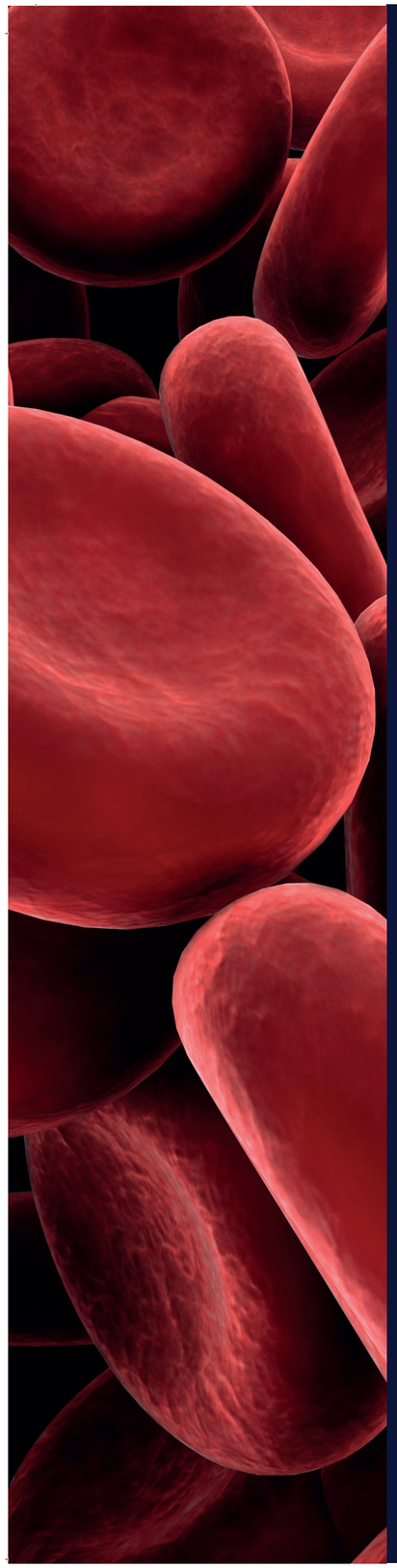

HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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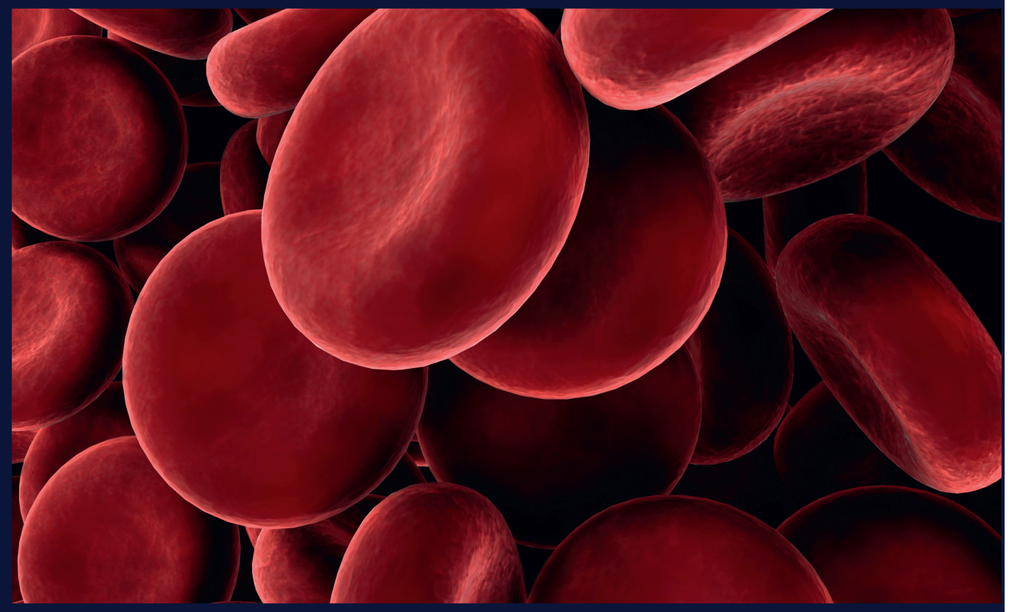
HEMATOLOGY, TRANSFUSION AND CELL THERAPY

VOLUME 42, SUPPLEMENT 1, OTOBER, 2020

ISSN 2531-1379



HEMATOLOGY, TRANSFUSION AND CELL THERAPY

VOLUME 42,
Supplement 1,
Otober, 2020

XIth Eurasian Hematology Oncology Congress

Abstract Book

21-24 October 2020

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Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular

HEMATOLOGY,
TRANSFUSION AND
CELL THERAPY

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de Hematologia, Hemoterapia
e Terapia Celular

XIth Eurasian

Hematology Oncology

EHOC 2020
Virtual

Abstract Book

21-24 October 2020

EHOG
Eurasian Hematology Oncology Group

Welcome Address

Distinguished Colleagues,

Eurasian Hematology Oncology Group has been expanding its network to the Americas, Africa and EMEA during recent years.

EHOG is a non-profit organization established to build a bridge in the field of hematology and oncology between these regions.

The main core of this formation is the HSA (Hematology Specialist Association), but the goal is to transform EHOG into an international society in the nea future.

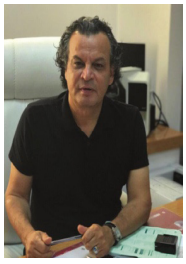
We believe that EHOG will fill a gap in these regions not only in a scientific way but also culturally. Our main objective is to bring together scientists from different countries, to know each other and to start joint projects and studies in the future.

This meeting was originally was supposed to be held in beautiful city of Istanbul however it has been transformed to a virtual congress on 21-24 October 2020 due to the COVID-19 pandemic that effected everyone around the would.

We believe deep in our hearts that with its special online concept, EHOC 2020 will fill in a significant gap in our region.

The attendees will be able to enjoy scientific programs in both Adult & Pediatric Hematology as well as Nursing. There will be online oral and poster presentations sessions. Pharmaceutical companies will get an opportunity to interact with the attendees live in the virtual exhibition area.

We hope that you will benefit in the best way possible in this virtual version of EHOC 2020 and we are looking forward to meeting you in face - to - face EHOC 2021 meeting in Istanbul.



Birol Güvenç

President of Hematology Specialist Association

Giuseppe Saglio

President of EHOC 2020 Virtual
President of EHOG

Hematology Specialist Association

President

Birol Güvenç

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Speaker Biographies

Adnan Abdul Jabbar

Associate Professor, Section Head Medical Oncology, The Aga Khan University, Pakistan

Dr. Adnan Abdul Jabbar is Section Head of Medical Oncology at one of the premier University Hospitals in Pakistan, The Aga Khan University. He is a graduate of Dow Medical College, Karachi and trained in Internal Medicine at the Nassau University Medical Center, New York and earned his Ph.D. in Immunology from RUSH University, Chicago, USA. Dr. Jabbar completed his Hematology/Oncology Fellowship from the Winship Cancer Institute, Emory University, Atlanta, USA. He has served as the Chief Resident Department of Internal Medicine, Nassau University Medical Center, New York and then as Adjunct Clinical Assistant Professor Department of Medicine, New York College of Osteopathic Medicine of New York Institute of Technology, Chief Fellow Winship Cancer Institute, Emory University, Atlanta and as Assistant Professor, department of Oncology Aga Khan University, Karachi, Pakistan.
Dr. Jabbar during his career is a recipient of numerous awards and grants. He serves on Boards of various committees and is currently the President Elect of the Society of Medical Oncology of Pakistan. He has several publications and poster presentations to his credit. He is Principle Investigator of many clinical trials and mentors post-graduate medical oncology trainees and supervises graduates for their Master's and PhD degrees.

Ali Ünal

Haematology-Oncology Department, Erciyes University, Turkey

He is working at Erciyes University Haematology-Oncology department and Bone Marrow Transplantation Center, in Kayseri, Turkey.
He received his MD degree at Erciyes University Medical School in Kayseri. He started his post graduated training in the department of Haematology at Ankara University Ibni Sina Hospital and subsequently completed at the London University Royal Postgraduate School of Medicine Hammersmith Hospital.
His scientific training in Bone Marrow transplantation and cancer immunotherapy was gained at the Hebrew University Hadassah Medical School Bone Marrow Transplantation (Jerusalem, Israel).
Ali Unal's main areas of research interests focus on: Haematological malignancy, Bone marrow transplantation, lymphoma, stem cell transplantation and therapeutic apheresis. His clinical research activities are mainly in the area of the lymphoma, leukaemia and tumour immunotherapy.
He was the president of Turkish Apheresis Society and member of, and Co-President of WAA 2012 Congress. He is member of National Haematology Association, European Society for Medical Oncology, American Society for Hematology and European Haematology Association.
He is serving on the editorial board of Turkish Haematology-Oncology Journal. He has published more than 200 scientific articles in international and national journals, peer-reviewed papers, review articles, book chapters, congress abstracts and oral presentations.

Ahmad Ibrahim

Hematology/Oncology and Physiological Sciences, National Lebanese University, Lebanon

He is a full Professor of Medicine, Hematology/ Oncology and Physiological Sciences at the Faculty of Medicine of the National Lebanese University, a Professor of Medicine at the Arab University of Beirut, an Associate Professor of Oncology at University of Paris XI, and Clinical Associate-Department of Internal Medicine at the American University of Beirut.
He graduated, from the University of Paris VII-School of Medicine in 1987. Then, he pursued a fellowship in Hematology/ Oncology, Immunology (HLA Lab, Professor Jean Dausset- Noble price of Medicine), and Bone Marrow Transplantation at the University of Paris; then, a post fellowship in the department Bone Marrow Transplantation at Fred Hutchinson Cancer Center -Seattle, USA (Professor E.D. Thomas- Noble price of Medicine).
Doctor Ibrahim was appointed in 1993 as a full-time Attending Physician/Associate professor in the Department of Hematology and Bone Marrow Transplantation at the Institute Gustave Roussy (IGR)-Villejuif/ University of Paris XI. In 1997, he moved to Lebanon where he established the first Bone Marrow Transplantation Program at Makassed Hospital-Beirut which was affiliated with IGR/University of Paris XI in a French-Lebanese cooperation. Since 1997, Dr. Ibrahim has been the head of the Division of Hematology/Oncology and the Director of the Bone Marrow Transplantation Program at Makassed Hospital. Since 2004, he has been appointed associate director of research for PhD Programs at the Faculty of Pharmacy/University Paris V. Since 2012. He has been board member of Masters Programs in stem cell engineering and applications at the faculty of Sciences of the National Lebanese University. In 2018, Dr. Ibrahim was the coordinator of the guidelines for Hematological Diseases established for the Ministry of Public Health in Lebanon in cooperation of UNDP. Dr. Ibrahim is currently in advisor of International Clinical Practice Guidelines on the Treatment and Prophylaxis of Venous Thromboembolism in Patients with Cancer (ITAC-CME CPGS).
Dr. Ibrahim is actively involved in research particularly in the fields of hematological malignancies and hematopoietic stem cell transplantation. In 1993, he was nominated a core member of the European Organization for Research and Treatment of Cancer (EORTC)-Leukemias Cooperative Groups. In 1996, he was elected member of the French College of Hematology. Since 2009, he has been member of the Board of Directors of the Eastern Mediterranean Group for Blood and Bone Marrow Transplantation (EMBMT). He is member of the American Society of Hematology (ASH), European School of Medical Oncology (ESMO), European Hematology Association (EHA), European Group for Blood and Marrow Transplantation/ Acute Leukemias and Lymphoma working parties (EBMT), and the American Society for Blood and Marrow Transplantation (ASBMT).
Dr. Ibrahim is currently the President of the Lebanese Society of Hematology and Blood Transfusion, Key partner of the ASH and EHA.
Dr. Ibrahim has taken an active role in the medical community-participating in numerous scientific meetings. He has authored and co-authored more than 300 medical publications and books chapters. He is also co-editor of a book in Hematology (edited in Paris-Maloine Publisher -1992).
In 1992, he received the Research Award of the Medical School of the University of Paris VII. In 1993, he received the award of the French League Against Cancer. In 2013, Dr. Ibrahim was awarded by the Lebanese Ministry of Health for his achievement in the field of hematopoietic stem cell transplantation in Lebanon. In 2018, he

received the award of achievement from the Pan Arab Hematology Association / EHA in Cairo, Egypt

Alina Antipova
Hematology, N.N. Blokhin National Medical Research Center of Oncology, Russian Federation

Alina Antipova has got her eduction Clincal Residence and Reserch fellowship in N.N Blokhin National Medical Research Center of Oncoogy. During her studies , she has become interesed in hematology and continued her professional activity in the Deparment of Chemotheapy of Hemoblastosis. Her research interests are focused on the treatment patients with acute leukemias, myelodysplastic syndromes. Thus, she finished her PhD work on theme "Diagnostic and treatment of rare types of acute leukemias". Alina Antipova is participant of many conferences and grant winner.

Angelo Maiolino
Internal Medicine and Hematology, Rio de Janeiro Federal University, Brazil

Graduate in Medicine (1982), Universidade Federal do Estado do Rio de Janeiro
Residence in Internal Medicine and Hematology (1986-88) at the University Hospital Clementino Fraga Filho, Federal University of Rio de Janeiro.
Fellow in Hematology and Bone Marrow Transplantation at the Hospital San Martino, Genova, Italy (1986-1988)
PhD in Internal Medicine - Hematology, Federal University of Rio de Janeiro (2000)
Professor of Medicine, Department of Internal Medicine, Federal University of Rio de Janeiro.
Chief of Hematology Service, Americas Centro de Oncologia Integrado, Rio de Janeiro
Member of the "International Myeloma Working Group"

Carmino Antonio De Souza
Internal Medicine and Hematology and Hemotherapy, University of Campinas – São Paulo State, Brazil

Professor Carmino Antonio De Souza graduated in Medicine in 1975, Medical Residency in Internal Medicine and Hematology and Hemotherapy 1976-1979, PhD in 1987, Free Professor in 1996 and Full Professor in 2001 of the Department of Internal Medicine of the Faculty of Medical Sciences - University of Campinas – São Paulo State - Brazil. He completed postdoctoral studies at the Department of Hematology, San Martino Hospital, University of Genoa, Italy, in 1997-1998. Onco hematologist, working in the Malignant Lymphomas, Chronic Myeloid Leukemia and Bone Marrow Transplantation.
He has about of 365 published papers, mainly in English and Portuguese, more than 1200 abstracts in national and international congresses; 25 chapters of scientific books and 45 approved theses of master and doctorate degrees. H index - 58 and Hi10 index - 282 (Google Scholar – 20th July 2020).
He is member of the Hematology, Hemotherapy and Cell Therapy Brazilian Association, the American Society of Hematology (ASH), the European Association of Hematology (EHA), the European Bone Marrow Transplant Group (EBMT) and founder member of LALNET (Latin America Leukemia Net) and AIBE (Brazilian Italian Association of Hematology). Head of the Hematology and Hemotherapy Center 1985 – 1993 and 2006 – 2011. São Paulo State Minister of Health – 1993 – 1994. Scientific Director of Brazilian Hematology and Hemotherapy Association (ABHH) – 2005-2009 and President of Brazilian Hematology and Hemotherapy Association (ABHH) – 2009-2013.

Education and Training

1970 - 1975	Graduation in Medicine at University of Campinas, São Paulo, Brazil
1976 - 1978	Medical Residency at University of Campinas – São Paulo –Internal Medicine and Hematology Department
1987	Doctoral Thesis at School of Medicine, Campinas-SP, UNICAMP

Post Doctor Training

1997 - 1998	University of Genoa – Italy – Ospedale San Martino – tutor - Dr. Gino Santini – Aggressive Malignant Lymphomas

Charles A. Schiffer
Hematology & Oncology, Wayne State University, USA

Charles A. Schiffer, MD, is Professor of Medicine and Oncology and the Joseph Dresner Chair for Hematologic Malignancies at Wayne State University School of Medicine and the Karmanos Cancer Institute in Detroit, Michigan. He is the director of the Leukemia/Lymphoma Multidisciplinary Program.

Dr. Schiffer earned his BA cum laude at Brandeis University and his M.D. at New York University School of Medicine. He completed his internship, residency, and chief residency in Internal Medicine at Bellevue Hospital under the auspices of New York University School of Medicine and had subsequent training and positions at the Baltimore Cancer Research Institute, National Cancer Institute and the University of Maryland School of Medicine, where he served as Chief of the Division of Hematology. He has also served as Chief of the Division of Hematology/Oncology and Director of Clinical Research at the Karmanos Cancer Institute.
Dr. Schiffer has authored and co-authored more than 330 articles and 80 book chapters on topics concerning the treatment of leukemia in adults, platelet transfusion, and granulocyte transfusion therapy, among others. He has served on the Editorial Boards for Blood, the Journal of Clinical Oncology, International Journal of Hematology, Transfusion Medicine Reviews and Transfusion, and reviews articles for multiple journals. Committee memberships have included Chairman of the Leukemia Committee of the Cancer and Leukemia Group B, Chairman of the Food and Drug Administration Oncologic Drug Advisory Committee, member of the American Board of Internal Medicine – Medical Oncology Board, and grant reviews for the NCI, ASH, DOD, ASCO and Leukemia/Lymphoma Society of America. Dr. Schiffer has been named among Castle Connelly's "Best Doctors in America," and Newsweek's "Best Cancer Specialists in the US." In 2006, he received the Dr. John J. Kenney Award from the Leukemia/Lymphoma Society of America and the Celgene Award for Career Achievement in Hematology. He has received numerous teaching awards from the School of Medicine and was recently inducted into the Academy of Scholars of Wayne State University, the highest recognition accorded to academic faculty at the University.

Christian Gisselbrecht
Hematology, Paris Diderot VII University Institut d'hématologie Hôpital Saint Louis, France

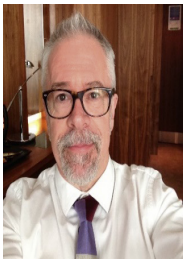
Christian Gisselbrecht, MD is emeritus professor of hematology at Paris Diderot University VII at the Hôpital Saint Louis in Paris, France. He has been co-founder and president of the Groupe d'Etude des Lymphomes de l'Adulte (GELA), a French-Belgian cooperative group which has organized numerous randomized trials in lymphoma since 1984. GELA has extended its activities and changed its name to LYSA (Lymphoma Study Association). Dr Gisselbrecht has been lead investigator of several major phase II and phase III clinical trials, which investigated the place of autologous stem cell transplantation in the treatment of lymphoma. Currently, he is chair of the international CORAL study on relapsed diffuse large B-cell lymphoma. His research interests include clinico-pathologic correlative studies in lymphoma, the pharmacology of novel antineoplastic agents, and stem cell transplantation with a focus on relapses or poor prognosis lymphoma and T cell lymphoma.
Dr Gisselbrecht is an active member of several European and American scientific societies and is an expert with the European Medical Agency (EMA) as well as several cancer research agencies. He has published over 300 peer-reviewed papers and several book chapters and is on the editorial board of a number of highly respected journals.

Dieter Hoelzer
Hematology, Onkologikum Frankfurt, Germany

Dieter Hoelzer is Professor of Medicine and Hematology. His main research is Acute Leukemias. He founded the German Adult ALL Study Group (GMALL) which so far conducted 7 multicenter studies in >145 participating hospitals, where more than 7000 patients were treated.

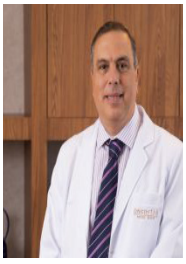
Prof. Hoelzer was one of the five founders and President of the European Hematology Association (EHA), currently Vice President of the European and German Competence Network Leukemias and he also founded the European
Working Group on Adult Acute Lymphoblastic Leukemia (EWALL). He currently chairs the Medical Advisory Board of the German Carreras Leukemia Foundation. Recently he was also the President of the Society for Hemato Oncology (SOHO). He is a member of the Medical Council and the Foundation Board of the DKMS (Deutsche Knochenmark Spender Datei).
Prof. Hoelzer received several awards for cancer research and therapy including those of the German Cancer Society, the "Deutsche Krebshilfe", the Johann-Georg-Zimmermann-Price, the San Salvatore Award and the European Leukemia Network Merit Award. He is a honorary member of the Hematological Societies of Austria, Hungary and Germany (DGHO) and received the doctor honoris causa from the University of Athens and First Pavlov State Medical University of Saint Petersburg.
Prof. Hoelzer is author or co-author of more than 800 peer-reviewed publications and co-author of international text books, such as Oxford textbook of Oncology and Harrison´s principles of Internal Medicine 2018 and forthcoming 2020.

Drew Provan
Hematology, The London School of Medicine and Dentistry, UK



Drew Provan is Emeritus Reader in Autoimmune Haematology at Barts and The London School of Medicine and Dentistry in London, UK. He studied molecular genetics at Leicester University, UK before completing his medical degree. After junior medical posts in the UK, Dr Provan undertook research at The Dana–Farber Cancer Institute in Boston, USA on an American Travelling Fellowship awarded by the UK's Medical Research Council. He subsequently became a Consultant Haematologist at Southampton University NHS Trust before assuming his current position. Dr Provan's research interests include immune thrombocytopenia (ITP), neutropenia and haemolytic anaemia. He established the UK Adult ITP Registry, a clinical and laboratory database of patients with ITP for symptom recording, genetic analysis and remote monitoring, with the hope of establishing the underlying mechanisms leading to autoantibody production and identifying treatment response genes and surrogate markers. Along with international colleagues, Dr Provan published the consensus guidelines for the diagnosis and management of ITP in children and adults which is being updated and will be submitted early August 2019. He has written numerous peer-reviewed papers and book chapters, and has authored several medical books including Molecular Hematology, Oxford Handbook of Clinical Haematology, Oxford Handbook of Clinical and Laboratory Investigation, and ABC of Clinical Haematology.

Eduardo M. Rego
Hematology, Faculty of Medicine of USP (FM-USP), Brazil



Dr. Eduardo Rego graduated in Medicine from the Medical School of Ribeirão Preto - USP (FMRP-USP) in 1988 and obtained his Ph.D. in Medicine (Clinical Medicine) from the University of São Paulo in 1997. He was a Post Doctoral Fellow at Memorial Sloan Kettering Cancer Center of New York (1998-2001). Upon returning to Brazil, he was nominated as Full Professor at FMRP-USP in 2010 where he worked until 2018. He is currently a Full Professor at the Faculty of Medicine of USP (FM-USP) and coordinator of the Acute Leukemia Service of the Cancer Institute of the State of São Paulo (ICESP). He is the Coordinator of the Hematology Services of the D'Or Network (Oncology D'Or). His areas of interest is the hematological neoplasias, with special emphasis on the study of pathophysiology and the development of new treatment strategies for acute leukemias. Among his most cited works are: "Retinoic acid (RA) and As2O3 treatment in transgenic models of acute promyelocytic leukemia (APL) unravel the distinct nature of the leukemogenic process induced by the PML-RAR alpha and PLZF-RAR alpha oncoproteins" Proceedings of the National Academy of Sciences of the United States of America (2000); "Role of promyelocytic leukemia (PML) protein in tumor suppression" - Journal of Experimental Medicine (2001); "Identification of a myeloid committed progenitor as the cancer-initiating cell in acute promyelocytic leukemia" - Blood (2009) and "Improving acute promyelocytic leukemia (APL) outcome in developing countries through networking, results of the International Consortium on APL" - Blood 2013). He is member of the Steering Committee and Coordinator in Brazil of the International Consortium of Acute Leukemias (ICAL) of the American Society of Hematology. The clinical studies developed by ICAL in Latin America aim to improve the outcomes of treatments for acute leukemias in the region and

promote the scientific advancement of hematology. Prof. Rego is the Chair of International Members Committee of the American Society of Hematology and Scientific Vice-Director of the Brazilian Association of Hematology and Hemotherapy (2018/2019). He is Editor of the Brazilian Journal of Medical and Biological Research; Deputy Editor of Hematology, Transfusion and Cell Therapy Journal (HTCT) and Associate Editor of the Annals of Hematology.

Elias Jabbour
Leukemia, University of Texas MD Anderson Cancer Center (MDACC), Houston, USA

Elias Jabbour, MD, is professor of medicine, Department of Leukemia, at The University of Texas MD Anderson Cancer Center (MDACC), Houston, Texas. He graduated from the Saint Joseph University School of Medicine, Beirut, and joined the Hotel Dieu de France University Hospital as a resident. He pursued a fellowship in hematology-oncology at the Gustave Roussy Institute, France. In 2003, he joined MDACC as a fellow in the Department of Hematology/Leukemia and Stem Cell Transplantation. He later joined the faculty in the Leukemia Department as assistant professor.

Dr Jabbour is actively involved in research in both acute and chronic forms of leukemia. He was involved in clinical trials that led to the approval of several drugs in chronic myeloid leukemia (CML), myelodysplastic syndromes (MDS), and acute lymphoblastic leukemia (ALL). He actively assisted in developing chemotherapeutic and biologic agents in leukemias and contributed to the development of others. Dr Jabbour has designed more than a dozen clinical trials assessing new combinations for the management of de novo ALL, elderly ALL, and relapsed/refractory disease. Of note, he developed a protocol that has shown significant improvements in survival rates for patients with Philadelphia chromosome-positive ALL. In addition, he developed another innovative treatment approach for these patients by combining blinatumomab, a bispecific monoclonal antibody, with ponatinib, offering a chemotherapy-free regimen that it is hoped will further increase cure rates. Another area on which he focused his research is elderly patients with ALL. The aggressive biology of the disease and elderly patients' poor tolerance of intensive chemotherapy leads to low survival rates for this patient population.

Dr Jabbour is currently investigating an innovative strategy combining new monoclonal antibodies such as inotuzumab ozogamicin, a conjugated anti-CD22 antibody, and blinatumomab with minimal chemotherapy. If successful, such strategies will likely increase the cure rates of adult patients with ALL to the high level achieved in pediatric patients.

Dr Jabbour has taken an active role in the medical community, participating in numerous scientific meetings. He has authored or co-authored numerous publications (>550 peer-reviewed publications) and abstracts, and serves as a reviewer for many scientific journals. He has received several prestigious awards, among them merit awards from the American Society of Clinical Oncology (2005, 2006, 2007) and the American Society of Hematology (2005, 2006, 2007). He also received several other honors, including the Kimberly Patterson and Shannon Timmons fellowships and the highly coveted Celgene Future Leader in Hematology (2007) and Young Investigator in Hematology (2016) awards.

Evangelos Terpos
Hematology, National & Kapodistrian University of Athens, School of Medicine, Greece

Evangelos Terpos, MD, PhD is a Professor of Hematology and Director of Stem Cell Transplantation Unit in the Department of Clinical Therapeutics of the National & Kapodistrian University of Athens, School of Medicine, Athens, Greece.
His main research interest is the biology of plasma cell dyscrasias and especially the biology of bone disease in multiple myeloma. Dr Terpos has evaluated the effect of bisphosphonates and different anti-myeloma therapies including ASCT, IMiDs-, proteasome inhibitor- and daratumumab-based regimens on bone metabolism. He has studied the biology and prevalence of osteonecrosis of the jaw in myeloma patients who receive bisphosphonates and denosumab as well as the role of modern imaging (including whole-body low-dose CT and DWI-MRI) for myeloma. He also studies the role of MRD in plasma cell neoplasms.
In the clinical research era, Dr Terpos participates in many important clinical trials with novel agents in the field of multiple myeloma and he is the PI in several real-world evidence studies with these novel agents. His research work was reported in more than 520 papers in peer-reviewed journals and Dr Terpos has more 20,000 citations and an h-index of 70 in ISI/Web of Knowledge (July 2020).
Dr Terpos is co-chairing the Bone Subgroup of the International Myeloma Working Group and the Guideline Subgroup of the European Myeloma Network. Dr Terpos has given lectures at ASH, ASCO & EHA meetings, International Myeloma Workshops and in several national meetings. He is reviewer of scientific papers in more than 50 medical journals and has reviewed abstracts for ASH, EHA & EBMT meetings. He is Associate Editor of HemaSphere (official journal of EHA) for Myeloma and member of the Editorial Board of Haematologica and Blood Cancer Journal.

Dr Evangelos Terpos can be reached via e-mail at eterpos@med.uoa.gr and eterpos@hotmail.com

Francesco Saglio
Hematology, AOU Città della Salute e della Scienza di Torino, Italy

Education
MD Università degli Studi di Torino (Italy) 2001- 2007
Pediatrics Università degli Studi di Torino (Italy) 2009-2014
Post-doctoral Fellowship Baylor College of Medicine, TX, US 2011-2012
PhD Biomedical Sciences & Oncology Università degli Studi di Torino (Italy) 2014- 2018

Professional Experiences
2014 - 2015 Part-time Attending Physician Pediatric Emergency Room, AOU Città della Salute e della Scienza di Torino, Turin, Italy
2015 - 2017 Attending Physician Pediatric Onco-Hematology, Cell Therapy and Stem Cell Transplantation Unit, AOU Città della Salute e della Scienza di Torino, Turin, Italy
2017- now Full-time position Attending Physician Pediatric Onco-Hematology, Cell Therapy and Stem Cell Transplantation Unit, AOU Città della Salute e della Scienza di Torino, Turin, Italy
Main areas of interest
Main areas of interest are the immunological aspects of hematopoietic stem cell transplantation in the pediatric population especially in relation to the opportunity to generate virus and leukemia directed cytotoxic T cell lines to be used in adoptive cell therapy

protocols. Experience in translational research and in the management of GCP compliant phase I-II and III clinical trials.

Giuseppe Saglio
Hematology, University of Torino and Ospedale Mauriziano, Italy

Giuseppe Saglio is a Professor of Internal Medicine and Haematology at the University of Turin. He is Director of the Department of Clinical and Biological Sciences o at the San Luigi University Hospital, Director of the Division of Hematology of the Mauriziano Hospital in Turin and Coordinator of the PhD programme in Molecular Medicine.

Chronic Myeloid Leukemia (CML) is likely to represent in modern medicine the most successful achievement of the so called targeted therapy and precision medicine. Since the discovery of the Philadelphia chromosome and of its closer association with this specific disease, a continuous flow of biological and clinical research has progressively provided insights on the CML pathogenesis of and on mechanisms leading to its progression to an acute phase, that until two decades ago was the major cause of death for the CML patients. This situation totally changed since the introduction of imatinib, the first tyrosine kinase inhibitor (TKI) introduced in clinical medicine. Several studies indeed suggest that after 10 years from the start of therapy, the OS of the CML patients is almost overlapping that of a control population without leukemia. These results however are not only due to imatinib, but also to other TKIs of second and third generation like nilotinib, dasatinib, bosutinib, radotinib, ponatinib and others. These TKIs are generally used as second or third line treatment in cases (approximately 35-40% of all patients) who are intolerant or resistant to imatinib therapy, but nilotinib, dasatinib and bosutinib have been used and registered also as first line therapy in the attempt to improve the first-line therapy results that can be obtained with imatinib. The decision to change therapy is based on the molecular quantification by quantitative RQ PCR of the amount of the BCR/ABL transcript at specific time points that is corresponding to the amount of the residual disease. The selection of the TKI to be used as first or second line therapy is also in many cases established based on the profile of the BCR-ABL mutation present. In other cases is the toxicity profile of each TKI the factor determinant for the choice. The enormous success of the TKI therapy however should not overshadow the fact that most of them are bound to continue the TKI therapy for the rest of their life. Therefore the new frontier of the CML therapy is represented by the treatment free remission (TFR) that means that the patient can discontinue the TKI therapy without experiencing a relapse of the disease. This in the net year will certainly represent a new challenge in which the so called precision medicine will play a major role.

Guillermo Garcia-Manero
Leukemia, Texas MD Anderson Cancer Center, USA

Guillermo Garcia-Manero is the Dr. Kenneth B. McCredie Chair in Clinical Leukemia Research in the Department of Leukemia at the University of Texas MD Anderson Cancer Center. He also serves as the Chief of the Section of Myelodysplastic Syndromes, Vice Chairman for Translational Research, Leader of the AML/MDS Moon Shot Program and Program Director of the Leukemia Fellowship Program (September 2019). He recently was elected as Chair-elect of the Faculty Senate of the University of Texas MD Anderson Cancer Center, which also starts in September 2019.
Dr. Garcia-Manero was born in Spain and received his medical degree and training at the University of Zaragoza in Spain and at the Royal Free Hospital in London, UK. From 1993-1996, he performed his internship and residency in Internal Medicine at Thomas Jefferson University Hospital in Philadelphia, PA. He then continued his training with a fellowship in Hematology and Medical Oncology at the Cardeza Foundation for Hematology Research, Sidney Kimmel Cancer Center, also at Thomas Jefferson University Hospital, where he served as chief fellow. In 1999, he became Assistant Professor in the Department of Leukemia at the University of Texas MD Anderson Cancer Center where he has remained for the rest of his academic career.
Dr. Garcia-Manero focuses on the understanding the cellular and molecular biology of MDS and AML with an aim to improve therapeutic options for patients with these disorders. His work has been funded by NIH, DoD, LLS, CPRIT, and the MDS/AML Moon Shot project. He has co-authored over 682 manuscripts. His last H-index is 119 and his i10-Index is 630 with over 58,000 citations to his work. Currently, he is PI or Co-PI on over 25 active clinical trials focusing on AML and MDS. He directs what is likely the largest single institution unit for patients with MDS in the world, with over 400 patients referred annually, and maintains one of the busiest clinics at MD Anderson. The Section of MDS is comprised of leukemia faculty dedicated to care for patients with MDS and two research laboratories directed by Dr. Colla and Dr. Wei. In addition, the section coordinates the work of over 15 research nurses. Dr. Garcia-Manero has received a number of significant awards, such as The Otis W. and Pearl L. Walters Faculty Achievement Award in Clinical Research and the Emil J. Freireich Award for Excellence in Translational Research at MD Anderson. He has also been recognized as one of the Best Doctors in America each year since 2007. He has trained over 100 fellows and post doctoral fellows and has been a speaker at multiple national and international forums.

Giovanni Martinelli
Scientific Director, Istituto Scientifico romagnolo per lo Studio e la cura dei Tumori (IRST) – IRCC, Italy

Education
Degree in Medicine at Verona University in 1985
Residency in Hematology at Verona University in 1988
Residency in Medical Genetics at Verona University in 1992

Careers
Scientific Director of Hematology Unit at Istituto Scientifico Romagnolo per lo Studio e la cura dei Tumori (IRST) IRCCS, Italy (2018-today)
Medical doctor at University of Bologna Institute of Hematology "L. E A. Seràgnoli", Italy (1993-2001)
Professor at Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Italy (2001-2017)

Achievements
Responsible of the individual program - "Diagnosis and treatment of acute leukemias and myelodysplastic syndromes" Sant' Orsola Hospital, Bologna.
Was the coordinator of Next Generation Sequencing platform for targeted Personalized Therapy of Leukemia (NGS-PTL) Eu-funded project
Winner of 2016 Investigator Grant, AIRC, Associazione Italiana per la Ricerca sul Cancro
WP LEADER (2017), IMI2 consortium "healthcare alliance for resourceful medicines offensive against neoplasms in hematology"
WP LEADER of H2020 project ONCORELIEF
WP LEADER of Erapermed Project SYNTHERAPY

Irina Poddubnaya
Hematology, Russian Society of Oncohematology, Russian Federation

Ph. D., Professor, Vice-rector for Educational Work and International Cooperation, Heard of Oncology and Palliative Medicine Chair, Russian Medical Academy for Continual Professional Education of Russian Ministry of Health. Since 1974 she works in Russian Medical Academy for Continual Professional Education (RMACPE) as assistant lecturer, associate professor, professor, and since 1989-Heard of department . In 2003 she was appointed as a vice- rector RMACPE. Prof. Poddubnaya since 2005 is a corresponding Member and since 2014 is Academician of Russian Academy of Sciens.
Her main sphere of scientific interests includes all aspects of diagnosis and treatment of malignant lymphoproliferative disorders and different forms of solid tumors; her activities include scientific clinical research, teaching and lecturing, as well as developing international scientific cooperation projects.
In 1994 she received the ESSO Sekiyu Kabushiki Kaisha Reseach grant (Japan)
for her Reseach "Study of different features of nodal and extranodal non-Hodgkin adult lymphomas and development of effective treatment". In 2002 prof. Poddubnaya was awarded as a Honorary Educational Worker of Russia.
In 1999-2002 she was a member of Annal Oncology Editorial Board as a member of the ESMO Publishing Working Group. She is Editor-in- Chief of quarterly Russian journal " Contemporary Oncology" since 1999. 2012-2016 she was Editot-in-Chief of Russian edition of Journal of Clinical Oncology (ASCO) She is the organizer and chair of annual Russian Conference with International Participation " Malignant Lymphomas". Since 2011 she is president of Russian Society of Oncohematologists".
Prof. Poddubnaya actively participates in numerous International and Russian clinical trials as principal investigator or co- investigator. She is author more than 550 articles, 8 monographies, chapters in manuals. Since 2012 she is editor-in-chief of Russian National Clinical Recomendations on Diagnostics and Treatment of Lymphoproliferative Diseases (in 2018 - the 4-th edition).

Jean François Rossi
Hematology, University of Montpellier, France

Jean-François Rossi University of Montpellier He is professor of Hematology at the University of Montpellier. He has over 30 years of experience in medicine and was certified in Rhumatology, Medical Oncology, Hematology, Immunology and Internal Medicine. He received his MD and PhD degrees in Hematology Immunology at the University of Montpellier and had post-doc at the Universities of Arizona (Tucson) and San Antonio (Texas) for multiple myeloma and bone research. He was associate professor at the University of Suzhou (China) for more than 10 years. He is member of 7 international scientific societies and the Scientific Advisory Board of the Castleman Disease Collaborative Network (CDCN). He was in charge of Medical Oncology for 5 years in Montpellier Cancer Center. He became the head of the Hematology Department during 14 years and he developed with Professor Bernard Klein the Biotherapy Saint-Eloi site (ImmunotherapyRegenerative Medicine (Chu/Inserm/University). He is particularly active in Immunotherapy for cancer and programs on crossed information analysis for algorithms including epigenetics with microbiota with 198 PubMed publications and 4 patents. He participated or activated different clinical or bio-clinical research programs with pharmaceutical companies (more than 150) or with academic institutes. He obtained an Award from the American Association for Cancer Research on April 2017 for his work on inflammatory process and interleukin 6 (http://aacrjournals.org/content/j-f-rossi-bio and The Best of the AACR Journals). He was a consultant for different for more than 20 years, in the domain of immune precision medicine and the development of different drugs, notably siltuximax (Centocor, EUSAPHARMA) TACI-Ig (Serono Merck), IPH1101 (Innate Pharma), anti-CD20 LFB-R603 (LFB), polyoxidinium (Petrovax Pharm LLC), POC for Horiba Medical, and for Marc Cluzel, Sanofi Research. He participated to the creation of 4 start-ups. He is an active member of the Scientific Advisory Boards for 3 start-ups such as Urodelia and Beta Innov. With E-Sana as a co-founder with Pr Kalle Levon (Polytechnic Institute of NYU, Brooklyn, USA) and Césare Massart, he participates to new programs based on innovative technology for tests including in-Home and biological monitoring, with dynamic follow-up. Nowadays, he develops a new Institute For Precision Medicine and Immunotherapy at the Cancer Institute Sainte Catherine, Avignon, France, with the collaboration of LABOSUD/INOVIE, academic labs (linked to the University Hospital in Montpellier and the Institute Paoli-Calmette, in Marseille) and start-ups. This platform integrates an international scientific committee and will use new technologies in Telemedicine.

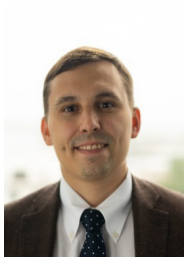
Joseph (Yossi) Schwartz
Transfusion Medicine & Cellular Therapy Service, Columbia University, USA

Joseph (Yossi) Schwartz is a Professor of Pathology and Cell Biology at the Vagelos College of Physician and Surgeons of Columbia University and the Director of the Transfusion Medicine & Cellular Therapy Service at the Columbia University Irving Medical Center campus of the New York Presbyterian Hospital. As the Director of the Transfusion Medicine & Cellular Therapy Service, Dr. Schwartz oversees the Blood Bank, The Apheresis unit and the Cell Therapy facility. As a major tertiary & transplantation center, those facilities collect, receive & process blood products for transfusion in variety of indications such as patients with Sickle Cell Disease, complex cardiac surgery, Hematopoietic Progenitor Cell transplantation, and all types of solid organ transplantation. He was until recently the chair of the FACT-JACIE international standards for cellular therapy and just finished his term as he Immediate Past-President of the American Society for Apheresis (ASFA). He was part of the writing committee in the last 5 editions of ASFA's special issue published every 3 years describing current evidence-based clinical applications of Therapeutic Apheresis.

Kinuko Mitani
Hematology, Dokkyo Medical University, Japan

Kinuko Mitani, MD & PhD, is Chair and Professor of the Department of Hematology and Oncology at Dokkyo Medical University in Tochigi, Japan. She graduated from the University of Tokyo in 1984. Thereafter, she received a postdoctoral training at her home institute and at The Rockefeller University in NY until 1994. She joined Dokkyo Medical University as a professor of medicine in 2000. She has cloned a leukemia-causing gene, RUNX1-EVI1, and analysed its functions in vitro and in vivo. Currently, Professor Mitani is a vice president of the Japanese Society of Hematology and is a secretary general in the Asian-Pacific division of International Society of Hematology.
E-mail address: Kinukom-tky@umin.ac.jp

Kirill Lepik
Hematology, Pavlov University, Russian Federation



Kirill Lepik completed residency in hematology in Pavlov University in 2016 and PhD program in 2019. His PhD work was related to the implementation of immune checkpoint inhibitors in the treatment of classical Hodgkin lymphoma. During last several years he actively participated in several research projects in Pavlov University including the optimization of immunotherapy strategy in resistant lymphomas, analysis of the mechanisms of resistance to PD-1 inhibition in Hodgkin lymphoma, approaches of immune checkpoint inhibitors combinations as a bridge to allogeneic hematopoietic stem cells transplantation. His research was presented at the EHA, EBMT and ASH meetings.

Koichi Akashi
Hematology, Kyushu University, Japan

1985 Graduated from Faculty of Medicine, Kyushu Univ.
1985 Resident, and Research Fellow, First Department of Internal Medicine, Kyushu Univ.
1994 Postdoctoral Fellow, Department of Pathology, Stanford Univ. School of Medicine, (Irving L. Weissman's lab)
2000 Associate Professor, Dept. of Cancer Immunology and AIDS, Dana-Farber Cancer Institute, Harvard Medical School
2008-present Professor and Chair, Department of Medicine and Biosystemic Science, Kyushu University, JAPAN

Marcio Nucci
Hematology, Medicine at Rio de Janeiro Federal University, Brazil

He is Professor of Medicine at Federal University of Rio de Janeiro, Brazil, and has been responsible for the Program of Infection in the Hematology and Bone Marrow Transplantation unit at the University Hospital for over 25 years. He has received his medical degree in 1981 from the Federal University of Rio de Janeiro State, has completed his residency in Hematology at Federal University of Rio de Janeiro in 1985 and has trained in Infectious Diseases at Università la Sapienza, Roma, Italy in 1991. Dr. Nucci is also consultant in Infectious complications of cancer and bone marrow transplantation in two hospitals, working in a telehealth platform.
His clinical and research interests include the epidemiology, diagnosis and management of invasive fungal diseases in immunocompromised hosts and infectious complications in in hematologic patients and hematopoietic cell transplant recipients.
Marcio Nucci has published over 200 peer-reviewed articles, and has been speaker in several medical conferences. He is member of the American Society of Hematology and of the European Confederation of Medical Mycology. He is past member of the Immunocompromised Host Society Council and the Mycosis Study Group Steering and Educational Committees, and is a reviewer of various medical scientific journals.

Martin H. Ellis
Hematology, Tel Aviv University, Israel

Professor Ellis is the head of the Hematology Institute and Blood Bank at the Meir Medical Center and is Associate Professor of Hematology at the Tel Aviv University. He is also the Chairman-elect of the Israel Society of Hematology. He was the founding chairman of the Israel Myeloproliferative Neoplasms (MPN) Working Group and currently heads the Israel MPN Registry.
Prof Ellis is a member of the MPN working groups of the European Leukemia Network and the European Hematology Association.
Prof. Ellis's clinical and research interests are the pathophysiology of MPN-related thrombosis and it's treatment as well as anticoagulant therapy for thrombotic diseases.
He has published numerous papers focused on the current management of MPNs and using meta-data, has demonstrated in a "real-world" context the importance of appropriate dosing of the direct oral anticoagulants.
He has performed a number of national and international studies of JAK inhibitor treatment for myelofibrosis and of the treatment of thrombotic complications of the myeloproliferative neoplasms.

Mehmet Yılmaz
Hematology, Sanko University, Turkey

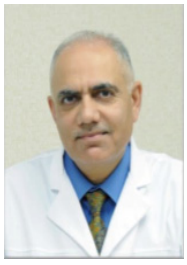
Mehmet Yilmaz, MD is a Professor of Internal Medicine Department of Hematology in SANKO University School of Medicine, Gaziantep. He was graduated from Cukurova University School of Medicine. Post graduate training; Internal Medicine and Hematology 1995-2002 Ankara Numune Education and Research Hospital, Immunohematology, Therapeutic Apheresis and blood transfusion as observer Leiden Medical Center 2007, Therapeutic Apheresis and Clinical Education of Blood and Bone Marrow Transplantation 2008, Erciyes University Department of Hematology Bone Marrow transplant and Therapeutic Apheresis Center, Kayseri. He founded hematology discipline at 2004, therapeutic apheresis center 2010 as a chief and bone marrow transplant as vice-chairman in Gaziantep University School of Medicine at 2009. His main research interest is hematologic malignancies and therapeutic apheresis. In clinical research era Dr. Yilmaz participated some important clinical trials (deferasirox, Rituximab, The World CML Registry, Bosutinib, SC Rutiximab, Obinituzumab) on the fields hematologic malignancies. Dr. Yilmaz has written over the 200 publications, abstracts and other scientific presentations. Throughout his career had received numerous national abstract awards. Dr. Yilmaz is member of several professional, national and international scientific societies including EHA, EHOC, Turkish Society of Hematology, Experimental Hematology and Turkish Society of Apheresis.

Mustafa Cetiner
Hemtology, Acibadem Maslak Hospital, Turkey

He was born in Kayseri in 1964. He received his MD degree at Ankara University School of Medicine in 1988. He pursued his career at the Department of Hematology in Marmara University Faculty of Medicine as a fellow, an attending physician and an associated professor respectively. He participated in research projects of the Hematopoietic Stem Cell Transplant Program in Northwestern University Robert Lurie Cancer Center, Chicago, US as a visiting scholar between 2004 and 2005 for 6 months.

He established Bone Marrow Transplantation Program in Sisli Memorial Hospital and became a director in 2011-2012.
Dr. Cetiner was a professor of the Hematology Department at Koc University School of Medicine between years of 2013 and 2018. He served as a founder and head of the Internal Medicine Department at Koc University School of Medicine in 2015-2018. He worked at the Hematology Department of V.K.V. American Hospital from 2008 to 2019.
He has been working as an official doctor of "United Nations" since 2010.
He is an active member of several national and international medical societies including Turkish Medical Association, the Turkish Society of Hematology, American Society of Hematology, European Hematology Association and MDS Foundation.
He has been a co-chairman of the recognized international meeting "New Trends in Hematology" organized in Istanbul since 2007.
Besides his academic career, Dr. Cetiner remarkably contributes to social responsibility projects. He is among the founders of "Cancer Warriors" in Turkey that is dedicated to providing care and support for cancer patients and their families.
He has an extensive and prominent career as an author. He has published over 50 articles in peer-reviewed scientific national and international journals also 3 books about hematological malignancies. Besides, he has also 3 popular science books titled "To Your Health", "Portraits from the History of Lymphoma" and "The Milestones in the History of Hematology".
He published over 500 columns under the title of "Actual Medicine" in national "Cumhuriyet (Republic) Newspaper" for 10 years till 2017. Currently, he continues to write his columns in weekly "Science and Technology Magazine".
He is currently working at the Hematology Department of Acibadem Maslak Hospital.

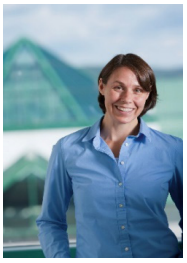
Naeem Arshad Chaudhri
Hematology, King Faisal Specialist Hospital & Research Centre, Saudi Arabia



College of Medicine, Alfaisal University Director, Research Unit, Oncology Centre Consultant, Adult Hematology/HSCT King Faisal Specialist Hospital & Research Centre Riyadh, Saudi Arabia

Dr. Chaudhri is a Consultant in Hematology and Hematopoietic Stem Cell Transplantation at KFSH&RC. He is board certified in Internal Medicine, Medical Oncology and Hematology from American Board of Internal Medicine and he completed his fellowship in Hematology and Medical Oncology in 1995 at Lombardi Cancer Center, Georgetown University Hospital, Washington D. C. He joined King Faisal Specialist Hospital and Research Centre in 1996. KFSH&RC is the major tertiary care referral centre in Saudi Arabia and Middle East with Oncology Centre being accredited by the World Health Organization (WHO) as a Collaborating Centre for Cancer Prevention and Control.
His main interest is Malignant Hematology, specifically Acute and Chronic Leukemia as well as Hematopoietic Stem Cell Transplant.
Dr. Chaudhri is also the Director/Head of Research Unit overseeing clinical research in the Oncology Centre at KFSH&RC. He is the principal investigator of the South West Oncology Group (SWOG) for KFSH&RC and principal investigator of numerous ongoing clinical trials. He is an Associate Editor-in-chief of Annals of Saudi Medicine and an Editorial Board of other journals. He has around 130-140 publications and abstracts in peer-reviewed journals.
At the same time, Dr. Chaudhri is the Congress Chairman of the annual conference of the Critical Reviews in Hematological Malignancies in Riyadh, Saudi Arabia and also a member of organizing and scientific committees of numerous national and international meetings. He is invited speaker on national and international scientific meetings.

Nancy M. Dunbar
Hematology, Dartmouth-Hitchcock Medical Center, USA



Nancy M. Dunbar, MD is an Associate Professor of Pathology and Laboratory Medicine and of Medicine at the Geisel School of Medicine at Dartmouth. She serves as the Medical Director of the Blood Bank and the Associate Medical Director of the Transfusion Medicine Service at Dartmouth-Hitchcock Medical Center. She currently serves as co-chair of the American Society for Apheresis (ASFA) Journal of Clinical Apheresis Special Issue Writing Committee and edited the most recent issue "Guidelines on the Use of Therapeutic Apheresis in Clinical Practice: Evidence-Based Approach" published in June 2019. These guidelines are widely used by healthcare personnel and provide the current level of evidence and strength of the recommendation for the use of apheresis in human disease.

Ozan Salim
Hematology, Akdeniz University School of Medicine, Turkey

Ozan Salim, MD is an associate professor of hematology at Akdeniz University Hospital in Antalya, Turkey.

Education
Fellow - Hematology: Akdeniz University School of Medicine
Resident - Internal Medicine: Istanbul University Cerrahpasa School of Medicine
Medical School, Internship: Istanbul University Cerrahpasa School of Medicine

Professional details
Member, Turkish Society of Hematology (TSH)
Member, European Hematology Association (EHA)
Lymphoma master class graduate organized by the TSH, 2017
Secretary of the lymphoma scientific subcommittee of TSH, 2018 - present
Chief, Hematology Department, Akdeniz University Hospital, 2012 - 2018
Director, Special Hematology Laboratory, Akdeniz University Hospital, 2012 - present
Director, Blood Bank, Akdeniz University Hospital, 2012-2013.

Publications
Author of approximately 30 published articles on hematologic subjects.

Personal details
Dr. Ozan Salim has a particular interest in non-Hodgkin's and Hodgkin's lymphoma. He has been involved in writing lymphoma guideline for TSH. He lives in Antalya with his wife and son. He likes fishing, playing football and swimming.

Panayiotis Panayiotidis
Hematology, National and Kapodistrian University of (NKUA), Greece

-Graduated from the Medical School of University of Athens in 1982.
-Trained in Haematology in the 1st Department of Internal Medicine, University of Athens (Head prof Faidon Fessas).
-Diploma in Haematology 1992
- Post graduate studies:
a) Karolinska Hospital, Stockholm, Hematology Clinic (Head Prof Peter Reisentaein)1984-1985.

b) Royal Free Hospital, London, Haematology Clinic (Head Prof Victor Hoffbrand, 1992- 1996) as an ESMO fellow and Hon. Lecturer.
-Present Position: from 1996- present : National and Kapodistrian University of (NKUA) Athens, 1st Department of Propaedeutic Medicine, Laikon General Hospital, professor of Haematology

Head of the Haematology Research Laboratory, NKUA
-Member of the ERIC and IG-CLL groups., of ELN.
-Member of the EUTOS commitee "path to cure group in CML" of the ELN
-National representative for Greece in the EUTOS CML European Group of ELN.
-Member of the Steering Committee of the EURO-SKI trial of ELN.
-Member of Hellenic Society of Haematology (President 20017-2018)
-President of the Educational committee of the Hellenic Society of Haematology (2018-2020)
-158 publications in neoplastic hematologic diseases with >6000 citations

Rajko Kusec
Consultant Hematologist, Dubrava University Hospital, Croatia

I was born and I practice hematology in Zagreb, the capital of Croatia, a historical, today modern and vibrant city that celebrated its 900th birthday recently. My parents were chemists, but I think I knew relatively early that I was going to study medicine. So, I did, at Zagreb University and after finishing my residence and fellowship in internal medicine I left to Vienna for postgraduate study in hematology at Medical university, department of hematology and hemostaseology. This was very important experience where, besides the clinic, I was introduced to molecular hematology, something which is part of my professional activity in form of molecular diagnostics today. Another important and interesting aspect of understanding hematological disorders, particularly neoplasms, was opened to me at University of Oxford at Haematology research unit of Nuffield department of medicine. Hunting for candidate tumour suppressor gene(s) in the deleted region of long arm of chromosome 5 in MDS was a unique perspective for a clinician! I eventually returned home and since then I am active as clinical hematologist that also supervises molecular hematology diagnostics at University hospital Dubrava and, as professor of internal medicine at Zagreb School of medicine, I teach undergraduate and postgraduate students. When thinking of myself as a physician, medical professional and a person who had opportunity to experience different but complementary levels of hematology I can say that through all this I became more aware of the challenges and complexity of blood diseases. Through this unique "journey" I had privilege to encounter many interesting people, made many true and lasting friendships and also retained international connections resulting in collaborations and projects in hematology, particularly in myeloid neoplasms. Through my "case ". I may suggest that it is visible that interconnecting, exchanging ideas and experiences, will move us all forward in our mission of being better doctors for our patients!

Robert Peter Gale
Hematology, UCLA, USA

He was born in New York in 1945 where he attended Erasmus Hall Academy and the Pratt Art Institute studying industrial design. He received his AB with high honors in biology and chemistry from Hobart College in 1966, MD from the State University of New York at Buffalo in 1970 and PhD in microbiology and immunology from the University of California, Los Angeles (UCLA) in 1976). His postgraduate training was at UCLA 1970-74. 1983-4 he was the Meyerhoff Visiting Scholar at the Weizmann Institute of Science in molecular biology. From 1973-1993, Gale was on the faculty of the UCLA School of Medicine and remains on the UCLA Ronald Regan Medical Center Staff.
From 1980-1997, Gale was Chairman of the Scientific Advisory Committee of the Center for International Blood and Marrow Transplant Research (CIBMTR), 1989-2003 he chaired the Scientific Advisory Board of the Center for Advanced Studies in Leukemia. From 1986-1993, he was President of the Armand Hammer Center for Advanced Studies in Nuclear Energy and Health, and 1985-1990 he was the Wald Scholar in Biomedical Communications at UCLA. Gale is currently Visiting Professor of Haematology at the Haematology Research Center, Division of Experimental Medicine, Department of Medicine, Imperial College London and Honorary Professor of Hematology at the Institute of Hematology at Peking Union Medical College. He is the Editor-in-Chief of LEUKEMIA, Associate Editor of CLINICAL TRANSPLANTATION, Executive Editor of BONE MARROW TRANSPLANTATION and a reviewer for many scientific journals in hematology, oncology, immunology, transplantation, radiation biology and internal medicine. Prof. Gale is also an expert on the medical response to nuclear and radiation accidents. From 2007-2019 he was executive director of clinical research and development at Celgene Corp and an honorary member of the Russian and Chinese Academies of Medical Science.
Gale has published over 1,100 scientific articles and 25 books on medical topics, nuclear energy and weapons and politics of US-Russian relations with articles for the New York Times, Los Angeles Times, Washington Post, USA Today, Der Spiegel, the Wall Street Journal and others. Dr. Gale has also written popular books on Chernobyl and US nuclear energy policy and screenplays for and/or appeared in several movies and received an Emmy award. His latest book "Radiation: What it is, What you need to know" was published in 2013 by A. Knopf.
Awards for his scientific achievements include the Presidential Award, New York Academy of Sciences, Scientist of Distinction Award, Weizmann Institute of Science, Distinguished Alumni Award, Hobart College and Intra-Science Research Foundation Award. He holds honorary degrees including DSc from Albany Medical College, LHD from Hobart College and DPS from MacMurray College.

Robin Foà
Hematology, Sapienza' University, Italy

Professor of Hematology, 'Sapienza' University of Rome. He earned his medical degree in Turin, Italy, and specialized in pediatrics and in hematology. Worked at the MRC Leukaemia Unit, Hammersmith Hospital, London between 1976 and 1979. Sabbatical at Memorial Sloan-Kettering Cancer Center, New York, between 1991 and 1992.
He is part of the European Leukemia Network and referee for national and international funding agencies.
Chairman of the Scientific Committee of the 4th EHA Congress, Barcelona 1999, councilor of EHA until December 2002, and member of the Education Committee of EHA until December 2005.
President-Elect, President and Past-President of EHA during the years 2007-2013.
Chairman Education Committee and Outreach Unit of EHA up to June 2017.
Member of EHA's Global Outreach Committee.
Chairman of the GIMEMA Working Party for chronic lymphoproliferative disorders, and member of
the board of the Working Party for acute leukemias.
Has authored over 750 papers, reviews and books. Has been co-editor of Leukemia and Lymphoma, and associate editor of the British Journal of Hematology and of The Hematology Journal. Editor-in-chief of The Hematology Journal up to December 2004 and of Haematologica from January 2005 to February 2008.

Rodrigo T. Calado
Hematolgy, University of Sao Paulo, Brazil

Dr. Rodrigo T. Calado received his MD in 1997 and his PhD in 2003 both from the University of Sao Paulo, Brazil. He received his postdoctoral training in hematology at the National Heart, Lung, and Blood Institute, National Institutes of Heath, Bethesda, Maryland, where he also worked as Staff Scientist. His main research focus is in hematopoietic stem cell failure, including inherited and acquired aplastic anemia. Dr. Calado has helped to characterize the molecular genetics of telomeropathies and acquired aplastic anemia and developed novel therapies for these disorders.

He is currently Scientific Director of the Ribeirao Preto Blood Bank, and Head of the Hematology Laboratory, University of Sao Paulo, Brazil.

Rüdiger Hehlmann
Hematology, Germany

Prof. Dr. med. Dr. h. c. Rüdiger Hehlmann, chief of medicine at the Mannheim Medical Faculty of Heidelberg University until 2007. Founder and chair of the German CML Study Group 1982-2017, the German Competence Network for Acute and Chronic Leukemias 1997 to present, and the European LeukemiaNet (ELN) 2002 to present. Past president of the German Society of Hematology and Oncology, past Dean of his faculty and past Secretary General of the International Association of Comparative Research on Leukemia and Related Diseases (IACRLRD). He is honorary member of the Polish and German Societies for Hematology and Oncology. His focus is fostering cooperative research for curing leukemia.

Selected publications
Hehlmann R. Review: Chronic myeloid Leukemia in 2020. HemaSphere 2020, in press
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Salam Alkindi
Hematology, Sultan Qaboos university, Oman

Following my graduation from Trinity college-Dublin Ireland, in 1993, I have completed my general medicine as well as haematology/oncology training in Dublin, Ireland as well as the Fred Hutch cancer centre in Seattle USA, where I did my training in Bone marrow transplant. In 1999 I have joined Sultan Qaboos University and in 2005 I was appointed as head of department of haematology for 10 years. Previously also I held the position of deputy director of Sultan Qaboos university hospital for clinical affairs (clinical director in effect) for about 5 years. Research interests include sickle cell disease, chronic leukaemia and autoimmune disorders with over100 articles published in international peer reviewed journals.

Tariq I. Mughal
Hematology/Oncology, Imperial College London, UK

Tariq trained in medicine at St George's Hospital in London, followed by postgraduate training at Imperial College London at the Hammersmith Hospital, London, and the University of Colorado School of Medicine, Denver. He has specialist credentials in internal medicine, medical oncology, hematology, and stem cell transplantation in the UK and USA. He has held senior clinical leadership roles in centers of excellence for the treatment of cancer, as well as positions of increasing seniority in pharmaceutical medicine, focusing on the interface between academia, clinical practice and industry. He is involved in humanitarian activities to co-ordinate cancer care in Africa since 2011, when he founded Alpine Oncology Foundation, a Swiss-registered cancer charity, in memory of his mother, with the principal objective to help improve the clinical management of children and adults in Tanzania diagnosed to have blood cancer by enhancing the understanding of these diseases and promoting access to affordable molecular diagnostic and monitoring tools. He has published over 130 peer reviewed papers, 30 cancer text book chapters and 13 cancer books. He is the recipient of several awards, including those from the UK Royal College of Physicians, American College of Physicians, Swiss humanitarian groups and runner-up for the Highly Commendable British Medical Association (UK) Book Award.

Tomasz Sacha
Hematology, Jagiellonian University, Poland

Ass. Prof. Tomasz Sacha MD.PhD. graduated from the Medical Academy in Kraków in 1992. During his studies, he worked actively in the research team at the Department of Internal Medicine in Kraków and won twice the prize of the Students' Scientific Society competition for the best scientific project. He worked as an assistant in the Haematology Department at the Jagiellonian University in Kraków after initial specialization in internal medicine. He specialized further in haematology after several pieces of training in Basel, Genoa and Turin, and became a lecturer and professor at the Jagiellonian University in Kraków. He received his PhD for his work on molecular diagnostics of Chronic Myeloid Leukemia (CML). In 2008, he completed his specialization in laboratory diagnostics and, in 2013, he habilitated at the Jagiellonian University. Dr Sacha established a National Molecular Reference Laboratory for quantitative BCR/ABL analysis and is responsible for the standardization of this procedure in Polish Molecular Laboratories. In 2002 he contributed to the organization of Polish Advocacy Group of patients suffering from chronic myeloid leukaemia. For his activity, he was awarded the prize: "Service for Life Award" and became an Honorary Member No 1 of this Society.
Since 2013, he is a president of the Molecular Hematology Section of the Polish Society of Human Genetics, and since 2017 he is the president of Chronic Myeloid Leukemia Section of the Polish Adult Leukemia Group, and since May 2019 he is the head of The Chair and Department of Hematology in Jagiellonian University Hospital. He has extensive clinical experience in the use of tyrosine kinase inhibitors and in the field of molecular monitoring of chronic myeloproliferative neoplasms. He is also interested in the clinical research of myeloproliferative neoplasms aiming at eliminating the leukemic stem cells.

Valeh Huseynov
Hematology,Educational-Therapeutic Clinic of Azerbaijan Medical University, Azerbaijan

Education
Azerbaijan Medical University 1992-1998
Azerbaijan Medical University, Oncology Hospital, Oncology – Hematologist 1998-1999
Oncology course on rehabilitation. Kazakhstan.Almaty. 1999
Rehabilitation course on hematology and bone marrow transplantation. Sample education and research hospital. Turkey Ankara2002
Regional Blood Banking Implementation Course. Turkey. 2002
WHO training course. Quality management in the blood transfusion service. 2005

Course of Quality Standarts of Cellular Therapy Products in Current/ 2015
Republic Oncology Center, Oncologist-Hematologist. Junior researcher. Kazakhstan, Almaty.1999-2001
WHO course. Quality control during bleeding. Baku. 2005

Course at the Medical Univesrsity of Vienna. Vyana, Avstriya. Hematologiya və Sümük iliyi transplantasiyası. 2010
Hematology and Bone Marrow Transplantation Course. Memorial Hospital. Istanbul, Turkey. 2013
Ankara Univ., Department of Hematology, Bone Marrow Transplant Unit. Ankara. Turkey.2014
Oncological hematology and bone marrow transplantation. Tennesi University. Memphis, USA. 2016
WORK EXPERIENCE:
City Oncology Dispensary, chemical therapy. Internship. Azerbaijan Baku. 1998-1999
Republic Oncology Center, Oncologist-Hematologist. Small scientific worker in Kazakhstan, Almaty.1999-2000
Institute of Hematology and Transfusiology, Hematologist named after B. Eivazov. Scientist. Azerbaijan Baku 2000-2002
Central Clinical Hospital. Hematologist. Azerbaijan Baku. 2001-2015
Head of Hematology and Oncology Department and Blood Bank Central Clinic. Azerbaijan Baku. 2003-2009
Head of the Therapy Center. Central Clinic. Azerbaijan Baku.2009-2012
Head of Department of Hematology at Educational-Therapeutic Clinic of Azerbaijan Medical University. Azerbaijan Baku.2013-until now
Director of the Thalassemia Center 2017- until now
Member Societies
European Hematology Society (EHA)
American Hematology Society (ASH)
Chairman of the Society of Hematology Professionals of Azerbaijan.

Vera Donnenberg
Cardiothoracic Surgery / Pharmaceutical Sciences, University of Pittsburgh, USA

Dr. Vera Donnenberg is an Associate Professor of Cardiothoracic Surgery in the School of Medicine at the University of Pittsburgh with a secondary appointment in the Department of Pharmaceutical Sciences in the School of Pharmacy. She is a Representative to the Council of Faculty and Academic Societies for the Association of American Medical Colleges (CFAS-AAMC), where is she is a member of the Administrative Board. She is also a Regent of the Board of the American College of Clinical Pharmacology (ACCP) and serves as an Ambassador to the Eurasian Hematology Oncology Group, an international organization that promotes oncology research and clinical interventions in Europe, Asia, Africa, and Americas.
Dr. Donnenberg earned her MS in Clinical Pharmacology in 1994 from Johns Hopkins University and her PhD with Honors in Pharmaceutical Sciences in 2002 from the University of Pittsburgh.
Dr. Donnenberg's research focuses on:

- Tumorigenic stem cells in lung cancer, esophageal cancer, and breast cancer
- Pleural metastases
- Therapeutic resistance
- Interaction of tumor cells and regenerating tissue
- Lung immunology
- Pleural immuno-oncology

Dr. Donnenberg has written over 395 publications, abstracts, book chapters, and other scientific presentations. Throughout her career she has received numerous awards for her academic and service efforts including the Nathaniel Kwitt Distinguished Service Award from the ACCP (2020), the Marylou Ingram Woman in Science Award from the Coulter Foundation, the Governor's Distinguished Citizenship Award, Maryland, and the Service Award from the National Society of Black Engineers. She is a member of several editorial boards including the Journal of Clinical Pharmacology and is an Associate Editor of Cytometry, Stem Cells, a leading journal in the field of imaging and cytometry, and served as the first female President of the Great Lakes Flow Cytometry Association.

View a list of Dr. Donnenberg's publications here [http://www.ncbi.nlm.nih.gov/pubmed?term=((%22johns%20hopkins%20university%22)%20OR%20%22university%20of%20pittsburgh%22)%20AND%20%22donnenberg%2C%20vera%20s%22].

Zeba AZIZ
Hematology, Hameed Latif Hospital, Pakistan

Zeba Aziz is a medical oncologist with a busy clinical practice based in Hameed Latif Hospital, Lahore, Pakistan. She previously served as the Head of Department of Oncology and Professor at Jinnah Hospital Lahore. Currently she is Dean of Medical Oncology for the College of Physicians and Surgeons Pakistan and is also the Program Director for the Medical Oncology Fellowship at Hameed Latif Hospital. She is currently the President of Society of Medical Oncology of Pakistan formed recently. Her international efforts include being on the steering committee for the Australian & Asia Pacific Oncology Research Development (ACORD) Workshop and being an invited panel list and speaker for multiple conferences around the world. She has made contributions to research through her 79 peer-reviewed publications on Oncology. Her specific fields of interest are malignant haematology and breast cancer.

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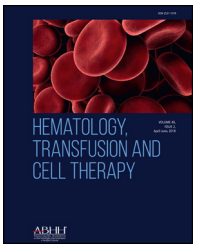

SPEAKER PRESENTATIONS

SP01

TIM-3/Gal-9 signaling is the molecular target for human myeloid leukemia treatment

Koichi Akashi

Acute myeloid leukemia (AML) originates from self-renewing leukemic stem cells (LSCs), an ultimate therapeutic target. The T-cell immunoglobulin mucin-3 (TIM-3) is expressed on the surface of LSCs in most AML patients. We have reported that targeting TIM-3 by anti-TIM-3 monoclonal antibodies could eradicate human AML LSCs in vivo by utilizing xenograft models (Cell Stem Cell, 2011). We then tested the role of TIM-3 signaling evoked by its ligand, galectin-9 (Gal-9), and found that TIM-3+ AML cells secreted Gal-9 into sera, and the ligation of TIM-3 by serum galectin-9 positively regulate the self-renewal capacity of TIM-3+ LSCs through activating the beta-catenin pathway (Cell Stem Cell, 2015). Furthermore, this TIM-3/Gal-9 "autocrine stimulatory loop" is involved in development of LSCs from preleukemic status, including myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPN); frequencies of TIM-3+ cells progressively increased and accumulate driver mutations along with disease progression from early/chronic phase to overt leukemia. Thus, signaling molecules downstream of TIM-3 as well as surface TIM-3 itself might be good target to regulate transformation from preleukemic status.

https://doi.org/10.1016/j.htct.2020.09.002

SP 02

Development of novel therapies in MDS

Kinuko Mitani

Myelodysplastic syndrome (MDS) is one of the bone marrow failure syndromes that usually develop for the elderly. Ineffective hematopoiesis and abnormal morphology are specific characters of the disease. MDS is a hematopoietic stem cell neoplasm caused by gene mutation. About half of the patients transform to acute myelogenous leukemia (AML). Although stem cell transplant (SCT) is the sole curable treatment, cytokine, molecular and immune therapies have been and are being developed to improve survival and QOL of the patients.

Technical progresses in genomic analysis have brought us large amounts of findings regarding molecular pathogenesis in MDS. Gene mutations found in MDS patients are classified into five groups, genes regulating epigenetics, RNA splicing, transcription and signal transduction, and others including *TP53*, *NPM1*, *BCOR*. Through accumulation of these mutations, MDS develops and progresses to AML. Among them, Splicing gene mutations are rather specific to MDS and one of them, *SF3B1* gene mutation, has been employed to sub-classify MDS in the revised 4th version of WHO classification 2017.

When we consider the treatment of MDS patients, we divide them into two risk groups, low and high, according to IPSS and IPSS-R. Supportive therapies for bone marrow failure are employed for low-risk patients, while SCT as a curable therapy or hypomethylating agents (HMAs) aimed at prolonging life are selected for high-risk patients. Supportive therapy includes cytokine therapy such as darbepoietin α and G-CSF, lenalidomide for 5q- patients, immunosuppressive therapy for borderline patients with aplastic anemia, and azacytidine (AZA). Luspatercept inhibits exaggerated TGF-β signaling that underlies a molecular basis on ineffective hematopoiesis. The Medalist trial showed that Luspatercept is especially effective for patients with MDS-RS and/or *SF3B1* mutation. Major part of MDS patients are old and ineligible for SCT, even if they belong to high risk group. For such patients, HMAs (azacytidine and decitabine) that elongate overall survival and time to leukemic transformation are the first-line therapy. Oral AZA (CC-486 and ASTX727) and guadecitabine, and combinations of HMAs with pevonedistat and venetclax are under development. Further, combination of HMA with checkpoint inhibitors such as nivolumab and ipilimumab is promising especially for therapy-naïve patients.

https://doi.org/10.1016/j.htct.2020.09.003

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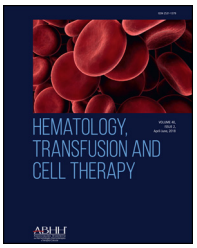

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SP 03

Risk scores and risk factors in CML, are they helpful?

Tomasz Sacha

There are multiple risk scores developed in the last decades to describe entry disease characteristics, enable risk stratification, and predict the clinical outcome of chronic myeloid leukemia (CML) therapy. The treatment-free remission is a new goal of CML therapy postulated and defined also by recent ELN recommendations. In this context, early predictors of good response and chance to reach this ambitious goal are of special interest. The importance of Sokal, EURO (Hasford), EUTOS, and ELTS scores will be discussed. The other risk factors such as additional chromosomal aberrations, additional genetic mutations, BCR/ABL1 transcript type, the dynamics of early BCR/ABL1 transcript decline, the presence of ABL1 KD mutations, and the quality of molecular response could have an important role in planning the optimal treatment. In the era of tyrosine kinase inhibitors and many possible choices, the analysis of risk factors could be considered as a key factor in the decision-making process. This will be discussed during the presentation.

https://doi.org/10.1016/j.htct.2020.09.004

SP 04

Minimal residual disease detection in multiple myeloma: methods and prognostic significance

Evangelos Terpos

The novel response criteria in antimyeloma therapy, published by the International Myeloma Working Group (IMWG), include minimal residual disease (MRD) assessment in multiple myeloma (MM), aiming to identify better definitions of complete response (CR) than those traditionally defined by conventional methods. IMWG has defined new response categories including (i) marrow MRD negativity with the use of next generation flow cytometry (NGFC) or next generation gene sequencing (NGS), with a cut-off value of 10^{-5}; (ii) imaging MRD negativity using PET/CT; and (iii) sustained MRD negativity (marrow and imaging MRD negativity that remains for 12 months).

The sensitivity of NGS seems to be similar than that of NGF and can be used for detection of rare residual myeloma BM cells at the level of 10^{-6}. However, an advantage of NGS is that it can be applied retrospectively on stored material including not only cryopreserved cells but also archival BM slides. On the other hand, the most commonly utilized NGS-based ClonoSEQ (Adaptive Biotechnologies) platform for MRD evaluation has high cost and requires specialized centers for sample preparation and data interpretation, which, in its current form, makes it challenging for daily clinical management. The major advantage of NGF is its high applicability in 99% of MM patients and the relatively simple manual set-up in diagnostic labs equipped with the appropriate 8-color cytometers, following the standardized EuroFlow guidelines. The cost of the technique is significantly more affordable and the results may be available within a few hours upon BM aspiration. There is no need for a prior diagnostic sample evaluation due to the elegantly elaborated 8-color marker combinations that can efficiently discriminate between normal and aberrant plasma cells in the whole spectrum of intra-phenotypic heterogeneity. Furthermore, NGF methodology allows for an intra-quality control check for hemodiluted samples – the major pitfall for both NGF and NGS approaches- by identifying cellular components (i.e., mast cells, B cell precursors, erythroblasts) that are mainly present in the BM. This point is commonly underestimated, though it consists one of the major advantages of NGF; the multiparametric panels allow for the global characterization of BM cells.

There is no doubt that the achievement of MRD negativity confers a more favorable outcome for treated MM patients. The first meta-analysis by Landgren et al in 2016 and the one that followed by Munshi et al in 2017 have verified the prognostic impact of MRD negativity in the clinical outcome. The latter meta-analysis showed a 59% reduced risk of progression and 43% reduced risk of death for MRD negative patients with a median PFS of 54 months vs. 26 months and a median OS of 98 months vs. 82 months for MRD negative vs. MRD positive patients respectively.

When compared with other prognostic factors, MRD has been shown to be superior and the most relevant predictor of clinical outcome. In multivariate analyses, the achievement of MRD negativity is proven to be the strongest independent prognostic factor which surpasses other favorable prognostic parameters. Patients with high-risk baseline cytogenetics who achieved MRD negativity after treatment, had significantly improved outcomes when compared with MRD persistent counterpart, but most importantly, they experienced similar survival outcomes with standard-risk patients who also achieved MRD negativity. It is important to stress that the favorable prognostication of MRD negativity stands independent of the assigned treatment.

https://doi.org/10.1016/j.htct.2020.09.005

SP 05

Treatment of relapsed, refractory multiple myeloma: focus on new drugs

Angelo Maiolino

In recent years several new drugs were approved for multiple myeloma (MM) treatment. Three classes are included in almost all lines of MM treatment: proteasome inhibitors (bortezomib, carfilzomib, and ixazomib), immunomodulators (thalidomide, lenalidomide, and pomalidomide) and monoclonal antibodies (daratumumab and elotuzumab) in different combinations.[1] In a relapsed setting, the decision about the new line of treatment should consider patient's related factors and previous MM treatment. Age, frailty, cytogenetics risk, and performance status at relapse have to be analyzed combined with the relapse aggressiveness, exposition to prior therapies, and the history of disease's responses.[2] Patients previously unexposed or those not refractory to lenalidomide, have better outcomes with a triple combination of lenalidomide and

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Treatment of relapsed, refractory multiple myeloma: focus on new drugs

Angelo Maiolino

In recent years several new drugs were approved for multiple myeloma (MM) treatment. Three classes are included in almost all lines of MM treatment: proteasome inhibitors (bortezomib, carfilzomib, and ixazomib), immunomodulators (thalidomide, lenalidomide, and pomalidomide) and monoclonal antibodies (daratumumab and elotuzumab) in different combinations.[1] In a relapsed setting, the decision about the new line of treatment should consider patient's related factors and previous MM treatment. Age, frailty, cytogenetics risk, and performance status at relapse have to be analyzed combined with the relapse aggressiveness, exposition to prior therapies, and the history of disease's responses.[2] Patients previously unexposed or those not refractory to lenalidomide, have better outcomes with a triple combination of lenalidomide and

dexamethasone plus daratumumab (POLLUX TRIAL),[3] carfilzomib (ASPIRE TRIAL),[4] ixazomib (TOURMALINE TRIAL),[5] or elotuzumab (ELOQUENT TRIAL).[6] In all these trials, results confirmed that triplet regimens were superior in response rate and progression-free survival. If the patient is considered refractory to lenalidomide, a proteasome inhibitör combination is a standard for treatment in early relapse. Carfilzomib plus dexamethasone was compared to bortezomib and dexamethasone in the Endeavor study and demonstrated superiority in progression-free survival (PFS) and overall survival (OS).[7] Carfilzomib + dexamethasone (KD) combination was recently compared as a control arm versus daratumumab plus KD (Candor Trial).[8] In this phase[3] trial, a superiority in PFS was demonstrated for the triple combination. Daratumumab, bortezomib, dexamethasone combination (Castor Trial)[9] and pomalidomide, bortezomib, dexamethasone (OPTIMISMM)[10] are also good options for this subset of patients, previously exposed and refractory to lenalidomide. Both trials demonstrated superiority in response rate and PFS. New clinical trials are addressing innovative strategies, particularly with belantamab mafodotin, an anti-BCMA antibody, and with anti-BCMA – CAR T-cell. Both demonstrated high efficacy in terms of response rate in Phase1/2 Trials, including heavily pretreated and Penta-refractory patients.[11,12] Large phase 3 trials are planned for hopefully incorporate these strategies to MM treatment.

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https://doi.org/10.1016/j.htct.2020.09.006

SP 06

Current therapy for indolent lymphomas

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Introduction: Indolent lymphomas are neoplasms of the mature B-cell that have the survival measure in years even without direct treatment. This group contains follicular lymphoma, lymphoplasmacytic lymphoma and marginal zone lymphoma. Mantle cell lymphoma, although can have an indolent course, it's not included here.

Follicular lymphoma (FL): FL is the second in prevalence between non-Hodgkin's lymphomas (NHL) and the most common with an indolent presentation.[1] Patients can have a heterogeneous evolution, from asymptomatic disease without need for therapy until an aggressive course with poor chemotherapy response. The latter tends to belong in a group of progressive disease within two years of first therapy (POD24).[2] Although a better knowledge of the disease biology, there are current no clear prognostic system that can separate patients in need for aggressive treatment versus those with no need for treatment at all. But it is considered standard only treat patients with high tumor burden or symptomatic. Generally, patients that do need therapy receive CHOP/CVP or Bendamustine with additional anti-CD20 antibody. There seems to be a favorable group that can be treated with Rituximab monotherapy and remain without need for new treatment for a long period.[3] After the GALLIUM trial,[4] where Obinutuzumab was associated with 34% reduction in progression versus Rituximab, this novel anti-CD20 antibody became an option. Although a progression-free survival (PFS) benefit was demonstrated, there was no gain in overall survival (OS) at this point. Maintenance with Rituximab or Obinutuzumab is generally recommended (every 2 months for 2 years), with long term follow up from the PRIMA trial showing a sustained difference in PFS.[5] However, no OS superiority was observed. To reduce toxicity while maintaining efficacy, Lenalidomide plus Rituximab regimen was tested in untreated FL patients ("R^{2}").[6] This "chemo-free" protocol had an equal

dexamethasone plus daratumumab (POLLUX TRIAL),[3] carfilzomib (ASPIRE TRIAL),[4] ixazomib (TOURMALINE TRIAL),[5] or elotuzumab (ELOQUENT TRIAL).[6] In all these trials, results confirmed that triplet regimens were superior in response rate and progression-free survival. If the patient is considered refractory to lenalidomide, a proteasome inhibitör combination is a standard for treatment in early relapse. Carfilzomib plus dexamethasone was compared to bortezomib and dexamethasone in the Endeavor study and demonstrated superiority in progression-free survival (PFS) and overall survival (OS).[7] Carfilzomib + dexamethasone (KD) combination was recently compared as a control arm versus daratumumab plus KD (Candor Trial).[8] In this phase[3] trial, a superiority in PFS was demonstrated for the triple combination. Daratumumab, bortezomib, dexamethasone combination (Castor Trial)[9] and pomalidomide, bortezomib, dexamethasone (OPTIMISMM)[10] are also good options for this subset of patients, previously exposed and refractory to lenalidomide. Both trials demonstrated superiority in response rate and PFS. New clinical trials are addressing innovative strategies, particularly with belantamab mafodotin, an anti-BCMA antibody, and with anti-BCMA – CAR T-cell. Both demonstrated high efficacy in terms of response rate in Phase1/2 Trials, including heavily pretreated and Penta-refractory patients.[11,12] Large phase 3 trials are planned for hopefully incorporate these strategies to MM treatment.

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PFS rate at 3 years compared with Rituximab plus Chemotherapy, with less hematological toxicity and neutropenic fever. The combination was also effective in the relapse setting, with a median of 40 months in PFS.[7] Chimeric antigen receptor-modified T cells (CAR-T) against CD19 is becoming widely use in lymphoma and has showed efficacy in relapse/refractory FL patients, with report of high complete remission rate and sustained remissions.[8]

Lymphoplasmacytic lymphoma (LPL): LPL is a lymphoma characterize by lymphoplasmacytic cells that produces monoclonal protein (IgM) and infiltrate the bone marrow and lymph nodes. When there is a measure IgM monoclonal production, LPL is a synonymous of Waldenström macroglobulinemia (WM). The *MYD88* L265P mutation occurs in over 90% of cases,[9] serving as a strong diagnostic marker (although not specific of WM). This mutation also has a prognostic role, with patients with the wild type showing a worse prognosis.[10] *CXCR4* is another frequent and important mutation (prevalence of 30% in WM), that together with *MYD88* can guide the treatment choice.[11] WM is an incurable disease of normally elderly patients and the treatment, when needed, focus on achieving a response (rarely complete remission) while maintaining low toxicity.[12] DRC is an option for low tumor burden and more frail patients that do not need urgent treatment. BDR serves well patients for patients with cytopenias and no neuropathy, while BR maybe prefer in bulky disease with high tumor burden.[13] Ibrutinib with or without rituximab can be used in first line[14] or relapsed patients,[15] especially with the *MYD88* mutation. Acalabrutinib and Venetoclax are other new options, with the last as one of the few active treatments in patient's refractory to ibrutinib.[16]

Marginal Zone B-cell lymphomas (MZL): The marginal zone B-cell lymphomas (MZLs) comprise extra nodal MZL (EMZL) of mucosa-associated lymphoid tissue (MALT), splenic MZL (SMZL) with or without villous lymphocytes and nodal MZL (NMZL) with or without monocytoid B cells. These are three distinct clinical entities with specific diagnostic criteria, clinical and therapeutic implications.[17]

Regarding to localize H. pylori-positive gastric MZL, the initial treatment should be H. pylori eradication. This treatment can induce lymphoma regression and long-term clinical disease control in the most of 50% of the patients.[18] In patients who do not achieve lymphoma regression following antibiotic therapy, irradiation and systemic oncological therapies should be used, depending on the stage of disease. Patients who require systemic treatment, chemotherapy, immunotherapy or both are all effective.[19] SMZL in asymptomatic patients, watch-and-wait is recommended and splenectomy is considered as the recommended first treatment. Rituximab therapy alone can be indicated and has an important response rate with minimal toxicity, particular useful in patients with autoimmune disorders.[20] For asymptomatic patient diagnosed with NMZL is also recommended only observation. If systemic treatment is indicated, chemo-immunotherapy can be performed.[21]

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https://doi.org/10.1016/j.htct.2020.09.007

SP 07

Bone marrow failure

Rodrigo T. Calado

Aplastic anemia may be the result of the immune attack against hematopoietic stem and progenitor cells or the impairment of appropriate hematopoietic stem cell function due to inherited genetic defects. Although bone marrow transplantation is the preferential therapy for severe cases, the majority of patients lack a suitable sibling donor. The thrombopoietin receptor agonist eltrombopag has been recently added to immunosuppressive therapy, reaching high response rates and overall survival, rivaling matched-donor transplant results. Additionally, genetic defects in telomere-maintenance genes appear to be the most prevalence etiology of inherited aplastic anemia. Sex hormones may recover hematopoiesis in these cases. The occurrence of somatic genetic mutations in immune and inherited aplastic anemia may help to understand the complex dynamics of hematopoietic stem cells in vivo.

https://doi.org/10.1016/j.htct.2020.09.008

SP 08

Immunocompromised patients: prevention, diagnosis and therapy of infection

Marcio Nucci

Patients with bone marrow failure are at increased risk to develop severe infection. The main immunodeficiency is neutropenia, particularly in patients with acute leukemia and severe aplastic anemia. In addition, treatment-related immunodefficiencies further increase the risk of infection, including mucositis caused by intensive chemotherapy, and T-cell immunodeficiency that follows immunosuppressive therapies for aplastic anemia. In neutropenic patients, prophylactic strategies focus on the prevention of bacterial and fungal infections. A key element in the management is the prompt initiation of empiric antibiotic therapy in febrile neutropenic patients, focusing on Gram-negative bacteria. With this regard, the emergence infection caused by multi-drug resistant Gram-negative bacteria is a major challenge, because inappropriate antibiotic coverage is associated with high mortality rates. Therefore, it is imperative to know local epidemiology in order to select the most appropriate antibiotic regimen. Likewise, changes in the initial empiric antibiotic regimen should be driven by objective parameters and not just fever. For invasive fungal disease, while the empiric antifungal therapy is still used, this strategy has been replaced by a preemptive diagnostic-driven approach. In this strategy, serial (2–3×/week) serum galactomannan and chest tomograpy drive the start of antifungal therapy. Finally, while the wise and appropriate employment of all these strategies is very important, recovery from neutropenia is the main prognostic factor. Therefore, every efforts must be devoted to control the underlying disease.

https://doi.org/10.1016/j.htct.2020.09.009

SP 09

Paroxysmal nocturnal hemoglobinuria pnh

Hanan Hamed

Objective: PNH is a condition in which uncontrolled complement activity leads to systemic complications, principally through intravascular hemolysis and platelet activation. It arises through a somatic mutation of the phosphatidylinositol glycan A (PIG-A) gene in bone marrow stem cells,[1,2] resulting in disruption to glycosylphosphatidylinositol (GPI) biosynthesis.[3]

Results: Among the deficient proteins are the complement regulatory proteinsCD55 andCD59, resulting in increased complement sensitivity of PNH cells, intravascular hemolysis, promotion of inflammatory mediators, and systemic hemoglobin release.[4] Patients with PNH can present with multisystemic clinical manifestations due to intravascular hemolysis, thrombosis and bone marrow failure.[5] Symptoms are therefore often non-specific, ranging from loss of vision (due to retinal thrombosis), headache and nausea/vomiting (due to cerebral thrombosis), pulmonary hypertension (due to pulmonary embolism), anaemia, through to pain and swelling in the lower extremities (due to deep vein thrombosis), renal failure and other symptoms affecting different systems.[6] Thromboembolism is the most common cause of mortality in patients with PNH and accounts for approximately 40% to 67% of deaths of which the cause is known. Further, 29% to 44% of patients with PNH have been reported to have at least 1 thromboembolic event during the course of their disease, although the reason(s) a thrombotic event may suddenly occur remains an enigma.[7–9] Platelet activation, complement-mediated hemolysis, impaired nitric oxide (NO) bioavailability, impairment of the fibrinolytic system, and inflammatory mediators are all proposed mechanisms and thought to be responsible for the increased thrombotic risk in patients with PNH. Multiple factors are likely to contribute to any one thrombotic event in patients with PNH.[10]

Conclusion: Therapeutic strategies include terminal complement blockade and bone marrow transplantation. Eculizumab, a monoclonal antibody complement inhibitor, is highly effective and the only licensed therapy for PNH.[11] The therapeutic anti-C5 antibody eculizumab (Soliris, Alexion)

lymphoid tissue lymphoma. Clin Gastroenterol Hepatol. 2010;8:105e110.
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Aplastic anemia may be the result of the immune attack against hematopoietic stem and progenitor cells or the impairment of appropriate hematopoietic stem cell function due to inherited genetic defects. Although bone marrow transplantation is the preferential therapy for severe cases, the majority of patients lack a suitable sibling donor. The thrombopoietin receptor agonist eltrombopag has been recently added to immunosuppressive therapy, reaching high response rates and overall survival, rivaling matched-donor transplant results. Additionally, genetic defects in telomere-maintenance genes appear to be the most prevalence etiology of inherited aplastic anemia. Sex hormones may recover hematopoiesis in these cases. The occurrence of somatic genetic mutations in immune and inherited aplastic anemia may help to understand the complex dynamics of hematopoietic stem cells in vivo.

https://doi.org/10.1016/j.htct.2020.09.008

SP 08

Immunocompromised patients: prevention, diagnosis and therapy of infection

Marcio Nucci

Patients with bone marrow failure are at increased risk to develop severe infection. The main immunodeficiency is neutropenia, particularly in patients with acute leukemia and severe aplastic anemia. In addition, treatment-related immunodefficiencies further increase the risk of infection, including mucositis caused by intensive chemotherapy, and T-cell immunodeficiency that follows immunosuppressive therapies for aplastic anemia. In neutropenic patients, prophylactic strategies focus on the prevention of bacterial and fungal infections. A key element in the management is the prompt initiation of empiric antibiotic therapy in febrile neutropenic patients, focusing on Gram-negative bacteria. With this regard, the emergence infection caused by multi-drug resistant Gram-negative bacteria is a major challenge, because inappropriate antibiotic coverage is associated with high mortality rates. Therefore, it is imperative to know local epidemiology in order to select the most appropriate antibiotic regimen. Likewise, changes in the initial empiric antibiotic regimen should be driven by objective parameters and not just fever. For invasive fungal disease, while the empiric antifungal therapy is still used, this strategy has been replaced by a preemptive diagnostic-driven approach. In this strategy, serial (2–3×/week) serum galactomannan and chest tomograpy drive the start of antifungal therapy. Finally, while the wise and appropriate employment of all these strategies is very important, recovery from neutropenia is the main prognostic factor. Therefore, every efforts must be devoted to control the underlying disease.

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SP 09

Paroxysmal nocturnal hemoglobinuria pnh

Hanan Hamed

Objective: PNH is a condition in which uncontrolled complement activity leads to systemic complications, principally through intravascular hemolysis and platelet activation. It arises through a somatic mutation of the phosphatidylinositol glycan A (PIG-A) gene in bone marrow stem cells,[1,2] resulting in disruption to glycosylphosphatidylinositol (GPI) biosynthesis.[3]

Results: Among the deficient proteins are the complement regulatory proteinsCD55 andCD59, resulting in increased complement sensitivity of PNH cells, intravascular hemolysis, promotion of inflammatory mediators, and systemic hemoglobin release.[4] Patients with PNH can present with multisystemic clinical manifestations due to intravascular hemolysis, thrombosis and bone marrow failure.[5] Symptoms are therefore often non-specific, ranging from loss of vision (due to retinal thrombosis), headache and nausea/vomiting (due to cerebral thrombosis), pulmonary hypertension (due to pulmonary embolism), anaemia, through to pain and swelling in the lower extremities (due to deep vein thrombosis), renal failure and other symptoms affecting different systems.[6] Thromboembolism is the most common cause of mortality in patients with PNH and accounts for approximately 40% to 67% of deaths of which the cause is known. Further, 29% to 44% of patients with PNH have been reported to have at least 1 thromboembolic event during the course of their disease, although the reason(s) a thrombotic event may suddenly occur remains an enigma.[7–9] Platelet activation, complement-mediated hemolysis, impaired nitric oxide (NO) bioavailability, impairment of the fibrinolytic system, and inflammatory mediators are all proposed mechanisms and thought to be responsible for the increased thrombotic risk in patients with PNH. Multiple factors are likely to contribute to any one thrombotic event in patients with PNH.[10]

Conclusion: Therapeutic strategies include terminal complement blockade and bone marrow transplantation. Eculizumab, a monoclonal antibody complement inhibitor, is highly effective and the only licensed therapy for PNH.[11] The therapeutic anti-C5 antibody eculizumab (Soliris, Alexion)

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SP 10

Access to cancer medicines and targeted therapies in developing countries

Zeba Aziz

In LMIC national cancer control programs are barely existent. Emphasis is mainly focused on fighting infectious disease, maternal child mortality and now fighting the Covis-19 catastrophe.

Pakistan is a LMIC with allocation of only 2.7% of the GDP to health. We have approximately 173,937 new cancers and a mortality of 118,442. Health expenditures do not correlate with outcomes especially for the marginalized population. Development and implementation of national NCD control programs for screening of common cancers and early detection are either non-existent or sporadic as a result cancers are usually diagnosed late and present challenges to therapy on all fronts especially in the indigent population.

Challenges include poverty, ignorance, lack of access to cancer centers, lack of access to basic cancer therapy and suboptimal treatment. This includes surgery, radiation and cancer therapy including supportive care. Simultaneously there is a dearth of human resource and cancer care providers to diagnose treat and provide supportive care to cancer patients.

Access to new biologics and targeted therapies present a challenge to the already strained health care budget. Current status of cancer care will be discussed in Pakistan.

https://doi.org/10.1016/j.htct.2020.09.011

SP 11

Ph-positive and ph-like all: how can we further improve?

Robin Foà

While in childhood ALL the cure rates can be over 80%, in adults the prognosis still remains unsatisfactory. Important advancements have however occurred in the management of adult patients based on the biology of the disease. Ph+ ALL is an illuminating example of how the understanding of a specific genetic abnormality has led over time to the use of targeted therapies. The results obtained with tyrosine kinase inhibitors (TKI) used upfront in adult Ph+ ALL have changed our approach to this condition in patients of all ages. It is thus mandatory that the abnormality is rapidly investigated at presentation. In the GIMEMA network, the presence or absence of the BCR-ABL fusion is tested centrally within one week from diagnosis of ALL, during the steroid pre-phase. TKIs – alone or in combination with chemotherapy – have markedly improved the rates of response and overall survival of Ph+ ALL. The Italian cooperative group GIMEMA over the years has been using an induction strategy based on the use of a TKI (1st, 2nd and 3rd generation) plus steroids and CNS prophylaxis, with no systemic chemotherapy. This has led to a hematologic CR in 94–100% of patients (with no upper age limit) with virtually no deaths in induction. A proportion of patients can obtain a molecular response. Some elderly patients treated only with TKIs are alive and well after many years from diagnosis. Other groups have used a combination between a TKI and de-intensified chemotherapy, in order to reduce the toxicities (and deaths) associated with conventional chemotherapy plus a TKI. With the advent of TKIs, the induction of Ph+ ALL patients – if identified promptly – is a solved issue. Since patients who achieve a molecular response fare significantly better, a molecular response should be the primary endpoint of treatment. Allogeneic stem cell transplant has always been considered the only curative strategy for Ph+ ALL patients. New strategies are however under active investigation. In the last GIMEMA LAL 2116 front-line trial an induction-consolidation strategy based on the use of dasatinib followed by at least two cycles of the bispecific monoclonal antibody blinatumumab were used. This chemo-free induction-consolidation approach is associated with very high rates of molecular response (Chiaretti et al, ASH 2019). In childhood Ph+ ALL, the protocols so far still use an induction based on a combination of chemotherapy plus a TKI.

Great attention has been raised by the so-called Ph-like ALL, a subgroup associated with an unfavorable prognosis. Evidence has been provided that this is contributed by the persistence of minimal residual disease following conventional chemotherapy. Attempts are being carried out by incorporating TKIs or other inhibitors. The GIMEMA LAL 2317 has used blinatumomab in the front-line Ph- ALL protocol (recently

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https://doi.org/10.1016/j.htct.2020.09.012

SP 12

CAR T-cell in children all

Francesco Saglio[1,2]

[1] *Pediatric Onco-Hematology, Stem Cell Transplantation and Cellular Therapy Division, Regina Margherita Children's Hospital, Torino, Italy*
[2] *University of Turin, Turin, Italy*

Chimeric Antigen Receptor (CAR)-T cell therapy is emerging as one of the most powerful and promising therapeutictool for the treatment of malignat diseases. CAR-T cells are T-lymphocytes modified *in vitro* to harbor an artificial molecular construct (CAR) made by an extracellular domain consisting of a single-chain variable fragment (scFv) recognizing a specific tumor antigen joined to a transmembrane domain which is linked to the signaling unit CD3ζ and co-stimulatory units CD28 or 4-1BB of the T-cell receptor, making them capable to recognize and to kill tumor's cell in a HLA-independent manner.CAR T-cell therapy consists in the selection of patient's normal T-cells via leukapheresis, activation, transduction to express CARs using lentiviral or retroviral vectors, expansion of transduced cells and infusion of the final product back to the patient. After the CAR T-cells are infused back into the patient, the engineered cells proliferate, recognize and kill tumor cells bearing the specific antigen the CAR is directed against. Most of the current clinical trials have been with anti-CD19 CAR T-cells directed against the antigen CD19, mainly expressed by Acute Lymphoblastic Leukemia and B-cells Non Hodgkin Lymphomas.

In recent years US Food and Drug Administration (FDA) and European Medicine Agency (EMA) approved CD19 CAR T-cells in patients affected by relapsed and refractory ALL under the age of 25 years and this technology is moving from an experimental approach available for very selected patients treated in a small number of Centers to a standard-of-care therapy available almost worldwide.

The diffusion of this technology requires a re-definition of the role of all the other therapy options currently available including other forms of immuno-therapy as monoclonal antibodies, bi-specific monoclonal antibodies and, upon all, allogeneic hematopoietic stem cell transplantation (alloHSCT).

Until now data are limited, and the above-mentioned question is far from being answered but there are some observations derived from pivotal clinical trials that probably will help us in building future trials aimed to define this topic.

Another open question is represented by the persistence of these cells in the patients that is related to the definition of the need for patients responding to CAR-T cells to proceed to other therapies, especially to alloHSCT, to consolidate disease remission. Moreover CAR-T cells are characterized by some peculiar side effects as the Cytokines Release Syndrome or CNS toxicity that if are not properly detected and treated may lead to very severe consequences with a significant mortality rate.

Finally, some technological, practical and economical considerations need to be defined in order to extend the use of this technology worldwide, in respect to the other currently available therapies.

https://doi.org/10.1016/j.htct.2020.09.013

SP 13

Update on chimeric antigen receptor – T cells (CAR-T) CD19 therapy: the Sheba experience

Arnon Nagler

Chimeric antigen receptor (CAR) T-cell therapy for hematologic malignancies is a cutting edge therapeutic advancement which is leading the immunotherapy frontier and cancer therapy. CD19-specific CARs are the most commonly used. CD19 is expressed on the surface of most B-cell malignancies and thus can be used as a target for immunotherapies for ALL, and NHL. Phase II trials have showed that anti-CD19 CAR T-cell therapy can induce durable responses in patients with relapse/refractory (R/R) ALL and aggressive B cell NHL. Some of the AMLs with 8:21 translocation expressed CD19, as well. We initiated a single center program in which patients with R/R ALL and NHL were treated with academic produced anti-CD19 CAR T-cells (autologous T-cells expressing anti-CD19 CAR construct with CD28 co-stimulatory domain). Inclusion criteria were age between 1 and 50 years, failure of at least two prior therapeutic protocols, a CD3 count greater than 250/μL blood, absence of clinical signs of graft-versus-host disease and no immunosuppressive treatment. Depending on age, the minimal performance score was 50 on a Lansky scale or on a Karnofsky scale. Patients with prior CD19 directed therapies were eligible for the study. Lympho-depleting conditioning was inducted by fludarabine 25 mg/m^2 for 3 days and cyclophosphamide 900 mg/m^2 for 1 day, followed by infusion of 1–1.5 × 10^6 transduced CAR-T cells per kilogram weight. Primary endpoints of the study were production feasibility, patient safety and best overall response rates, documented 1 to 2 months after infusion. 93 patients with r/r B-cell malignancies. All patients were heavily pretreated. Three enrolled patients (3%) dropped out from the study due to clinical deterioration ($n = 2$) or failure to produce CAR-T cells ($n = 1$; absence of CAR-T cells in the infusion product). One patient was treated twice. Of the treated patients, 37 patients had r/r ALL and 53 patient's r/r NHL, including DLBCL ($n = 36$), Burkitt lymphoma ($n = 3$), PMBCL ($n = 7$), follicular lymphoma ($n = 4$), gray zone lymphoma ($n = 1$), mediastinal lymphoma ($n = 1$) and high-grade lymphoma ($n = 1$). The median age of pts with ALL was 17 ± 14 years and median age of those with NHL was 44 ± 15 years. Both, ALL and NHL patients received an average of three prior lines of therapy. Thirty-two of 90 patients (36%) received a stem cell transplantation(SCT) prior CAR-T therapy, including 17 allogenic or haloidentical SCT in patients with ALL ($n = 15$) and NHL ($n = 2$). Ten of 37 (27%) ALL patients received prior

closed) and Ph-like cases are being identified using a predictor described by our group (Chiaretti et al, BJH, 2018). In adult B-lineage ALL, Ph+ and Ph-like ALL account for 35–60% of cases, depending on age, making them the most prevalent genetic ALL subgroup.

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In recent years US Food and Drug Administration (FDA) and European Medicine Agency (EMA) approved CD19 CAR T-cells in patients affected by relapsed and refractory ALL under the age of 25 years and this technology is moving from an experimental approach available for very selected patients treated in a small number of Centers to a standard-of-care therapy available almost worldwide.

The diffusion of this technology requires a re-definition of the role of all the other therapy options currently available including other forms of immuno-therapy as monoclonal antibodies, bi-specific monoclonal antibodies and, upon all, allogeneic hematopoietic stem cell transplantation (alloHSCT).

Until now data are limited, and the above-mentioned question is far from being answered but there are some observations derived from pivotal clinical trials that probably will help us in building future trials aimed to define this topic.

Another open question is represented by the persistence of these cells in the patients that is related to the definition of the need for patients responding to CAR-T cells to proceed to other therapies, especially to alloHSCT, to consolidate disease remission. Moreover CAR-T cells are characterized by some peculiar side effects as the Cytokines Release Syndrome or CNS toxicity that if are not properly detected and treated may lead to very severe consequences with a significant mortality rate.

Finally, some technological, practical and economical considerations need to be defined in order to extend the use of this technology worldwide, in respect to the other currently available therapies.

https://doi.org/10.1016/j.htct.2020.09.013

SP 13

Update on chimeric antigen receptor – T cells (CAR-T) CD19 therapy: the Sheba experience

Arnon Nagler

Chimeric antigen receptor (CAR) T-cell therapy for hematologic malignancies is a cutting edge therapeutic advancement which is leading the immunotherapy frontier and cancer therapy. CD19-specific CARs are the most commonly used. CD19 is expressed on the surface of most B-cell malignancies and thus can be used as a target for immunotherapies for ALL, and NHL. Phase II trials have showed that anti-CD19 CAR T-cell therapy can induce durable responses in patients with relapse/refractory (R/R) ALL and aggressive B cell NHL. Some of the AMLs with 8:21 translocation expressed CD19, as well. We initiated a single center program in which patients with R/R ALL and NHL were treated with academic produced anti-CD19 CAR T-cells (autologous T-cells expressing anti-CD19 CAR construct with CD28 co-stimulatory domain). Inclusion criteria were age between 1 and 50 years, failure of at least two prior therapeutic protocols, a CD3 count greater than 250/μL blood, absence of clinical signs of graft-versus-host disease and no immunosuppressive treatment. Depending on age, the minimal performance score was 50 on a Lansky scale or on a Karnofsky scale. Patients with prior CD19 directed therapies were eligible for the study. Lympho-depleting conditioning was inducted by fludarabine 25 mg/m^2 for 3 days and cyclophosphamide 900 mg/m^2 for 1 day, followed by infusion of 1–1.5 × 10^6 transduced CAR-T cells per kilogram weight. Primary endpoints of the study were production feasibility, patient safety and best overall response rates, documented 1 to 2 months after infusion. 93 patients with r/r B-cell malignancies. All patients were heavily pretreated. Three enrolled patients (3%) dropped out from the study due to clinical deterioration ($n = 2$) or failure to produce CAR-T cells ($n = 1$; absence of CAR-T cells in the infusion product). One patient was treated twice. Of the treated patients, 37 patients had r/r ALL and 53 patient's r/r NHL, including DLBCL ($n = 36$), Burkitt lymphoma ($n = 3$), PMBCL ($n = 7$), follicular lymphoma ($n = 4$), gray zone lymphoma ($n = 1$), mediastinal lymphoma ($n = 1$) and high-grade lymphoma ($n = 1$). The median age of pts with ALL was 17 ± 14 years and median age of those with NHL was 44 ± 15 years. Both, ALL and NHL patients received an average of three prior lines of therapy. Thirty-two of 90 patients (36%) received a stem cell transplantation(SCT) prior CAR-T therapy, including 17 allogenic or haloidentical SCT in patients with ALL ($n = 15$) and NHL ($n = 2$). Ten of 37 (27%) ALL patients received prior

closed) and Ph-like cases are being identified using a predictor described by our group (Chiaretti et al, BJH, 2018). In adult B-lineage ALL, Ph+ and Ph-like ALL account for 35–60% of cases, depending on age, making them the most prevalent genetic ALL subgroup.

https://doi.org/10.1016/j.htct.2020.09.012

SP 12

CAR T-cell in children all

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[2] *University of Turin, Turin, Italy*

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SP 14

Treatment of sickle cell crises

Salam Alkindi

Sickle cell disease (SCD) is an inherited disorder prevalent in Sub-Saharan Africa, Middle East and parts of India. Its characterized by repetitive episodes of vaso-occlusive (VOC) process leading to recurrent painful episodes, hemolytic anemia and predisposition to infection. Sickle cell crises varies and this what brings patients to hospital including VOC leading to recurrent painful episodes, or organ specific complications such as acute chest syndrome, stroke, splenic sequestration, and many skeletal complications. Although the prognosis of patients with SCD has improved, however still these events contributes to decrease quality of life and increased risk of death. Also unfortunately, progress on the management of these acute complications is slow, and tended to be supportive including vaccination, use of antibiotics prophylaxis and blood transfusions. Better understanding of pathophysiology of the disease has allowed more accelerated progress on preventing these complications and development of more focused pharmacological therapies. Hemoglobin polymerization is a primary triggering event in the pathophysiology of the disease, leading to the sickling process, this usually ignite an inflammatory process/tissue ischemia and increased adhesions. This understanding of the pathophysiology has allowed scientist to develop drugs that interfere with these processes such as Voxeletor & Hydroxyurea (interfere with polymerization-both approved by FDA), L-glutamine and Omega 3 (interfere with inflammatory process and oxidative stress) and crizanlizumab and Tinzaparin (works by inhibiting adhesion molecules). This will allow patients and physicians the freedom for a number of therapeutic interventions including development of combinations protocols. SCD is very complex and require a drug with multi-faceted action such as Hydroxyurea and this is of the limiting factors in the new recently approved drugs, limiting the patients who can benefit from each of them. Further progress is also seen in the area of bone marrow transplant (including alternative donor pool) and gene therapy/gene editing.

https://doi.org/10.1016/j.htct.2020.09.015

SP 15

Secondary acute leukemia evolving from myeloproliferative neoplasm (MPN)

Tariq Mughal

The natural history of myeloproliferative neoplasms (MPNs), both Philadelphia-chromosome positive – [chronic myeloid leukemia(CML)] and negative – [essential thrombocythemia (ET), polycythemia vera (PV), and primary myelofibrosis (PMF)] has been well documented but the mechanism underlying the apparently inexorable progression from an initial, rather indolent or chronic phase (CP) to advance phase, a term including accelerated phase (AP) and blast crisis (BC) remains obscure. Most patients with MPNs present in the indolent phase, during which myeloid progenitor numbers are greatly increased in the bone marrow and blood. This phase may continue for as little as one year or as long as 20 years or more, but eventually it transforms into acute leukaemia (BC), in which an increasing proportion of blast cells are found in the marrow and peripheral blood. The risk associated with the development of advanced-phase disease differs depending on the MPN subtype and is influenced by a number of factors such as duration of disease, clinical factors, the presence of

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unique molecular genetic features, and in some cases, the therapeutic interventions. ET probably carries the lowest rate of transformation to acute myeloid leukaemia (AML), whereas MF may carry a relatively high risk; lymphoid transformation has been reported in rare cases. The risk of transformation in CML to BC in the *ABL1*-tyrosine kinase inhibitors (TKI) era appears to be quite low, <2% per annum. Transformed disease in general tends to be difficult to be managed and is associated with a poor prognosis. The best treatment strategy, therefore, remains the prevention of transformation. Allogeneic stem cell transplantation is currently the only treatment that has been observed to confer long-term benefit to a small minority of patients who qualify for it. In this presentation, I will address the evolving genetic landscape, translational research efforts and investigational therapies for transformed MPNs.

https://doi.org/10.1016/j.htct.2020.09.016

SP 16

The new European leukemianet recommendations for treating CML

Rüdiger Hehlmann

Twenty-two years after the first patients with chronic myeloid leukemia (CML) were treated with the tyrosine kinase inhibitor (TKI) imatinib, outcome exceeds all expectations: the vast majority of CML patients have achieved normal life expectancy and some patients in sustained deep molecular remissions (DMR) may even be operationally cured in durable treatment-free remissions (TFR). However, some expectations remain unmet. Most patients are not yet cured and require life-long maintenance therapy. Also, progression to blast crisis still occurs in 5–7% of patients and remains a challenge. CML has not become the expected model disease for treating other leukemias or cancers, but the principle of elucidating the pathogenesis as a successful approach for cancer treatment has been impressively demonstrated in CML.

New insights have emerged from maturing long-term academic and commercial clinical trials regarding optimum management of CML. Velocity of response has unexpectedly proved less important than hitherto thought, does not predict survival, and is of unclear relevance for TFR. Serious and cumulative toxicity has been observed with TKI that had been expected to replace imatinib. Generic imatinib has become cost-effective first-line treatment in chronic phase despite chronic low-grade side-effects in many patients. Earlier recognition of CML end-phase by genetic assessment might improve prospects for blast crisis. Treatment discontinuation and TFR has become an important new treatment goal of CML. Duration of DMR (MR4, MR4.5) may be the best predictor of success. To reflect this new situation, the European LeukemiaNet has recently revised and updated its recommendations for treating CML. The presentation will focus on recent developments and on current evidence for treating CML in 2020.

https://doi.org/10.1016/j.htct.2020.09.017

SP 17

Ex vivo activation of pleural T cells in pleural malignancies

Vera S. Donnenberg, James D. Luketich, Albert D. Donnenberg

Introduction: MPE are uniformly fatal. It is estimated that the incidence of MPE in the United States is more than 150,000 cases per year, making this a common terminal pathway for a variety of cancers and a dire problem without a solution. Currently available cellular therapeutics are costly and often lack polyclonality, polyfunctionality, and the ability to persist as central memory. The treatment of this deadly complication is potentially at a turning point if the rich immune infiltrates that characterize the majority of effusions can be redirected to an efficacious anti-tumor response. Despite this promise, pleural immune infiltrates have not been used to generate effector cells for adoptive cellular therapy.

Objectives: We have exploited the heterogeneous cellular composition of MPE by piloting the generation of therapeutic T-cell products, using conventional methods used for expanding tumor-infiltrating lymphocytes (TIL). The advantages of plural T cells are: (1) Fewer cycles of expansion owing to several orders of magnitude greater starting number of T cells; (2) Greater initial clonal and functional heterogeneity; (3) Likelihood of preserving polyclonality, polyfunctionality and central memory.

Results: MPE have abundant tumor infiltrating CD3+ T-cells, CD19+ B-cells, CD14+ macrophages, and EpCAM-/Cytokeratin+ mesothelial cells. Regulatory T-cells, which may be abundant in TIL, are low or absent in MPE. Our laboratory's average recovery of viable nucleated cells per MPE is $7.8 \pm 4.0 \times 10^8$ cells, with viability exceeding 95%. The cellular composition (tumor, lymphocytes, macrophages, neutrophils, mesothelial cells) varies from patient to patient, but T-cell recovery averages $2.0 \pm 1.6 \times 10^8$ (mean, SD). In pilot experiments we cultured whole breast cancer MPE in the presence of anti-CD3/anti-CD28 Dynal beads, IL-2 and IL-7 for 96 h. CD3+ T cells were FACS-sorted and added to autologous tumor monolayer cultures and expanded for an additional passage (2 weeks). Expanded passage 2 T cells were compared to freshly isolated T cells (2nd MPE drainage) for ability to kill autologous tumor and non-tumor targets (live cell imaging). Expanded T cells were potently cytotoxic, whereas freshly isolated MPE had no activity against autologous tumor. Expanded T cells did not kill the autologous non-tumor target (adherent cells isolated from peripheral blood). Additionally, we tested freshly isolated breast cancer MPE T cells for the ability to secrete cytokines associated with expansion and effector generation (IL-2, IFNγ and TNFα). We also measured the immunosuppressive cytokine IL-10. Freshly isolated plastic nonadherent cells from a breast cancer MPE were incubated with TPA+ ionomycin for 1 h, followed by brefeldin for 2 h. CD4+ T cells (85%) and CD8+ T cells (9%) were gated on cells co-expressing intracellular IL-2 and IFNγ. Polyfunctional T cells, defined as IL-2+/IFNγ+/TNFα+/IL-10-, comprised 0.38%, and 0.82% of CD4+ and CD8+ T cells. Unstimulated control cultures constitutively secreted IL-10 and IFNγ but not IL-2 or TNFα.

unique molecular genetic features, and in some cases, the therapeutic interventions. ET probably carries the lowest rate of transformation to acute myeloid leukaemia (AML), whereas MF may carry a relatively high risk; lymphoid transformation has been reported in rare cases. The risk of transformation in CML to BC in the *ABL1*-tyrosine kinase inhibitors (TKI) era appears to be quite low, <2% per annum. Transformed disease in general tends to be difficult to be managed and is associated with a poor prognosis. The best treatment strategy, therefore, remains the prevention of transformation. Allogeneic stem cell transplantation is currently the only treatment that has been observed to confer long-term benefit to a small minority of patients who qualify for it. In this presentation, I will address the evolving genetic landscape, translational research efforts and investigational therapies for transformed MPNs.

https://doi.org/10.1016/j.htct.2020.09.016

SP 16

The new European leukemianet recommendations for treating CML

Rüdiger Hehlmann

Twenty-two years after the first patients with chronic myeloid leukemia (CML) were treated with the tyrosine kinase inhibitor (TKI) imatinib, outcome exceeds all expectations: the vast majority of CML patients have achieved normal life expectancy and some patients in sustained deep molecular remissions (DMR) may even be operationally cured in durable treatment-free remissions (TFR). However, some expectations remain unmet. Most patients are not yet cured and require life-long maintenance therapy. Also, progression to blast crisis still occurs in 5–7% of patients and remains a challenge. CML has not become the expected model disease for treating other leukemias or cancers, but the principle of elucidating the pathogenesis as a successful approach for cancer treatment has been impressively demonstrated in CML.

New insights have emerged from maturing long-term academic and commercial clinical trials regarding optimum management of CML. Velocity of response has unexpectedly proved less important than hitherto thought, does not predict survival, and is of unclear relevance for TFR. Serious and cumulative toxicity has been observed with TKI that had been expected to replace imatinib. Generic imatinib has become cost-effective first-line treatment in chronic phase despite chronic low-grade side-effects in many patients. Earlier recognition of CML end-phase by genetic assessment might improve prospects for blast crisis. Treatment discontinuation and TFR has become an important new treatment goal of CML. Duration of DMR (MR4, MR4.5) may be the best predictor of success. To reflect this new situation, the European LeukemiaNet has recently revised and updated its recommendations for treating CML. The presentation will focus on recent developments and on current evidence for treating CML in 2020.

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Ex vivo activation of pleural T cells in pleural malignancies

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SP 18

Are there really cancer stem cells and how do they operate?

Robert Gale

Some but not all data suggest within a cancer not all cancer cells are the same, namely, there are diverse cell types. The *stem cell* theory of cancer proposes amongst all cancer cells a very few act as *stem cells*. These cells reproduce themselves and sustain the cancer much like normal stem cells renew and replenish organs and tissues like the haematopoietic system. There are important therapy implications if cancers are really driven by a few *stem cells*. For instance, many anti-cancer therapies are evaluated based on their ability to make a cancer smaller. This can happen without killing cancer *stem cells*. If so, the cancer is likely to recur, perhaps in a more dangerous form such as metastases. In fact, most people with cancer die from metastases, not the primary cancer. The analogy is selecting a more virulent microbe by indiscriminate use of antibiotics.

One component of the cancer *stem cell* theory concerns how cancers arise. Typically, for a cell to become cancerous it must accumulate substantial numbers of mutations. A leukaemia such as chronic myeloid leukaemia (CML) is an exception caused by 1 mutation (*BCRABL1*). Conventional cancer theory is that any cell has the potential to become a cancer. However, other data suggest only some cells, those with *stem cell* potential, can develop into a cancer. This may explain why some normal people can have cancer-related mutations without having cancer, for example normals with *BCRABL1* or normals with t(14;18) without CML or without a lymphoma. The hypothesis is the cell(s) in which these mutations occur are not *stem cells* and therefore lack the potential to cause cancer. However, we must also consider the possibility some mutations can re-programme a cell without *stem cell* potentially to become a *stem cell*. An example of this are induced pluripotent stem cells iPSC) which are adult (non-stem) cells reverted to an *embryonic stem cell* state by introducing 4 genes. Another notion is only cells with *stem cell* like features survive sufficiently long to accumulate the typically large number of mutations required for cancer development. The theory, therefore, is cancer *stem cells* arise from normal *stem cells* or *precursor cells* produced by normal *stem cells*.

Another important implication of the cancer *stem cell* theory is cancer *stem cells* are closely related to normal *stem cells* and share many properties. Cancer cells produced by cancer *stem cells* should follow many of the rules observed by normal daughter cells. In this regard cancer cells can be considered a caricature of normal cells with similar but distorted features. If so, it may be possible to use knowledge about normal *stem cells* to identify and attack cancer *stem cells*.

Lastly, it may not be necessary to eradicate all cancer stem cells to cure a cancer. For example, in CML, therapy with tyrosine kinase-inhibitors (TKIs) markedly reduces numbers of mature leukaemia cells but not any and certainly not all CML *stem cells*. Regardless, in a substantial proportion of people with CML responding favorably to TKI-therapy it is possible to stop therapy without leukaemia returning. In sum, increasing knowledge of cancer stem cells should improve our understanding of and ability to treat diverse cancers.

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https://doi.org/10.1016/j.htct.2020.09.019

SP 19

Challenges in treating solid tumors in developing countries

Adnan Abdul Jabbar

There is an increasing number of cancers worldwide due to epidemiological transition. Longer life spans resulting in aging population is among some of the reasons for growing burden in cancer worldwide. The number of new cancer cases is expected to increase by nearly 75% by 2030 (107,000 additional cases per annum), with 60% of cases in the elderly (aged ≥65). The extent of cancer related morbidity and mortality is directly linked to the effectiveness of efforts to prevent, control and treat cancer, particularly in the developing world. In 2012, almost 57% of all cancer cases and 65% of cancer deaths occurred in low-and middle-income countries. If the current trend continues, the burden of cancer will increase to 22 million new cases annually by 2030, with 81% of new cases and almost 88% of mortality occurring in less developed countries. Cancer care in a country like Pakistan is challenging because of lack of strategic information and national planning for cancer control. Cancer registry provides important information that helps in directing and planning cancer prevention and care. Lack of national cancer registry limits estimation of true burden, identification of areas that require special need and thereby proper treatment strategy. Health systems required to deliver comprehensive life-saving treatments are limited in the country. Out of pocket payments and private health care usage remains high. A number of patients are not covered by insurance and individuals face catastrophic expenditure in seeking treatment. As a result, there is disparity in access to quality care. High incidence of later stage disease is very common due to social stigma associated with cancer treatment, myths, lack of awareness and preference for alternative treatment options. Drugs that have lately revolutionized cancer management are either not available in the country and if present, are extremely expensive for a common person to afford. Palliative care and access to supportive care medicines is almost nonexistent. Pain management is restricted to analgesics without narcotics. With cancer rates steadily rising in low- and middle-income countries, the disease will inevitably

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frustrate global development efforts unless urgent action is taken.

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SP 20

Lymphoblastyc lymphoma/leukemia: a single center experience

Alina Antipova, Olga Baranova

Introduction: Lymphoblastic lymphoma (LBL) is a rare neoplasm of lymphoblasts or precursor T- and B-cell with predominantly involves lymph nodes, mediastinum or extranodal tissues with minimal persistence in bone marrow. LBL amount 2% of all non-Hodgkin lymphomas. T-phenotype is the most common one and reaches above 80% of LBL. LBL and acute lymphoblastic leukemia (ALL) have the same biological entity according WHO Classification of Tumors of Haematopoietic and Lymphoid Tissues 2017. Distinguishing criterion between two diseases is the number of bone marrow blasts 25%. ALL-regimen provide better overall (OS) and disease-free survival (DFS) in contrast with CHOP-like schemes.

Patients and methods. A retrospective review of LBL patients from **N.N. Blokhin National Medical Research Center of Oncology** (Russia, Moscow) during period between 2009 and 2020 was done. Patients were treated according ALL-2009 protocol (Russian ALL-Study Group, ClinicalTrials.gov NCT01193933). Kaplan–Meier curves and log-rank test were used to evaluate the OS and DFS. This study includes 20pts with primary ($n=15$) and relapse LBL ($n=5$). T-cell LBL pts were 18, and 2 were of B-cell lineage. Most patients were males 85% (17 of 20). Stage II and IV both at 45%, stage III 10%. All T-LBL patients showed a mediastinal tumor, B-LBL pts had involved peripheral lymph nodes and soft tissues. The rate of LBL among all primary lymphoid precursor neoplasms (LBL and ALL) was 17.6%. Median follow up was 28 months (0.5–170.5 mo).

Results: All 5 relapse patients were pre-treated out of our center: after CHOP-like treatment with relapse in initial zones and all died from disease ($n=3$), after HyperCVAD, later followed alloHSCT ($n=1$, alive) and 1 pts after ALL-BFM-2002 with mediastinum and CNS relapse. CR rate of primary LBL ($n=15$) was 93%, 1 pts was refractory and later died. Radiotherapy has been carried out in 40% (6 of 15) patients with residual tumor mass after chemotherapy consolidation. 1 patient was been undergoing autoSCT. The 10-year OS of patients with LBL, T-ALL and B-ALL was 73.8%, 48.7% and 54.5% respectively ($p=0.3$). The 10-year DFS in the same groups was 75%, 56.3% and 64.5% respectively ($p=0.2$). Although the results are not statistically significant, we see a trend towards better survival outcomes in patients with LBL. AlloSCT was performed in 2 patients LBL in CR2, one of them alive, the other died of complications.

Conclusion: The results of treatment of LBL pts in **N.N. Blokhin National Medical Research Center of Oncology** are comparable to most of the similar reported studies. The survival results of LBL patients with ALL-regimen therapy seem to be better compared with patients ALL. CHOP-like chemotherapy is a very poor prognostic factor for LBL patients. The role of autoSCT has not been developed. In our center we have satisfied outcomes of LBL with minimal rate of high dose consolidation with autoSCT. Radiotherapy at postconsolidation phase in patients with residual tumor mass reduces the risk of relapse.

https://doi.org/10.1016/j.htct.2020.09.021

SP 21

Relapsed and refractory classical Hodgkin lymphoma immunotherapy

Kirill Lepik

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Background: Introduction of PD-1 inhibitor nivolumab (Nivo) into a clinical practice revolutionized the treatment of relapsed and refractory classical Hodgkin lymphoma (r/r cHL). Yet there is a set of unresolved clinical questions including the assessment of response, the prognostic factors influencing the survival of patients during immunotherapy, and optimal treatment strategy in patients resistant to nivolumab, as well as the possibility of discontinuation of therapy in case of persistent complete remission. This report presents the results of analysis of nivolumab treatment outcomes in Pavlov University.

Methods: This retrospective study included r/r cHL patients treated with standard-dose nivolumab (3 mg/kg q2w). Therapy was continued until the disease progression, signs of intolerance or could be stopped at the discretion of treating physicians in selected patients with prolonged complete remission. In patients with r/r disease after nivolumab monotherapy, 48 received nivo and bendamustine (Benda) in a 28-day cycle. Benda (90 mg/m^2) was infused on day 1,2 and Nivo – on day 1 of the cycle. The response was assessed by PET-CT scan every 3 months according to LYRIC criteria.

Results: The analysis included 116 patients treated with nivolumab monotherapy (56 m/60 f) with a median age of 32 years (range 14–63). With a median follow-up of 41 (6–54) months after treatment initiation, 108 (93%) patients were alive, the median OS was not reached. Median PFS was 19 mo (13.7–24.4) with a 3-year PFS of 27%. The best overall response was CR in 33%, PR in 34%, SD in 5%, PD in 9%, an indeterminate response (IR) in 20% of pts. Patients with early CR at 3mo after treatment initiation had significantly better prognosis (median PFS 35 mo vs. 17 mo, $p=0.008$). Other clinical factors that predicted prognosis were B-symptoms (median PFS 15 mo vs. 26 mo, $p=0.017$), extranodal disease at the moment of the treatment initiation (median PFS 14 mo vs. NR, $p=0.000$), >4 prior lines of therapy (median PFS 18mo vs. 27 mo, $p=0.05$). In a group of patients ($n=23$) who discontinued nivolumab in complete response (CR), the possibility of durable remission achievement was demonstrated (2-year PFS was 55.1%). The nivolumab retreatment has demonstrated the efficacy with high overall response rate (ORR) and CR (67 and 33.3% respectively). In the group of patients receiving nivo-benda combination after nivolumab monotherapy failure, the

frustrate global development efforts unless urgent action is taken.

https://doi.org/10.1016/j.htct.2020.09.020

SP 20

Lymphoblastyc lymphoma/leukemia: a single center experience

Alina Antipova, Olga Baranova

Introduction: Lymphoblastic lymphoma (LBL) is a rare neoplasm of lymphoblasts or precursor T- and B-cell with predominantly involves lymph nodes, mediastinum or extranodal tissues with minimal persistence in bone marrow. LBL amount 2% of all non-Hodgkin lymphomas. T-phenotype is the most common one and reaches above 80% of LBL. LBL and acute lymphoblastic leukemia (ALL) have the same biological entity according WHO Classification of Tumors of Haematopoietic and Lymphoid Tissues 2017. Distinguishing criterion between two diseases is the number of bone marrow blasts 25%. ALL-regimen provide better overall (OS) and disease-free survival (DFS) in contrast with CHOP-like schemes.

Patients and methods. A retrospective review of LBL patients from **N.N. Blokhin National Medical Research Center of Oncology** (Russia, Moscow) during period between 2009 and 2020 was done. Patients were treated according ALL-2009 protocol (Russian ALL-Study Group, ClinicalTrials.gov NCT01193933). Kaplan–Meier curves and log-rank test were used to evaluate the OS and DFS. This study includes 20pts with primary ($n=15$) and relapse LBL ($n=5$). T-cell LBL pts were 18, and 2 were of B-cell lineage. Most patients were males 85% (17 of 20). Stage II and IV both at 45%, stage III 10%. All T-LBL patients showed a mediastinal tumor, B-LBL pts had involved peripheral lymph nodes and soft tissues. The rate of LBL among all primary lymphoid precursor neoplasms (LBL and ALL) was 17.6%. Median follow up was 28 months (0.5–170.5 mo).

Results: All 5 relapse patients were pre-treated out of our center: after CHOP-like treatment with relapse in initial zones and all died from disease ($n=3$), after HyperCVAD, later followed alloHSCT ($n=1$, alive) and 1 pts after ALL-BFM-2002 with mediastinum and CNS relapse. CR rate of primary LBL ($n=15$) was 93%, 1 pts was refractory and later died. Radiotherapy has been carried out in 40% (6 of 15) patients with residual tumor mass after chemotherapy consolidation. 1 patient was been undergoing autoSCT. The 10-year OS of patients with LBL, T-ALL and B-ALL was 73.8%, 48.7% and 54.5% respectively ($p=0.3$). The 10-year DFS in the same groups was 75%, 56.3% and 64.5% respectively ($p=0.2$). Although the results are not statistically significant, we see a trend towards better survival outcomes in patients with LBL. AlloSCT was performed in 2 patients LBL in CR2, one of them alive, the other died of complications.

Conclusion: The results of treatment of LBL pts in **N.N. Blokhin National Medical Research Center of Oncology** are comparable to most of the similar reported studies. The survival results of LBL patients with ALL-regimen therapy seem to be better compared with patients ALL. CHOP-like chemotherapy is a very poor prognostic factor for LBL patients. The role of autoSCT has not been developed. In our center we have satisfied outcomes of LBL with minimal rate of high dose consolidation with autoSCT. Radiotherapy at postconsolidation phase in patients with residual tumor mass reduces the risk of relapse.

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SP 22

Literature review: the year in apheresis – what is new?

Joseph Schwartz

Since 1986, the American Society for Apheresis (ASFA) has published practice guidelines on the use of therapeutic apheresis in the Journal of Clinical Apheresis. Since 2007, the guidelines are published in regular intervals to reflect current evidence-based apheresis practice with the most recent edition published in 2019. The ASFA guidelines are written in a user-friendly fact sheet format and represent a concise yet comprehensive review of the English language literature on the use of apheresis to treat disease. The role of the guidelines is to provide the most current information available to apheresis practitioners. The PEXIVAS study is an international, randomized controlled trial comparing therapeutic plasma exchange (TPE) versus no TPE and steroid dosing regimen on the primary composite outcome of end stage renal disease or death in patients with ANCA-associated vasculitis. The study was published in early 2020 in the NEJM. This is the largest study on the role of therapeutic apheresis in ANCA-associated vasculitis published to date. The study showed the TPE does not reduce the risk of ESRD or death in patients with ANCA-associated vasculitis. Based on these findings, an interim updated fact sheet was recently published. In this interim fact sheet, the category recommendation for rapidly progressive glomerulonephritis in the setting of microscopic polyangiitis, granulomatosis with polyangiitis, or renal-limited vasculitis with Cr $\geq$5.7 mg/dL (includes "on dialysis") was changed from category I to category II. Similarly, the grade of evidence was changed from IA to IB to acknowledge previously described important limitations of the PEXIVAS study including the lack of biopsy to define disease severity and the long follow-up period, which may make it difficult to detect initial improvement in the subset of patients at first presentation. This recent seminal publication and its implication for therapeutic apheresis will be discussed. Other topics with new information that will be addressed in this presentation include Hereditary TTP. A recent review on the prevalence, pathogenesis, clinical features of this disorder, as well as therapeutic options was published. Although Hereditary TTP is not currently categorized in the Therapeutic Apheresis guidelines, indications for TPE as well as the use of plasma infusion, and eventually rhADAMTS13 enzyme in this disorder will be discussed. Similarly, Hemophagocytic Lymphohistiocytosis/Macrophage Activating Syndrome (HLH/MAS) will be reviewed including a recent retrospective case series showing use of TPE in combination with immunosuppressive therapy in this disorder.

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SP 23

The ASFA therapeutic apheresis guidelines – 8th edition – overview with focus on hematology/oncology indications

Nancy M. Dunbar

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SP 24

Essential molecular characterization of AML patients

Mehmet Yilmaz

Several recurrent somatic mutations have been identified as important features in defining the molecular landscape of AML. Targeting mutations such as FLT3 remained an area with active investigations and variable success while targeting other common mutations such as NPM1, DNMT3A, and TET2 remains challenging.

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Literature review: the year in apheresis – what is new?

Joseph Schwartz

Since 1986, the American Society for Apheresis (ASFA) has published practice guidelines on the use of therapeutic apheresis in the Journal of Clinical Apheresis. Since 2007, the guidelines are published in regular intervals to reflect current evidence-based apheresis practice with the most recent edition published in 2019. The ASFA guidelines are written in a user-friendly fact sheet format and represent a concise yet comprehensive review of the English language literature on the use of apheresis to treat disease. The role of the guidelines is to provide the most current information available to apheresis practitioners. The PEXIVAS study is an international, randomized controlled trial comparing therapeutic plasma exchange (TPE) versus no TPE and steroid dosing regimen on the primary composite outcome of end stage renal disease or death in patients with ANCA-associated vasculitis. The study was published in early 2020 in the NEJM. This is the largest study on the role of therapeutic apheresis in ANCA-associated vasculitis published to date. The study showed the TPE does not reduce the risk of ESRD or death in patients with ANCA-associated vasculitis. Based on these findings, an interim updated fact sheet was recently published. In this interim fact sheet, the category recommendation for rapidly progressive glomerulonephritis in the setting of microscopic polyangiitis, granulomatosis with polyangiitis, or renal-limited vasculitis with Cr $\geq$5.7 mg/dL (includes "on dialysis") was changed from category I to category II. Similarly, the grade of evidence was changed from IA to IB to acknowledge previously described important limitations of the PEXIVAS study including the lack of biopsy to define disease severity and the long follow-up period, which may make it difficult to detect initial improvement in the subset of patients at first presentation. This recent seminal publication and its implication for therapeutic apheresis will be discussed. Other topics with new information that will be addressed in this presentation include Hereditary TTP. A recent review on the prevalence, pathogenesis, clinical features of this disorder, as well as therapeutic options was published. Although Hereditary TTP is not currently categorized in the Therapeutic Apheresis guidelines, indications for TPE as well as the use of plasma infusion, and eventually rhADAMTS13 enzyme in this disorder will be discussed. Similarly, Hemophagocytic Lymphohistiocytosis/Macrophage Activating Syndrome (HLH/MAS) will be reviewed including a recent retrospective case series showing use of TPE in combination with immunosuppressive therapy in this disorder.

https://doi.org/10.1016/j.htct.2020.09.023

SP 23

The ASFA therapeutic apheresis guidelines – 8th edition – overview with focus on hematology/oncology indications

Nancy M. Dunbar

The ASFA Journal of Clinical Apheresis (JCA) Special Issue Writing Committee is charged with reviewing, updating, and categorizing indications for the evidence-based use of therapeutic apheresis every 3 years to produce "Guidelines on the Use of Therapeutic Apheresis in Clinical Practice: Evidence-Based Approach" which is published in the Journal of Clinical Apheresis. Guideline preparation incorporates systematic review published peer reviewed literature and applies evidence-based approaches in the grading and categorization of apheresis indications. These guidelines serve as a key resource to guide the utilization of therapeutic apheresis in the treatment of human disease. In this session, we will review the evolution of the guidelines and highlight significant changes in the 2019 Journal of Clinical Apheresis 8th Special Issue published in June 2019. Recommendations for the use of therapeutic apheresis for Hematology/Oncology Indications will be briefly reviewed.

https://doi.org/10.1016/j.htct.2020.09.024

SP 24

Essential molecular characterization of AML patients

Mehmet Yilmaz

Several recurrent somatic mutations have been identified as important features in defining the molecular landscape of AML. Targeting mutations such as FLT3 remained an area with active investigations and variable success while targeting other common mutations such as NPM1, DNMT3A, and TET2 remains challenging.

Cytogenetic characterization of AML: These abnormalities include: AML with t(8;21)(q22;q22); RUNX1-RUNX1T1, AML with inv (16)(p13.1q22) or t (1 6; 1 6) (p 1 3. 1; q 2 2); CBFB-MYH11, AML with t(15;17)(q22;q12); PML-RARA, AML with t(9;11)(p22;q23);MLLT3-MLL, AML with t(6;9)(p23;q34); DEK-NUP214, AML with inv (3)(q21q26.2) or t(3;3)(q21;q26.2); RPN1-EVI1, AML (megakaryoblastic) with t(1;22)(p13;q13); RBM15-MKL14, A recent revision of WHO classification in 2016 has recognized new provisional category of AML with BCR-ABL1. Patients with BCR-ABL1 AML are less likely to have splenomegaly or peripheral basophilia and usu-

ally have lower bone marrow cellularity and myeloid/erythroid ratios compared to CML-BC.

Mutations in signaling pathways: Mutations in FLT3 receptor can lead to constitutive activation that in turn can lead to decrease in apoptosis and increase in leukemia proliferation and survival. Patients with FLT3/ITD mutations typically have high white cell counts at disease presentation and have normal or intermediate risk karyotypes. FLT3/TKD mutations tend to confer slightly better prognosis. NPM1 mutations usually occur in exon 12 in the C-terminus of the protein and can lead to cytoplasmic localization of NPM1 protein. Studies have shown that NPM1 mutations usually carry a favorable prognosis in the absence of FLT3-ITD and mainly in the presence of IDH1-2.

Other gene mutations in AML: ASXL1 gene encodes a chromatin binding protein, which in turn enhance or repress gene transcription in localized areas by chromatin structure modification. The overall frequency of ASXL1 mutations in AML is approximately 3–5% but its incidence is higher in patients with intermediate risk AML. DNMT3A is a DNA methyltransferase that regulates epigenetic alterations through DNA methylation. DNMT3A mutations are frequently found with FLT3-ITD, NPM1, IDH1-2 mutations though rarely associated with t (15; 17) and CBF leukemia's. IDH1 and IDH2 are two enzymes that play an important role in DNA methylation and histone modification and affect the active isocitrate binding site and lead to increased level of 2-hydroxyglutarate. IDH2 mutations occur in 8–12% of adult AML. 2-HG can be detected in vast excess in the serum and BM of AML patients with IDH1/2 mutations, suggesting that it may serve as a biomarker for this genetically defined subset of AML patients and as a measure of residual disease after AML therapy.

Mutations in cohesion complex members; BCOR, PHF6;

Mutations in splicing machinery: The most common splicing factor gene abnormalities involved in AML are SF3B1, U2AF1, SRSF2, and ZRSR2. These mutations are mutually exclusive and can be defined as founder mutations or associated with certain phenotype in a subset of patients such as SF3B1 mutations in MDS patients with ring sideroblasts and SRSF2 in chronic CMML.

https://doi.org/10.1016/j.htct.2020.09.025

SP 25

How clinical networking may be a powerful strategy to face the challenges faced by hematologists treating acute leukemias in the developing world. The experience of the International Consortium on Acute Leukemia (ICAL)

Eduardo M. Rego

The International Consortium on Acute Promyelocytic Leukemia (IC-APL), later renamed as International Consortium on Acute Leukemias (ICAL), was founded in 2004 as an initiative of the International Members Committee of the American Society of Hematology (ASH). Its goal was to create a network of institutions in developing countries that would exchange experience and data and receive support from well-established cooperative groups, bringing together clinical investigators from Europe, North America and Latin America. The Consortium selected acute promyelocytic leukaemia (APL) as a model disease to test the impact of networking on the outcome of patients treated in developing countries, because it is a highly curable disease, if early diagnosis and specific treatment are promptly established. By the end of the 1990's, European and American groups reported complete remission (CR) and long-term disease-free survival (DFS) rates of approximately 90% and 85%, respectively, in studies of cohorts of APL patients who were treated with all trans retinoic acid (ATRA) and anthracyclines (Soignet et al., 1997; Sanz et al., 1999). In contrast, a retrospective analysis of 134 Brazilians patients with APL treated between 2003 and 2006 reported a death rate of 32% during induction, with most of the deaths caused by APL-associated coagulopathy (Jacomo et al., 2007). In this study the long-term overall survival (OS) rate at 2 years was less than 60%, indicating a clearly unmet medical need. The consortium adopted the combination of ATRA and anthracycline, using the same design of the PETHEMA/HOVON LPA2005 protocol (Sanz et al., 2010, 2015), except that idarubicin was replaced by daunorubicin at a ratio of 1:5. Importantly, medical educational activities, centralized laboratory diagnosis and monitoring and specific guidelines for supportive treatment were adopted. Here we will present the analysis of 306 Brazilian patients treated according to the IC-APL protocol and discuss the achievements and pitfalls that the group has faced during its 16-year experience. In total Number of screened patients: 374 patients were screened and 306 were considered elegible with an average of 25.4 pts/year. The main reasons of ineligibility were PML/RARA was not detected (36%); previous chemo or radiotherapy (12%), drug unavailability (10%); age >75 y (8%); pregnancy (7%). One case of ZBTB16/RARA rearrangement was detected. The median time of follow up was of 50 months. The Complete Hematological Remission was of 88.9% and the number of deaths during induction among eligible patients was of 33 (10.7%). The Cummulative Incidence of Relapse was 13% (35/265 pts) and most relapses occurred during maintenance relapse (21 pts). Monitoring was successfully performed by RT-qPCR and conventional RT-PCR. With discrepant results in only 7 patients (in whom relapse was first detected by RT-qPCR). The 10-year overall survival rate was of 75% (95% CI: 68–80%) and the 10-year disease free survival was of 82% (95% CI: 75–87). The ICAL experience confirmed that the establishment of clinical networks involving developing and developed countries may be a powerful strategy to face the challenges faced by hematologists treating acute leukemias in the developing world.

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Novel approaches to the treatment of polycythemia vera

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ductive agents have been added to achieve hematocrit control in patients at high risk for thrombosis. Thus PV has lagged behind other hematologic malignancies in the implementation of novel and targeted drug therapy. This has changed recently with the development of novel therapies for this disease, a number of which have received regulatory approval internationally.

Ruxolitinib has been approved as second line therapy for PV patients intolerant of or resistant to hydroxyurea on the basis of the RESPONSE trial. In this study 222 patients were randomized to receive ruxolitinib or best available therapy (BAT) in the second line setting. At 5 years 60% of the ruxolitinib patients versus 19% of the BAT patients maintained hematocrit control without need for phlebotomy. Reduction in spleen volume was also more frequent among ruxolitinib patients (89 vs. 49%). There were decreases in *JAK2* V617F allele burden in both groups but complete molecular remissions were rare. Importantly, herpes zoster infections occurred among ruxolitinib treated patients.

Interferon has become an important drug in the treatment of PV with the publication of interim and final results of a number of studies of pegylated versions of interferon. The Myeloproliferative Disorders Research Consortium (MPD-RC) 112 and MPD-RC 111 randomized studies previously treated and untreated patients respectively. Good clinical responses with manageable toxicity were attained and further follow up is awaited. The 3 year results of the combined PROUD-PV and CONTINUATION-PV, randomized, phase 3 trials comparing ropeginterferon (a novel, long-acting, mono-pegylated proline interferon) to hydroxyurea in newly diagnosed PV patients show improved complete haematological response and reduced *JAK2* V617F allele burden with ropeginterferon. The drug is also under study in patients with low-risk PV in whom hematocrit levels at or below 45% compared with those who received monthly phlebotomy alone were more common according to interim findings from the ongoing LOW-PV trial.

Novel agents for PV include MDM2 inhibitors, nutlins. MDM2, an inhibitor of *TP53* is up-regulated in PV CD34+ cells and exposure to a nutlin induced *TP53* and selective stem cell depletion in preclinical models. Early trials of idasanutlin, an oral MDM2 antagonist demonstrated a 58% overall response rate and median duration of response of 16.8 months in high-risk PV patients after failing prior therapy. Idasanutlin is being evaluated in a multinational phase 2 trial.

A unique approach to controlling the hematocrit in PV by targeting iron metabolism is currently in early testing. Hepcidin is the major physiologic regulator of iron metabolism. PTG-300 is a first-in-class synthetic hepcidin mimetic that is in phase 2 clinical trial development. The agent reduces iron available for erythropoiesis and in a preliminary study was able to maintain the hematocrit at <45% without need for phlebotomy in a small number of PV patients all of whom were previously phlebotomy dependent.

These novel agents and others will likely change treatment paradigms in PV.

https://doi.org/10.1016/j.htct.2020.09.027

SP 27

New drugs for low grade lymphoproliferative diseases

Argiris Symeonidis

For asymptomatic patients with low-grade lymphoproliferative disorders and low tumor burden, watchful waiting represents a rational approach. For symptomatic patients or for those with high tumor burden, initial treatment is usually chemoimmunotherapy with an anti-CD20 monoclonal antibody (mo-Ab), most commonly Rituximab or Obinutuzumab plus an alkylator, such as bendamustine or chlorambucil and/or a pourine analog, such as fludarabine or cladribine. For the Refractory/Relapsed (RR) setting treatment options depend on patient's background, initial PFS and on various prognostic parameters. Newer anti-CD20 mo-Abs, such as Ublituximab appear equally effective, but have not yet been tested comparatively with the previous ones. Radioconjugates such as 90Y-ibritumomab tiuxetan and 131I-tositumomab are no more in broad use due to unpredicted myelotoxicity. The newer 90Y-epratuzumab tetratexan appears safe as consolidation following R-CHOP in DLBCL patients. Polatuzumab vedotin, Pinatuzumab vedotin and Tafasitamab targeting CD19 have mainly been used, combined with an anti-CD20 mo-Ab to treat RR-DLBCL with success, which render them candidates for indolent lymphomas also. BTK inhibitors represent one main treatment option, either as initial treatment or in the RR setting. Ibrutinib, the first in class drug, is used either alone or in combination with Mo-abs and/or alkylators. Acalabrutinib, already approved for CLL/SLL and MCL, is now being tested for other B-cell malignancies. Zanubrutinib, a newer analog not exhibiting some of ibrutinib's AE, has been approved for RR-MCL and is currently being evaluated alone or in combination with Mo-Abs, lenalidomide and other agents. Idelalisib, the first PI3K-inhibitor, the second family of highly used targeted agents, has been approved for CLL/SLL and FL. Duvelisib, Copanlisib and Umbralisib are newer agents coming up and are currently being tested usually in combination with mo-Abs or other agents. Bimiralisib, a dual PI3K/mTOR inhibitor is a promising agent still in phase I. Hepatotoxicity, the major AE of this class, is reversible and dose-dependent. The BCL2 inhibitor venetoclax, alone or combined with mo-Abs and/or bendamustine (BRVen) or with Ibrutinib (ongoing trial), is a breakthrough approach, being tested in several disease entities with impressive results. Bispecific antibodies engaging CD19 (Blinatumomab) or CD22 (Inotuzumab ozogamycin) to a T/NK-cell surface antigen have received approval for more aggressive B-cell lymphomas. Lenalidomide combined with Rituximab (R2) has demonstrated impressive results as initial treatment in FL and the newer cereblon-modifier Avadomide is now being tested in combination with Obinutuzumab in RR B-cell lymphomas of all types. Lenalidomide with Blinatumomab is also tested in an ongoing study. mTOR/NF-κB inhibitors (temsirolimus, everolimus) are not so effective as single agents but can be combined with various targeted and/or cytotoxic agents and construct synergistic regimens. Tazemetostat a novel EZH2 inhibitor recently received accelerated approval by FDA for patients with RR-FL and EZH2 gene mutations, following the

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New drugs for low grade lymphoproliferative diseases

Argiris Symeonidis

For asymptomatic patients with low-grade lymphoproliferative disorders and low tumor burden, watchful waiting represents a rational approach. For symptomatic patients or for those with high tumor burden, initial treatment is usually chemoimmunotherapy with an anti-CD20 monoclonal antibody (mo-Ab), most commonly Rituximab or Obinutuzumab plus an alkylator, such as bendamustine or chlorambucil and/or a pourine analog, such as fludarabine or cladribine. For the Refractory/Relapsed (RR) setting treatment options depend on patient's background, initial PFS and on various prognostic parameters. Newer anti-CD20 mo-Abs, such as Ublituximab appear equally effective, but have not yet been tested comparatively with the previous ones. Radioconjugates such as 90Y-ibritumomab tiuxetan and 131I-tositumomab are no more in broad use due to unpredicted myelotoxicity. The newer 90Y-epratuzumab tetratexan appears safe as consolidation following R-CHOP in DLBCL patients. Polatuzumab vedotin, Pinatuzumab vedotin and Tafasitamab targeting CD19 have mainly been used, combined with an anti-CD20 mo-Ab to treat RR-DLBCL with success, which render them candidates for indolent lymphomas also. BTK inhibitors represent one main treatment option, either as initial treatment or in the RR setting. Ibrutinib, the first in class drug, is used either alone or in combination with Mo-abs and/or alkylators. Acalabrutinib, already approved for CLL/SLL and MCL, is now being tested for other B-cell malignancies. Zanubrutinib, a newer analog not exhibiting some of ibrutinib's AE, has been approved for RR-MCL and is currently being evaluated alone or in combination with Mo-Abs, lenalidomide and other agents. Idelalisib, the first PI3K-inhibitor, the second family of highly used targeted agents, has been approved for CLL/SLL and FL. Duvelisib, Copanlisib and Umbralisib are newer agents coming up and are currently being tested usually in combination with mo-Abs or other agents. Bimiralisib, a dual PI3K/mTOR inhibitor is a promising agent still in phase I. Hepatotoxicity, the major AE of this class, is reversible and dose-dependent. The BCL2 inhibitor venetoclax, alone or combined with mo-Abs and/or bendamustine (BRVen) or with Ibrutinib (ongoing trial), is a breakthrough approach, being tested in several disease entities with impressive results. Bispecific antibodies engaging CD19 (Blinatumomab) or CD22 (Inotuzumab ozogamycin) to a T/NK-cell surface antigen have received approval for more aggressive B-cell lymphomas. Lenalidomide combined with Rituximab (R2) has demonstrated impressive results as initial treatment in FL and the newer cereblon-modifier Avadomide is now being tested in combination with Obinutuzumab in RR B-cell lymphomas of all types. Lenalidomide with Blinatumomab is also tested in an ongoing study. mTOR/NF-κB inhibitors (temsirolimus, everolimus) are not so effective as single agents but can be combined with various targeted and/or cytotoxic agents and construct synergistic regimens. Tazemetostat a novel EZH2 inhibitor recently received accelerated approval by FDA for patients with RR-FL and EZH2 gene mutations, following the

results of a phase-II study. Combinations of this drug with other agents are also expected. Immune check point inhibitors (Nivolumab, Pemprolizumab, Atezolizumab) are promising as third line treatment and beyond. Other agents under investigation include the inhibitor of nuclear export selinexor, the SYK inhibitor entospletinib, the dual SYK/JAK inhibitor certulatinib and the CDK inhibitors flavopiridol and dinaciclib.

https://doi.org/10.1016/j.htct.2020.09.028

SP 28

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SP 30

Exosomes in heme malignancies and pre-cancerous states

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Diverse physiologic and pathologic processes, such as angiogenesis, immune cell phenotype, cell differentiation and fate, epithelial to mesenchymal transition and apoptosis are maintained by extracellular vesicles (EV), small membrane vesicles released from most cell types into the extracellular space as vehicles of intercellular communication. EV subtype are exosomes, 30–100 nm in diameter structures containing microRNA (miRNA), cytokines, chemokines, and other types of proteins that can be internalized by and function within recipient cells. In cancer biology cellular interactions within the microenvironment lead to tumor growth and progression. The most abundant stromal cells within the tumor microenvironment are macrophages and circulating monocytes, recruited into the tumor sites are differentiated into tumor associated macrophages (TAMs) that correlate with a poor prognosis of cancers. Cancer cells derived exosomes contain abundance of miRNAs influencing various stromal cells in the tumor microenvironment and also induce polarization of macrophages with pro- or anti-inflammatory properties. TAMs are also significant source of miRNAs that affect transcriptional activities of different oncogenes or cellular pathway regulators. There are now determined miRNAs for particular cancer type, e.g. miR-16 for breast cancer, miR-21 and miR-29 for NSCLC, miR-155 and miR-301a-3p for pancreatic cancer, miR-21-3p, miR-940, miR-181d-5p, miR-222-3p, miR-125b-5p for ovarian cancer, miR-25-3p, miR-130b-3p, miR-145, miR-203 and miR-425-5p for colorectal cancer, miR-146, and miR-150 for hepatic cancer. In hematological malignancies the cancerogenic role of exosome delivered miRNAs, cytokines and other molecules is identical: evasion of immune surveillance, progression of leukemia (miR-146a, miR-150, miR-155, miR-320) and training the leukemia microenvironment for protecting neoplastic clone with increasing neo-angiogenesis (miR-126, miR-17-92 cluster, miR-210, miR-155, miR-135b). There is a growing interest in clinical applications of EVs (including exosomes) as biomarkers with the identification of the signature miRNAs for specific cancer type and in the development of anti-cancer therapeutics.

https://doi.org/10.1016/j.htct.2020.09.031

HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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ORAL PRESENTATIONS

ADULT HEMATOLOGY
ACUTE LEUKEMIAS

OP 01

Isolated myeloid sarcoma causing obstructive jaundice in duodenal ampulla: a very rare case

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Objective: Isolated myeloid sarcoma (MS) is a malignant neoplasm of myeloid origin that is located in extramedullary tissues. MS is quite rare and only 5–6% of MS cases originate from the gastrointestinal tract (GIT). Established treatment options for MS include local therapies (surgery or radiotherapy or a combination), systemic chemotherapy, allogeneic hematopoietic stem-cell transplantation (alloHSCT), and targeted therapies. In this article, we present a case of isolated MS localized in the duodenal ampulla that presented with cholestatic jaundice.

Case report: A 19-year-old male patient presented to our hospital with abdominal pain, nausea, and bilious vomiting that had persisted for one week and jaundice in the body that had persisted for one month. Laboratory test results were as follows; complete blood count was normal, total bilirubin 20.7 mg/dl; direct bilirubin 16.7 mg/dl. MRI and MRCP visualized a 3.8 cm × 3.5 cm mass lesion consistent with a tumor that was localized lateral to the pancreatic head and in the duodenal ampulla and causing a sudden interruption in the choledochal duct and dilatation proximally. In the ERCP performed, a mass lesion with fragile mucosa that obstructed the lumen at the level of the duodenal papilla and extended distally was detected. A tissue biopsy was obtained from the lesion; however, transpapillary biliary cannulation could not be performed due to the change in the anatomical position secondary to the lesion. Histopathological sections of the duodenum biopsy specimens showed that medium to large cells with pronounced nucleoli and minimal to moderate eosinophilic cytoplasm infiltrate the lamina propria diffusely. Immunohistochemically, MPO, CD117 and CD34 were diffuse positive in tumor cells. In contrast, positive immunoreactivity was not observed with CD3, CD20, CD10, terminal deoxynucleotidyl transferase (TdT), and cytokeratin (not shown). According to these results, the patient was diagnosed with MS. The peripheral blood smear, bone marrow aspiration, and biopsy performed after the tissue diagnosis was made did not detect AML infiltration and immunophenotyping was normal. A fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) was performed prior to the treatment. A focal lesion with moderate metabolic activity was detected in the pancreatic head and duodenal ampulla region (standardized uptake value maximum [SUV max], 4.2). A standard idarubicin and cytarabine regimen (12 mg/m^2 idarubicin on days 1–3 and 100 mg/m^2 cytarabine on days 1–7) was administered. After induction chemotherapy, tumor size decreased significantly. One course of high-dose cytarabine (3 g/m2 q12 h on days 1, 3, 5) was administered as post-remission therapy. And then the patient received alloHSCT from an HLA-matched, related donor as consolidation therapy. The patient currently remains in remission under follow-up in the 6th post-transplant month.

Conclusion: The optimal treatment of the isolated MS is not elucidated due to the lack of relevant data and large prospective studies in the literature. The most recommended treatments are the systemic chemotherapies used in AML remission induction treatment. The authors think that alloHSCT must be considered after the induction of remission in MS, as it offers an advantage in terms of overall survival and leukemia-free survival.

https://doi.org/10.1016/j.htct.2020.09.033

OP 02

Blinatumomab therapy in a relapsed acute lymphoblastic leukemia with isolated radius involvement following allogeneic bone marrow transplant: a case report

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Introduction: Treatment of relapsed acute lymphoblastic leukaemia after allogeneic bone marrow transplant can be challenging to clinicians and have a grim prognosis. Relapse sites other than bone marrow are generally central nervous system and gonads. Blinatumomab is a bi-specific T-cell engager(BiTE) antibody that mainly targets leukemic cells CD19 protein. Blinatumomab is effective in relapsed ALL with medullary involvement but in extramedullary relapsed setting its activity is not well-know. Here, we report an effective treatment with blinatumomab in a case of acute lymphoblastic leukaemia that recurred with isolated bone involvement after allogeneic bone marrow transplantation (ABMT).

CASE: A 20-year-old woman diagnosed with a Philadelphia chromosome-negative precursor B cell ALL and remission achieved with HyperCVAD/MA regimen. While in remission after two cycles of HyperCVDAD/MA regimen, 100% compatible sibling donor allogeneic bone marrow transplant was performed. İmmunosupresive therapy continued after six months of a transplant due to chronic GVHD that affects eye and skin. The patient presented with pain in the right elbow three years after the transplant. F-18 fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) imaging revealed increased signs of FDG uptake in the right radius. There was no recurrence in aspirate and biopsy from the iliac bone marrow. In the biopsy taken from the right radius, leukemic cell infiltration was detected. Blinatumomab therapy was started. No side effects were observed. After two cycles of blinatumomab therapy, pet/ct showed total metabolic response and remission.

Discussion: In acute lymphoblastic leukemia, Blinatumomab therapy may be an effective salvage treatment in patients with extramedullary relapse.

Keywords: Relapsed acute lymphoblastic leukemia, blinatumomab, allogenic bone marrow transplantation.

https://doi.org/10.1016/j.htct.2020.09.034

CHRONIC LEUKEMIAS

OP 03

Cardiovascular risk reduction in chronic myeloid leukemia patients treated with the tyrosine kinase inhibitors

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Objective: To identify factors that should be taken into account for the assessment of the necessity the cardiovascular (CV) risk reduction for chronic myeloid leukemia (CML) patients treated with BCR-ABL1 tyrosine kinase inhibitors (TKIs) in the decision making for strategy prevention.

Case report: CV risk reduction is an important consideration in patients with CML based on the necessity to improve prognosis in such a group of patients. The success and high effectiveness of TKIs have increased the focus on survivorship and late toxicity include CV toxicity in CML patients. Survivorship in CML patients depends on CV disease prevention, given its prevalence in the general population. The separate clinical guidelines for CML patients treated with TKIs for CV risk reduction are absent in clinical practice.

Methodology: We observed clinical trials expected TKIs effectiveness and toxicity (we especially focused on cardiotoxicity and hepatotoxicity), clinical guidelines on CV disease prevention for the general population. We also analyzed TKIs and HMG-CoA reductase inhibitors biotransformation, drug-drug interaction TKIs and HMG-CoA reductase inhibitors.

Results: TKIs demonstrated high effectiveness in CML patients based on the published clinical trials. Nilotinib and ponatinib have been linked to the development of vascular occlusive events, CV disease. Type 2 diabetes mellitus development can be associated with nilotinib treatment and as a result, could enhance CV disease. Dasatinib has been associated with pleural/pericardial effusions and pulmonary hypertension. Dasatinib based on clinical trial data is the most liver safe TKI, bosutinib, nilotinib, ponatinib have higher risks of hepatotoxicity in CML patients (ENESTnd trial, BELA Trial, DASISION trial, PACE study). The individual CV risk of the patient and the necessity of CV risk reduction should be based on the personal scores assessment with the cardiac risk score calculator, ASCVD algorithm based on the clinical guidelines on CV disease prevention for the general population. TKIs for CML treatment is the group of drugs that required liver biotransformation through CYP 3A4 cytochrome enzyme and are the inhibitors of CYP 3A4. Atorvastatin and simvastatin are required liver biotransformation with the CYP 3A4. Rosuvastatin and pravastatin are not required CYP 3A4 for their

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Objective: To identify factors that should be taken into account for the assessment of the necessity the cardiovascular (CV) risk reduction for chronic myeloid leukemia (CML) patients treated with BCR-ABL1 tyrosine kinase inhibitors (TKIs) in the decision making for strategy prevention.

Case report: CV risk reduction is an important consideration in patients with CML based on the necessity to improve prognosis in such a group of patients. The success and high effectiveness of TKIs have increased the focus on survivorship and late toxicity include CV toxicity in CML patients. Survivorship in CML patients depends on CV disease prevention, given its prevalence in the general population. The separate clinical guidelines for CML patients treated with TKIs for CV risk reduction are absent in clinical practice.

Methodology: We observed clinical trials expected TKIs effectiveness and toxicity (we especially focused on cardiotoxicity and hepatotoxicity), clinical guidelines on CV disease prevention for the general population. We also analyzed TKIs and HMG-CoA reductase inhibitors biotransformation, drug-drug interaction TKIs and HMG-CoA reductase inhibitors.

Results: TKIs demonstrated high effectiveness in CML patients based on the published clinical trials. Nilotinib and ponatinib have been linked to the development of vascular occlusive events, CV disease. Type 2 diabetes mellitus development can be associated with nilotinib treatment and as a result, could enhance CV disease. Dasatinib has been associated with pleural/pericardial effusions and pulmonary hypertension. Dasatinib based on clinical trial data is the most liver safe TKI, bosutinib, nilotinib, ponatinib have higher risks of hepatotoxicity in CML patients (ENESTnd trial, BELA Trial, DASISION trial, PACE study). The individual CV risk of the patient and the necessity of CV risk reduction should be based on the personal scores assessment with the cardiac risk score calculator, ASCVD algorithm based on the clinical guidelines on CV disease prevention for the general population. TKIs for CML treatment is the group of drugs that required liver biotransformation through CYP 3A4 cytochrome enzyme and are the inhibitors of CYP 3A4. Atorvastatin and simvastatin are required liver biotransformation with the CYP 3A4. Rosuvastatin and pravastatin are not required CYP 3A4 for their

biotransformation. As a result, if atorvastatin or simvastatin are use with TKIs for CV risk reduction the HMG-CoA reductase inhibitors exposure increase and it should be taken into account in patients with abnormal liver tests due to TKIs using. Rosuvastatin or pravastatin exposure does not change due to simultaneous treatment with TKIs and could be a beneficial role for CV disease prevention.

Conclusion: The decision for the necessity of the CV risk reduction for CML patients treated with TKIs through strategy prevention should be based on the assessment the next factors: individual CV risk of the patient and the necessity of CV risk reduction, liver function, the metabolism peculiarities of TKIs using for CML treatment, the metabolism peculiarities of the HMG-CoA reductase inhibitor potential recommended for CV risk reduction, drug–drug interactions TKI and HMG-CoA reductase inhibitor.

https://doi.org/10.1016/j.htct.2020.09.035

CHRONIC MYELOPROLIFERATIVE DISEASES

OP 04

Analysis of demographic and clinical characteristics of primary myelofibrosis and post-polycythemia vera/essential thrombocythemia myelofibrosis patients

P. Akyol, A. Yıldız, M. Albayrak, H. Afacan Öztürk, S. Maral, M. Reis Aras*, F. YıLmaz, B. Saglam, M. Tıglıoglu, U. Malkan

Diskapi Yildirim Beyazit Training and Research Hospital, Ankara, Turkey

Objective: Myelofibrosis (MF), could be de novo (primary myelofibrosis [PMF]), as well as developing in the clinical course of polycythemia vera (PV) or essential thrombocythemia (ET). PMF and post-PV/ET MF have many common features with clinical course and laboratory findings. However, there are insufficient studies showing the etiological or morphological differences between these patients. In this context, the aim of this study was to contribute to the literature by comparing PMF and PV/ET patients who developed MF.

Case report: . . .

Methodology: This retrospective study included 31 patients who were diagnosed with PMF and post-PV/ET MF in the Hematology Department of Dışkapı Yıldırım Beyazıt Training and Research Hospital between 2008–2019. The diagnosis of PMF was made according to the WHO criteria and the IWG-MRT group criteria were used for the diagnosis of PPV-MF and PET-MF. The two groups were compared in terms of demographic and clinical features. The diagnosis date, demographic and clinical features, physical examination findings, mutation analyses, treatment management and follow-up times of all the patients were recorded. Hematological parameters including Hb, hematocrit (Hct), leukocyte (WBC), neutrophil, lymphocyte, monocyte, platelet, platelet distribution width (PDW), mean platelet volume (MPV), LDH, ferritin and Vitamin B12 levels were examined.

Results: Evaluation was made of a total of 31 patients, including 16 PMF and 15 post-PV/ET MF. The mean follow-up period was 31.1 months [1–107.5]. JAK-2 V617F gene mutation was detected 10 (62.5%) PMF patients and 12 (80%) post-PV/ET MF patients. Splenomegaly was detected at the time of diagnosis in all PMF and post-PV/ET MF patients. When the size of the spleen was examined, there was no statistically significant difference between the two groups.JAK-2 V617F gene mutation was detected 10 (62.5%) PMF patients and 12 (80%) post-PV/ET MF patients. In terms of JAK-2 V617F mutation positivity, there was no statistically significant difference between the two groups. JAK-2 V617F mutation, and allele burden of ≥60% was detected in 70% of PMF patients and in 90% of post-PV/ET MF patients. The allele burden was not determined to affect OS in patients with MF. Hydroxyurea was most frequently used as the first line treatment in PMF (81.3%), while ruxolitinib was preferred in post ET/PV MF (53.3%). Throughout the follow-up period, thromboembolic complications developed in 12.5% of PMF patients and in 13.3% of post-PV/ET MF patients. There was no statistically significant difference between the two groups in terms of thromboembolic complications. Acute myeloid leukemia transformation was observed in 1 (6.25%) patient from the PMF group during the follow-up period. The OS of patients was mean 63.6 months in the PMF group, and mean 78.3 months in the post-PV/ET MF group. As a result of the Log Rank test, no significant difference was observed between the two groups in terms.

Conclusion: The results of this study demonstrated that PMF and post-PV/ET MF patients showed similar demographic, clinical and prognostic features in general. Therefore, patients with ET and PV should be closely monitored for MF development and should be managed as PMF if MF develops.

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OP 05

Incidence in PH-negative myeloproliferative neoplasms in armenia from 2005 to 2019

L. Sahakyan[1,*], A. Ter-Grigoryan[1], M. Badikyan[2], Y. Hakobyan[1], A. Saharyan[2], A. Shaljyan[2], S. Danelyan[1]

[1] *Armenian Haematology center aft. prof. R. Yeolyan, Yerevan, Armenia*
[2] *YSMU aft. M. Heratsi, Yerevan, Armenia*

Objective: Enhancements of laboratory diagnostics and the emergence of new therapies had a significant impact on incidence, prevalence and survival of patients with MPN. Published epidemiology data are scarce, and multiple sources are needed to assess the disease burden.

Case report: The aim of our work was to identify the patterns and trends of incidence, prevalence and survival of patients with MPN in the Republic of Armenia for the period 2005–2019.

Methodology: The data from Hematology Center blood diseases register, Oncological Center cancer register, as well as the data from death registration were basis of our research. Demographic data were obtained from National Statistical Office PA (http://www.armstat.am). The calculation of standardized indicators has been based upon the data from the Demographic compendium of Armenia from 2005 to 2019.

biotransformation. As a result, if atorvastatin or simvastatin are use with TKIs for CV risk reduction the HMG-CoA reductase inhibitors exposure increase and it should be taken into account in patients with abnormal liver tests due to TKIs using. Rosuvastatin or pravastatin exposure does not change due to simultaneous treatment with TKIs and could be a beneficial role for CV disease prevention.

Conclusion: The decision for the necessity of the CV risk reduction for CML patients treated with TKIs through strategy prevention should be based on the assessment the next factors: individual CV risk of the patient and the necessity of CV risk reduction, liver function, the metabolism peculiarities of TKIs using for CML treatment, the metabolism peculiarities of the HMG-CoA reductase inhibitor potential recommended for CV risk reduction, drug–drug interactions TKI and HMG-CoA reductase inhibitor.

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CHRONIC MYELOPROLIFERATIVE DISEASES

OP 04

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Case report: . . .

Methodology: This retrospective study included 31 patients who were diagnosed with PMF and post-PV/ET MF in the Hematology Department of Dışkapı Yıldırım Beyazıt Training and Research Hospital between 2008–2019. The diagnosis of PMF was made according to the WHO criteria and the IWG-MRT group criteria were used for the diagnosis of PPV-MF and PET-MF. The two groups were compared in terms of demographic and clinical features. The diagnosis date, demographic and clinical features, physical examination findings, mutation analyses, treatment management and follow-up times of all the patients were recorded. Hematological parameters including Hb, hematocrit (Hct), leukocyte (WBC), neutrophil, lymphocyte, monocyte, platelet, platelet distribution width (PDW), mean platelet volume (MPV), LDH, ferritin and Vitamin B12 levels were examined.

Results: Evaluation was made of a total of 31 patients, including 16 PMF and 15 post-PV/ET MF. The mean follow-up period was 31.1 months [1–107.5]. JAK-2 V617F gene mutation was detected 10 (62.5%) PMF patients and 12 (80%) post-PV/ET MF patients. Splenomegaly was detected at the time of diagnosis in all PMF and post-PV/ET MF patients. When the size of the spleen was examined, there was no statistically significant difference between the two groups.JAK-2 V617F gene mutation was detected 10 (62.5%) PMF patients and 12 (80%) post-PV/ET MF patients. In terms of JAK-2 V617F mutation positivity, there was no statistically significant difference between the two groups. JAK-2 V617F mutation, and allele burden of ≥60% was detected in 70% of PMF patients and in 90% of post-PV/ET MF patients. The allele burden was not determined to affect OS in patients with MF. Hydroxyurea was most frequently used as the first line treatment in PMF (81.3%), while ruxolitinib was preferred in post ET/PV MF (53.3%). Throughout the follow-up period, thromboembolic complications developed in 12.5% of PMF patients and in 13.3% of post-PV/ET MF patients. There was no statistically significant difference between the two groups in terms of thromboembolic complications. Acute myeloid leukemia transformation was observed in 1 (6.25%) patient from the PMF group during the follow-up period. The OS of patients was mean 63.6 months in the PMF group, and mean 78.3 months in the post-PV/ET MF group. As a result of the Log Rank test, no significant difference was observed between the two groups in terms.

Conclusion: The results of this study demonstrated that PMF and post-PV/ET MF patients showed similar demographic, clinical and prognostic features in general. Therefore, patients with ET and PV should be closely monitored for MF development and should be managed as PMF if MF develops.

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OP 05

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Objective: Enhancements of laboratory diagnostics and the emergence of new therapies had a significant impact on incidence, prevalence and survival of patients with MPN. Published epidemiology data are scarce, and multiple sources are needed to assess the disease burden.

Case report: The aim of our work was to identify the patterns and trends of incidence, prevalence and survival of patients with MPN in the Republic of Armenia for the period 2005–2019.

Methodology: The data from Hematology Center blood diseases register, Oncological Center cancer register, as well as the data from death registration were basis of our research. Demographic data were obtained from National Statistical Office PA (http://www.armstat.am). The calculation of standardized indicators has been based upon the data from the Demographic compendium of Armenia from 2005 to 2019.

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OP 04

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OP 05

Incidence in PH-negative myeloproliferative neoplasms in armenia from 2005 to 2019

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Methodology: The data from Hematology Center blood diseases register, Oncological Center cancer register, as well as the data from death registration were basis of our research. Demographic data were obtained from National Statistical Office PA (http://www.armstat.am). The calculation of standardized indicators has been based upon the data from the Demographic compendium of Armenia from 2005 to 2019.

Results: Analysis of the data obtained has shown that, during the reporting period the average annual incidence of MPN was 1.84 per 100,000 inhabitants, including 2.1 for male and 1.64 for female. Analysis of incidence rates of MPN in relation to sex and age in the period under study revealed high rates in patients in groups 65–74 (8.3) and 55–64 (5.12 per 100 thousand years), respectively. According to the data obtained in the group of patients with MPN, the high annual average incidence rates are noted in PMF (1.09 in 2018) and PV (0.89 in 2016), the lowest for ET (0.7 in 2016) per 100,000 population, respectively. In comparing our data to those obtained for 1966–1971 and 1998–2004 periods, one may detect a statistically significant increase in the total incidence of PMF and PV ($p < 0.001$).

Conclusion: Analysis of the incidence rate in MPNs adjusted for age and gender shown prevalence in group 65–74 (8.3) and in group 55–64 (5.13) per 100,000 inhabitants. The peak of incidence rate for both males and females was the age 65–74 and the male female incidence ratio in this age group was 11.3:6.2. The increasing incidence rate in MPNs in Armenia depends on the improvement of laboratory diagnosis. Thrombotic complications are observed in patients with MPN in 45.3% of cases. In most cases, thrombosis is the first clinical symptom of a myeloproliferative disease, which determines the need for the introduction into clinical practice of molecular genetic testing methods among patients with thrombosis, an increase in blood levels, splenomegaly for the early diagnosis of clonal hematopoiesis and the use of a targeted drug.

https://doi.org/10.1016/j.htct.2020.09.037

LYMPHOMA

OP 06

The importance of next generation sequence in patients with diffuse large B cell lymphoma

A. Bolaman[1], I. Yavasoglu[1], I. Erdogdu[2], A. Ozcalimli[1,*]

[1] *Adnan Menderes University, School of Medicine, Division of Hematology, Aydın, Turkey*
[2] *Adnan Menderes University, School of Medicine, Division of Molecular Pathology, Aydın, Turkey*

Objective: Diffuse large B cell lymphomas (DLBCL) are clinically and morphologically heterogen diseases. There are more than 150 gene mutations in DLBCL. Mutations effect disase survey by histon modification, cell proliferation, cell metabolism and differentiation, apoptosis, response to DNA injury, B cell and Toll-like receptor signalization, angiogenesis and immun regulation in patients with DLBCL. We aim to search gene expression frequency, the relation of mutative genes expression with treatment response and survey in patients with DLBCL.

Methodology: The DNAs of patients with DLBCL obtained from formalin fixed paraffin embedded biopsy material in Pathology Department as retrospectively. Illumina genom analyzer and qiaqen method for bioinformatic software was used. Total 141 gene were evaluated. SPSS 17.0 were used for statistically analyses. We used Shapiro-Wilk test relevance for distrubition. The results were described as a number, frequency, and percentage. The chi-squared and Student's *T*, Mann–Whitney *U* tests were used for the analysis. The results were assessed at a 95% confidence interval and a *p*-value of less than 0.05 was accepted as significant.

Results: We found mutation in 13 of 141 genes. The pathological genes were ANKRD26, BRCA1, BRCA2, EZH2, KMT2C, MSH6, MYC, MYD88, NF1, NOTCH1, PMS2, PTEN and WRN. There were relations among ANKRD26, BRCA2, MYD88, NOTCH1 genes with prognosis. The remission rates in patients with ANKRD26, BRCA2, MYD88, NOTCH1 were 33.3% ($p < 0.05$), 52.4% ($p < 0.05$), 0% ($p < 0.05$), 37.5% ($p > 0.05$), respectively. The relapse rates in patients with ANKRD26, BRCA2, MYD88, NOTCH1 gene mutation were 58.3% ($p < 0.05$), 38.1% ($p = 0.37$), 66.7% ($p = 0.23$), 62.5% ($p = 0.03$), respectively.

Conclusion: ANKRD26, BRCA2, MYD88, NOTCH1 genes effect prognosis in patients with DLBCL. Aggressive treatment can be useful in patients DLBCL that have ANKRD26, BRCA2, MYD88, NOTCH1 gene mutations.

https://doi.org/10.1016/j.htct.2020.09.038

OP 07

Real experience of brentuximab vedotin for cutaneous T cell lymphomas

F. Keklik Karadag*, A. Arslan, T. Pashayev, N. Akad Soyer, F. Sahin, F. Vural, M. TöBü, G. Saydam

Ege University, Department of Hematology, Izmir, Turkey

Objective: Patients with relapsed/refractory CD30 positive lymphomas have relatively poor outcomes, with reported 3–5-year overall survival (OS) of only 30–50%. Mycosis fungoides (MF) and its leukemic variant, Sézary syndrome (SS), are the most common subtypes of cutaneous T cell lymphoma (CTCL). Brentuximab vedotin (BV) is an antibody-drug conjugate linking a CD30 antibody to four molecules of the microtubule inhibitor monomethyl auristatin E (MMAE), which has multiple proposed mechanisms of action BV is FDA-approved for relapsed Hodgkin's lymphoma (HL) and systemic anaplastic large cell lymphoma (sALCL). National Comprehensive Cancer Network guidelines have already incorporated BV as a primary treatment option in multifocal primary cutaneous anaplastic large cell lypmhoma (pcALCL) and MF.

Methodology: Between January 2018 and June 2020, 10 patients with CD30+ cutaneous T cell lymphoma (MF and pcALCL) who were treated with BV are evaluated in our study. One cycle of BV typically involves 1.8 mg/kg being administered intravenously once every 3 weeks. We detail our experience with BV and the position of BV in our treatment methods for CTCL.

Results: Ten patients (6 male and 4 female) have received BV in our center. Median age at time of commencing brentuximab was 54.5 years (range 34–72 years), 80% of patients had experienced at least one prior line of chemotherapy (range 0–2). Six patients with Mycosis Fungoides (MF) and large cell transformation (LCT) and one with high burden Sezary

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Results: Analysis of the data obtained has shown that, during the reporting period the average annual incidence of MPN was 1.84 per 100,000 inhabitants, including 2.1 for male and 1.64 for female. Analysis of incidence rates of MPN in relation to sex and age in the period under study revealed high rates in patients in groups 65–74 (8.3) and 55–64 (5.12 per 100 thousand years), respectively. According to the data obtained in the group of patients with MPN, the high annual average incidence rates are noted in PMF (1.09 in 2018) and PV (0.89 in 2016), the lowest for ET (0.7 in 2016) per 100,000 population, respectively. In comparing our data to those obtained for 1966–1971 and 1998–2004 periods, one may detect a statistically significant increase in the total incidence of PMF and PV ($p < 0.001$).

Conclusion: Analysis of the incidence rate in MPNs adjusted for age and gender shown prevalence in group 65–74 (8.3) and in group 55–64 (5.13) per 100,000 inhabitants. The peak of incidence rate for both males and females was the age 65–74 and the male female incidence ratio in this age group was 11.3:6.2. The increasing incidence rate in MPNs in Armenia depends on the improvement of laboratory diagnosis. Thrombotic complications are observed in patients with MPN in 45.3% of cases. In most cases, thrombosis is the first clinical symptom of a myeloproliferative disease, which determines the need for the introduction into clinical practice of molecular genetic testing methods among patients with thrombosis, an increase in blood levels, splenomegaly for the early diagnosis of clonal hematopoiesis and the use of a targeted drug.

https://doi.org/10.1016/j.htct.2020.09.037

LYMPHOMA

OP 06

The importance of next generation sequence in patients with diffuse large B cell lymphoma

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Objective: Diffuse large B cell lymphomas (DLBCL) are clinically and morphologically heterogen diseases. There are more than 150 gene mutations in DLBCL. Mutations effect disase survey by histon modification, cell proliferation, cell metabolism and differentiation, apoptosis, response to DNA injury, B cell and Toll-like receptor signalization, angiogenesis and immun regulation in patients with DLBCL. We aim to search gene expression frequency, the relation of mutative genes expression with treatment response and survey in patients with DLBCL.

Methodology: The DNAs of patients with DLBCL obtained from formalin fixed paraffin embedded biopsy material in Pathology Department as retrospectively. Illumina genom analyzer and qiaqen method for bioinformatic software was used. Total 141 gene were evaluated. SPSS 17.0 were used for statistically analyses. We used Shapiro-Wilk test relevance for distrubition. The results were described as a number, frequency, and percentage. The chi-squared and Student's *T*, Mann–Whitney *U* tests were used for the analysis. The results were assessed at a 95% confidence interval and a *p*-value of less than 0.05 was accepted as significant.

Results: We found mutation in 13 of 141 genes. The pathological genes were ANKRD26, BRCA1, BRCA2, EZH2, KMT2C, MSH6, MYC, MYD88, NF1, NOTCH1, PMS2, PTEN and WRN. There were relations among ANKRD26, BRCA2, MYD88, NOTCH1 genes with prognosis. The remission rates in patients with ANKRD26, BRCA2, MYD88, NOTCH1 were 33.3% ($p < 0.05$), 52.4% ($p < 0.05$), 0% ($p < 0.05$), 37.5% ($p > 0.05$), respectively. The relapse rates in patients with ANKRD26, BRCA2, MYD88, NOTCH1 gene mutation were 58.3% ($p < 0.05$), 38.1% ($p = 0.37$), 66.7% ($p = 0.23$), 62.5% ($p = 0.03$), respectively.

Conclusion: ANKRD26, BRCA2, MYD88, NOTCH1 genes effect prognosis in patients with DLBCL. Aggressive treatment can be useful in patients DLBCL that have ANKRD26, BRCA2, MYD88, NOTCH1 gene mutations.

https://doi.org/10.1016/j.htct.2020.09.038

OP 07

Real experience of brentuximab vedotin for cutaneous T cell lymphomas

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Objective: Patients with relapsed/refractory CD30 positive lymphomas have relatively poor outcomes, with reported 3–5-year overall survival (OS) of only 30–50%. Mycosis fungoides (MF) and its leukemic variant, Sézary syndrome (SS), are the most common subtypes of cutaneous T cell lymphoma (CTCL). Brentuximab vedotin (BV) is an antibody-drug conjugate linking a CD30 antibody to four molecules of the microtubule inhibitor monomethyl auristatin E (MMAE), which has multiple proposed mechanisms of action BV is FDA-approved for relapsed Hodgkin's lymphoma (HL) and systemic anaplastic large cell lymphoma (sALCL). National Comprehensive Cancer Network guidelines have already incorporated BV as a primary treatment option in multifocal primary cutaneous anaplastic large cell lypmhoma (pcALCL) and MF.

Methodology: Between January 2018 and June 2020, 10 patients with CD30+ cutaneous T cell lymphoma (MF and pcALCL) who were treated with BV are evaluated in our study. One cycle of BV typically involves 1.8 mg/kg being administered intravenously once every 3 weeks. We detail our experience with BV and the position of BV in our treatment methods for CTCL.

Results: Ten patients (6 male and 4 female) have received BV in our center. Median age at time of commencing brentuximab was 54.5 years (range 34–72 years), 80% of patients had experienced at least one prior line of chemotherapy (range 0–2). Six patients with Mycosis Fungoides (MF) and large cell transformation (LCT) and one with high burden Sezary

Syndrome (SS) and 3 patients with multifocal primary cutaneous anaplastic large cell lymphoma (pcALCL). The median follow-up was 21.5 (range: 4–60) months from the date of diagnosis. Adverse events were grade 1–2 peripheral neuropathy (40%) and gastro-intestinal disturbances (10%). Peripheral neuropathy resolved by discontinuation of therapy. All there pcALCL patients achieved complete remission after 5 cycle of BV. One patient with MF had progressive disease due to nodal involvement and one died of fungal pneumonia after 2 cycles of BV and could not evaluated for disease response.

Conclusion: BV has proven efficacy in both CD30- expressing MF, pcALCL. Same as previous studies, CR could be achieved more frequently in pcALCL than MF in our study. BV is found significantly higher response rates compared to traditional agents like methotrexate or bexarotene and 75% of patients had underwent these therapies before BV. In summary, BV is a promising agent for relapsed refractory CTCL patients with durable remission.

https://doi.org/10.1016/j.htct.2020.09.039

OP 08

The prognostic impact of comorbidity, nutritional and performance status on patients with diffuse large B cell lymphoma

B. Saglam, M. Albayrak, A. Yıldız, P. Akyol, M. Tiglioglu, M. Aras*, F. Yılmaz, S. Maral, H. Ozturk

University of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital, Department of Hematology, Ankara, Turkey

Objective: The aim of the study was to investigate the impact of nutritional status, comorbidity and performance status on patients with diffuse large B cell lymphoma (DLBCL).

Methodology: A retrospective study was conducted on DLBCL patients who was diagnosed in our centre between 2009–2018. The study included a total of 112 patients. Demographic and disease characteristics and labaratory test results were recorded. Overall and progression free survival were measured from these data. The methods for the assessments are Charlson comorbidity index for comorbidity, albumin level for nutritional status and ECOG score for performance status.

Results: The average age of the patients was found to be 62.63 ± 15.16 years. The ECOG score of 65 patients (69.1%) is in the range of 0–1. The mean follow-up time of the patients was determined to be 25.24 ± 25.11 (months), and at the end of the follow-up period, 64 patients (57.1%) were found to be alive. The median of 5-year PFS was 13.2 months, and the 5-year OS was 59.8%. Those with CCI-A score <4 and those with ≥4 were compared. PFS, OS and 5-year OS values of those with CCI-A >4 were found to be significantly lower than those with CCI-A score ≤4 ($p < 0.05$). As a result of the Cox-Regression (Backward: LR method) analysis, ECOG and albumin values were found to be independent risk factors for both OS and PFS ($p < 0.05$).

Conclusion: This study demonstrated that CCI-A, ECOG and nutritional status are independent prognostic markers for DLBCL patients. Initial evaluation of these patients should include all of these parameters which are easily available at the time of diagnosis.

https://doi.org/10.1016/j.htct.2020.09.040

OP 09

Can sarcopenia be a risk factor for bleomycin toxicity?

M. Koyuncu

Mersin University, Mersin, Turkey

Objective: Hodgkin Lymphoma (HL) constitutes 10 percent of lymphomas. It is one of the most curable malignancies with a response rate of around 85%. Most recent guidelines recommend ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) regimen in the first-line treatment of classical HL. Epidemiological studies showed that around 20% of patients treated with bleomycin developed bleomycin pulmonary toxicity (BPT). Risk factors for BPT are under investigation by most lymphoma working groups. Some studies suggested that bleomycin dose could be a risk factor for BPT. Sarcopenia is defined as a syndrome characterized by the loss of muscle mass, strength, and performance. Recent studies suggested that psoas muscle indexes could be used to identify sarcopenic patients. We hypothesized that the same bleomycin dose especially in patients with muscle loss due to the subsequent chemotherapy cycles might be a risk factor BPT.

Methodology: A total of 48 patients with newly diagnosed classical HL were included in the study. All of the patients received at least 2 cycles of a standard dose of ABVD chemotherapy. Sarcopenia was assessed using the psoas muscle index (PMI), which was calculated using values measured on PET/CT images before ABVD chemotherapy and the following formula: cross-sectional area of the bilateral psoas muscle/height^2. Patients were divided into two groups according to the PMI: the sarcopenia group (≤443 mm^2/m^2 for men and ≤326 mm^2/m^2 for women) and the non-sarcopenia group (>443 mm^2/m^2 for men and >326mm^2/m^2 for women). PMI was calculated both prior to the initial chemotherapy and after 2 cycles of ABVD. chemotherapy-related complications such as bleomycin toxicity, hospitalizations, the time course of neutropenia, and hospitalization due to the neutropenic fevers were recorded. Chi-square test and Mann Whitney *U* tests were used for statistical analyses. A *p*-value less than 0.05 were considered as statistically significant.

Results: 29 (60.4%) of the patients were male. 13 of 48 patients (27%) developed BPT after starting chemotherapy. Body Mass Index (BMI) status of these patients with BPT did not change after 2 cycles of ABVD. Mean psoas indexes prior to chemotherapy were 581.36[PLUSMN]188.08 in patients who did not have BPT and 465.29[PLUSMN]149.64 in patients with BPT ($p = 0.052$). Mean psoas indexes after 2 cycles of ABVD were 597.43[PLUSMN]207.38 in patients who did not have BPT and 400.46[PLUSMN]109.21 ($p < 0.001$). 11 of 13 patients with BPT had sarcopenia after 2 cycles of ABVD. There were no statistically significant association with stage, mortality status, time of neutropenia, relapsed disease, neutropenic fever episodes, and psoas muscle indexes.

Syndrome (SS) and 3 patients with multifocal primary cutaneous anaplastic large cell lymphoma (pcALCL). The median follow-up was 21.5 (range: 4–60) months from the date of diagnosis. Adverse events were grade 1–2 peripheral neuropathy (40%) and gastro-intestinal disturbances (10%). Peripheral neuropathy resolved by discontinuation of therapy. All there pcALCL patients achieved complete remission after 5 cycle of BV. One patient with MF had progressive disease due to nodal involvement and one died of fungal pneumonia after 2 cycles of BV and could not evaluated for disease response.

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https://doi.org/10.1016/j.htct.2020.09.039

OP 08

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B. Saglam, M. Albayrak, A. Yıldız, P. Akyol, M. Tiglioglu, M. Aras*, F. Yılmaz, S. Maral, H. Ozturk

University of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital, Department of Hematology, Ankara, Turkey

Objective: The aim of the study was to investigate the impact of nutritional status, comorbidity and performance status on patients with diffuse large B cell lymphoma (DLBCL).

Methodology: A retrospective study was conducted on DLBCL patients who was diagnosed in our centre between 2009–2018. The study included a total of 112 patients. Demographic and disease characteristics and labaratory test results were recorded. Overall and progression free survival were measured from these data. The methods for the assessments are Charlson comorbidity index for comorbidity, albumin level for nutritional status and ECOG score for performance status.

Results: The average age of the patients was found to be 62.63 ± 15.16 years. The ECOG score of 65 patients (69.1%) is in the range of 0–1. The mean follow-up time of the patients was determined to be 25.24 ± 25.11 (months), and at the end of the follow-up period, 64 patients (57.1%) were found to be alive. The median of 5-year PFS was 13.2 months, and the 5-year OS was 59.8%. Those with CCI-A score <4 and those with ≥4 were compared. PFS, OS and 5-year OS values of those with CCI-A >4 were found to be significantly lower than those with CCI-A score ≤4 ($p < 0.05$). As a result of the Cox-Regression (Backward: LR method) analysis, ECOG and albumin values were found to be independent risk factors for both OS and PFS ($p < 0.05$).

Conclusion: This study demonstrated that CCI-A, ECOG and nutritional status are independent prognostic markers for DLBCL patients. Initial evaluation of these patients should include all of these parameters which are easily available at the time of diagnosis.

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OP 09

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Mersin University, Mersin, Turkey

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Methodology: A total of 48 patients with newly diagnosed classical HL were included in the study. All of the patients received at least 2 cycles of a standard dose of ABVD chemotherapy. Sarcopenia was assessed using the psoas muscle index (PMI), which was calculated using values measured on PET/CT images before ABVD chemotherapy and the following formula: cross-sectional area of the bilateral psoas muscle/height^2. Patients were divided into two groups according to the PMI: the sarcopenia group (≤443 mm^2/m^2 for men and ≤326 mm^2/m^2 for women) and the non-sarcopenia group (>443 mm^2/m^2 for men and >326mm^2/m^2 for women). PMI was calculated both prior to the initial chemotherapy and after 2 cycles of ABVD. chemotherapy-related complications such as bleomycin toxicity, hospitalizations, the time course of neutropenia, and hospitalization due to the neutropenic fevers were recorded. Chi-square test and Mann Whitney *U* tests were used for statistical analyses. A *p*-value less than 0.05 were considered as statistically significant.

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Conclusion: Sarcopenia after 2 cycles of chemotherapy may be a risk factor for BPT. All patients with sarcopenia received same dose of bleomycin in this study. A significant relation between loss of muscle mass and BPT indicates that higher bleomycin doses in accordance with muscle mass may be a risk factor for BPT development. Dose reductions according to muscle mass can be more logical even if the BMI status of the patients remains the same after 2 cycles of chemotherapy. Randomized clinical trials are needed in this very important topic.

https://doi.org/10.1016/j.htct.2020.09.041

MYELOMA

OP 10

Bendamustine-bortezomib-dexamethasone (BVD) in heavily pretreated multiple myeloma: old/new in novel agents' era

C. Cerchione[1,*], L. Catalano[2], D. Nappi[3], S. Rocco[4], S. Palmieri[4], A. Pareto[2], F. Pane[2], F. Ferrara[4], G. Martinelli[1]

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[4] *Hematology, A. O. R. N. Cardarelli, Naples, Italy*

Objective: Bendamustine is an old bi-functional alkylating agent which has proved to be effective in relapsed, refractory and in new diagnosed Multiple Myeloma (MM).

Case report: Thus, aiming to provide further insights in this field, also in novel agents' era, we present here a retrospective, real-life analysis of patients with relapsed/refractory MM (rrMM), who had received salvage therapy with bendamustine in combination with bortezomib and dexamethasone (BVD).

Methodology: 81 patients (44 M/37 F), with rrMM, median age at diagnosis 59.4 years (r. 36–82), median age at start of treatment 63.6 years (r.37–86) treated with several lines of treatments (median 6, r. 2–11), every refractory to all the drugs previously received (also Bortezomib), received BVD (B 90 mg/sqm days 1,2; V 1.3 mg/sqm days 1,4,8,11, D 20 mg days 1,2,4,5,8,9,11,12, Pegfilgrastim day +4) every 28 days, until progression. All patients had previously received bortezomib-based and IMIDs-based treatments, and 32% (26/81) had also received radiotherapy. 69% (56/81) had undergone single or double autologous and three (2%) allogeneic stem cell transplant. All patients were relapsed and refractory to last therapies received before BVD.

Results: Bendamustine was well tolerated, with grade 3–4 transfusion-dependent anemia in 56% (46/81) of patients, and 43% (35/81) grade 3–4 neutropenia (no ospedalization was required, no septic shocks were observed). No severe extrahematologic toxicity was observed, only grade 1 gastrointestinal side effect (nausea), treated by common antiemetic drugs. According to IMWG, ORR was 63% (51/81: 7 CR, 18 VGPR, 15 PR, 11 MR) with 11 PD and 19 patients in SD, which can be considered as an impressive result in this subset of rrMM patients. In particular, for 11 patients, BVD was, after having achieved at least a PR, a bridge to second auSCT, and for two patients a bridge to alloSCT. Eight patients have surprisingly achieved a notable PR after failure of novel agents (i.e. Carfilzomib, Daratumumab and Pomalidomide). Median time to response was 1.3 months (r.1–3), median OS from diagnosis was 67.3 months (r.6–151), median OS from start of Bendamustine was 9.6 months (r.2–36).

Conclusion: The triplet Bendamustine-Bortezomib-Dexamethasone has shown significant efficacy in a particularly severe setting of patients, relapsed and refractory to all available therapeutic resources, and, in particular cases, it could be considered as a bridge to a second autologous or allogenic SCT, also after failure of novel agents.

https://doi.org/10.1016/j.htct.2020.09.042

OP 11

Efficacy and safety of daratumumab with dexamethasone in patients with relapsed/refractory multiple myeloma and severe renal impairment: results of the phase 2 dare study

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Objective: Patients (pts) with multiple myeloma (MM) and severe renal impairment (RI) have poorer overall survival. Daratumumab (DARA), an IgG1κ human monoclonal antibody that targets CD38, has shown efficacy and a favorable safety profile in pts with relapsed or refractory MM (RRMM). Moreover, in population pharmacokinetic analyses, no clinically important differences in exposure to DARA were observed

Conclusion: Sarcopenia after 2 cycles of chemotherapy may be a risk factor for BPT. All patients with sarcopenia received same dose of bleomycin in this study. A significant relation between loss of muscle mass and BPT indicates that higher bleomycin doses in accordance with muscle mass may be a risk factor for BPT development. Dose reductions according to muscle mass can be more logical even if the BMI status of the patients remains the same after 2 cycles of chemotherapy. Randomized clinical trials are needed in this very important topic.

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MYELOMA

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Objective: Bendamustine is an old bi-functional alkylating agent which has proved to be effective in relapsed, refractory and in new diagnosed Multiple Myeloma (MM).

Case report: Thus, aiming to provide further insights in this field, also in novel agents' era, we present here a retrospective, real-life analysis of patients with relapsed/refractory MM (rrMM), who had received salvage therapy with bendamustine in combination with bortezomib and dexamethasone (BVD).

Methodology: 81 patients (44 M/37 F), with rrMM, median age at diagnosis 59.4 years (r. 36–82), median age at start of treatment 63.6 years (r.37–86) treated with several lines of treatments (median 6, r. 2–11), every refractory to all the drugs previously received (also Bortezomib), received BVD (B 90 mg/sqm days 1,2; V 1.3 mg/sqm days 1,4,8,11, D 20 mg days 1,2,4,5,8,9,11,12, Pegfilgrastim day +4) every 28 days, until progression. All patients had previously received bortezomib-based and IMIDs-based treatments, and 32% (26/81) had also received radiotherapy. 69% (56/81) had undergone single or double autologous and three (2%) allogeneic stem cell transplant. All patients were relapsed and refractory to last therapies received before BVD.

Results: Bendamustine was well tolerated, with grade 3–4 transfusion-dependent anemia in 56% (46/81) of patients, and 43% (35/81) grade 3–4 neutropenia (no ospedalization was required, no septic shocks were observed). No severe extrahematologic toxicity was observed, only grade 1 gastrointestinal side effect (nausea), treated by common antiemetic drugs. According to IMWG, ORR was 63% (51/81: 7 CR, 18 VGPR, 15 PR, 11 MR) with 11 PD and 19 patients in SD, which can be considered as an impressive result in this subset of rrMM patients. In particular, for 11 patients, BVD was, after having achieved at least a PR, a bridge to second auSCT, and for two patients a bridge to alloSCT. Eight patients have surprisingly achieved a notable PR after failure of novel agents (i.e. Carfilzomib, Daratumumab and Pomalidomide). Median time to response was 1.3 months (r.1–3), median OS from diagnosis was 67.3 months (r.6–151), median OS from start of Bendamustine was 9.6 months (r.2–36).

Conclusion: The triplet Bendamustine-Bortezomib-Dexamethasone has shown significant efficacy in a particularly severe setting of patients, relapsed and refractory to all available therapeutic resources, and, in particular cases, it could be considered as a bridge to a second autologous or allogenic SCT, also after failure of novel agents.

https://doi.org/10.1016/j.htct.2020.09.042

OP 11

Efficacy and safety of daratumumab with dexamethasone in patients with relapsed/refractory multiple myeloma and severe renal impairment: results of the phase 2 dare study

E. Terpos[1,*], A. Symeonidis[2], S. Delimpasi[3], E. Zamagni[4], E. Katodritou[5], E. Rivolti[6], M. Kyrtsonis[7], D. Fotiou[1], N. Kanellias[1], M. Migkou[1], M. Roussou[1], M. Gavriatopoulou[1], E. Hatjiharissi[8], M. Cavo[4], M. Dimopoulos[1]

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[8] *First Department of Internal Medicine, Aristotle University of Thessaloniki, School of Medicine, AHEPA University Hospital, Thessaloniki, Greece*

Objective: Patients (pts) with multiple myeloma (MM) and severe renal impairment (RI) have poorer overall survival. Daratumumab (DARA), an IgG1κ human monoclonal antibody that targets CD38, has shown efficacy and a favorable safety profile in pts with relapsed or refractory MM (RRMM). Moreover, in population pharmacokinetic analyses, no clinically important differences in exposure to DARA were observed

Conclusion: Sarcopenia after 2 cycles of chemotherapy may be a risk factor for BPT. All patients with sarcopenia received same dose of bleomycin in this study. A significant relation between loss of muscle mass and BPT indicates that higher bleomycin doses in accordance with muscle mass may be a risk factor for BPT development. Dose reductions according to muscle mass can be more logical even if the BMI status of the patients remains the same after 2 cycles of chemotherapy. Randomized clinical trials are needed in this very important topic.

https://doi.org/10.1016/j.htct.2020.09.041

MYELOMA

OP 10

Bendamustine-bortezomib-dexamethasone (BVD) in heavily pretreated multiple myeloma: old/new in novel agents' era

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[4] *Hematology, A. O. R. N. Cardarelli, Naples, Italy*

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Methodology: 81 patients (44 M/37 F), with rrMM, median age at diagnosis 59.4 years (r. 36–82), median age at start of treatment 63.6 years (r.37–86) treated with several lines of treatments (median 6, r. 2–11), every refractory to all the drugs previously received (also Bortezomib), received BVD (B 90 mg/sqm days 1,2; V 1.3 mg/sqm days 1,4,8,11, D 20 mg days 1,2,4,5,8,9,11,12, Pegfilgrastim day +4) every 28 days, until progression. All patients had previously received bortezomib-based and IMIDs-based treatments, and 32% (26/81) had also received radiotherapy. 69% (56/81) had undergone single or double autologous and three (2%) allogeneic stem cell transplant. All patients were relapsed and refractory to last therapies received before BVD.

Results: Bendamustine was well tolerated, with grade 3–4 transfusion-dependent anemia in 56% (46/81) of patients, and 43% (35/81) grade 3–4 neutropenia (no ospedalization was required, no septic shocks were observed). No severe extrahematologic toxicity was observed, only grade 1 gastrointestinal side effect (nausea), treated by common antiemetic drugs. According to IMWG, ORR was 63% (51/81: 7 CR, 18 VGPR, 15 PR, 11 MR) with 11 PD and 19 patients in SD, which can be considered as an impressive result in this subset of rrMM patients. In particular, for 11 patients, BVD was, after having achieved at least a PR, a bridge to second auSCT, and for two patients a bridge to alloSCT. Eight patients have surprisingly achieved a notable PR after failure of novel agents (i.e. Carfilzomib, Daratumumab and Pomalidomide). Median time to response was 1.3 months (r.1–3), median OS from diagnosis was 67.3 months (r.6–151), median OS from start of Bendamustine was 9.6 months (r.2–36).

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OP 11

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Objective: Patients (pts) with multiple myeloma (MM) and severe renal impairment (RI) have poorer overall survival. Daratumumab (DARA), an IgG1κ human monoclonal antibody that targets CD38, has shown efficacy and a favorable safety profile in pts with relapsed or refractory MM (RRMM). Moreover, in population pharmacokinetic analyses, no clinically important differences in exposure to DARA were observed

between pts with MM and RI regardless of renal function. The aim of the DARE study [NCT03450057] was to assess the safety and efficacy of DARA in pts with RRMM and severe RI or requiring hemodialysis.

Methodology: DARE is a prospective, open-label, multicenter, phase 2 study, which included pts with documented RRMM and severe RI (eGFR < 30 ml/min/1.73m^2) or requiring hemodialysis. Participating pts must have ≥2 lines of therapy with both bortezomib- and lenalidomide-based regimens and an Eastern Cooperative Oncology Group performance status (ECOG PS) score ≤2. Exclusion criteria include previous DARA or other anti-CD38 therapy exposure. Pts receive 28-day treatment cycles with 16 mg/kg intravenous DARA (weekly for cycles 1–2, every 2 weeks [wks] for cycles 3–6, and every 4 wks thereafter) and oral dexamethasone (40 mg weekly, each cycle). The primary endpoint is progression-free survival (PFS). Secondary endpoints are overall response rate (ORR; proportion of pts with partial response or better), renal response rate (RRR; proportion of pts with best response of renal partial response or better), and safety. All responses are based on investigators' assessment per International Myeloma Working Group criteria.

Results: Thirty-eight pts with obtained informed consent, enrolled in 7 centers, were included in this analysis. The pts median age was 72 years, and most were male (75%). At study initiation 7% and 93% of pts had International Staging System (ISS) stage II and III disease, respectively; 51% and 49% of pts had revised ISS stage II and III, respectively. At baseline, the median time from MM diagnosis was 4.2 years; 24%, 72%, and 4% pts had ECOG PS 0, 1, and 2, respectively; the median eGFR was 13.0 mL/min/1.73 m^2. Median number of prior lines of therapy was 3, and 35% pts had previous autologous stem cell transplantation. The median number of therapy cycles received per patient was 7.0. The median follow-up was 8 months and the 6-month PFS rate was 51%. The ORR was 41% (including VGPR in 29% of pts). The RRR was 22%. The median time from first DARA dose to first partial response or better was 1.5 months. Of all grade 3 or 4 AEs, the most frequent were anemia (21%), thrombocytopenia (13%), hyperkalemia (11%), and hyperglycemia (8%).

Conclusion: DARA plus dexamethasone was efficacious with a favorable safety profile in pts with RRMM and severe RI or requiring dialysis. Hematologic responses were high in these heavily pretreated pts, while more than one-fifth of them also achieved a renal response.

https://doi.org/10.1016/j.htct.2020.09.043

OP 12

A novel microrna signature with clinical significance in multiple myeloma

A. Papanota[1,*], P. Artemaki[2], P. Karousi[2], C. Liacos[1], M. Gavriatopoulou[1], E. Kastritis[1], C. Kontos[2], M. Dimopoulos[1], A. Scorilas[2], E. Terpos[1]

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Objective: MicroRNAs (miRNA) are single-stranded, small non-coding RNA molecules (~21 nucleotides) that regulate protein-coding gene expression at the post-transcriptional level, mainly through interactions with the 3′-untranslated region of target mRNAs. Such interactions lead to mRNA degradation and/or translational repression, depending on the complementarity of the miRNA seed sequence with the mRNAs 3′-untranslated region. They can function as oncogenes or tumor suppressors, possessing a vital role in all stages of tumorigenesis and cancer progression. In the present study, we have investigated the clinical significance of a molecular signature consisting of 10 cancer-related miRNAs in multiple myeloma (MM): miR-15a, miR-16, miR-21, miR-221, miR-222, miR-25, miR-125, miR-155, miR-223, and miR-181a. These molecules were selected due to their well-documented role and clinical significance in numerous human malignancies.

Methodology: Bone marrow aspiration samples were collected from 94 patients with multiple myeloma (MM) and smoldering multiple myeloma (sMM) at the time of diagnosis and CD138+ plasma cells were positively selected using magnetic beads coated with an anti-CD138 antibody. Total RNA was isolated using TRIZol, 200ng RNA of each sample were polyadenylated at the 3′ end and reversely transcribed. An in-house developed real-time quantitative PCR assay was conducted and the results were biostatistically analyzed. For the normalization of the expression levels of each miRNA, the mean expression of two small nucleolar RNAs (RNU43 and RNU48) was used as reference.

Results: Seventy-six out of the 94 BM aspiration samples were derived from MM patients and 18 from sMM patients. The MM patients were classified, according to the R-ISS staging system, as follows: 15 patients with stage I disease, 42 patients with stage II, and 19 patients with stage III. Forty-nine myeloma patients presented with osteolytic lesions at diagnosis. The statistical analysis revealed significantly lower expression levels of miR-16 ($p = 0.036$) and miR-155 ($p = 0.045$) in CD138+ cells of MM patients, compared to those from sMM patients. Furthermore, miR-221 and miR-222 expression levels were negatively correlated with R-ISS; thus, miR-221 and miR-222 expression was significantly downregulated in MM patients with R-ISS stage III ($p = 0.004$ and 0.034, respectively). Interestingly, the expression levels of miR-15a ($p = 0.048$) and miR-16 ($p = 0.047$) were decreased in

between pts with MM and RI regardless of renal function. The aim of the DARE study [NCT03450057] was to assess the safety and efficacy of DARA in pts with RRMM and severe RI or requiring hemodialysis.

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MM patients with osteolytic lesions at the time of diagnosis, compared to those without osteolyses.

Conclusion: We conclude that miR-221/222 cluster correlates with more favorable R-ISS stage, revealing a potential favorable prognostic value in MM patients. MiR-15a and miR-16 correlate with the presence of osteolytic disease in MM. The observed decreased expression of these two miRNAs in symptomatic MM patients with osteolytic lesions could constitute a possible biomarker for the occurrence of bone disease. Moreover, decreased expression of miR-16 and miR-155 in MM patients, compared to sMM patients may indicate a putative predictive biomarker able to distinguish symptomatic patients from sMM patients. This ongoing study will further reveal the possible prognostic significance of this 10 miRNAs signature studied, when response to therapy, progression-free and overall survival is available.

https://doi.org/10.1016/j.htct.2020.09.044

OP 13

Peripheral blood immune profiling of multiple myeloma patients at diagnosis: correlations with circulating plasma cells

K. Papadimitriou[1,*], I. Ntanasis-Stathopoulos[2], N. Tsakirakis[1], M. Gavriatopoulou[2], I. Kostopoulos[1], E. Kastritis[2], N. Orologas-Stavrou[1], M. Dimopoulos[2], O. Tsitsilonis[1], E. Terpos[2]

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[2] *Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece*

Objective: Circulating Tumor Plasma Cells (CTPCs) detected in the peripheral blood (PB) of newly diagnosed Multiple Myeloma (MM) patients have been associated with adverse prognostic features and poor overall survival. The correlation of CTPCs with the immune profile in PB remains unknown. The aim of the present study was to evaluate the immune profile in the PB of patients with newly diagnosed MM and correlate the results with the presence of low or high number of CTPCs.

Methodology: We analyzed myeloid-derived suppressor cells (MDSCs) and major immune T cell subpopulations, including regulatory T cells (Tregs), in the PB of newly diagnosed MM patients. The percentages of MDCSs and Tregs were correlated with the concomitant presence of low (<0.003%) or high (>0.05%) CTPCs. PB samples of 26 newly diagnosed MM patients were analyzed with flow cytometry using the following panels: (a) the minimal residual disease EuroFlow-based next-generation flow cytometry (NGF) panel, for the detection and identification of PB CTPCs; (b) a panel comprising the surface markers CD15, HLA-DR, CD14, CD124, CD33, CD11b, and LinCD56-CD3-CD19, for the detection of polymorphonuclear MDSCs (PMN-MDSCs), monocytic MDSCs (M-MDSCs) and early-stage MDSCs (eMDSCs); and c) two panels comprising the surface and intra-cellular markers CD25, CD3, CD39, CTLA-4, CD4, CD8, CD45RO, CD45RA, HLA-DR, CD127, Ki67, and FoxP3, for the detection of CD4, CD8 T cells and Tregs. For the evaluation of (b) and (c), prior to staining, mononuclear cells (PBMCs) were isolated from PB using density-gradient centrifugation on Ficoll-paque.

Results: Using NGF, 12 MM patients had high and 14 low CTPCs in their PB. MDSCs averaged $5.42 \pm 5.9\%$ of PBMCs, whereas PMN-MDSCs were the most abundant subpopulation ($4.38 \pm 5.7\%$ of PBMCs) and displayed great heterogeneity between patients. Additionally, 22 distinct T subpopulations were phenotypically identified and analyzed, including CD4 and CD8 T cells, naive Tregs (CD45RA+), effector Tregs (CD45RO+), terminal effectors (HLADR+), CD39+ suppressor Tregs, CD8 Tregs and their proliferating (Ki67+) counterparts. Comparing the percentages of the immune populations among patients with high versus low CTPCs, M-MDSCs were significantly more abundant ($p < 0.05$) in patients with low CTPCs, whereas immune profiling of T cells revealed (although not reaching statistical significance) the presence of increased percentages of proliferating Tregs in those with low CTPCs and increased percentages of naïve CD4 T cells in patients with high CTPCs.

Conclusion: To our knowledge, this is the first study correlating the presence of high versus low CTPCs with the immune profile in PB of MM patients. Low CTPCs correlated with the presence of higher percentage of M-MDSCs. Since the latter has been associated with the CCR5-dependent recruitment of Tregs into the tumor site, our findings suggest that, in low CTPC MM patients, a more effective immune surveillance mechanism, mediated by the interaction of M-MDSCs – Tregs, likely controls CTPC expansion and may contribute to a more favorable prognosis. Analysis of more samples, which is ongoing, will validate our findings and provide more solid results.

https://doi.org/10.1016/j.htct.2020.09.045

OTHER DISEASES

OP 14

COVID-19 infection in cancer patients: a systematic review and meta-analysis with emphasizing the risk and prognosis stratification

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Objective: Various cancer societies worldwide have released guidelines to care for cancer patients suffering from COVID-19. Given the findings from our meta-analysis, in the absence of prospective data, we recommend diligent preventive care measures, full supportive care for immunosuppressed patients to minimize the risk of infection, limiting patient's visits to the hospital when possible and using telecommunication technology. Future studies should focus on collecting all the baseline characteristics of cancer patients suffering from COVID-19, all cancer and chemotherapy or radiation-related variables as well as the detailed COVID-19 care protocol followed in these patients and the dynamic biochemical and inflammatory profile of these patients during the infection.

MM patients with osteolytic lesions at the time of diagnosis, compared to those without osteolyses.

Conclusion: We conclude that miR-221/222 cluster correlates with more favorable R-ISS stage, revealing a potential favorable prognostic value in MM patients. MiR-15a and miR-16 correlate with the presence of osteolytic disease in MM. The observed decreased expression of these two miRNAs in symptomatic MM patients with osteolytic lesions could constitute a possible biomarker for the occurrence of bone disease. Moreover, decreased expression of miR-16 and miR-155 in MM patients, compared to sMM patients may indicate a putative predictive biomarker able to distinguish symptomatic patients from sMM patients. This ongoing study will further reveal the possible prognostic significance of this 10 miRNAs signature studied, when response to therapy, progression-free and overall survival is available.

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Conclusion: To our knowledge, this is the first study correlating the presence of high versus low CTPCs with the immune profile in PB of MM patients. Low CTPCs correlated with the presence of higher percentage of M-MDSCs. Since the latter has been associated with the CCR5-dependent recruitment of Tregs into the tumor site, our findings suggest that, in low CTPC MM patients, a more effective immune surveillance mechanism, mediated by the interaction of M-MDSCs – Tregs, likely controls CTPC expansion and may contribute to a more favorable prognosis. Analysis of more samples, which is ongoing, will validate our findings and provide more solid results.

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OTHER DISEASES

OP 14

COVID-19 infection in cancer patients: a systematic review and meta-analysis with emphasizing the risk and prognosis stratification

G. Elgohary

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Objective: Various cancer societies worldwide have released guidelines to care for cancer patients suffering from COVID-19. Given the findings from our meta-analysis, in the absence of prospective data, we recommend diligent preventive care measures, full supportive care for immunosuppressed patients to minimize the risk of infection, limiting patient's visits to the hospital when possible and using telecommunication technology. Future studies should focus on collecting all the baseline characteristics of cancer patients suffering from COVID-19, all cancer and chemotherapy or radiation-related variables as well as the detailed COVID-19 care protocol followed in these patients and the dynamic biochemical and inflammatory profile of these patients during the infection.

MM patients with osteolytic lesions at the time of diagnosis, compared to those without osteolyses.

Conclusion: We conclude that miR-221/222 cluster correlates with more favorable R-ISS stage, revealing a potential favorable prognostic value in MM patients. MiR-15a and miR-16 correlate with the presence of osteolytic disease in MM. The observed decreased expression of these two miRNAs in symptomatic MM patients with osteolytic lesions could constitute a possible biomarker for the occurrence of bone disease. Moreover, decreased expression of miR-16 and miR-155 in MM patients, compared to sMM patients may indicate a putative predictive biomarker able to distinguish symptomatic patients from sMM patients. This ongoing study will further reveal the possible prognostic significance of this 10 miRNAs signature studied, when response to therapy, progression-free and overall survival is available.

https://doi.org/10.1016/j.htct.2020.09.044

OP 13

Peripheral blood immune profiling of multiple myeloma patients at diagnosis: correlations with circulating plasma cells

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Objective: Circulating Tumor Plasma Cells (CTPCs) detected in the peripheral blood (PB) of newly diagnosed Multiple Myeloma (MM) patients have been associated with adverse prognostic features and poor overall survival. The correlation of CTPCs with the immune profile in PB remains unknown. The aim of the present study was to evaluate the immune profile in the PB of patients with newly diagnosed MM and correlate the results with the presence of low or high number of CTPCs.

Methodology: We analyzed myeloid-derived suppressor cells (MDSCs) and major immune T cell subpopulations, including regulatory T cells (Tregs), in the PB of newly diagnosed MM patients. The percentages of MDCSs and Tregs were correlated with the concomitant presence of low (<0.003%) or high (>0.05%) CTPCs. PB samples of 26 newly diagnosed MM patients were analyzed with flow cytometry using the following panels: (a) the minimal residual disease EuroFlow-based next-generation flow cytometry (NGF) panel, for the detection and identification of PB CTPCs; (b) a panel comprising the surface markers CD15, HLA-DR, CD14, CD124, CD33, CD11b, and LinCD56-CD3-CD19, for the detection of polymorphonuclear MDSCs (PMN-MDSCs), monocytic MDSCs (M-MDSCs) and early-stage MDSCs (eMDSCs); and c) two panels comprising the surface and intra-cellular markers CD25, CD3, CD39, CTLA-4, CD4, CD8, CD45RO, CD45RA, HLA-DR, CD127, Ki67, and FoxP3, for the detection of CD4, CD8 T cells and Tregs. For the evaluation of (b) and (c), prior to staining, mononuclear cells (PBMCs) were isolated from PB using density-gradient centrifugation on Ficoll-paque.

Results: Using NGF, 12 MM patients had high and 14 low CTPCs in their PB. MDSCs averaged $5.42 \pm 5.9\%$ of PBMCs, whereas PMN-MDSCs were the most abundant subpopulation ($4.38 \pm 5.7\%$ of PBMCs) and displayed great heterogeneity between patients. Additionally, 22 distinct T subpopulations were phenotypically identified and analyzed, including CD4 and CD8 T cells, naive Tregs (CD45RA+), effector Tregs (CD45RO+), terminal effectors (HLADR+), CD39+ suppressor Tregs, CD8 Tregs and their proliferating (Ki67+) counterparts. Comparing the percentages of the immune populations among patients with high versus low CTPCs, M-MDSCs were significantly more abundant ($p < 0.05$) in patients with low CTPCs, whereas immune profiling of T cells revealed (although not reaching statistical significance) the presence of increased percentages of proliferating Tregs in those with low CTPCs and increased percentages of naïve CD4 T cells in patients with high CTPCs.

Conclusion: To our knowledge, this is the first study correlating the presence of high versus low CTPCs with the immune profile in PB of MM patients. Low CTPCs correlated with the presence of higher percentage of M-MDSCs. Since the latter has been associated with the CCR5-dependent recruitment of Tregs into the tumor site, our findings suggest that, in low CTPC MM patients, a more effective immune surveillance mechanism, mediated by the interaction of M-MDSCs – Tregs, likely controls CTPC expansion and may contribute to a more favorable prognosis. Analysis of more samples, which is ongoing, will validate our findings and provide more solid results.

https://doi.org/10.1016/j.htct.2020.09.045

OTHER DISEASES

OP 14

COVID-19 infection in cancer patients: a systematic review and meta-analysis with emphasizing the risk and prognosis stratification

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Objective: Various cancer societies worldwide have released guidelines to care for cancer patients suffering from COVID-19. Given the findings from our meta-analysis, in the absence of prospective data, we recommend diligent preventive care measures, full supportive care for immunosuppressed patients to minimize the risk of infection, limiting patient's visits to the hospital when possible and using telecommunication technology. Future studies should focus on collecting all the baseline characteristics of cancer patients suffering from COVID-19, all cancer and chemotherapy or radiation-related variables as well as the detailed COVID-19 care protocol followed in these patients and the dynamic biochemical and inflammatory profile of these patients during the infection.

Case report: Our meta-analysis, suffers from several limitations. All the included studies are retrospective, the number of cancer patients is small, and many important data were not reported in these studies (cancer types, stages, and treatments).

Methodology: Several groups have published on outcomes of cancer patients infected with of the SARS-CoV-2 virus causing the COVID-19 infection. However, most of these reports are single-center studies with a limited number of patients. We performed a systematic review and meta-analysis to evaluate the impact of COVID-19 infection on cancer patients. We searched PubMed, Web of Science, and Scopus for studies that reported the risk of infection and complications of COVID-19 in cancer patients. The literature search retrieved 22 studies (1018 cancer patients).

Results: The analysis showed that the frequency of cancer among COVID-19 confirmed patients was 2.1% (95% CI: 1.3%, 3%) in the overall cohort. These patients had a mortality of 21.1% (95% CI: 14.7%, 27.6%), severe/critical disease rate of 45.4% (95% CI: 37.4%, 53.3%), ICU admission rate of 14.5% (95% CI: 8.5%, 20.4%), and mechanical ventilation rate of 11.7% (95% CI: 5.5%, 18%). The double-arm analysis showed that cancer patients had higher risk of mortality (OR = 3.23, 95% CI: 1.71, 6.13), severe/critical disease (OR = 3.91, 95% CI: 2.70, 5.67), ICU admission (OR = 3.10, 95% CI: 1.85, 5.17), and mechanical ventilation (OR = 4.86, 95% CI: 1.27, 18.65), compared to non-cancer patients. Further, cancer patients had significantly lower platelet levels and a significantly higher D-Dimer, C-reactive protein, and prothrombin time

Conclusion: cancer patients are at a higher risk of COVID-19 infection-related complications. Therefore, cancer patients need diligent preventive care measures and aggressive surveillance for earlier detection of COVID-19 infection.

https://doi.org/10.1016/j.htct.2020.09.046

PLATELET DISEASES

OP 15

The factors that affect the results of the response to rituximab treatment in ITP patients

O. Beyler, A. Gunes*, G. Korkmaz Akat, F. Ceran, S. Dagdas, G. Ozet

Ankara City Hospital, Ankara, Turkey

Objective: ITP is an acquired thrombocytopenia caused by antibodies that develop against platelet antigens. The underlying mechanism is thought to be specific immunoglobulin G (IgG) autoantibodies produced by the patient\'s B cells, mostly formed against platelet membrane glycoproteins such as GPIIb/IIIa. Preventing serious bleeding is in the decision to start treatment. Patient with platelet count <30,000/microL or signs of severe bleeding (intracranial or gastrointestinal), platelet transfusion along with glucocorticoid and/or IVIG therapy should be started immediately. If there are still signs of bleeding or platelet count <20,000/microL following glucocorticoid-based treatments, three principal choices such as rituximab, splenectomy, TPO agonists can be used as a second-line therapy. The aim of our study is to determine the factors that affect the results of the response status to rituximab treatment in ITP patients.

Methodology: Twenty five patients with the diagnosis of ITP who were treated in Hematology Clinic at Ankara Numune Hospital, Ankara City Hospital and Şanlıurfa Mehmet Akif İnan Hospital Hematology Clinic. The dose of rituximab administered in patients is 375 mg/m^2 once a week for four consecutive weeks. Treatment response criteria are; those with a platelet >30,000 were defined as a response, and those with >100,000 as a complete response.

Results: Seventeen of the patients (68%) were female and 8 (32%) were male. Median age was 34 (18-71). All Patients who treated with Rituximab was received corticosteroid as a first line treatment. Twenty (80%) of the patients was responded to Methyl prednisolone (MP) treatment, 5 patients (20%) were resistant to MP treatment. Eleven patients (44%) had steroid dependent disease before Rituximab treatment. Thirteen (52%) of the patients were underwent splenectomy. Three patients (12%) received Eltrombopag treatment before Rituximab treatment. The response was observed in 20 of 25 patients who received Rituximab so overall response rate (ORR) is 80%. Complete Response (CR) was observed in 17 (68%) of the patients and partial response was in 3 (12%) of the patients. In patients with complete response, the median response time was on the 15th day (6–90 days). In patients with partial response, the median time was 12th day. After a median follow-up of 48 months (12–186), for 20 patients who were rensponsive to Rtiuximab, median duration of response was 15 months (2–68 months). In the follow-up period, clinical recurrence was detected in 12 (60%) of 20 patients, while permanent remission was achieved with Rituximab in 8 patients (40%). In patients with MP-dependent group, the Rituximab response rate is significantly higher than patients with non-dependent ($p = 0.027$). There was no difference in response to Rituximab treatment in splenectomized patients, those who received eltrombopag therapy before or whom have steroid resistant disease. In addition, the median time for Rituximab response in the MP dependent group is significantly higher than the MP resistant group (9.4 months vs. 17.4 months, $p = 0.006$).

Conclusion: Rituximab is a second line treatment for ITP patients especially whom are not suitable for splenecetomy. It should have more priority to TPO agonists regarding the success to obtain long-term remission.

https://doi.org/10.1016/j.htct.2020.09.047

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Methodology: Several groups have published on outcomes of cancer patients infected with of the SARS-CoV-2 virus causing the COVID-19 infection. However, most of these reports are single-center studies with a limited number of patients. We performed a systematic review and meta-analysis to evaluate the impact of COVID-19 infection on cancer patients. We searched PubMed, Web of Science, and Scopus for studies that reported the risk of infection and complications of COVID-19 in cancer patients. The literature search retrieved 22 studies (1018 cancer patients).

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STEM CELL TRANSPLANT

OP 16

The role of T helper 22 cells during engraftment at hematopoietic stem cell transplantation

O. Yucel[1,*], M. Ulubahsi[1], T. Ulas[2], O. Salim[1], D. Ekinci[1], L. Undar[1]

[1] *Department of Hematology Akdeniz University School of Medicine, Antalya, Turkey*
[2] *Department of Hematology Near East University School of Medicine, Nicosia, Cyprus*

Objective: T helper 22 (Th22) and T helper 17 (Th17) cells that are especially a subtype of CD4+ T lymphocyte are known to secrete interleukin 22 (IL-22). Th22 cells have been reported to play a role in infection, chronic inflammation, tumor development, autoimmune disease pathogenesis, and cell development. However, the role and number of cells whose carrying IL-22 in patients with hematopoietic stem cell transplantation is unknown. In this study, the number of circulating cells carrying IL-22, IL-17A, TNF-α and IFN-γ were investigated before hematopoietic stem cell transplantation (at stem cell infusion day) and during engraftment.

Methodology: A total of 10 patients who underwent autologous or allogeneic hematopoietic stem cell transplantation consecutively at the Department of Stem Cell Transplantation at Akdeniz University School of Medicine between July and December 2019 and 10 healthy people as a control group were included in this study. After separating the peripheral blood mononuclear cells (PBMCs) from the peripheral blood both at the transplantation day (before stem cell infusion) and at the engraftment, PBMCs were incubated by phorbol myristate acetate (PMA), ionomycin and monensin for 4 h. After that, the number of absolute lymphocytes carrying IL-22, IL-17A, TNF-α and IFN-γ among CD3 and CD4 double-positive T cells were determined by flow cytometry in patient and control groups, respectively.

Results: The diagnosis of patients' were multiple myeloma (6/10), B cell acute lymphoid leukemia (1/10), acute myeloid leukemia (1/10), non-hodgkin lymphoma (1/10), and gestational trophoblastic disease (1/10), respectively. While 6 of patients (') had autologous stem cell transplantation, 4 patients (@) had allogeneic stem cell transplantation. The number of absolute lymphocytes carrying IL-22, IL-17A, TNF-α and IFN-γ was found significantly lower in the patient group compared with the control group as shown in Table 1. In the patient group, although, there was no statistically significant difference between them, the number of absolute lymphocytes carrying IL-22, IL-17A, TNF-α and IFN-γ at engraftment were higher than stem cell infusion day (D0). Table 1 The absolute count of lymphocytes carrying IL-22, IL-17A, TNF-α and IFN-γ at stem cell infusion day (D0).

Conclusion: In our study, we detected that the number of absolute lymphocytes carrying IL-22, IL-17A, TNF-α and IFN-γ at stem cell infusion day (D0) were significantly lower in the patient group compared with control group. This might be related with previous received treatments including conditioning regimen, chemotherapy or radiotherapy. In addition to, although there was a trend increased the absolute count of lymphocytes carrying IL-22, IL-17A, TNF-α and IFN-γ at engraftment in the patient group, there was no significant difference between D0 and engraftment. This could be related to small sample size as well. In conclusion, we think that further larger prospective studies are needed to clarify for this issue in patients with hematopoietic stem cell transplantation.

https://doi.org/10.1016/j.htct.2020.09.048

OP 17

Story of success of haploidentical hematopoietic stem cell transplantation in aplastic anemia: a systematic review and meta-analysis of clinical outcome and risk assessment

G. Elgohary

Ain shams university Hospitals, Heliopolis, Egypt

Objective: Story Of Success Of Haploidentical Hematopoietic Stem Cell Transplantation in Aplastic Anemia: A Systematic Review and Meta-analysis of Clinical Outcome and risk assessment. Authors: Ghada ElGohary1,2 1King Khalid University Hospital, Riyadh, Saudi Arabia 2Faculty of Medicine Ain Shams University, Cairo Egypt Running title: Haploidentical Stem Cell Transplantation in Aplastic Anemia.

Case report: Abstract Aplastic anemia (AA) is a very serious hematological disorder which can be solely cured by hematopoietic stem cell transplantation (HSCT). Haploidentical HSCT is a new emerging modality with encouraging outcomes in several blood conditions,yet it is still under several trials in AA Objectives: To assess the feasibility and safety of the haploidentical HSCT in patients with severe and very severe AA.

Methodology: This is a systematic review and meta-analysis of studies related to haploidentical stem cell transplantation in idiopathic aplastic anemia emphasizing the investigating rates of successful engraftment, acute graft-versus-host-disease (aGvHD), chronic GvHD (cGvHD), besides the transplant-related mortality (TRM), and post-transplantation viral infections (including cytomegalovirus [CMV]) in patients with AA.

Results: The effects of reduced intensity (RIC) and non-myeloablative conditioning (NMA) as well as various GvHD-prophylaxis regimens on these outcomes were evaluated in our study. In total of fifteen studies that were identified, (577 patients, 58.9% males), successful engraftment was observed in 97.3% of patients (95% CI, 95.9–98.7) while grade II-IV aGvHD and cGvHD has been reported in 26.6% and 25.0%, respectively. The incidence of TRM was 6.7% per year (95% CI, 4.0 to 9.4). RIC regimens were associated with higher proportions of successful engraftment (97.7% vs. 91.7%, $p = 0.03$) and aGvHD (29.5% vs. 18.7%, $p = 0.008$) when compared to NMA regimens with no differences in cGvHD or mortality incidence. When compared to methotrexate-containing regimens and other regimens, post-transplant-cyclophosphamide-containing regimens (PTCy) has helped to reduce the rates of aGvHD (28.6%, 27.8%, and 12.8%, respectively, $p = 0.02$), CMV viremia (55.7%, 38.6%, and 10.4%,

STEM CELL TRANSPLANT

OP 16

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O. Yucel[1,*], M. Ulubahsi[1], T. Ulas[2], O. Salim[1], D. Ekinci[1], L. Undar[1]

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OP 17

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G. Elgohary

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Objective: Story Of Success Of Haploidentical Hematopoietic Stem Cell Transplantation in Aplastic Anemia: A Systematic Review and Meta-analysis of Clinical Outcome and risk assessment. Authors: Ghada ElGohary1,2 1King Khalid University Hospital, Riyadh, Saudi Arabia 2Faculty of Medicine Ain Shams University, Cairo Egypt Running title: Haploidentical Stem Cell Transplantation in Aplastic Anemia.

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respectively, $p < 0.001$), and CMV disease in initially-viremic patients (2.1%, 33.0%, and 0%, respectively, $p < 0.001$).

Conclusion: We can conclude that Haploidentical HSCT is associated with promising outcomes in terms of successful engraftment and reduced complications. Engraftment success has been noticed in the majority of patients with severe and very severe AA, while TRM and GvHD rates were acceptable. NMA conditioning was better in terms of lower CMV viremia and acute GVHD but not in terms of RRT, mortality and engraftment. The addition of PTCy regimens have showed lower GvHD and lower CMV incidence at a price of non-significant increase in the incidence of mortality per year. NMA vs. RIC and PTCy vs others may be used depending on both patient's and donor's profiles besides each institution's setup and resources Recommendation: Still we are in need of more studies to weigh the risk and benefits of Haplo SCT in AA.

https://doi.org/10.1016/j.htct.2020.09.049

OP 18

Long-term results of allogeneic peripheral blood hematopoietic stem cell transplantation for severe aplastic anemia

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Objective: Aplastic anemia (AA) is a life-threatening disorder of hematologic stem cell which, if untreated, may be associated with significant morbidity and mortality due to the recurrent infections or bleeding. Currently, the first treatment option is allogeneic hematopoietic stem cell transplant (allo-HSCT) for patients younger than 40 years. Bone marrow is recommended as the stem cell source due to less graft versus host disease (GVHD) risk and better outcomes than peripheral blood (PB)-derived stem cell. Recently, a few data of PB-derived allo-HSCT in AA has been published, due to its easy applicability and early engraftment advantage. The aim of this study is to share the data of AA patients who have underwent PB-derived allo-HSCT in our bone marrow transplantation center.

Methodology: Twenty-seven patients who underwent PB-derived allo-HSCT from human leukocyte antigen matched sibling donors were analyzed retrospectively.

Results: The median follow-up time of the patients was 95.2 months (range, 4.8–235 months). The 10-year survival was 89%. The median neutrophil and platelet engraftment time was 11 days (range, 9–16 days) and 13 days (range, 11–29 days, respectively. Primary platelet engraftment failure was observed in only 1 patient (3.7%). Acute and chronic GVHD observed in 2 (7.4%) and 3 (11.1%) patients, respectively. Neutropenic fever was observed in 13 (44.8%) of patients until the engraftment after allo-HSCT. One patient died due to CMV infections, two died due to septic shock secondary to fungal infection.

Conclusion: This study demonstrated that PB is the stem cell source of choice for patients with SAA.

https://doi.org/10.1016/j.htct.2020.09.050

PEDIATRIC HEMATOLOGY
HEMATOLOGY – GENERAL

OP 19

Hematological parameters and peripheral blood morphologic abnormalities in children with COVID-19

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Objective: The aim of this study is to evaluate the hematologic parameters and peripheral blood cell morphological changes in children with COVID-19 and compare them with those of children suspected but then confirmed to be negative for SARS-CoV-2.

Methodology: Thirty children were tested to be positive for SARS-CoV-2 and the remaining 40 were negative. Hemoglobin, leukocyte, neutrophil, lymphocyte, monocyte counts according to age-specific intervals, platelet, large unstained cell counts, and delta neutrophil index were recorded. Differential counts were formulated by manual counting and morphology of the blood cells were evaluated.

Results: The mean leukocyte counts of the SARS-CoV-2 positive and negative groups were $7.0 \pm 3.7 \times 10^9$/L and $10.4 \pm 7.1 \times 10^9$/L, respectively ($p < 0.05$). Nine (30%) children with COVID-19 had lymphopenia. Among children with COVID-19, absolute lymphocyte count was lower in those with pneumonia ($p < 0.05$). Reactive lymphocytes were noted in 77.8% and 90% in the SARS-CoV-2 test positive and negative groups, respectively ($p > 0.05$). Mean absolute neutrophil counts of the SARS-CoV-2 test positive and negative groups were $3.7 \pm 2.9 \times 10^9$/L and $5.4 \pm 4.2 \times 10^9$/L ($p < 0.05$). Four patients (13.3%) with SARS-CoV-2 test positive had neutrophilia and seven (23.3%) had mild neutropenia. In the peripheral smear, vacuolated monocytes and dysplastic changes in neutrophils and platelets were noted in both groups.

Conclusion: Leukocyte, neutrophil and monocyte counts were significantly lower in children with COVID-19 compared with symptomatic children without COVID-19. Lymphopenia, reactive lymphocytosis and dysplasia, could be noted in children with COVID-19. Further studies on hematological findings linked with the course of the disease in children are warranted.

https://doi.org/10.1016/j.htct.2020.09.051

respectively, $p < 0.001$), and CMV disease in initially-viremic patients (2.1%, 33.0%, and 0%, respectively, $p < 0.001$).

Conclusion: We can conclude that Haploidentical HSCT is associated with promising outcomes in terms of successful engraftment and reduced complications. Engraftment success has been noticed in the majority of patients with severe and very severe AA, while TRM and GvHD rates were acceptable. NMA conditioning was better in terms of lower CMV viremia and acute GVHD but not in terms of RRT, mortality and engraftment. The addition of PTCy regimens have showed lower GvHD and lower CMV incidence at a price of non-significant increase in the incidence of mortality per year. NMA vs. RIC and PTCy vs others may be used depending on both patient's and donor's profiles besides each institution's setup and resources Recommendation: Still we are in need of more studies to weigh the risk and benefits of Haplo SCT in AA.

https://doi.org/10.1016/j.htct.2020.09.049

OP 18

Long-term results of allogeneic peripheral blood hematopoietic stem cell transplantation for severe aplastic anemia

E. Aladag[1,*], H. Goker[2], H. Demiroglu[2], S. Aksu[2], N. Sayınalp[2], I. Haznedaroglu[2], O. Ozcebe[2], Y. Buyukasık[2]

[1] *Hacettepe University Department Hematology, Ankara, Turkey*
[2] *Hacettepe University Department Hematologyacettepe University Department Hematology, Ankara, Turkey*

Objective: Aplastic anemia (AA) is a life-threatening disorder of hematologic stem cell which, if untreated, may be associated with significant morbidity and mortality due to the recurrent infections or bleeding. Currently, the first treatment option is allogeneic hematopoietic stem cell transplant (allo-HSCT) for patients younger than 40 years. Bone marrow is recommended as the stem cell source due to less graft versus host disease (GVHD) risk and better outcomes than peripheral blood (PB)-derived stem cell. Recently, a few data of PB-derived allo-HSCT in AA has been published, due to its easy applicability and early engraftment advantage. The aim of this study is to share the data of AA patients who have underwent PB-derived allo-HSCT in our bone marrow transplantation center.

Methodology: Twenty-seven patients who underwent PB-derived allo-HSCT from human leukocyte antigen matched sibling donors were analyzed retrospectively.

Results: The median follow-up time of the patients was 95.2 months (range, 4.8–235 months). The 10-year survival was 89%. The median neutrophil and platelet engraftment time was 11 days (range, 9–16 days) and 13 days (range, 11–29 days, respectively. Primary platelet engraftment failure was observed in only 1 patient (3.7%). Acute and chronic GVHD observed in 2 (7.4%) and 3 (11.1%) patients, respectively. Neutropenic fever was observed in 13 (44.8%) of patients until the engraftment after allo-HSCT. One patient died due to CMV infections, two died due to septic shock secondary to fungal infection.

Conclusion: This study demonstrated that PB is the stem cell source of choice for patients with SAA.

https://doi.org/10.1016/j.htct.2020.09.050

PEDIATRIC HEMATOLOGY
HEMATOLOGY – GENERAL

OP 19

Hematological parameters and peripheral blood morphologic abnormalities in children with COVID-19

N. Yarali*, Y. Akcabelen, Y. Unal, A. Ozkaya-Parlakay

Ministry of Health Ankara City Hospital, Ankara, Turkey

Objective: The aim of this study is to evaluate the hematologic parameters and peripheral blood cell morphological changes in children with COVID-19 and compare them with those of children suspected but then confirmed to be negative for SARS-CoV-2.

Methodology: Thirty children were tested to be positive for SARS-CoV-2 and the remaining 40 were negative. Hemoglobin, leukocyte, neutrophil, lymphocyte, monocyte counts according to age-specific intervals, platelet, large unstained cell counts, and delta neutrophil index were recorded. Differential counts were formulated by manual counting and morphology of the blood cells were evaluated.

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Conclusion: Leukocyte, neutrophil and monocyte counts were significantly lower in children with COVID-19 compared with symptomatic children without COVID-19. Lymphopenia, reactive lymphocytosis and dysplasia, could be noted in children with COVID-19. Further studies on hematological findings linked with the course of the disease in children are warranted.

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HEMATOLOGY – GENERAL

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OP 20

Risk factors and outcomes related to intensive care unit admission of children with hematological and solid organ malignancies: single-center experience

C. Kaya[1,*], Z. Guzelkucuk[2], D. Ozyoruk[2], N. Ozbek[2], N. Yarali[2]

[1] *University of Health Sciences, Ankara City Hospital, Department of Pediatric, Ankara, Turkey*
[2] *University of Health Sciences, Ankara City Hospital, Department of Pediatric Hematology and Oncology, Ankara, Turkey*

Objective: Despite the developments in the diagnosis and treatment of cancer, malignancy remains one of the important causes of mortality in children. Aggressive chemotherapy leads to severeinfections or complicationsaffecting many systems, causing admissions to intensive care units (ICU). In our study, we aimed to evaluate the demographic data, clinical findings, and prognostic factors affecting hospitalization in the intensive care unit of the patients with hematological malignancy (HM) and solid organ malignancy (SOM).

Methodology: Between June 2013 and December 2018, patients were enrolled in our study between 28 and 18 years of with HM and SOM, who were hospitalized in the Pediatric Intensive Care of the University of Health Sciences Ankara Children's Hematology Oncology Training and Research Hospital. Demographic, clinical, laboratory, and treatment characteristics and survival in ICU were recorded.

Results: During the study period, 232 admissions of 158 patients with HM and SOM who were treated in ICU were evaluated. Patients diagnosed with acute lymphoblastic leukemia (ALL) and central nervous system (CNS) tumors were the most frequently hospitalized patients in the ICU, respectively. One hundred fifty-eight patients included in our study, 89 (56.3%) died. There was no statistically significant difference between HM and SOM patients in terms of mortality rate. The overall survival rate was calculated as 51.7%. Mortality was found to be higher in patients who need ICU admission while staying in the hospital, patients between the ages of 15–18, patients needed respiratory support before ICU and underwent mechanical ventilation (MV) during the first 24 h of hospitalization, and patients needed inotropic support. Neutropenia, thrombocytopenia, hypoglycemia, hypoalbuminemia, and high levels of AST/ALT, urea, creatinine, total and direct bilirubin, LDH, and CRP values were associated with mortality. Detection of recurrenceor refractory disease and organ dysfunction is an independent risk factor on mortality.

Conclusion: One-year overall survival rate of our patients was 51.7%. Relapse/refractory disease and organ dysfunction were identified as two independent risk factors on mortality. Prospective, multicenter studies are needed to determine the increasing importance of factors in the follow-up of patients with hematological and solid organ malignancies and to determine long-term survival rates.

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OP 21

A case report of RAS-associated autoimmune lymphoproliferative disorder

C. Coskun[1,*], F. Gumruk[1], M. Cemaloglu[1], M. Orhan[2], I. Tezcan[3], S. Unal[4]

[1] *Hacettepe University, Department of Pediatric Hematology, Ankara, Turkey*
[2] *Sakarya University, Department of Pediatric Hematology, Sakarya, Turkey*
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[4] *Hacettepe University, Research Center for Fanconi Anemia and Other Inherited Bone Marrow Failure Syndromes, Ankara, Turkey*

Objective: Clinically, RAS-associated autoimmune lymphoproliferative disorder (RALD) is characterized by splenomegaly, peripheral lymphadenopathy and autoimmunity. The autoimmune phenotype can present in childhood or adulthood and primarily includes autoimmune hemolytic anemia, immune thrombocytopenia (ITP) and neutropenia. In this report, we present a patient with RALD. The patient showed somatic mutation for NRAS mutation.

Case report: A two-year-old boy was referred with the complaints of ecchymoses. There was no consanguinity between parents and he had a healthy sibling. It was learned that the patient presented with bruises at the age of 12 months, and was follow up with thrombocytopenia, which responded partially and transiently to intravenous immunglobin (IVIG) and steroids. Physical examination at admission revealed hepatosplenomegaly and cervical lymphadenopathies. Complete blood count showed hemoglobin (Hb) 10.6 g/dL, mean corpuscular volume (MCV) 74 fL, white blood count 11.3×10^9/L and platelet 15×10^9/L with monocytosis on blood film. Bone marrow of the patient showed megaloblastic changes and no increase in megakaryocytes. Additionaly, patient was found to have hypergamaglobulinemia. Double-negative (CD4-CD8-) T cells were 2% and a decrease in lymphocyte activation was observed with T and B cell subgroups. Mycophenolate mofetil was started. The patient was followed up with the autoimmune lymphoroliferative syndrome (ALPS) phenotype and genetic work-up revealed NRAS c.38G>A heterozygous mutation. The patient was diagnosed with ALPS type 4 (NRAS somatic mutation). Thrombocytopenia responded to mycophenolate mofetil.

Results: Genetic analysis of the RAS mutation should be performed in cases that does not meet the defined diagnostic criteria of ALPS or JMML.

Conclusion: RAS-related lymphoproliferative disease is a rare genetic disorder of the immune system and is a newly classified disease. RALD presents with autoimmunity, lymphadenopathy, and/or splenomegaly, but without a defect in FAS-dependent apoptosis or an increase in peripheral double negative T lymphocytes. The absolute or relative monocytosis in particular is an important characteristic of this disorder and help differentiate it from ALPS. JMML may be characterized with autoimmunity and may be similar to RALD as a clinical and laboratory phenotype. Approximately 15–30% of patients

OP 20

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diagnosed with JMML have somatic, activating RAS mutations. Response to steroids/IVIG in our patient prompted RALD diagnosis, rather than JMML. Finally genetic analysis of the RAS mutation should be performed in cases that does not meet the defined diagnostic criteria of ALPS or JMML.

https://doi.org/10.1016/j.htct.2020.09.053

LEUKEMIA/LYMPHOMA/HISTIOCYTE DISORDERS

OP 22

Bone mineral density and bone resorption in the acute leukemia during childhood

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[2] *University of Ankara, Faculty of Medicine, Department of Pediatrics Hematology-Oncology, Ankara, Turkiye*

Objective: Acute leukemia is the most common malignancy in children and has been reported to be associated with low bone mass. The urinary cross-links lysyl-pyridinoline (dipyridinoline [Dpd]) are established biochemical markers of osteoclastic bone resorption and collagen degradation. We believe that acute leukemia treatment; we wanted to investigate the effect on bone mineral density (BMD, g/cm^2) and bone resorption. It has been asked to investigate whether this effect is continuing or not with the passing years.

Methodology: Our materials were 29 leukemia patients who completed their treatments. The patients were divided into two groups. Group I consisted of 19 patients (the ones in the 1.00 ± 0.15th months after treatment) and Group II consisted of 10 patients (the ones in the 43.36 ± 18.39th month). 52 healthy children formed BMD group and 20 children formed Dpd control group. The BMD and urine Dpd values of the healthy ones and the patients were measured.

Results: In 10 of total 29 cases (4.48) osteopeni and osteoporosis were determined. A meaningful difference could not be found in the average values of BMD between the groups. In the evaluation of all cases and the groups separately, any effect of the chemotheraphy could not be found on BMD. It was found that age had a meaningful effect on BMD in the Group I ($p < 0.05$). The age and the time after the treatment affected BMD in a meaningful level in Group II ($p < 0.00001$, $p < 0.05$, respectively). BMD was increasing significantly with age and interval. The average BMD of 29 cases was 0.66 ± 0.17 g/cm^2, while of control group was 0.65 ± 0.16 g/cm^2. Average Dpd levels in urine were 32.92+13.74 and 30.15 ± 13.48 nmol/mmol Cr in the patients and control group respectively. The average BMD and Dpd values of the patients were not different than of the control group. A meaningful negative relation was determined between BMD and Dpd values separately in both all cases and Group II. Dpd value in urine decreased with the increase in the value of BMD. As the age of diagnosis increased, BMD increased. When the age of diagnosis increased, Dpd was determined as decreased. In the evaluation of all cases and groups separately, bone resorption and BMD were not different between the one taking radiotherapy (0.60 ± 0.15 g/cm^2 and 31.29 ± 18.09 nmol/mmol Cr) and the one not taking radiotherapy (0.67 ± 0.20 g/cm^2 and 37.29 ± 11.91 nmol/mmol Cr). In Group I, there was a meaningful difference ($p < 0.05$) between Bsds of the patients taking cranial radiotherapy (1.04 ± 0.74) and the ones not taking cranial radiotherapy (-0.19 ± 0.80) and taking extracranial radiotherapy (-1.36 ± 0.93). Cranial radiotherapy effected Bsds negatively in Group I while this effect could not be seen in Group II.

Conclusion: It was concluded that the childrens completing acute leukemia treatment could reach carry out the ideal height and weight with a sufficient and balanced nutrition program and maintain BMD values proper to their ages.

https://doi.org/10.1016/j.htct.2020.09.054

LEUKEMIA/LYMPHOMA/HISTIOCYTE DISORDERS

OP 23

A girl with SAMD9L mutation presenting with pancytopenia, immunodeficiency and myelodsyplasia

D. Gurlek Gokcebay[1,*], I. Yaman Bajin[2], Y. Akcabelen[1], A. Koca Yozgat[1], O. Arman Bilir[1], I. Ok Bozkaya[1], N. Yarali[1], N. Ozbek[1]

[1] *Ankara City Hospital, Ankara, Turkey*
[2] *Hacettepe University Faculty of Medicine, Ankara, Turkey*

Objective: Several monogenic causes of familial myelodysplastic syndrome (MDS) have recently been identified. Genetic studies disclosed heterozygous missense mutations in SAMD9L, a tumor suppressor gene located on chromosome arm 7q. Consistent with a gain-of-function effect, ectopic expression of the 2 identified SAMD9L mutants decreased cell proliferation relative to wild-type protein.

Case report: A one month old girl was referred to our hospital with bruising. She was followed-up at a local hospital with thrombocytopenia for three weeks. She had normal physical examination findings except petechiaes on her extremities, trunk, and face. There was no bleeding diathesis and consanginous marriage in her family history. Complete blood count showed hemoglobin of 7.2 g/dL, reticulocyte of 2.4%, leukocyte count of 3.1×10^9/L, absolute neutrophil count of 0.3×10^9/L, platelet count of 2×10^9/L. Coagulation tests, liver and kidney functions were normal. Her viral serologies were negative for EBV, CMV, rubella, hepatitis and parovirus B19. However, vitamin B12 level was below normal limits, then cyanocobalamin treatment was started. Her mother's serum vitamin B12 level was normal. Immune thrombocytopenia was considered and intravenous immunoglobulin (IVIG) was given to her, and platelets raised to 87×10^9/L, thereafter decreased to 14×10^9/L within a few days. Bone marrow aspiration showed hypocellularity with dysplastic changes in myeloid lineage. Karyotype analysis revealed 46,XX der(20), and negative for monosomy 7. Her neurologic examination was normal except bulging of anterior fontanel, cranial ultrasonography was performed and it showed triventricular hydrocephalus and left cerebellar hypoplasia. A

diagnosed with JMML have somatic, activating RAS mutations. Response to steroids/IVIG in our patient prompted RALD diagnosis, rather than JMML. Finally genetic analysis of the RAS mutation should be performed in cases that does not meet the defined diagnostic criteria of ALPS or JMML.

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Results: In 10 of total 29 cases (4.48) osteopeni and osteoporosis were determined. A meaningful difference could not be found in the average values of BMD between the groups. In the evaluation of all cases and the groups separately, any effect of the chemotheraphy could not be found on BMD. It was found that age had a meaningful effect on BMD in the Group I ($p < 0.05$). The age and the time after the treatment affected BMD in a meaningful level in Group II ($p < 0.00001$, $p < 0.05$, respectively). BMD was increasing significantly with age and interval. The average BMD of 29 cases was 0.66 ± 0.17 g/cm^2, while of control group was 0.65 ± 0.16 g/cm^2. Average Dpd levels in urine were 32.92+13.74 and 30.15 ± 13.48 nmol/mmol Cr in the patients and control group respectively. The average BMD and Dpd values of the patients were not different than of the control group. A meaningful negative relation was determined between BMD and Dpd values separately in both all cases and Group II. Dpd value in urine decreased with the increase in the value of BMD. As the age of diagnosis increased, BMD increased. When the age of diagnosis increased, Dpd was determined as decreased. In the evaluation of all cases and groups separately, bone resorption and BMD were not different between the one taking radiotherapy (0.60 ± 0.15 g/cm^2 and 31.29 ± 18.09 nmol/mmol Cr) and the one not taking radiotherapy (0.67 ± 0.20 g/cm^2 and 37.29 ± 11.91 nmol/mmol Cr). In Group I, there was a meaningful difference ($p < 0.05$) between Bsds of the patients taking cranial radiotherapy (1.04 ± 0.74) and the ones not taking cranial radiotherapy (-0.19 ± 0.80) and taking extracranial radiotherapy (-1.36 ± 0.93). Cranial radiotherapy effected Bsds negatively in Group I while this effect could not be seen in Group II.

Conclusion: It was concluded that the childrens completing acute leukemia treatment could reach carry out the ideal height and weight with a sufficient and balanced nutrition program and maintain BMD values proper to their ages.

https://doi.org/10.1016/j.htct.2020.09.054

LEUKEMIA/LYMPHOMA/HISTIOCYTE DISORDERS

OP 23

A girl with SAMD9L mutation presenting with pancytopenia, immunodeficiency and myelodsyplasia

D. Gurlek Gokcebay[1,*], I. Yaman Bajin[2], Y. Akcabelen[1], A. Koca Yozgat[1], O. Arman Bilir[1], I. Ok Bozkaya[1], N. Yarali[1], N. Ozbek[1]

[1] *Ankara City Hospital, Ankara, Turkey*
[2] *Hacettepe University Faculty of Medicine, Ankara, Turkey*

Objective: Several monogenic causes of familial myelodysplastic syndrome (MDS) have recently been identified. Genetic studies disclosed heterozygous missense mutations in SAMD9L, a tumor suppressor gene located on chromosome arm 7q. Consistent with a gain-of-function effect, ectopic expression of the 2 identified SAMD9L mutants decreased cell proliferation relative to wild-type protein.

Case report: A one month old girl was referred to our hospital with bruising. She was followed-up at a local hospital with thrombocytopenia for three weeks. She had normal physical examination findings except petechiaes on her extremities, trunk, and face. There was no bleeding diathesis and consanginous marriage in her family history. Complete blood count showed hemoglobin of 7.2 g/dL, reticulocyte of 2.4%, leukocyte count of 3.1×10^9/L, absolute neutrophil count of 0.3×10^9/L, platelet count of 2×10^9/L. Coagulation tests, liver and kidney functions were normal. Her viral serologies were negative for EBV, CMV, rubella, hepatitis and parovirus B19. However, vitamin B12 level was below normal limits, then cyanocobalamin treatment was started. Her mother's serum vitamin B12 level was normal. Immune thrombocytopenia was considered and intravenous immunoglobulin (IVIG) was given to her, and platelets raised to 87×10^9/L, thereafter decreased to 14×10^9/L within a few days. Bone marrow aspiration showed hypocellularity with dysplastic changes in myeloid lineage. Karyotype analysis revealed 46,XX der(20), and negative for monosomy 7. Her neurologic examination was normal except bulging of anterior fontanel, cranial ultrasonography was performed and it showed triventricular hydrocephalus and left cerebellar hypoplasia. A

diagnosed with JMML have somatic, activating RAS mutations. Response to steroids/IVIG in our patient prompted RALD diagnosis, rather than JMML. Finally genetic analysis of the RAS mutation should be performed in cases that does not meet the defined diagnostic criteria of ALPS or JMML.

https://doi.org/10.1016/j.htct.2020.09.053

LEUKEMIA/LYMPHOMA/HISTIOCYTE DISORDERS

OP 22

Bone mineral density and bone resorption in the acute leukemia during childhood

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[2] *University of Ankara, Faculty of Medicine, Department of Pediatrics Hematology-Oncology, Ankara, Turkiye*

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Methodology: Our materials were 29 leukemia patients who completed their treatments. The patients were divided into two groups. Group I consisted of 19 patients (the ones in the 1.00 ± 0.15th months after treatment) and Group II consisted of 10 patients (the ones in the 43.36 ± 18.39th month). 52 healthy children formed BMD group and 20 children formed Dpd control group. The BMD and urine Dpd values of the healthy ones and the patients were measured.

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ventrculo-peritoneal shunt was inserted to her. She had cellular and humoral immunodeficiency with decreased peripheral blood B and natural killer (NK) cell numbers (C19+20 cell number of 1%) and low immunoglobulin levels. On the follow-up, she received monthly IVIG prophlylaxis and platelet transfusions as needed. Genetic analysis disclosed that a heterozygous missense variant in SAMD9L (c.2627T > C). Bone marrow aspiration was planned to done in every 3 months on the follow-up. Platelet count and hemoglobin levels gradually increased over the time, but monosomy 7 was positive at the age of 2 in the 52% of the cells. She underwent hematopoietic stem cell transplantation (HSCT) from a matched unrelated donor with myeloablative conditioning regimen.

Methodology: We herein report a girl presenting with pancytopenia and immunodeficiency which was revealed SAMD9L mutation.

Results: SAMD9L, the gene is located in a region of chromosome 7 that is commonly deleted in myeloid malignancies. In mice, Samd9l deficiency causes development of MDS with age, suggesting that SAMD9L is a tumor suppressor. Heterozygous SAMD9L missense mutations may cause of familial MDS like Ataxia-pancytopenia syndrome which is associated with neurological findings (ataxia and nystagmus), cytopenias and predisposition to myeloid leukemia involving −7/del(7q). In addition, SAMD9L may regulate differentiation of diverse immune cell lineages like B and NK cells, however cellular basis of neurological manifestations in the carriers remains unclear.

Conclusion: In conclusion, SAMD9L mutation screening should be considered in all pediatric patients with MDS, AML, or JMML with chromosome 7 aberrations, even in the absence of neurological symptoms or a family history of myeloid malignancies.

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RED BLOOD CELL DISORDERS

OP 24

The effects of vitamin D deficiency on myocardial deformation and functions in patients with β-thalassemia

A. Koca Yozgat[1,*], E. Azak[2], D. Kaçar[1], M. Işık[1], O. Arman Bilir[1], I. Çetin[2], N. Ozbek[1], N. Yaralı[1]

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Objective: β-Thalassemia major (TM) is an inherited hemoglobin disorder resulting in chronic hemolytic anemia, and regular lifelong transfusion therapy remains the mainstay in the treatment of patients. Cardiac involvement is the leading cause of death in patients with β-TM. The association between vitamin D deficiency and left ventricular systolic and diastolic dysfunction has been previously demonstrated in the literature. Speckle-tracking echocardiography (STE) is feasible and valid for the evaluation of cardiac function via an assessment of the longitudinal deformation of the myocardium through the cardiac cycle. Our study aims to evaluate the effect of vitamin D deficiency on myocardial deformation and functions in children with thalassemia major by STE.

Methodology: In this prospective study, 33 patients with β-TM, receiving regular blood transfusions, and undergoing iron chelation therapy were enrolled in April 2018-January 2020. Vitamin D and ferritin levels, cardiac magnetic resonance (MR) T2* value, conventional echocardiography, and speckle tracking were evaluated. LV regional circumferential, and longitudinal strain values were measured. Vitamin D levels considered <20 ng/ml, 20–30 ng/ml, >30 ng/ml as deficient, insufficient, and sufficient, respectively. Myocardial functions of patients with vitamin D deficiency or insufficiency were evaluated by STE before and after vitamin D replacement.

Results: The mean age of patients was 15.4 ± 3.09 years; the male/female ratio was 18/15, and mean ferritin levels were 2017 ± 1573 ng/ml. Vitamin D level deficiency was detected in 30 (90%) and insufficient in 3 (10%) of our patients. Cardiac T2* value was normal in 21 patients and 12 patients had iron accumulation on cardiac T2* MR. The mean of left ventricular ejection fraction (LVEF) was 64 ± 4.7%, and the mean left ventricular shortening fraction (LVSF) was 34.2 ± 3.8% before vitamin D replacement, and LVEF was 65.1 ± 5.2% and LVSF 35 ± 3.7% after vitamin D replacement ($p > 0.05$). The mean left ventricle global longitudinal strain (LVGLS) was 19 ± 2.7% before replacement and 24 ± 2.7% after replacement (p: 0.04). The left ventricle global circumferential strain (LVGCS) was 20 ± 2.8% before replacement and 25 ± 3.8% after replacement (p: 0.03). While there was no significant difference in right ventricular functions before and after vitamin D replacement, but a statistically significant increase was observed in parameters showing left ventricular diastolic functions after replacement. There was a significant improvement in the global longitudinal strain of left ventricular after vitamin D replacement.

Conclusion: Vitamin D deficiency is frequently observed in patients with β-TM. It is reported that vitamin D deficiency causes decreased contractility and leads to an increase in cardiac iron involvement accordingly cardiomyopathy in these patients. Speckle tracking echocardiography could be used as a feasible method for evaluating subclinical myocardial dysfunction in patients with β-TM. In patients with β-TM, diastolic functions are primarily affected in the case of cardiac toxicity. In our study, we observed that our patients' diastolic functions had improved after vitamin D replacement therapy.

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OP 25

The molecular spectrum of patients with hereditary spherocytosis: a single center experience

C. Coskun[*], S. Unal, F. Gumruk

Hacettepe University, Department of Pediatric Hematology, Ankara, Turkey

Objective: Hereditary spherocytosis (HS) is a hemolytic anemia with variably severity, caused by defects in the

ventrculo-peritoneal shunt was inserted to her. She had cellular and humoral immunodeficiency with decreased peripheral blood B and natural killer (NK) cell numbers (C19+20 cell number of 1%) and low immunoglobulin levels. On the follow-up, she received monthly IVIG prophlylaxis and platelet transfusions as needed. Genetic analysis disclosed that a heterozygous missense variant in SAMD9L (c.2627T > C). Bone marrow aspiration was planned to done in every 3 months on the follow-up. Platelet count and hemoglobin levels gradually increased over the time, but monosomy 7 was positive at the age of 2 in the 52% of the cells. She underwent hematopoietic stem cell transplantation (HSCT) from a matched unrelated donor with myeloablative conditioning regimen.

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components of red cell membranes. It is characterized by anemia, jaundice, splenomegaly and cholelithiasis. The clinical manifestations vary widely, ranging from nearly asymptomatic to transfusion-dependent or severe life-threatening anemia. It is difficult to identify atypical cases with classical approaches. The known HS gene mutations are SPTA1 gene, SPTB gene, ANK1 gene, SLC4A1 gene and EPB42 gene. In this report, the next-generation sequencing (NGS) was used to analyze our patients with HS and we identified mutations responsible for HS.

Methodology: Patients who were diagnosed with hereditary spherocytosis with osmotic fragility testing between 2007–2019; ten were further tested for molecular background. Diagnosed in our center were analyzed retrospectively. Either NGS or ANK1 Sanger testing were used.

Results: The 10 cases of HS comprised 8 males and 2 females. The age of patients ranged from 5 months to 17 years. Hemolytic anemia, jaundice and splenomegaly were the most common findings in our cases. Gallstones were detected in four patients (40%). The family history was positive in 5 (50%) patients. Splenectomy and cholecystectomy was performed in two cases and three cases, respectively. The results corfirmed ANK1 gene mutation in 50%; SPTB gene mutation in 20%, EBP42 gene mutation in 10%; SPTA1 gene mutation in 10%. The clinical features of the patients are summarized in the Table 1. Table 1. Patient Age Sex Age of diagnosis Family history Splenomegaly Gallstone Splenectomy/Cholecystectomy Mutated gene 1 1 Female 1 year Yes + – –/– SPTB 2 10 Female 10 years Yes + – +/– ANK1 3 12 Female 7 years Yes + + +/+ ANK1 4 12 Female 2 years Yes – + –/+ ANK1 5 10 Male 6 years No – + –/– ABCG8 6 2 Female 5 months No + – –/– ANK1 7 13 Female 15 years Yes + – –/– ANK1 8 8 Female 7 years No + + –/+ EBP42 9 2.5 Male 2 years No + – –/– SPTB 10 19 Female 17 years No + – –/– SPTA1.

Conclusion: Consistent with the literature, the most common gene mutated was ANK1. Collectively, our results suggest that mutation analyses will complement other conventional tests for accurate diagnosis of HS, especially in those who are under transfusion programme and are followed with a diagnosis of unspecified hemolytic anemia.

https://doi.org/10.1016/j.htct.2020.09.057

STEM CELL TRANSPLANTATION

OP 26

Eltrombopag for thrombocytopenia following pediatric allogeneic hematopoietic stem cell transplantation

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Inonu University School of Medicine, Malatya, Turkey

Objective: Failure of platelet recovery is a complication occurring after allogeneic hematopoietic stem cell transplantation (HSCT). Poor graft function, relapse, viral infections, drug toxicity, immune processes may lead to decreased platelets production. Treatment options are limited for thrombocytopenia caused by poor platelet production. While the use of Eltrombopag (ELT) was retrospectively investigated in adult patients, data regarding the potential benefit of these agent for pediatric posttransplant thrombocytopenia are lacking. We report three pediatric patients who received ELT for thrombocytopenia occurring after HSCT.

Case report: The median patients' age at HSCT was 13.3 years (10–18). All patients had HSCT from a sibling donor with the bone marrow stem cell source. All patients were treated with a myeloablative conditioning regimen. Patients engrafted at a median time of 19 days (10–24) for neutrophils and 49 days (44–49) for platelets. Bone marrow aspirates showed a decrease number of megakaryocytes, and all patients had been ineffectively treated with high-dose intravenous gamma globulin and with steroids before ELT initiation.

Methodology: ELT was started at a median time after HSCT of 57 days (42–90), the starting dose being 25 mg/day, and the maximum administered dose was 75 mg/day. ELT was continued for a median period of 64 days (28–286). All patients reached sustained platelets count >50,000/μL after a median time from starting ELT of 197 days (87–210). The median platelet count at last evaluation was 115,000/μL (range 66,000–125,000/μL). ELT was well tolerated, and no patient have developed important side effect.

Results: Our cases became transfusion independent after a median time from starting ELT of 197 days. In the pediatric post-HSCT setting, only few previously published case reports described the successful use of ELT as a treatment for thrombocytopenia. Li et al. reported three children transplanted for nonmalignant disease treated for both primary and secondary failure of platelet engraftment. Treatment was effective in two patients, but not in one patient transplanted for Gaucher disease. In Masettis' study, the 60-day cumulative incidence of platelet recovery >50,000/μL after ELT treatment was 75%. Similarly, Tanaka et al. described 12 adults treated for primary and secondary post-HSCT thrombocytopenia who reached platelet count>50,000/μL in 60% and 71% of cases respectively.

Conclusion: Our study supports the safety and efficacy of ELT for treatment of prolonged thrombocytopenia after allogeneic HSCT in children. Future prospective studies are needed to confirm these findings.

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components of red cell membranes. It is characterized by anemia, jaundice, splenomegaly and cholelithiasis. The clinical manifestations vary widely, ranging from nearly asymptomatic to transfusion-dependent or severe life-threatening anemia. It is difficult to identify atypical cases with classical approaches. The known HS gene mutations are SPTA1 gene, SPTB gene, ANK1 gene, SLC4A1 gene and EPB42 gene. In this report, the next-generation sequencing (NGS) was used to analyze our patients with HS and we identified mutations responsible for HS.

Methodology: Patients who were diagnosed with hereditary spherocytosis with osmotic fragility testing between 2007–2019; ten were further tested for molecular background. Diagnosed in our center were analyzed retrospectively. Either NGS or ANK1 Sanger testing were used.

Results: The 10 cases of HS comprised 8 males and 2 females. The age of patients ranged from 5 months to 17 years. Hemolytic anemia, jaundice and splenomegaly were the most common findings in our cases. Gallstones were detected in four patients (40%). The family history was positive in 5 (50%) patients. Splenectomy and cholecystectomy was performed in two cases and three cases, respectively. The results corfirmed ANK1 gene mutation in 50%; SPTB gene mutation in 20%, EBP42 gene mutation in 10%; SPTA1 gene mutation in 10%. The clinical features of the patients are summarized in the Table 1. Table 1. Patient Age Sex Age of diagnosis Family history Splenomegaly Gallstone Splenectomy/Cholecystectomy Mutated gene 1 1 Female 1 year Yes + – –/– SPTB 2 10 Female 10 years Yes + – +/– ANK1 3 12 Female 7 years Yes + + +/+ ANK1 4 12 Female 2 years Yes – + –/+ ANK1 5 10 Male 6 years No – + –/– ABCG8 6 2 Female 5 months No + – –/– ANK1 7 13 Female 15 years Yes + – –/– ANK1 8 8 Female 7 years No + + –/+ EBP42 9 2.5 Male 2 years No + – –/– SPTB 10 19 Female 17 years No + – –/– SPTA1.

Conclusion: Consistent with the literature, the most common gene mutated was ANK1. Collectively, our results suggest that mutation analyses will complement other conventional tests for accurate diagnosis of HS, especially in those who are under transfusion programme and are followed with a diagnosis of unspecified hemolytic anemia.

https://doi.org/10.1016/j.htct.2020.09.057

STEM CELL TRANSPLANTATION

OP 26

Eltrombopag for thrombocytopenia following pediatric allogeneic hematopoietic stem cell transplantation

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Objective: Failure of platelet recovery is a complication occurring after allogeneic hematopoietic stem cell transplantation (HSCT). Poor graft function, relapse, viral infections, drug toxicity, immune processes may lead to decreased platelets production. Treatment options are limited for thrombocytopenia caused by poor platelet production. While the use of Eltrombopag (ELT) was retrospectively investigated in adult patients, data regarding the potential benefit of these agent for pediatric posttransplant thrombocytopenia are lacking. We report three pediatric patients who received ELT for thrombocytopenia occurring after HSCT.

Case report: The median patients' age at HSCT was 13.3 years (10–18). All patients had HSCT from a sibling donor with the bone marrow stem cell source. All patients were treated with a myeloablative conditioning regimen. Patients engrafted at a median time of 19 days (10–24) for neutrophils and 49 days (44–49) for platelets. Bone marrow aspirates showed a decrease number of megakaryocytes, and all patients had been ineffectively treated with high-dose intravenous gamma globulin and with steroids before ELT initiation.

Methodology: ELT was started at a median time after HSCT of 57 days (42–90), the starting dose being 25 mg/day, and the maximum administered dose was 75 mg/day. ELT was continued for a median period of 64 days (28–286). All patients reached sustained platelets count >50,000/μL after a median time from starting ELT of 197 days (87–210). The median platelet count at last evaluation was 115,000/μL (range 66,000–125,000/μL). ELT was well tolerated, and no patient have developed important side effect.

Results: Our cases became transfusion independent after a median time from starting ELT of 197 days. In the pediatric post-HSCT setting, only few previously published case reports described the successful use of ELT as a treatment for thrombocytopenia. Li et al. reported three children transplanted for nonmalignant disease treated for both primary and secondary failure of platelet engraftment. Treatment was effective in two patients, but not in one patient transplanted for Gaucher disease. In Masettis' study, the 60-day cumulative incidence of platelet recovery >50,000/μL after ELT treatment was 75%. Similarly, Tanaka et al. described 12 adults treated for primary and secondary post-HSCT thrombocytopenia who reached platelet count>50,000/μL in 60% and 71% of cases respectively.

Conclusion: Our study supports the safety and efficacy of ELT for treatment of prolonged thrombocytopenia after allogeneic HSCT in children. Future prospective studies are needed to confirm these findings.

https://doi.org/10.1016/j.htct.2020.09.058

ONCOLOGY
SOLID TUMORS

OP 27

Bone marrow involvement in non-small cell lung cancer

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Objective: Purpose of the study is to evaluate the possibility of detection DOCs in BM and to identify the frequency of BM involvement in patients with NSCLC, as well as their effect on the population of bone marrow lymphocytes.

Case report: There is evidence that disseminated tumor cells (DOCs) in the bone marrow (BM) are precursors of subsequent distant metastases. There is evidence indicating an important role for bone marrow lymphocyte subpopulations in hematogenous metastasis. The detection of DOCs in non-small cell lung cancer (NSCLC) will provide important information about the features of metastasis, as well as the possibilities of identifying new targets for the treatment of NSCLC.

Methodology: 62 bone BM of NSCLC patients were studied by morphological and immunological methods. DOCs analysis was performed using flow cytometry (FACS Canto II, USA, Kaluza Analysis v2.1 software), monoclonal antibodies to CD45, cytokeratins directly labeled with various fluorochromes were used. Lymphocyte populations CD3, CD4, CD8, CD19, CD20, CD16, CD27 were studied.

Results: DOCs (EPCAM+CD45-) in the BM were found in 43.5% of patients (threshold level:1 cell per 10 million myelocaricytes). The presence of DOCs did not correlate with tumor size, lymph node status, stage of the tumor process. The highest detection rates of DOCs were observed at stages IA and IIA: 60.7% and 58.3% respectively. BM involvement in adenocarcinoma was observed in 45% cases, in squamous cell carcinoma - in 37% samples ($p = 0.501$). It was found that DOCs are more often detected in more differentiated tumors ($p = 0.023$). Significant correlations between the presence of DOCs in the BM and myelogram parameters have not been established. A decrease in the number of granulocyte germ cells was observed in 4% of BM involvement ($p = 0.036$). A significant increase in the level of subpopulations of CD16 + CD4-NK-cells ($p = 0.002$), CD27 + CD3 + T-cells ($p = 0.015$) with bone marrow damage was revealed.

Conclusion: The possibility of detecting DOCs in the BM of NSCLC patients has been established. BM involvement was 43.5%. DOCs are detected even in the early stages of NSCLC. Relationship between BM involvement and the degree of tumor differentiation was found. More frequent BM involvement was observed in adenocarcinoma compared with squamous cell carcinoma of the lung. The relationship between DOCs and bone marrow lymphocyte populations was revealed: subpopulations of CD16 + CD4−, CD27 + CD3+.

https://doi.org/10.1016/j.htct.2020.09.060

OP 28

The prognostic significance of neutrophil/lymphocyte ratio in patients with terminal cancer

M. Alemdar*, S. Sezgin Goksu, A. Tatli, H. Coskun

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Objective: Predicting the life expectancy in patients with terminal cancer is important in terms of clinical assessment and treatment approaches. Although, various prognostic scoring systems have been established and still often used, those are based on subjective parameters. There is a recently increased tendency to anticipate prognosis by prognostic laboratory tests that consist of objective parameters and are easily applied. The role of inflammation in cancer development and progress is a well-known topic. Neutrophil/lymphocyte ratio (NLR) is a objective parameter that could show the level of systemic inflammation. Increasing NLR has been associated with worse prognosis in many type of cancer. In this study, we evaluated the prognostic role of NLR in terminal cancer patients.

Methodology: Patients of 432 who were enrolled as a terminal cancer in Department of Medical Oncology were included in this study. The information of those patients were obtained retrospectively from medical archive records. Hemogram and biochemistry results which were examined on the first day of patients' last hospitalisation were used. Statistical analyses were done by Independent Sample T or Mann Whitney U test. Two main subgroup were defined; patients who died in first 30 days from last hospitalization or patients who died after 30 days from last hospitalization.

Results: Descriptive data and statistical analysis results are shown in Table 1. The median age of patients was 62. 268 (b) of patients were male and 164 (8) were female. The most frequent cancer type were lung (1), colorectal (%9), and esophagus/stomach (%8), respectively. While the median NLR was 11.36 (min–max, 0.11–367.67), the median thrombocyte/lymphocyte ratio (PLR) was 305.39 (min–max, 3.23–4150). 381 (88%) of the patients were in the group that died within 30 days after the last hospitalization. The median NLR was significantly higher in patients who died within 30 days compared with patients who died after 30 days (11.84 vs. 7.5, $p < 0.001$, respectively) as shown in Table 1. On the other hand, there were no differences between 2 group in terms of other parameters including hemoglobin, leukocyte count, lactate dehydrogenase (LDH), mean platelet volume (MPV), PLR, CRP/albumin ratio, monocyte count, and prognostic nutritional index (PNI) (Table 1).

Conclusion: There is a strong relationship between inflammation and cancer. NLR is a marker to show inflammation. In this study, we showed that increased NLR was associated with worse prognosis in patients with terminal cancer. There are few studies evaluating the prognostic role of NLR in terminal

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Conclusion: There is a strong relationship between inflammation and cancer. NLR is a marker to show inflammation. In this study, we showed that increased NLR was associated with worse prognosis in patients with terminal cancer. There are few studies evaluating the prognostic role of NLR in terminal

cancer patients in the literature, and our study results are compatible with those. The limitation of our study is to be a retrospective design and single-center study. Further prospective multi-center trials are needed to clarify the prognostic role of NLR. In conclusion, we think that NLR can be used safely for anticipating prognosis in terminal cancer patients due to its easy usage and objectivity.

https://doi.org/10.1016/j.htct.2020.09.061

OP 29

Anti-Yo positive paraneoplastic cerebellar degeneration associated with ovarian cancer: a rare case report

Y. Ilhan[1,*], M. Korkmaz[2], E. Taskiran Guzel[2], K. Mammadova[3], S. Sezgin Goksu[1], A. Tatlı[1], H. Coskun[1]

[1] *Akdeniz University Faculty of Medicine, Department of Medical Oncology, Antalya, Turkey*
[2] *Akdeniz University Faculty of Medicine, Department of Internal Medicine, Antalya, Turkey*
[3] *Akdeniz University Faculty of Medicine, Department of Neurology, Antalya, Turkey*

Objective: Paraneoplastic cerebellar degeneration (PCD) is a rare neurological complication of cancer characterized by rapid development of cerebellar ataxia resulting from tumor-induced autoimmunity against cerebellar purkinje cells. Anti-Yo antibody which is also known as anti-Purkinje cell cytoplasmic antibody type-1, is highly specific and the most frequent antibody in patients with PCD. Here we present a case of anti-Yo-associated PCD in a patient with ovarian cancer. After the patient was diagnosed with PCD, ovarian cancer recurrence was shown.

Case report: A 54-year-old female patient, who was in remission with ovarian cancer applied to us with a 6-month history of progressively worsening unsteadiness while walking. She was diagnosed as ovarian cancer in November 2016 and operated, and then 6 cycles of carboplatin plus paclitaxel adjuvant treatment was given. She did not have any other disease and history of drug, smoking, and alcohol use. There was no important family history. On physical examination, her speech was minimally dysarthric. While she was walking, ataxia was observed. Other system examinations were normal. Hemogram, biochemistry, muscle enzymes, thyroid function tests, vitamin B12, and 25-OH-D were in the normal range. CA-125 increased compared to 3 months ago.(23–53 U/mL)Because of the increased CA-125 level, computer tomography and then PET-CT scan was taken. There was a 1.5-cm diameter hypermetabolic nodular pelvic lesion. Brain MR and EMG were planned for complaints of walking and balance disorders. Nothing was found in the examinations and tests to explain the current condition of the patient. The paraneoplastic panel was taken from the blood and cerebrospinal fluid (CSF) samples. Anti-Yo antibodies were three positive in both the CSF and blood samples. The patient was diagnosed with PCD due to clinical findings and anti-Yo positivity both CSF and blood samples. Since the main treatment of paraneoplastic syndrome was the excision of the primary lesion, it was discussed for the excision of the recurrent mass. But this patient was not eligible for re-surgery. So carboplatin, gemcitabine plus bevacizumab treatment protocol was initiated for recurrent ovarian cancer. Plasmapheresis was performed 5 times, every other day. A significant improvement in walking were observed in the patient after 2 weeks from discharge.

Conclusion: Here we described a patient who developed ataxia 3 years after remission of ovarian cancer and diagnosed with PCD. Diagnosing a paraneoplastic syndrome and mild elevation of CA-125 level have led to the diagnosis of recurrence of ovarian cancer. In approximately 30% of patients, the ataxic symptoms occur when the cancer is in remission as it was in this reported case. Therefore, when a patient is diagnosed with PCD, whole-body screening is necessary to reveal the underlying malignancy. Although there is a strong association between PCD and Anti-yo; its pathological function is still not clear. Treatment of PCD is unfavorable and patients usually have a poor prognosis. Plasmapheresis, intravenous immunoglobulin (IVIG), and cyclophosphamide are the treatment options. Also, it is very important to treat underlying malignancy. In conclusion, in patients with unexplained neurological symptoms and a history of cancer, paraneoplastic syndromes should be considered and an underlying malignancy should be investigated.

https://doi.org/10.1016/j.htct.2020.09.143

OP 30

Gastroenteropancreatic neuroendocrine carcinoma: single center experience

A. Sakin[1], O. Can[2,*]

[1] *Internal Medicine Clinic, Van Training and Research Hospital, Van, Turkey*
[2] *Medical Oncology Clinic, Okmeydani Training and Research Hospital, Istanbul, Turkey*

Objective: In general, all high grade, poorly differentiated gastrointestinal neuroendocrine carcinomas (GIS-NEC) exhibit aggressive behavior characterized by widespread metastases in the early stages. It relapses very quickly, even in the early stages. The prognosis is extremely poor. These tumors show similarities with small cell carcinoma of the lung in terms of morphology, biological behavior and chemosensitivity. In this study, we aimed to investigate survival according to primary tumor localization and the stage besides clinical and demographic data of GIS-NECs.

Methodology: Twenty-seven patients with the diagnosis of GIS-NEC were included in the study. Patients under the age of 18, patients with another malignancy other than GIS-NEC and patients having GIS NEC but whose data were missed, were not included in the study.

Results: In this study, 15 male (55.6%) and 12 female (44.4%) patients were included. Median age was 66 years old. The primary localizations were as follows, in 15 (55.6%) patients; gastric, in 4 (14.8%) patients; esophagus, in 4 (14.8%) patients; colorectal, in 2 (7.4%) patients; pancreas and in 2 (7.4%) patients; small intestine. At the time of diagnosis, in 21 (77.8%) patients Stage 4 disease, in 5 (18.5%) patients stage 2 and 3 disease and in 1 (3.7%) patients stage 1 disease was present.

cancer patients in the literature, and our study results are compatible with those. The limitation of our study is to be a retrospective design and single-center study. Further prospective multi-center trials are needed to clarify the prognostic role of NLR. In conclusion, we think that NLR can be used safely for anticipating prognosis in terminal cancer patients due to its easy usage and objectivity.

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OP 30

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During the follow-up, 16 (59.3%) patients were ended up with exitus. Feature characteristics of the patients were summarized in (Table 1). While median survival was not achieved in stage 2 and 3 patients, it was 8 months in stage 4 patients. (Figure 1). Based on the primary tumor localization, mOS was 7 months in the gastric, 5 months in the pancreas, 7 months in the small intestine, 6 months in the esophagus. In colorectal localization mOS could not be reached (Table 2).

Conclusion: In our study, gastric localization was the most common in GIS-NECs. The shortest survival was observed in the pancreatic localization.

https://doi.org/10.1016/j.htct.2020.09.144

HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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POSTER PRESENTATIONS

ADULT HEMATOLOGY
ACUTE LEUKEMIAS

PP 01

Hypercalcemia due to the interaction between all trans retinoic acid and posaconazole used for acute promyelocytic leukemia treatment

H. Afacan Öztürk, M. Albayrak, S. Maral*, M. Reis Aras, F. YıLmaz, P. Akyol, M. Tiglioglu

University of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital, Department of Hematology, Ankara, Turkey

Objective: All-trans retinoic acid (ATRA), a physiological metabolite of vitamin A, has revolutionized acute promyelocytic leukemia (APL) treatment. Most APL cases show a t(15;17) (q22 q21) chromosomal translocation from which a PML/retinoic acid receptor a (RARa) fusion gene originates. The maturation of APL cells during myeloid differentiation is blocked at the promyelocyte stage, and ATRA induces the terminal differentiation and apoptosis of leukemia cells. Although very high rates of complete remission have been achieved using ATRA in APL patients, side effects associated with systemic ATRA treatment have also been reported in the literature. Hypercalcemia associated with ATRA has been reported among rare side effects of the drug. We report a case of hypercalcemia that resulted from the interaction of ATRA and posaconazole used in the treatment APL.

Case report: A 49-year-old woman was diagnosed with APL by tests and studies to investigate the etiology of pancytopenia, and was started on a combination of daunorubicin 60 mg/m^2/day (3 days), cytosine arabinoside 100 mg/m^2/day (7 days) plus ATRA 45 mg/m^2/day. Due to febrile neutropenia, piperacillin/tazobactam treatment and posaconazole treatment at a dose of 300 mg/day were added. She developed difficulty breathing and weight gain on the 6th day of therapy, which was attributed to the ATRA syndrome; thus, ATRA was stopped and dexamethasone was started. As she developed hyperbilirubinemia during her follow-up, posaconazole and prophylactic drugs were stopped. The patient entered remission after induction therapy, and ATRA plus idarubicin 5 mg/m^2/day (4 days) chemotherapy regimen, and prophylactic posaconazole were planned as the first consolidation therapy. Having a normal calcium level (9.79 mg/dL; normal range 8.6–10.2 mg/dL) prior to treatment, the patient developed a progressive rise of serum calcium (10.3 to 10.6 to 10.8 to 11.1 mg/dL) with the start of posaconazole and ATRA. Her Vitamin D level and PTH, both of which were in the normal range. Considering that hypercalcemia might have been caused by posaconazole and ATRA, both drugs were stopped. When the calcium level returned to normal by four days, ATRA but not posaconazole was reinstituted, and the patient developed no calcium elevation thereafter.

Conclusion: It is known that ATRA is metabolized by Cytochrome P450 pathway, and closely associated with the enzymes CYP 2C9 and CYP3A4. Azole antifungals have been shown to be strong inhibitors of the cytochrome P450 enzyme system. A case of hypercalcemia developing as a result of the addition of voriconazole to ATRA was reported in the literature, and another case of hypercalcemia developing as a result of combined use of itraconazole and ATRA. To reduce the incidence of side effects during ATRA treatment, it may be prudent to limit the use of any drug with the potential of inhibiting the cytochrome P450 enzyme system. A review of the literature has not provided any clear evidence as to when ATRA can be reinstituted after the cessation of a drug belonging to the azole group. This case highlights the importance of monitoring ATRA's side effects when it is used in combination with drugs inhibiting the cytochrome P450 enzymes.

https://doi.org/10.1016/j.htct.2020.09.063

PP 02

Acute cerebellar syndrome after high dose cytosine arabinoside treatment: case report

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Objective: Cytosine Arabinoside (cytarabine, ARA-C) discovered in the early 1950s from crptathetia crpta which is a type of sponge. It is a chemotherapeutic agent that is an analogue of primidine from the group of antimetabolites and it is used in AML (acute myeloid leukemia), ALL (acute lymphoblastic leukemia), CML (chronic myeloid leukemia), relapse or refractory hodgkin lymphoma, non-hodgkin lymphoma, primary central nervous system lymphoma treatment. The most common side effect is cytopenias due to the bone marrow suppression. In addition; side effects may occur such as nausea, vomiting, diarrhea, abdominal pain, hepatic dysfunction, neurological side effects. Beside many neurological side effects such as peripheral neuropaty, convulsion, cerebral dysfunction can be seen in systemic and intrathecal treatments, classical cytarabine neurotoxicity is acute cerebellar syndrome caused by high-dose systemic therapy.

Case report: A 61 year-old man who had lung cancer history and not suitable for allogeneic stem cell transplantation; was planned HyperCVAD A/B chemotherapy protocol with the diagnosis of B-ALL. Dysarthria and impaired coordination of hand and foot movements occurred on the sixth days of second cycle of HyperCVAD-B chemotherapy. In neurologic examination, dysarthric speech, measured and sequential motion tests for cerebral examination was failed and no motor deficits. No mass or vascular pathology were detected in imaging examinations that could explain the patient's complaint. As a result, the patient was evaluated acute cerebellar syndrome caused by high dose cytosine arabinoside side effect by neurology department. From the eleventh day of treatment patient's complaints was regressed and come back to normal at fifteenth days of treatment.

Conclusion: Acute cerebellar syndrome begins 3–8 days after the start of drug administration. Cerebellar symptoms such as dysarthria, dysdiadokokinesia, dysmetry and ataxia greatly improved after stopping the drug however these symptoms may not full recover in approximately 1/3 of patients. Therefore there is not any treatment for neurological side effects, it should be kept in mind in chemoterapy treatment planning. While planning treatment, dose adjustment considering side effects as performance and age of patient. Nearly monitored is most important for early diagnosed of neurological symptoms.

https://doi.org/10.1016/j.htct.2020.09.064

PP 03

An unusual case report: myeloid sarcoma presented with appendicitis

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Objective: Myeloid sarcomas (MS) also called as granulocytic sarcomas, myeloblastoma or chloromas are the representatives of extramedullary infiltrates of immatur myeloid cells. According to 2016 revısıon to the World Health Organization classification of myeloid neoplasms and acute leukemia; it is classified a subgroup of Acute myeloid leukemia (AML) and related neoplasms. MS has more aggressive clinical course than AML. MS may present simultaneously with or precede bone marrow disease or may be seen in relapse. Isolated myeloid sarcoma involvement is most frequently detected in the bone, periosteum, soft tissues and lymph nodes. Herein we reported an unusual case of a 44 year old man who presented to appendicitis and diagnosed with MS with appendicitis pathology report.

Case report: A 44 year-old man who had no history of smoking, alcohol or any chronic disease, was admitted to the hospital with sudden abdominal pain, nause and vomiting. The patient, who was diagnosed with appendicitis and was underwent appendectomy. The patient's appendectomy result was reported as MS. In the blood test examination; white blood cells (WBC): $43.2 \times 10^3/\mu L$; neutrophil: $36.3 \times 10^3/\mu L$; monocyte: $2 \times 10^3/\mu L$, hemoglobin:11.5 g/dL, and plateletes:$100 \times 10^3/\mu L$ were detected. Peripheral smear was applied to the patient due to leukocytosis. Blastic cell infiltration was detected in peripheral smear and the patient underwent bone marrow biopsy. More than 20% monoblasts were observed in bone marrow aspiration. Flowcytometric examination was performed and immunfenotypic finding MS of the patient were interpreted of AML M5. Remission induction chemotherapy (daunorubucin 60 mg/m^2 110 mg/daily throughout 3 days and ARA-C 100 mg/m^2 180 mg/daily, throughout 7 days) was planned.

Conclusion: Hematological malignancies could involve extramedullary soft tissue in relatively rare cases. MSs are rare extramedullary tumors, most commonly occur in patient with acute or chronic myeloid leukemia (1–3). De novo MS may represent the first sign of systemic disease. Untreated MS usually progress to AML in about 1 year. The clinical presentation of MS depends on location, size of mass. In the current case a sudden right lower abdominal pain, nause and vomiting due to blastic infiltraion and obstruction of appendix were initial symptoms. Total excision of the mass is to gold standard for diagnosis. In the current case, appendix patology results showed that monoblastic and localize inflitration of cell form of monocytoid with large nucleolus, prominent nucleoli, wide cytoplasm, Ki 67 proliferative activity >. There is no consensus of MS treatment. Recommended treatment regimen for isolated MS or MS with AML is conventional AML protocols. In conclusion, MS is a subgroup of AML present with myeloblastic

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infiltration of soft tissue. MS may present at any time of disease process and any localization. It should be kept in mind that hematological malignancies may be seen all over the body and may be present atypically because early diagnosis and treatment are very important cause of MS's aggressive clinical course.

https://doi.org/10.1016/j.htct.2020.09.065

PP 04

Postdural puncture superior sagittal sinus thrombosis during remission induction therapy for acute lymphoblastic leukemia

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[2] *University of Health Sciences Bakırkoy Dr. Sadi Konuk Training and Research Hospital, Department of Radiology, İstanbul, Turkey*

Objective: Superior sagittal sinus thrombosis (SSST) during the course of acute lymphoblastic leukemia (ALL) may arise during or even after treatment. Majority of the cases are either directly attributed to ALL or considered as a consequence of using chemotherapy agents including prednisone, vincristine, cytarabine and especially L-Asparaginase. Post-lumbar puncture intracranial hypotension is a rarely encountered cause of SSST in ALL.

Case report: A 27-year-old man was admitted with fatigue and following bone marrow aspiration and biopsy, he was diagnosed as having B-ALL. He received HyperCVAD regimen as remission induction therapy, which included doxorubicine, vincristine and cyclophosphamide, dexamethasone and intrathecal administration of methotrexate. Cranial computerized tomography (CT) prior to intrathecal methotrexate was normal. Cerebrospinal fluid analysis was acellular and showed no ALL infiltration. He complained of mild postural headache intrathecal treatment. Eight days after intrathecal administration of methotrexate on day 13 of HyperCVAD, he complained of newly developing non-postural headache and vomiting.

Methodology: At the time of symptoms, complete blood count showed the following: WBC: 5480/uL, Hgb: 12.3 g/dL and PLT: 148,000/uL. Coagulation profile studies showed prothrombin time of 13 s, partial thromboplastin time (PTT) of 30.9 s, and normal concentrations of fibrinogen. Neurologic examination including evaluation of his mental status, sensory, motor, and reflex functions of his extremities. Coronal plane contrast enhanced T1-weighted MRİ demonstrated a nonenhancing superior sagittal sinus with the empty delta sign, compatible with a diagnosis of SSVT. Enoxaparin 2×1 mg/kg was initiated. Platelet transfusions were given to keep platelet count over 50,000/uL during the course of anticoagulant therapy.

Results: SSST in the context of ALL has been ascribed to lymphoblastic infiltration of the superior sagittal sinus wall or to the chemotherapeutic agents used. L-Asparaginase decreases plasma antithrombin, plasminogen, and fibrinogen concentrations while prednisone may increase the levels of factor VIII. These hemostatic changes may predispose to thrombosis, especially in the setting of the turbulent flow in the superior sagittal sinus. Our patient harbored none of the aforementioned risk factors except for the use of corticosteroids. Any cause of intracranial hypotension, which induces a downward shift and traction of the brain, may disrupt the veins/sinus and hence may lead to venous dilatation and thrombosis.

Conclusion: Our patient most probably developed intracranial hypotension due to lumbar puncture, which resulted in SSST. The possibility of a dural venous thrombosis should be suspected in patients with ALL who had treatment with L-asparaginase and prednisone. However, SSST thrombosis should also be an important consideration in patients with dural puncture who report a changing pattern of their headache (postural headache becoming nonpostural in character) and severe nausea and vomiting.

https://doi.org/10.1016/j.htct.2020.09.066

PP 05

Retrospective analysis of all patients single center experience

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[2] *19 Mayıs University Department of Internal Medicine, Samsun, Turkey*

Objective: The aim of study was to evaluate the demographic, clinical, laboratory, genetic and pathological features of the patients followed with the diagnosis of adult ALL in our center and to evaluate their contribution to the prognosis, treatment responses and overall survival rates of the patients and to contribute to the literature.

Methodology: A total of 116 patients diagnosed with ALL in our center between 2006–2018 were included in the study. Patients under 18 years of age and patients with active solid organ malignancies were not included in our study. The data of the patients were obtained by scanning the hospital computer automation system and patient files.

Results: Sixty-two of our patients are male and 54 are female. The mean age of the patients was 43.1 years. Twenty patients were T-ALL and 96 patients were B-ALL. In a quarter of patients, the Philedelphia chromosome was positive. 22 of our patients had standard risk and 94 had high risk class. Total survival rate was 52.6%. The mean total survival time was 41,4 months. 83.6% of the patients were in remission with induction therapy. Forty patients underwent allogeneic stem cell transplantation. There was no statistically significant difference between B-ALL, T-ALL and Ph+ ALL patients in terms of remission induction and survival. Tyrosine kinase inhibitors improved the prognosis of Ph+ ALL patients. In patients who received TKI treatment, the decrease in PCR values at the 3rd month was found to be a good prognostic factor. PCR monitoring is important in predicting prognosis in patients receiving

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PP 05

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TKI. The presence of severe fibrosis in the bone marrow (Grade 2–4) was found to be poor prognostic.

Conclusion: In our study, although the overall survival rate is consistent with the literature, it is evident that it is still insufficient. Therefore, more study and innovation are needed in the treatment of adult ALL.

https://doi.org/10.1016/j.htct.2020.09.067

PP 06

Case report: acute lymphoblastic leukemia with bone involvement

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Objective: ALL is the most common type of acute leukemia in children, after AML in adults. At the time of diagnosis, there may be weakness due to anemia, signs of bleeding due to thrombocytopenia, signs of infection related to neutropenia. There may be bone pain due to expansion of the medullary cavity by the leukemic process. However, low back pain due to vertebral body collapse is one of the rare symptoms at the time of diagnosis. We are reporting an adult male patient with acute lymphoblastic leukemia who presented with paraparesis and multiple osteolytic lesions in lomber and thoracal vertebra.

Case report: A 63-year-old male patient had a complaint of back pain for 4 months, spreading to the left leg, accompanied by numbness and loss of strength. The patient without incontinence and painful walking was operated by the neurosurgery department. The patient with pancytopenia was consulted to us. In physical examination peripheral LAP was not detected and spleen size was determined as 16.5 cm by ultrasound. In the laboratory examination was remarkable for Hb: 9 g/dL, MCV: 79 fL, plt: $13*10^3$/uL, sedim 76 mm/h LDH: 1092 u/L. Other biochemical tests are normal. The L2 corpus pathological fracture biopsy result was determined as CD45+, Cd19+, Cd10+, TDT+, PAX 5+, c myc 30%+, Kİ 67% 50+, and was compatible with B lymphoblastic lymphoma infiltration. In bone marrow biopsy, 98% cellularıty, 99% blastic infiltration was detected. Blasts were CD34+, CD19+, PAX 5+, 80% CD10+, 80% TDT+, 50% CD22+, 30% CD20+, CD123+, respectively. Cytogenetics and fluorescence in situ hybridization (FISH) panel for ALL were normal; Philadelphia chromosome was not present. HyperCVAD chemotherapy was started for the patient who was diagnosed with B-ALL+ bone involvement. Intrathecal chemotherapies were given. After Hyper CVAD 2B chemotherapy, the patient was clapped due to sepsis.

Conclusion: Skeletal lesions can occur in a variety of malignant hematological conditions. In diseases such as multiple myeloma and waldenstrom macroglobulinemia, bone involvement is a common finding in diagnosis. Acute lymphoblastic leukemia and lymphomas can rarely present with osteolytic lesions and neurological involvement. ALL is a chemosensitive tumor, so chemotherapy is the main treatment option. In patients with bone involvement, radiotherapy and surgical resection are the other treatment options that can be applied.

https://doi.org/10.1016/j.htct.2020.09.068

CHRONIC LEUKEMIAS

PP 07

Chronic lymphocytic leukemia presenting as pulmonary involvement in an elderly patient: a case report

O. Ekinci[1,*], A. Dogan[2], M. Aslan[1], I. Aras[3], C. Demir[2]

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[2] *Department of Hematology, Faculty of Medicine, Yüzüncü Yıl University, Van, Turkey*
[3] *Department of Pathology, Faculty of Medicine, Yüzüncü Yıl University, Van, Turkey*

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Case report: An 82-year-old male patient presented to our hospital with progressive dyspnea, non-productive cough, and weight loss, which had persisted for one month. Chest X-ray radiography revealed opacity in the lower zone of the right lung. Contrast computed tomography (CT) of the chest visualized a soft-tissue density measuring approximately 74 mm × 75 mm in maximal axial dimensions in the inferior segment of the right middle lobe with surrounding ground-glass density and some air bronchogram localized near the medial hilum. Laboratory test results were as follows: hemoglobin level, 13.4 g/dL; total leukocyte count, 174×10^9/L; lymphocyte count, 148×10^9/L; platelet count, 192×10^9/L. Peripheral blood smear showed diffuse mature small lymphocytes and smudge cells. Peripheral blood flow cytometry revealed strong positivity for the CD5, CD20, CD19, and CD23 markers, consistent with CLL. A bronchoscopy was performed for diagnostic purposes and a transbronchial biopsy was taken from the lung parenchyma, and bronchoalveolar lavage (BAL) was performed. BAL cytology and microbiological tests were not diagnostic. On immunohistochemical examination of the parenchymal biopsy, neoplastic cells showed a CD20(+), CD5(+), CD23(+), CK(−), CK7(−), CK20(−), CD56(−), synaptophysin(−), chromogranin-A(−), CD3(−), TTF-1(−), Napsin A(−), and P63(−) staining pattern. The Ki67 proliferation index was 10%. The pathology clinic reported the result to be consistent with a chronic lymphocytic leukemia/small lymphoma infiltration. Cervical and abdominopelvic CT results of the patient were also considered and the CLL stage was determined as RAI 2

TKI. The presence of severe fibrosis in the bone marrow (Grade 2–4) was found to be poor prognostic.

Conclusion: In our study, although the overall survival rate is consistent with the literature, it is evident that it is still insufficient. Therefore, more study and innovation are needed in the treatment of adult ALL.

https://doi.org/10.1016/j.htct.2020.09.067

PP 06

Case report: acute lymphoblastic leukemia with bone involvement

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[2] *Afyonkarahisar Health Sciences University Hospital, Pathology Department, Afyonkarahisar, Turkey*

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CHRONIC LEUKEMIAS

PP 07

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PP 06

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CHRONIC LEUKEMIAS

PP 07

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(moderate risk) and Binet B (moderate risk). However, in consideration of his weight loss and symptomatic extranodal involvement, a chemotherapy protocol with bendamustine and the CD20 antibody rituximab (BR) was initiated. BR treatment was administered every 28 days for up to 6 courses. The patient's symptoms demonstrated marked improvement after two cycles of chemotherapy. After a total of 4 courses, lymphocytosis in the peripheral blood showed complete remission and the involvement that had been visualized on direct chest radiography and CT showed nearly complete remission. After 6 cycles of chemotherapy, the patient was considered in complete remission and follow-up was started.

Conclusion: Pulmonary complications and involvement in CLL typically occur after the diagnosis, in the course of the disease, while there are cases who present as pulmonary involvement (broncho-pulmonary infiltrates, hilar and mediastinal lymphadenopathies, pleural effusion, etc.), although much less frequently. Pulmonary involvement must be considered in patients diagnosed with CLL who have symptoms associated with the respiratory system. Particularly in patients diagnosed with broncho-pulmonary lesions based on peripheral blood analysis or lymph node biopsy, CLL-associated involvement should certainly be included in the differential diagnosis when the most common causes are excluded.

https://doi.org/10.1016/j.htct.2020.09.069

PP 08

Frequency of brucellosis and hepatitis b virus seropositivity in patients with chronic lymphocytic leukemia

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[1] *Department of Hematology, Faculty of Medicine, Fırat University, Elazığ, Turkey*
[2] *Department of Hematology, Faculty of Medicine, Yüzüncü Yıl University, Van, Turkey*

Objective: Chronic lymphocytic leukemia (CLL) is a disease characterized by an increase in mature neoplastic lymphocytes in tissues with a lymphoid component, such as peripheral blood, bone marrow, lymph node, spleen, and liver. Patients with CLL show defective cellular and humoral immune responses. Although such immune failure is known to be associated with an increase in the frequency of particularly gram-positive and -negative bacterial infections, data on the increase in the frequency of zoonoses such as brucellosis and viral infections such as the hepatitis B virus (HBV) are inconclusive. This study aims to investigate the frequency of brucellosis and HBV seropositivity in patients diagnosed with CLL.

Methodology: Patients followed-up for CLL between 2005 and 2019 were evaluated. Results of patients who were tested for HBsAg and anti-HBs serology using the ELISA assay and for Brucellosis using the serum (Wright) agglutination test were recorded. Demographic data and laboratory results of all patients included in the study were evaluated.

Results: This study included 188 patients diagnosed with CLL, of whom 56 (29.8%) were female and 132 (70.2%) were male. The median age was 62 (range: 33–92) years. Complete blood count parameters at diagnosis were as follows: median leukocyte count, 54.4×10^9/L; median lymphocyte count, 42.3×10^9/L; median platelet count, 148×10^9/L; median hemoglobin level, 13.4 g/dL. HBsAg and anti-HBs were tested in 142 patients. A total of 16 (11.27%) patients were HBsAg-positive; with 5 (3.52%) positive cases in females and 11 (7.75%) in males. A total of 105 (73.95%) patients were anti-HBs-positive; with 32 (22.54%) positive cases in females and 73 (51.41%) in males. The Wright agglutination test was performed on 82 patients. A total of 4 (4.88%) patients reacted positively to the Wright test; with 3 (3.66%) positive cases in females and 1 (1.22%) in males.

Conclusion: The immune system disorders that develop due to the nature of CLL make the patient more vulnerable to infections. Accordingly, many patients lose their lives due to a clinical picture of severe infection. Based on the present study, compared with the epidemiological studies conducted in the same region; the rate of positive reactions to the Wright agglutination test was consistent with the literature data; however, a higher rate of HBsAg positivity was determined. This may be linked to the increase in the risk of HBV transmission due to the immune defect caused by CLL or the immunosuppressive picture induced by the medication used in the treatment, or viral reactivation.

https://doi.org/10.1016/j.htct.2020.09.070

PP 09

Epidemiological spectrum and diagnosis patterns of hematological malignancies in the republic of moldova

V. Musteata[1,*], L. Catrinici[2], V. Stratan[2], L. Musteata[1]

[1] *State University of Medicine and Pharmacy, Chișinău, Republic of Moldova*
[2] *Institute of Oncology, Iași, Romania*

Objective: Hematological malignancies (HM) are the relatively frequent nosological entities within the structure of morbidity by malignant tumors, exhibiting a severe evolution, restrained prognosis and negative socio-economic impact in the advanced stages and phases. The objective of the study was to analyze the incidence and diagnosis patterns of HM in Moldova.

Methodology: The following research methods were used: epidemiological, descriptive statistics, clinico-analytic. The type of HM was identified according to the Revised 2017 WHO Classification of Tumours of Hematopoietic and Lymphoid Tissues. The diagnosis was proved by histopathological, cytological, cytogenetic, molecular and immunophenotyping examinations. The quantitative real-time PCR was used in order to assess the expression of BCR-ABL p210 and p190 transcripts for CML diagnosis. The quantitative detection of JAK2 V617F mutation served as a major criterion for diagnosis of polycythemia vera (PV) and primary myelofibrosis (PMF).

Results: The number of newly diagnosed and followed-up patients with HM at the Institute of Oncology in 2016, 2017, 2018 and 2019 amounted respectively to 725, 802, 613 and 628, the incidence (new cases per 100,000 population) being 17.6,

(moderate risk) and Binet B (moderate risk). However, in consideration of his weight loss and symptomatic extranodal involvement, a chemotherapy protocol with bendamustine and the CD20 antibody rituximab (BR) was initiated. BR treatment was administered every 28 days for up to 6 courses. The patient's symptoms demonstrated marked improvement after two cycles of chemotherapy. After a total of 4 courses, lymphocytosis in the peripheral blood showed complete remission and the involvement that had been visualized on direct chest radiography and CT showed nearly complete remission. After 6 cycles of chemotherapy, the patient was considered in complete remission and follow-up was started.

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PP 08

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[2] *Institute of Oncology, Iași, Romania*

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Methodology: The following research methods were used: epidemiological, descriptive statistics, clinico-analytic. The type of HM was identified according to the Revised 2017 WHO Classification of Tumours of Hematopoietic and Lymphoid Tissues. The diagnosis was proved by histopathological, cytological, cytogenetic, molecular and immunophenotyping examinations. The quantitative real-time PCR was used in order to assess the expression of BCR-ABL p210 and p190 transcripts for CML diagnosis. The quantitative detection of JAK2 V617F mutation served as a major criterion for diagnosis of polycythemia vera (PV) and primary myelofibrosis (PMF).

Results: The number of newly diagnosed and followed-up patients with HM at the Institute of Oncology in 2016, 2017, 2018 and 2019 amounted respectively to 725, 802, 613 and 628, the incidence (new cases per 100,000 population) being 17.6,

19.5, 14.9 and 17.7. In 2019 Hodgkin lymphoma was diagnosed in 9.4% of cases, non-Hodgkin lymphomas – in 36.4%, multiple myeloma and plasma cells neoplasms – in 8.6%, lymphoid leukemias – in 13.7%, myeloid leukemias – in 8.3%, monocytic leukemias – in 1.7%, and other leukemias – in 19.8%. The male's rate was 51.5%, the female's rate – 48.5%. The age of 50–79 years prevailed in both genders (males – 65%, females – 72.5%). The children constituted 4.0% of newly diagnosed cases and 4.8% of those under the follow-up at the end of the year. Regarding the chronic myeloproliferative neoplasms (CMN), prefibrotic stage of PMF was confirmed in 42.1% of cases, fibrotic stage – in 57.9%. The diagnosis of CML was asserted in chronic phase in 89.3% of patients and in accelerated phase in 10.7%. PV was diagnosed in erythremic stage in all cases: II A – in 87.1% of cases, IIB – in 12.9%. The age group of 60–69 years proved to be more numerous in PV (80.6%), as compared with CML (53.4%) and PMF (52.6%) cases. The disease span range from the onset to diagnosis was 1.4–7 months (median – 3.5 ± 0.63 months) in PMF, 1.5–12 months (median – 2.1 ± 0.37 months) in CML, and 1–8 months (median – 3.8 ± 0.54 months) in PV. The clinical onset and addressability of patients with CML and PMF did not significantly differ, the absolute majority (over 90%) being consulted by the family doctors because of the appearance of fatigue, left upper hemiabdomen heaviness and pain. The majority of PV patients (67.7%) addressed for the medical care by reason of a stable arterial hypertension and astheno-vegetative syndrome.

Conclusion: The incidence of malignant lymphomas and leukemias in Moldova emerged rather lower than in the majority of European countries mainly due to the migration of a workable population. Mostly the 50–79 years old males proved to be affected. PV yielded to be less frequently registered CMN, diagnosed more tardily due to the resemblance with cardiovascular disorders.

https://doi.org/10.1016/j.htct.2020.09.071

PP 10

A rare case: coexistence of small cell lung cancer and chronic lymphocytic leukemia

M. Tıglıoglu, B. Saglam, M. Reis Aras*, F. Yılmaz, U. Malkan, H. Afacan Ozturk, P. Akyol, M. Albayrak

Diskapi Yildirim Beyazit Training and Research Hospital, Department of Hematology, Ankara, Turkey

Objective: The most common type of leukemia in adults; chronic lymphocytic leukemia (CLL), which is detected in 25% of all leukemias. In epidemiological studies in western societies, its incidence was found to be 4/100,000. CLL is an advanced age disease and its incidence increases with age. While some of the patients are followed up asymptomatically and with lymphocytosis without any treatment indications, others may show aggressive clinical course, appear with cytopenia and cause chemotherapy indications. Suppression of immunity and B cell dysfunction in CLL can cause secondary malignancies. In a much rarer group of patients, the diagnosis of CLL and solid organ cancer is made simultaneously. In such cases, pathological or cytogenetic common mechanisms or common risk factors such as smoking and radiation may play a role in etiology. We also wanted to present the coexistence of small cell lung cancer (SCLC) and CLL, which are rarely diagnosed simultaneously, and may contribute to the literature.

Case report: In the examination of a 82-year-old male with a history of smoking 30 packs/year, who suffered from ongoing loss of balance for approximately 1 month, an irregular limited mass with a size of 3×2 cm was detected in the upper left lobe. The fine needle biopsy result from the mass was reported as SCLC and was considered Stage 3 in the evaluation. The patient was started on cisplatin 75 mg/m^2 + etoposide 100 mg/m^2 chemotherapy protocol treatment by department of pulmonary diseases. During the diagnosis process, the patient, who was found to have had long-standing lymphocytosis, was also asked for flow cytometry examination upon monitoring of mature lymphocyte infiltration and basket cells in the peripheral smear examination. In flow cytometric examination, CD5, CD19, CD20, CD23 were positive and CD10, CD103 were negative and these findings were reported as B-lymphoproliferative disease (CLL). The patient, who was evaluated as stage 1 CLL with detailed blood tests and imaging, was followed up without treatment. During follow-up, in the evaluation of the patient with deep anemia, the direct coombs test was positive (IgG) and the biochemical markers were compatible with hemolysis, 60 mg/day (1 mg/kg/day) methylprednisolone treatment was started for the patient who was diagnosed with autoimmune hemolytic anemia. With the initiation of corticosteroid therapy, a significant increase in both hemoglobin value and improvement in hemolysis parameters of the patient was observed and treatment was continued by decreasing the dose. The patient, whose steroid treatment is completed and hemogram parameters are monitored within normal limits, is followed up without treatment by the hematology department in terms of CLL. At the same time, the third cycle of chemotherapy has been completed with the diagnosis of SCLC and is followed by the department of pulmonary diseases.

Conclusion: CLL constitutes a high risk factor for many solid tumors such as lung, breast, colon and prostate cancer. In a study in which 4.869 CLL patients were screened for secondary malignancy, 33 lung cancers were detected and SCLC was 6% among all lung cancers.

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PP 11

Stevens–Johnson syndrome secondary to rituximab administration in a chronic lymphocytic leukemia patient

V. Tomacinschii*, M. Robu, S. Buruiana, V. Musteata

Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

Objective: Stevens–Johnson syndrome (SJS) is an acute hypersensitivity reaction that compromises the integrity of mucous membranes and cutaneous tissue. Chronic

19.5, 14.9 and 17.7. In 2019 Hodgkin lymphoma was diagnosed in 9.4% of cases, non-Hodgkin lymphomas – in 36.4%, multiple myeloma and plasma cells neoplasms – in 8.6%, lymphoid leukemias – in 13.7%, myeloid leukemias – in 8.3%, monocytic leukemias – in 1.7%, and other leukemias – in 19.8%. The male's rate was 51.5%, the female's rate – 48.5%. The age of 50–79 years prevailed in both genders (males – 65%, females – 72.5%). The children constituted 4.0% of newly diagnosed cases and 4.8% of those under the follow-up at the end of the year. Regarding the chronic myeloproliferative neoplasms (CMN), prefibrotic stage of PMF was confirmed in 42.1% of cases, fibrotic stage – in 57.9%. The diagnosis of CML was asserted in chronic phase in 89.3% of patients and in accelerated phase in 10.7%. PV was diagnosed in erythremic stage in all cases: II A – in 87.1% of cases, IIB – in 12.9%. The age group of 60–69 years proved to be more numerous in PV (80.6%), as compared with CML (53.4%) and PMF (52.6%) cases. The disease span range from the onset to diagnosis was 1.4–7 months (median – 3.5 ± 0.63 months) in PMF, 1.5–12 months (median – 2.1 ± 0.37 months) in CML, and 1–8 months (median – 3.8 ± 0.54 months) in PV. The clinical onset and addressability of patients with CML and PMF did not significantly differ, the absolute majority (over 90%) being consulted by the family doctors because of the appearance of fatigue, left upper hemiabdomen heaviness and pain. The majority of PV patients (67.7%) addressed for the medical care by reason of a stable arterial hypertension and astheno-vegetative syndrome.

Conclusion: The incidence of malignant lymphomas and leukemias in Moldova emerged rather lower than in the majority of European countries mainly due to the migration of a workable population. Mostly the 50–79 years old males proved to be affected. PV yielded to be less frequently registered CMN, diagnosed more tardily due to the resemblance with cardiovascular disorders.

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Case report: In the examination of a 82-year-old male with a history of smoking 30 packs/year, who suffered from ongoing loss of balance for approximately 1 month, an irregular limited mass with a size of 3×2 cm was detected in the upper left lobe. The fine needle biopsy result from the mass was reported as SCLC and was considered Stage 3 in the evaluation. The patient was started on cisplatin 75 mg/m^2 + etoposide 100 mg/m^2 chemotherapy protocol treatment by department of pulmonary diseases. During the diagnosis process, the patient, who was found to have had long-standing lymphocytosis, was also asked for flow cytometry examination upon monitoring of mature lymphocyte infiltration and basket cells in the peripheral smear examination. In flow cytometric examination, CD5, CD19, CD20, CD23 were positive and CD10, CD103 were negative and these findings were reported as B-lymphoproliferative disease (CLL). The patient, who was evaluated as stage 1 CLL with detailed blood tests and imaging, was followed up without treatment. During follow-up, in the evaluation of the patient with deep anemia, the direct coombs test was positive (IgG) and the biochemical markers were compatible with hemolysis, 60 mg/day (1 mg/kg/day) methylprednisolone treatment was started for the patient who was diagnosed with autoimmune hemolytic anemia. With the initiation of corticosteroid therapy, a significant increase in both hemoglobin value and improvement in hemolysis parameters of the patient was observed and treatment was continued by decreasing the dose. The patient, whose steroid treatment is completed and hemogram parameters are monitored within normal limits, is followed up without treatment by the hematology department in terms of CLL. At the same time, the third cycle of chemotherapy has been completed with the diagnosis of SCLC and is followed by the department of pulmonary diseases.

Conclusion: CLL constitutes a high risk factor for many solid tumors such as lung, breast, colon and prostate cancer. In a study in which 4.869 CLL patients were screened for secondary malignancy, 33 lung cancers were detected and SCLC was 6% among all lung cancers.

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Case report: We report the case of a 49 years old caucasian male that four years previously was diagnosed with CLL stage A Binet. The "watch and wait" strategy was adopted at that time. But the patient disappeared from the current supervision of the hematologist and returned after 4 years with B symptoms, giant splenomegaly, hepatomegaly, peripheral lymphadenopathy, and bicytopenia (anemia and thrombocytopenia) that accompanied the lymphocytosis in peripheral blood. Stage C Binet was established, and for this patient was proposed the initiation of treatment with chemoimmunotherapy type FCR according to guidelines. But, the patient refused to administer any type of chemotherapy and in the absence of new targeted therapeutic alternatives, the most plausible solution was to initiate monotherapy with Rituximab 375 mg/m^2 weekly. On the 3rd day after the second administration of rituximab, he experienced a febrile episode 38.5 °C, fatigue, and weakness, moderate pain all over the skin, which were aggravated by a slight touch and a non-pruritic widespread maculopapular rash, which affects the oral mucosa and also the skin in the genital area, palmar and plantar region. SJS was diagnosed affecting 12% of total body surface area according to the Lund-Browder Burn calculator. Rituximab therapy was stopped and immediate treatment of SJS has started. Patients received supportive care measures including hydration, wound debridement, systemic and topical antibiotics, topical and systemic corticosteroids, nutritional support, and pain management for 4 weeks with a total recovery of skin and mucosal lesions.

Conclusion: Although SJS is a rare complication of Rituximab therapy (0.01% in a series of 167,000 patients), it remains a dreaded complication with a 30% mortality rate among patients who develop it. Recognition of clinical signs and prompt diagnosis along with complex therapy can ensure adequate recovery of the case.

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CHRONIC MYELOPROLIFERATIVE DISEASES

PP 12

Concomitant essential thrombocythemia and mature B-lymphoproliferative disorder in a patient

A. Butt*, R. Qudus, N. Ali

Aga Khan University Hospital, Karachi, Pakistan

Objective: ET and B-LPD are two distinct, clonal hematologic malignancies with their concomitant existence in a single individual being exceedingly rare.

Case report: A 64-year-old male was admitted with cough, weight loss, maculopapular rash and elevated platelet counts. The rash was present on his face and trunk for 20 days and he had non-productive cough for the past two weeks. On examination, he was found to have cervical lymphadenopathy and splenomegaly (5 cm below left costal margin). His blood counts were as follows: hemoglobin 10.8 g/dl, hematocrit 37.2%, RBC mass 5.34×10^{12}/L, WBC 62.1×10^9/L, platelets 1169×10^9/L. LDH was found to be 816 IU/L and C-reactive protein was 2.43 mg/dl. Peripheral blood film showed anisocytosis, poikilocytosis, elliptical cells, tear-drop cells, nucleated red blood cells, myelocytes and metamyelocytes. Platelets were markedly increased on film. Leucoerythroblastic blood picture was noted. Suspecting a myeloproliferative disorder, additional investigations were sent while the patient was started on hydroxyurea 1gm daily and allopurinol 100 mg daily in addition to antibiotics. Bone marrow aspirate depicted increase in lymphoid cells that constituted around 35% of the total nucleated non-erythroid cell population. M:E ratio was 4:1. Bone trephine showed hypercellularity for age with overall cellularity 90 to 95%. Cellular areas exhibited increase in myeloid precursors along with prominent lymphoid cells and abundant megakaryocytes. Pan-T (CD03) and Pan-B (CD20) marker by immunohistochemistry was applied on bone trephine biopsy specimen which was interpreted as increase in B-lymphocytes. Reticulin stain showed grade MF-2 reticulin fibrosis. Overall findings were suggestive of essential thrombocythemia. In view of increased CD20 positive cells, immunophenotyping by flow cytometry was recommended. CD45 positive lymphoid cells population was 31%. This population showed reactivity to Pan-B-markers i.e. CD19 (26%), CD20 (27%), CD22 (26%), CD23 (11%) and cCD79a (30%) along with HLA-DR (12%) and CD45 (35%). Double bright positivity of CD19 and CD5 typical of CLL was absent. This population also showed positivity to lambda light chains restriction (kappa 0%, lambda 13%). Results were consistent with mature-B-lymphoproliferative disorder (B-LPD). JAK2 mutation was detected by PCR while BCR-ABL1 translocation was not detected by fluorescence in situ hybridization (FISH). Since double bright positivity for CD19 and CD5 was absent along with absence of FMC7, a diagnosis of mature-B-lymphoproliferative disorder was made. Cyclin D1 was applied on bone trephine, which was negative, and the infiltration did not reveal a follicular pattern. Ki67 was approximately 30%. A diagnosis of ET progressing to myelofibrosis and B-LPD was made. Patient was discharged in a stable condition and followed up on an outpatient basis. Ruxolitinib at a dose of 5 mg twice daily was initiated while hydroxyurea was reduced to 500 mg daily and then later to alternate day dosing. A wait and watch approach was adopted for the B-LPD Ruxolitinib was later increased to 10 mg twice daily. After a few months, ruxolitinib was switched to 15 mg daily with the counts remaining stable. The patient remains stable and asymptomatic two and half years later. The most recent blood counts show hemoglobin at 10.9 g/dl, WBC 31.1×10^9/L, and platelets 445×10^9/L.

Methodology: Retrospective review of case.

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Methodology: Retrospective review of case.

Conclusion: We report a rare case of ET with concomitant B-LPD. The patient is stable on Ruxolitinib and is on wait and watch approach for B-LPD.

https://doi.org/10.1016/j.htct.2020.09.074

PP 13

Acute phase reactants in chronic inflammation leading to secondary myelofibrosis in polycythemia vera and essential thrombocytosis

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Objective: Polycythemia vera and essential thrombocytosis are chronic and progressive myeloproliferative neoplasms characterized by a clonal increase in hematopoietic stem cells in the bone marrow. Myelofibrosis in the bone marrow has been shown to be secondary to an inflammatory process.

Methodology: To investigate the association between the secondary myelofibrosis and acute phase reactants in patients with polycythemia vera and essential thrombocytosis. Fourty-six PV and 28 ET patients without myelofibrosis above Grade 1 were included in the present study. Bone marrow evaluations were performed retrospectively. C-reactive protein, ferritin, and albumin levels were measured.

Results: C-reactive protein (0.55 ng/L vs. 4.2 ng/L, $p < 0.001$) and ferritin (18.5 ng/mL vs. 118 ng/mL, $p = 0.001$) levels in patients with secondary myelofibrosis were found to be increased compared to baseline levels. Mean albumin levels in patients with secondary myelofibrosis, and CRP, ferritin, and albumin levels in patients without secondary myelofibrosis were similar at the diagnosis and at last visit. There were also similar the baseline levels of CRP, ferritin, and albumin between the patients with and without secondary myelofibrosis.

Conclusion: The increase in CRP and ferritin, which are indicators of chronic inflammation, may be used to show the inflammation and relevant secondary fibrosis in the bone marrow. Due to the similar CRP, ferritin, and albumin levels at the diagnosis, the prediction for the development of the secondary myelofibrosis is not possible in the present study.

https://doi.org/10.1016/j.htct.2020.09.075

PP 14

Polycythemia vera: updates in diagnosis and treatment outcomes

L. Musteata[1,*], S. Pinzari[2], V. Musteata[1], N. Sghibneva-Bobeico[2], A. Dorogan[2]

[1] *State University of Medicine and Pharmacy, Chișinău, Republic of Moldova*
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Objective: The objective of the study was to analyze the contemporary clinical and laboratory features of polycythemia vera (PV), as well as to evaluate the short- and long-term results of different treatment options.

Methodology: The clinico-hematological evolution features, complications, short- and long-term results of cytoreductive treatment were evaluated in a group of 114 PV patients, aged at 28–78 years old, who were followed up at the Institute of Oncology of Moldova between 1987–2019. The diagnosis was proved by the bone marrow biopsy and quantitative detection of JAK2 V617F mutation in pending cases. Physical and histopathologic examinations were associated with the repeated complete blood counts and abdominal ultrasound scan. The treatment included phlebotomies and cytoreductive chemotherapy with busulfan (56 patients) and hydroxycarbamide (58 patients) in standard doses. The life-table method was used for Kaplan–Meier Survival Analysis in order to evaluate the long-term results of treatment.

Results: The disease was commonly diagnosed in males – 66 (57.9%) patients. The females prevailed in the age groups of 40–49 years (31.3% versus 24.6% in males) and 60–69 years (25% versus 19.8% in males). The disease span from the onset of the initial clinical manifestations until the diagnosis lasted 4–9 months (median – 5.8 months) in the majority of patients (86.8%), that led to the development of thromboembolic complications in 28.1% of cases. The diagnosis was proved in stage IIA disease in 105 (92.1%) patients, IIB in 9 (7.9%) patients. The skin hiperemia was registered in 112 (98.3%) cases, scleral congestion – in 109 (95.6%), splenomegaly – in 77 (67.5%), erythromelalgia – in 71 (62.2%), aquagenic skin itching – in 68 (59.6%), hepatomegaly – in 61 (53.5%), vascular thrombosis – in 32 (28.1%). The complete blood count revealed the increase of hemoglobin (18.0–23.5 g/dL) and red cells (5.5–6.7 × 1,000,000 [MICRO]/L). The platelets range was 180–1690 × 1000 [MICRO]/L, leukocytes range – 5.1–21.3 × 1000 [MICRO]/L. Leukocytosis occurred in 69 (60.5%) patients, thrombcytosis – in 61 (53.5%). The bone marrow biopsy detected a hyperplasia due to the proliferation of erythroid, granulocyte and megakaryocyte cell lines. The study of short-term results asserted the complete remissions in all cases under chemotherapy combined with phlebotomies. The overall one-, 5-, 10- and 15 year was 100%, 98.6%, 85.9% and 67.1%, respectively. 73 (64.04%) patients remain in stage II disease after the treatment during 5–26 years of follow-up. The survival median was not reached.

Conclusion: The reluctant evolution, progressive growth of hemoglobin and red cell count, gradual increase of blood hyperviscosity and the lack of hemato-oncological vigilance of primary care physicians may lead to the development of

Conclusion: We report a rare case of ET with concomitant B-LPD. The patient is stable on Ruxolitinib and is on wait and watch approach for B-LPD.

https://doi.org/10.1016/j.htct.2020.09.074

PP 13

Acute phase reactants in chronic inflammation leading to secondary myelofibrosis in polycythemia vera and essential thrombocytosis

E. Aladag[1], I. Haznedaroglu[1], N. Sayinalp[1], H. Demiroglu[1], H. Goker[1,*], S. Aksu[1], O. Ozcebe[1], A. Ayhan[2], Y. Buyukasik[1]

[1] *Hacettepe University Department of Hematology, Ankara, Turkey*
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Objective: Polycythemia vera and essential thrombocytosis are chronic and progressive myeloproliferative neoplasms characterized by a clonal increase in hematopoietic stem cells in the bone marrow. Myelofibrosis in the bone marrow has been shown to be secondary to an inflammatory process.

Methodology: To investigate the association between the secondary myelofibrosis and acute phase reactants in patients with polycythemia vera and essential thrombocytosis. Fourty-six PV and 28 ET patients without myelofibrosis above Grade 1 were included in the present study. Bone marrow evaluations were performed retrospectively. C-reactive protein, ferritin, and albumin levels were measured.

Results: C-reactive protein (0.55 ng/L vs. 4.2 ng/L, $p < 0.001$) and ferritin (18.5 ng/mL vs. 118 ng/mL, $p = 0.001$) levels in patients with secondary myelofibrosis were found to be increased compared to baseline levels. Mean albumin levels in patients with secondary myelofibrosis, and CRP, ferritin, and albumin levels in patients without secondary myelofibrosis were similar at the diagnosis and at last visit. There were also similar the baseline levels of CRP, ferritin, and albumin between the patients with and without secondary myelofibrosis.

Conclusion: The increase in CRP and ferritin, which are indicators of chronic inflammation, may be used to show the inflammation and relevant secondary fibrosis in the bone marrow. Due to the similar CRP, ferritin, and albumin levels at the diagnosis, the prediction for the development of the secondary myelofibrosis is not possible in the present study.

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Conclusion: The reluctant evolution, progressive growth of hemoglobin and red cell count, gradual increase of blood hyperviscosity and the lack of hemato-oncological vigilance of primary care physicians may lead to the development of

thrombotic and vascular complications in some PV cases. Chemotherapy improves significantly the patient's quality of life, reduces the rate of thromboembolic events and extends the life-span, comparable with that of total population of Moldova.

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PP 15

Disease and clinical characteristics of patients with chronic myeloproliferative neoplasms: 11-year single center experience

P. Akyol, A. Yıldız, H. Afacan Öztürk, S. Maral, M. Reis Aras*, F. Yılmaz, B. Saglam, M. Tıglıoglu, M. Albayrak

Diskapi Yildirim Beyazit Training and Research Hospital, Ankara, Turkey

Objective: BCR/ABL-negative myeloproliferative neoplasms are characterized by over-production myeloid lineages in the bone marrow. Polycythemia vera, essential thrombocythemia and primary myelofibrosis are the most common myeloproliferative neoplasms. Diagnosis is made according to the WHO diagnostic criteria from clinical data, hematological and biochemical analysis and BM histology. The aim of this study was to analyse patient demographic characteristics, clinical features, laboratory findings, mutational status together with complications, clinical course and survival.

Methodology: This study was conducted on patients diagnosed with myeloproliferative neoplasms between 2008 and 2019. Hemogram and biochemical parameters, demographic information, mutation analysis, management, complications and follow-up periods were recorded for all patients. Survival rates were calculated and the effect of the parameters on overall survival was analyzed.

Results: Evaluation was made of 247 patients, comprising 105 polycythemia vera, 126 essential thrombocythemia and 16 primary myelofibrosis patients. The overall frequency of driver mutations was 96.1% for PV, 71.4% for ET and 75% for PMF. Hydroxyurea was the most commonly used first-line treatment agent and the most common indication for switching to second-line treatment in all disease subgroups was the development of side-effects. During follow-up, 11 polycythemia vera, 14 essential thrombocythemia and 2 primary myelofibrosis patients developed thromboembolic complications. Median overall survival could not be reached in polycythemia vera and essential thrombocythemia patient and determined as 70.3 months in primary myelofibrosis patients. Age, LDH, ferritin and platelet/lymphocyte ratio at the time of diagnosis and thromboembolic complications were determined to have a statistically significant effect on survival in all patients.

Conclusion: Lower survival rates were seen in the primary myelofibrosis patients although thromboembolic complications were observed at similar rates in all 3 disease subgroups. In addition to known risk factors such as age and thromboembolic complications, parameters such as LDH, ferritin and PLR, which may be considered to indicate disease activity and inflammation, can also be used as prognostic markers.

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PP 16

The frequency of calreticulin and mpl gene mutations in bcr-abl and jak2 unmutated chronic myeloproliferative neoplasms and its effect on the outcome

T. Tiryaki[1], A. DağLar Aday[2], M. Güzel Mastanzade[1], M. ÖZbalak[1], D. Özlük[1], F.Y. Onal Hindilerden[1], M. Yenerel[1], A. Yavuz[1], S. Kalayoğlu Beşışık[1,*], M. Nalçacı[1]

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Objective: The World Health Organization (WHO) embedded calreticulin receptor (CalR) and myeloproliferative leukemia virus (MPL) gene mutation in diagnostic criteria for primary myelofibrosis (PMF) and essential thrombocythemia (ET), since 2016). We aimed to identify the frequency of CalR and MPL gene mutations and their effects on clinical outcomes in bcr-Abl and Jak2 unmutated chronic myeloproliferative neoplasms (MPNs).

Methodology: We screened bcr-abl negative and Jak2 unmutated MPNs diagnosed and treated between March 2004 and January 2013 at İstanbul Medical Faculty. We revised the MPN diagnosis according to the latest WHO classification. The association of CalR and MPL mutation with thrombotic complications, leukemic transformation, and survival was was defined.

Results: A total of 46 ET ($n = 34$) and PMF ($n = 12$) patients enrolled in the study. The demographic characteristics were similar between the two disease groups. Patients' mean age was 53.5 years (range 23–93 years) and gender distribution as 18 male to 28 female. A total of 18 patients (39.1%) had CalR mutation, and 4 (8.69%) patients MPL mutation. None of the ET patients had MPL mutations. CalR positive PMF patients' mean age was lower compared to patients without the mutation (p: 0.028). During the follow-up period, 8.3% of PMF and 5.9% of ET patients experienced leukemic transformation. None of the leukemic transformed patients had gene mutations. Among thrombosis complications, six patients developed thrombosis. All of them were ET patients, and 3 of them had CalR mutation two as CalR type 1 and one as CalR type 2. The mortality ratio was higher in patients in PMF, regardless of mutational status (p: 0.006).

Conclusion: Our study cohort is small to make a definite conclusion. Apart from the diagnostic guide, CALR mutations seem to have a prognostic effect is different in PMF and ET. This prognostic significance of CALR could be different among the MPN categories.

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Results: Evaluation was made of 247 patients, comprising 105 polycythemia vera, 126 essential thrombocythemia and 16 primary myelofibrosis patients. The overall frequency of driver mutations was 96.1% for PV, 71.4% for ET and 75% for PMF. Hydroxyurea was the most commonly used first-line treatment agent and the most common indication for switching to second-line treatment in all disease subgroups was the development of side-effects. During follow-up, 11 polycythemia vera, 14 essential thrombocythemia and 2 primary myelofibrosis patients developed thromboembolic complications. Median overall survival could not be reached in polycythemia vera and essential thrombocythemia patient and determined as 70.3 months in primary myelofibrosis patients. Age, LDH, ferritin and platelet/lymphocyte ratio at the time of diagnosis and thromboembolic complications were determined to have a statistically significant effect on survival in all patients.

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PP 17

Study of JAK2V617F gene allele burden in polycythemia vera

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National Center of Hematology and Blood Transfusion, Cầu Giấy, Viet Nam

Objective: In recent years, it became necessary to identify a new clinical form of polycythemia vera – latent polycythemia vera (LPV). Considering the significant role of the JAK2V617F gene in the pathogenesis of LPV, we investigated the relationship between the allele burden of the JAK2V617F gene and clinical and laboratory parameters of the disease.

Case report: Patient G.N., at the age of 64, complained of pain in the legs, itching during bathing, weakness, headaches. He had been ill for several years. He suffered from glaucoma, as a result of which he acquired blindness. For a long period paresthesias, erythromelalgia and a gradual impairment of movement in the lower extremities had been observed. The patient was observed by a neurologist with a diagnosis of sensory neuropathy. Recently pain in the legs intensified and there were difficulties in walking. Due to changes in the hemogram, the patient was sent for a consultation to a hematologist. During examination, hyperemia on the face, traces of scratching were visible on the skin. On palpation, the spleen was enlarged by 1.5 cm. In laboratory analysis in the hemogram Hb-185 g/L, RBC-6.96 $\times 10^{12}$/L, Ht-58.5%, WBC-13.4 $\times 10^{9}$/L, PLT-471 $\times 10^{9}$/L. Taking into account the clinical and laboratory data, the patient underwent trepanobiopsy and molecular genetic analysis for the JAK2V617F mutation. As a result of histological examination of the trepanobioptate, three-branch proliferation in the bone marrow was revealed. The allele burden of the JAK2V617F gene was 79.5%. The patient was diagnosed with PV. After phlebotomy 4 times at a dose of 500 ml + LDA, the patient's condition improved, the pain in the legs disappeared, and independent movement without the help resumed. Control parameters of the hemogram: Hb-131q/L, RBC-4.5 $\times 10^{12}$/L, Ht-40%, WBC-9.69 $\times 10^{9}$/L, PLT-394 $\times 10^{9}$/L.

Methodology: The data of 193 patients were analyzed: hemogram parameters, allele burden of the JAK2V617F gene, analysis of the risk groups of patients were carried out. The WHO classification of 2008 and 2016, the prognosis of the risk of thrombohemorrhagic complications (TC) according to the Marchioli scale was used.

Results: Out of 193 patients, 127 were with classic polycythemia vera (CPV), and 66 were with LPV. The age of the patients (M ± m) with CPV was 57.01 ± 1.1 years, with LPV – 55.03 ± 1.6 years ($p > 0.05$). 97% of patients had the mutation of JAK2V617F gene. Laboratory parameters of patients with CPV and LPV were compared (M ± m): hemoglobin – 182.66 ± 2.1 g/L and 157.97 ± 2.2 g/L ($p < 0.05$), hematocrit – 71.85 ± 1.4% and 63.5 ± 1.8% ($p < 0.05$), erythrocytes – 6.18 ± 0.1 $\times 10^{12}$/L and 5.46 ± 0.1 $\times 10^{12}$/L ($p < 0.05$), platelets – 526.85 ± 30.9 $\times 10^{9}$/L and 429.3 ± 34.7 $\times 10^{9}$/L ($p < 0.05$), leukocytes 11.92 ± 0.6 $\times 10^{9}$/L and 10.79 ± 0.7 $\times 10^{9}$/L ($p > 0.05$), allele burden of the JAK2V617F gene – 55.0 ± 6.4% and 27.0 ± 6.9% ($p < 0.05$). Allele burden was divided into quartiles. In CPV 21.78% of patients belonged to the 1st, 20.16% to the 2nd, 18.55% to the 3rd, 39.51% to the 4th quartile. In LPV – 20% of patients belonged to the 1st, 80% to the 2nd quartile, in the 3rd and 4th quartiles there were no patients. In CPV the highest leukocyte count was in the 4th quartile. In LPV patients with an allele burden of the JAK2V617F gene above 40% had higher leukocyte and platelet counts, while the allele burden did not exceed 50%. We did not find any more relationship between allele burden and other hemogram parameters in patients with CPV and LPV. TC risk groups in CPV-low – 56.34%, intermediate – 38.03%, high – 5.63%, in LPV- low – 51.3%, intermediate –16.2%, high – 32.5%. In the analysis of JAK2V617F gene allele burden in the 1st and 2nd quartiles, no differences were found between the risk groups of LPV patients.

Conclusion: Out of PV patients 65.8% were with CPV, and 34.2% with LPV. In LPV the allele burden was lower than in CPV and did not exceed 50%. In CPV and LPV more than 51% of patients were at low risk of TC. CPV patients with JAK2V617F allele burden >75% had higher leukocyte count. LPV patients with JAK2V617F allele burden >40% had higher leukocyte and platelet counts.

https://doi.org/10.1016/j.htct.2020.09.079

COAGULATION DISEASES

PP 18

Clinical and anamnestic signs of hypercoagulation in patients with β-thalassemia

N. Alieva*, P. Safarova, A. Kerimov

National Center for Hematology and Transfusiology, Cầu Giấy, Viet Nam

Objective: Hypercoagulation in β-thalassemia patients is known to manifest as arterial and/or venous thrombotic complications. Along with the clinical assessment of thrombotic complications (TC), it is also important to study latent (masked) hypercoagulation (LH) hypercoagulable state (HS) in patients with β-thalassemia. HS assessment is possible based on the analysis of various clinical symptoms and patient history.

Case report: In the National Centers of Hematology and Transfusiology, we studied 315 women aged 18–40 years: 130 with β-thalassemia Major (TM), 95 with β-thalassemia intermedia (TI), 60 with β-thalassemia minor (Tm), 30 blood donors (BD).

Methodology: The data were analyzed retrospectively and as a result of our survey on the increased thrombotic tendency. Statistics: data input system MS Excel, data processing using the program Statistics 6.

Results: In 10.0 ± 2.6% of TM patients and in 14.7 ± 3.6% of TI patients, various TCs were revealed: arterial thrombosis, venous thrombosis, chronic venous insufficiency (varicose nodes of the lower extremities, telangiectasia, trophic ulcer, venous eczema, swelling of the feet and lower legs). Such complications was not detected in patients with Tm and in the control group. Out of 60 splenectomized patients with

PP 17

Study of JAK2V617F gene allele burden in polycythemia vera

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National Center of Hematology and Blood Transfusion, Cầu Giấy, Viet Nam

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TM, arterial thrombosis was observed in 2 (3.3%) patients, venous thrombosis in 3 (5.0%) patients, and signs of chronic venous insufficiency in 4 (6.7%) patients. Out of 70 non-splenectomized patients with TM, venous thrombosis was observed in 1 (1.4%) patient, and signs of chronic venous insufficiency in 3 (4.3%) patients. Of the 40 splenectomized TI patients, arterial thrombosis was observed in 2 (5.0%), venous thrombosis in 3 (7.5%), and signs of chronic venous insufficiency in 4 (10%). Of 55 non-splenectomized TI patients, venous thrombosis was observed in 2 (3.6%), and signs of chronic venous insufficiency in 3 (5.4%). Assessment of thrombotic tendency was conducted among non-splenectomized patients. HS (the total score for the PTT questionnaire >30) was detected in 36.0 ± 6.8% of TM patients and 40.0 ± 7.7% of TI patients. In patients with TI and in BD, increased thrombotic tendency was not detected (the sum of the scores for the PTT questionnaire is <30).

Conclusion: TCs detected in patients with homozygous β-thalassemia was more common in patients with TI compared with patients with TM ($p \geq 0.05$). In patients, cases of venous thrombosis were detected 2 times more often than arterial thrombosis ($p \geq 0.05$). Chronic venous insufficiency was detected identically in patients with TM and TI. TCs was observed more often in splenectomized patients with TM and TI compared with non-splenectomized patients ($p \geq 0.05$). It was established that some patients with β-thalassemia who did not have clinical thrombotic complications had prethrombotic state. A study of clinical and anamnestic risk factors revealed a tendency to HS in 1/3 of patients with β-thalassemia. Based on the results of the survey, the risk factors (predictors) of HS were determined. The tendency to form blood clots in patients with anemia was associated with two groups of clinical and anamnestic symptoms: “comorbidity” and “chronic stress conditions”.

https://doi.org/10.1016/j.htct.2020.09.080

PP 19

Factor XIII deficiency case with posttravmatic subcutaneous bleeding

M. Reis Aras[1,*], M. Tıglıoğou[1], B. Sağlam[1], P. Akyol[1], Ü. Malkan[1], A. Alan[2], M. Albayrak[1]

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[2] *University of Health Sciences, Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital, Internal Medicine Department, Ankara, Turkey*

Objective: Factor XIII deficiency; is a rare hereditary bleeding disorder caused by heterogeneous mutations that can lead to life-threatening bleeding. Hereditary factor XIII deficiency's inheritance is autosomal recessive and its incidence is about 1–3/1,000,000. The form of bleeding can be seen in a wide spectrum, from life-threatening bleeding (such as intracranial bleeding) to skin bleeding. Umbilical cord hemorrhage and soft tissue hematoma is the most common and often first symptom of factor XIII deficiency (1). Lifelong bleeding diathesis can be seen in hereditary FXIII deficiency. Especially subcutaneous bleeding (57%), delayed umbilical cord bleeding (56%), muscle hematoma (49%), postoperative bleeding (40%), intracerebral bleeding (34%) and recurrent abortion can be seen. Bleeding after trauma or surgery (12–36 h) is pathognomonic in factor XIII deficiency. (2) Diagnosis of factor XIII deficiency is difficult due to its rarity. Because standard clotting screening tests including prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time (TT), platelet count or bleeding time are normal; therefore, specific factor XIII assays are required. For all these reasons, factor XIII deficiency remains one of the least diagnosed rare bleeding disorders (1).

Case report: 34-year-old male patient applied to the emergency department due to the swelling that developed after hitting his right arm on the door. He stated that he had a history of factor 13 deficiency. Fracture or fissure line was not observed in the patient's physical examination and direct radiography. Bleeding observed in skin and subcutaneous region. In the anamnesis, the patient stated that he had a history of skin-subcutaneous bleeding and hematoma after trauma. In hospital records, it was observed that he had posttraumatic intramuscular hematoma two times in the last 5 years (the largest is 75 mm × 25 mm × 40 mm). In these hematomas treatment; there was no need for factor XIII concentrate, it was regressed with fresh frosen plasma replacement. In the laboratory tests performed in emergency department; leukocyte value 12,370/μL, neutrophil 6720/μL, hemoglobin 16.7 g/dL, platelet 315,000, PT: 9.12 s, aPTT 23.2 s, INR 1.02 was detected. Fresh frozen plasma was replaced at a dose of 15 mL/kg. The patient, who did not have any additional systemic problem, was discharged by recommending polyclinic control.

Conclusion: Hereditary factor XIII deficiency is an autosomal recessive bleeding disorder with a serious course (4). Unlike other hereditary hemostatic protein deficiencies, clotting tests and platelet function tests are normal in factor XIII deficiency. For this reason, specific factor XIII assays should be performed and the factor XIII level should be checked. The basis of treatment is replacement of the missing factor with plasma, cryoprecipitate and FXIII concentrates (2). However, in cases where there is a serious decrease in factor XIII levels, prophylaxis strategies with factor XIII concentrate can be applied to minimize bleeding events (5). In cases with recurrent delayed bleeding after trauma, factor XIII deficiency should be considered if the clotting profile is normal (2).

https://doi.org/10.1016/j.htct.2020.09.081

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Objective: Factor XIII deficiency; is a rare hereditary bleeding disorder caused by heterogeneous mutations that can lead to life-threatening bleeding. Hereditary factor XIII deficiency's inheritance is autosomal recessive and its incidence is about 1–3/1,000,000. The form of bleeding can be seen in a wide spectrum, from life-threatening bleeding (such as intracranial bleeding) to skin bleeding. Umbilical cord hemorrhage and soft tissue hematoma is the most common and often first symptom of factor XIII deficiency (1). Lifelong bleeding diathesis can be seen in hereditary FXIII deficiency. Especially subcutaneous bleeding (57%), delayed umbilical cord bleeding (56%), muscle hematoma (49%), postoperative bleeding (40%), intracerebral bleeding (34%) and recurrent abortion can be seen. Bleeding after trauma or surgery (12–36 h) is pathognomonic in factor XIII deficiency. (2) Diagnosis of factor XIII deficiency is difficult due to its rarity. Because standard clotting screening tests including prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time (TT), platelet count or bleeding time are normal; therefore, specific factor XIII assays are required. For all these reasons, factor XIII deficiency remains one of the least diagnosed rare bleeding disorders (1).

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https://doi.org/10.1016/j.htct.2020.09.081

PP 20

Acute ischemic stroke presentation of otherwise asymptomatic covid-19 patient

E. Aksoy[1], Y. Tor[1], S. Kalayoglu Besisik[2,*], A. Alibeyoglu[1], M. Kose[1], N. Senkal[1], A. Cagatay[3], M. Erelel[4], T. Tukek[1]

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Objective: Coronavirus disease 2019 (COVID-19), first identified in Wuhan, China in December 2019, become widespread and may be mortal, especially in some high-risk group. Most of the reported experiences suggested that COVID-19 is associated with a distinct coagulation disorder resulting in fibrin thrombi within small vessels and capillaries. Data focusing on arterial thrombotic events is few. In milder COVID cases, both hemorrhagic and ischemic stroke may occur. Acute ischemic stroke seems to be higher than the rate identified among patients who visited the emergency departments (ED). On the other hand, SARS-CoV-2 has the potential for neurotropism. We here present a case who had neurological symptoms during pandemic days and has been diagnosed with imaging-proven ischemic stroke with COVID-19.

Case report: A 40-year-old female patient presented to the ED with an articulation of speech and numbness in the right arm and leg. She is not a smoker and denied any environmental exposure. Physical examination revealed fever and hypotension with a respiratory rate was 18 breaths/min. She had dysarthria, hypoesthesia, and frustrated hemiparesis on the right arm and leg. Oxygen saturation was 98% on room air. Mild normocytic anaemia and lymphopenia associated with a mild elevation in transaminases (AST 73 U/L, ALT 103 U/L) and in D-Dimer (1440 ng/ml) associated the clinical picture. Thoracic CT showed bilateral multifocal peripheral ground glass infiltrations (Picture-1). Conventional MRI imaging is consistent with acute ischemia of millimetre in size on the left parietal lobe (Picture-2). The patient was accepted as having COVID-19 and acute ischemic stroke. She commenced on hydroxychloroquine and azithromycin with enoxaparin. Nasopharynx swab sample was found to be severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive by RT-PCR. She did not progress to the hyperinflammation phase and discharged on 10th day of admission. One month later on, outpatient visit her neurological findings resolved, no weakness was detected.

Conclusion: For each patient with an acute stroke clinic, thoracic CT and SARS-CoV-2 PCR should be performed before transferring to stroke or neurointensive care unit. For our patient, she did not have apparent risk factors for stroke. She was nearly asymptomatic apart of the stroke-related clinic, which points to the direct effect of coronavirus on vascular endothelial cells apart of the relationship between inflammation and coagulopathic complications in COVID-19.

https://doi.org/10.1016/j.htct.2020.09.082

LYMPHOMA

PP 21

Isolated primary spinal mucosa-associated lymphoid tissue (malt) lymphoma: a rare case report

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Objective: Mucosa-associated lymphoid tissue (MALT) lymphoma, also known as extranodal marginal zone lymphoma (MZL), is a subtype of indolent B-cell non-Hodgkin's lymphoma (NHL). MALT lymphomas are encountered mainly in mucosal organs such as the stomach, however, they can also be found in non-mucosal organs and tissue regions. MALT lymphoma of the spinal dura is a very rare condition. Here, we present the clinical presentation pattern, histopathologic and radiographic findings, treatment options, and response to treatment in a rare case of isolated primary spinal MALT lymphoma.

Case report: A 74-year-old male presented to our hospital with progressive weakness and loss of sensation in bilateral lower extremities, and fecal and urinary incontinence. Spinal MRI examination visualized an extra-axial mass lesion of approximately 45 mm × 11 mm between the vertebral levels T5 and T7. The lesion markedly compressed the spinal cord, severely narrowing the spinal canal and bilateral neural foramina. In order to ensure early decompression of the spine and histopathological diagnosis of the epidural mass, a total laminectomy of T6 and a subtotal resection of the mass were performed. On immunohistochemical examination of the mass, neoplastic cells showed: LCA(+), CD20(+), CD79a(+), PAX5(+), bcl-6(−), fascin(−), CD3(−), CD5(−), cyclin D1(−),CD23(−), CD138(−), kappa (−), lambda (−), MUM1(−), CD10(−), tdt(−), CD15(−), CD30(−), reticulin(−), and a Ki67 proliferation index of 20%; and the pathology department reported the findings to be consistent with MALT lymphoma of the dura. Following mass resection, FDG-PET CT) was performed to determine the extent of the disease, and other regions of the body did not show 18-FDG uptake. Bone marrow aspiration and biopsy showed that there was no infiltration. Only systemic chemotherapy was planned as the patient refused to undergo radiotherapy. A systemic combination therapy with R-CHOP protocol every 3 weeks and central nervous system prophylaxis with intrathecal cytarabine and dexamethasone were carried for the patient. After

PP 20

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Objective: Coronavirus disease 2019 (COVID-19), first identified in Wuhan, China in December 2019, become widespread and may be mortal, especially in some high-risk group. Most of the reported experiences suggested that COVID-19 is associated with a distinct coagulation disorder resulting in fibrin thrombi within small vessels and capillaries. Data focusing on arterial thrombotic events is few. In milder COVID cases, both hemorrhagic and ischemic stroke may occur. Acute ischemic stroke seems to be higher than the rate identified among patients who visited the emergency departments (ED). On the other hand, SARS-CoV-2 has the potential for neurotropism. We here present a case who had neurological symptoms during pandemic days and has been diagnosed with imaging-proven ischemic stroke with COVID-19.

Case report: A 40-year-old female patient presented to the ED with an articulation of speech and numbness in the right arm and leg. She is not a smoker and denied any environmental exposure. Physical examination revealed fever and hypotension with a respiratory rate was 18 breaths/min. She had dysarthria, hypoesthesia, and frustrated hemiparesis on the right arm and leg. Oxygen saturation was 98% on room air. Mild normocytic anaemia and lymphopenia associated with a mild elevation in transaminases (AST 73 U/L, ALT 103 U/L) and in D-Dimer (1440 ng/ml) associated the clinical picture. Thoracic CT showed bilateral multifocal peripheral ground glass infiltrations (Picture-1). Conventional MRI imaging is consistent with acute ischemia of millimetre in size on the left parietal lobe (Picture-2). The patient was accepted as having COVID-19 and acute ischemic stroke. She commenced on hydroxychloroquine and azithromycin with enoxaparin. Nasopharynx swab sample was found to be severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive by RT-PCR. She did not progress to the hyperinflammation phase and discharged on 10th day of admission. One month later on, outpatient visit her neurological findings resolved, no weakness was detected.

Conclusion: For each patient with an acute stroke clinic, thoracic CT and SARS-CoV-2 PCR should be performed before transferring to stroke or neurointensive care unit. For our patient, she did not have apparent risk factors for stroke. She was nearly asymptomatic apart of the stroke-related clinic, which points to the direct effect of coronavirus on vascular endothelial cells apart of the relationship between inflammation and coagulopathic complications in COVID-19.

https://doi.org/10.1016/j.htct.2020.09.082

LYMPHOMA

PP 21

Isolated primary spinal mucosa-associated lymphoid tissue (malt) lymphoma: a rare case report

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Objective: Mucosa-associated lymphoid tissue (MALT) lymphoma, also known as extranodal marginal zone lymphoma (MZL), is a subtype of indolent B-cell non-Hodgkin's lymphoma (NHL). MALT lymphomas are encountered mainly in mucosal organs such as the stomach, however, they can also be found in non-mucosal organs and tissue regions. MALT lymphoma of the spinal dura is a very rare condition. Here, we present the clinical presentation pattern, histopathologic and radiographic findings, treatment options, and response to treatment in a rare case of isolated primary spinal MALT lymphoma.

Case report: A 74-year-old male presented to our hospital with progressive weakness and loss of sensation in bilateral lower extremities, and fecal and urinary incontinence. Spinal MRI examination visualized an extra-axial mass lesion of approximately 45 mm × 11 mm between the vertebral levels T5 and T7. The lesion markedly compressed the spinal cord, severely narrowing the spinal canal and bilateral neural foramina. In order to ensure early decompression of the spine and histopathological diagnosis of the epidural mass, a total laminectomy of T6 and a subtotal resection of the mass were performed. On immunohistochemical examination of the mass, neoplastic cells showed: LCA(+), CD20(+), CD79a(+), PAX5(+), bcl-6(−), fascin(−), CD3(−), CD5(−), cyclin D1(−),CD23(−), CD138(−), kappa (−), lambda (−), MUM1(−), CD10(−), tdt(−), CD15(−), CD30(−), reticulin(−), and a Ki67 proliferation index of 20%; and the pathology department reported the findings to be consistent with MALT lymphoma of the dura. Following mass resection, FDG-PET CT) was performed to determine the extent of the disease, and other regions of the body did not show 18-FDG uptake. Bone marrow aspiration and biopsy showed that there was no infiltration. Only systemic chemotherapy was planned as the patient refused to undergo radiotherapy. A systemic combination therapy with R-CHOP protocol every 3 weeks and central nervous system prophylaxis with intrathecal cytarabine and dexamethasone were carried for the patient. After

two chemotherapy cycles, there was a significant improvement in motor weakness and the fecal and urinary function impairment. After a total of 6 cycles, spinal MRI and FDG-PET CT showed complete disappearance of the lesion. The patient remains in remission, at 1-year follow-up.

Conclusion: This report presents a case of primary spinal MALT lymphoma, which is extremely rare. Lymphoma should be considered in the differential diagnosis of patients who present with a spinal mass and the subtype of the lymphoma must be identified. The management of MALT lymphomas is quite heterogenous and there exist no universally-accepted therapeutic guidelines for this rare condition. A treatment option must be selected in consideration of the disease subtype, stage, and the clinical characteristics of the patient. In spinal MALT lymphoma, both local and systemic treatment options are available. Local treatments such as surgical resection or radiotherapy can achieve complete remission in patients with MALT lymphomas confined to a single site or at early stages. Systemic treatment is an option for patients who are not suitable for local treatment and appropriate patients may be administered systemic chemotherapy regimens that include anti-CD20 monoclonal antibodies.

https://doi.org/10.1016/j.htct.2020.09.083

PP 22

Ir2 leading to complete remission in r/r richter syndrome – a case report

Emin Abdullayev*, Christoph Buhl, Judith Niederland, Herrad Baurmann, Bertram Glass

Helios Clinic Berlin Buch: Department of Hematology and of Stem Cell Transplantation, Berlin, Germany

Introduction: Relapsed and refractory diffuse large B Non-Hodgkin lymphoma (r/r DLBCL) is a severe condition with fatal outcome for the majority of the patients. (1) Richter Syndrome is defined as a transformation of chronic lymphatic leukemia in a highly aggressive B-Non-Hodgkin lymphoma, mainly DLBCL. 20% of Richters Syndromes are de novo DLBCL, implying comparable prognosis to other aggressive Non-Hodgkin Lymphoma, whereas 80% are clonally related to the CLL cells and imply a poor prognosis of one-year median overall survival. (2) Despite huge efforts that have been achieved recently by implementing CAR-T Cells for r/r DLBCL and transformed Follicular Lymphoma, treatment of r/r Richter syndrome remains desperate with poor outcome. Allogenic stem cell transplantation is recommended for eligible patients. The combination of Anti CD 20 Antibody Rituximab with IMiD Lenalidomide and Bruton-kinase inhibitor Ibrutinib iR2 has shown safety and efficacy in a breaking phase II study. (2)

We present the rare case of a patient with refractory DLBCL after CLL (Richter Transformation) who achieved complete remission with iR2 and was successfully transplanted.

Case report: Our by now 74-year old patient was first diagnosed with CLL in 08/2014. He showed ubiquitous lymph nodes and evidence of p53 mutation, Binet stage B & RAI I.

He was treated with Ofatumumab + Bendamustine in the first line, Rituximab + Idelalisib in first relapse and Ibrutinib in second relapse before evolving to highly aggressive B-NHL in 10/2019. Richters Syndrome was first treated with Standard Immunochemotherapy (R-CHOP), before switching to Rituximab + Ifosphamid + Etoposid + Carboplatin (R-ICE) for refractory disease. There was further progress (clearly progressive lymph nodes cervical) after first cycle R-ICE chemotherapy, we decided to treat with a combination of immunotherapy with the Anti CD 79a-Antibody Polatuzumab in combination with Rituximab. Unfortunately, we saw again progressive disease after three cycles, that lead to the decision of experimental application of Ibrutinib in combination with Rituximab and Lenalidomid.

We saw an immediate effect as Lactat-dehydrogenase normalized very soon and lymph nodes disappeared completely.

https://doi.org/10.1016/j.htct.2020.09.084

PP 23

Primary spinal extramedullary diffuse large B-cell lymphoma presenting with initial spinal cord compression: a case report

O. Ekinci[1,*], A. Dogan[2], M. Aslan[1], I. Aras[3], C. Demir[2]

[1] *Department of Hematology, Faculty of Medicine, Fırat University, Elazığ, Turkey*
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Objective: Extranodal lymphomas, by definition, can involve any organ or tissue. Brain parenchyma, spinal cord, eyes, cranial nerves, and meninx are extranodal regions that show involvement at much lower rates. It is quite rare for lymphoma patients to present to the hospital with symptoms and findings associated with spinal cord compression as the initial presentation. This condition can lead to irreversible autonomic dysfunction, and motor and sensory loss. Here, we present a rare primary spinal intradural extramedullary diffuse large B-cell lymphoma (DLBCL) case who presented with acute neurological symptoms and no findings of cerebral involvement or involvement at any other site.

Case report: A 41-year-old male patient presented to our hospital with thoracic back pain and progressive complaints of weakness, numbness and difficulty in ambulation in bilateral lower extremities. On spinal MRI examination, a well-circumscribed intradural extramedullary mass with a craniocaudal extension of 6 cm and an AP diameter of 1 cm that was isointense to the spinal cord on T1-weighted sequences and slightly hyperintense on T2-weighted series, and showed diffuse homogenous contrast enhancement after intravenous contrast agent injection was determined between the vertebral levels T6 and T8. In the surgical operation, the mass showed partial invasion of the vertebral bone and the surrounding muscle. The mass invading the dura was resected and laminectomy was performed at T6-T9. On histopathological examination of the mass, there was diffuse malignant

two chemotherapy cycles, there was a significant improvement in motor weakness and the fecal and urinary function impairment. After a total of 6 cycles, spinal MRI and FDG-PET CT showed complete disappearance of the lesion. The patient remains in remission, at 1-year follow-up.

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PP 22

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PP 23

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infiltration by large atypical lymphoid cells with prominent nucleoli and a coarse chromatin structure. On immunohistochemical examination, neoplastic cells showed; CD20 (+, diffuse), CD3 (–), MPO (–), Tdt (–), CD1a (–), S100 (–), ALK (–), CD68 (–), CK (–), actin (–), vimentin (–) staining, and the Ki67 proliferation index was 70%. The pathology department reported the mass to be consistent with a diffuse large B cell lymphoma (centroblastic type). Cervical-thoracic-abdominopelvic CT was performed to determine the extent of the disease, and no masses, organomegaly, or enlarged lymph nodes were detected. Bone marrow aspiration and biopsy did not show bone marrow involvement. The patient received chemotherapy consisted of R-CHOP and was administered with six cycles. After chemotherapy, radiotherapy was given at a total dose of 40 Gy as 2 Gy per fraction. The strength of the bilateral lower extremity muscle groups showed daily improvement and the patient was able to walk normally with two courses of chemotherapy, after approximately six weeks. The patient remains in remission without clinical or radiological relapse under follow up after nearly 3 years.

Conclusion: The differential diagnosis of patients who present with a spinal mass should be made carefully. It must be considered that, although rarely, DLBCLs can present as massive disease-causing spinal compression, and that clinically significant improvement can be achieved by timely and effective treatment. In patients who present with spinal compression, early decompression, particularly by means of surgery, is of great importance. Considering that spinal DLBCL is a malignant disease, appropriate treatment approaches play a vital role in achieving neurological recovery, longer survival times, and better life quality.

https://doi.org/10.1016/j.htct.2020.09.085

PP 24

Comparison of 68ga-psma and 18f-fdg pet/ct uptake in different lymphoma

S. Souza[1], M. Delamain[1], N. Tobar[1], V. Castro[1], F. Frasson[1], B. Amorim[1], E. Etchebehere[1], K. Mariana[1], J. Mengatti[2], E.B. Araujo[2], E. Perini[2], C. De Souza[1,*], A. Santos[1], I. Lorant-Metze[1], C. Ramos[1]

[1] *University of Campinas – UNICAMP, Campinas, Brazil*
[2] *Nuclear and Energy Research Institute – IPEN, São Paulo, Brazil*

Objective: Few reports have documented the uptake of radiolabeled Prostate-Specific Membrane Antigen (PSMA) in lymphomas.[1,2] It is not known how PSMA uptake varies among various histological subtypes and how it correlates with 18F-FDG uptake in lymphomas. This study aimed to compare 68Ga-PSMA and 18F-FDG in different lymphoma subtypes.

Methodology: Nine randomly selected patients with biopsy-proven lymphoma with a median age 43 (32–70) years, 5 female – were submitted to whole-body 18F-FDG and 68Ga – PSMA PET/CT (time interval: 1–6 days between procedures). Lymphoma subtypes included: nodular-sclerosis Hodgkin's lymphoma (HL; 2 patients); diffuse large B-cell lymphoma (DLBCL; 1); marginal-zone lymphoma (2); MALT lymphoma (ML; 1); follicular lymphoma (FL; 1); lymphoplasmacytic lymphoma (1); and B-cell non-Hodgkin's lymphoma, unspecified (BCNHL-U; 1). Eight patients were under initial staging and 1 (HL) with disease relapse after treatment. Two experienced nuclear physicians analyzed the images by consensus. The intensity of tracer uptake was visually classified as marked, moderate or mild. The affected sites (lymph node chains, spleen, diffuse bone marrow involvement and non-lymphatic focal lesions) were counted in both sets of images and their respective maximum SUV (SUVmax) were measured.

Results: PSMA PET/CT was positive in all patients except for one with ML. FDG PET/CT was positive in all patients. At visual analyses, FDG uptake was higher than PSMA uptake in all patients, except for one patient with BCNHL-U (both tracers with similar low-intensity uptake). The intensity of FDG and PSMA uptake was respectively classified as marked in 3/9 and 0/8 patients, moderate in 4/9 and 1/8 and mild in 2/9 and 7/8. One patient (FL) presented a "mismatch" uptake pattern with different parts of an extensive lesion presenting predominant uptake of PSMA or FDG. Brain infiltration in one patient (DLBCL) was more easily identified on PSMA than on FDG images. FDG detected a total of 58/58 and PSMA 43/58 affected sites in all patients with a median SUVmax of respectively 5.4 (2.0–31.1) and 2.8 (1.3–5.4), $p < 0.0001$. The median SUVs of the 43 lesions with uptake of both tracers was respectively 5.5 (2.0–28.9) and 2.8 (1.3–5.4) for FDG and PSMA, $p < 0.0001$.

Conclusion: Distinct lymphoma subtypes present PSMA uptake, with less intensity than FDG uptake. Although PSMA uptake is usually mild, several lymphoma subtypes might cause false-positive results in PSMA PET/CT performed to assess prostate cancer.

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https://doi.org/10.1016/j.htct.2020.09.086

PP 25

Prognostic value of pre-treatment neutrophil-lymphocyte and platelet-lymphocyte ratio in diffuse large B-cell lymphoma: a single-center experience

G. Dagci[1], M. Guzel Mastanzade[1], M. Ozbalak[2], D. Ozluk[2], T. Tiryaki[2], I. Yonal Hindilerden[2], M. Yenerel[2], M. Nalcaci[2], S. Kalayoglu Besisik[2,*]

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[2] *Istanbul University School of Medicine Department of Hematology, İstanbul, Turkey*

Objective: The neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) as inflammatory biomarkers have emerged as prognostic factors for patients with cancer.

infiltration by large atypical lymphoid cells with prominent nucleoli and a coarse chromatin structure. On immunohistochemical examination, neoplastic cells showed; CD20 (+, diffuse), CD3 (–), MPO (–), Tdt (–), CD1a (–), S100 (–), ALK (–), CD68 (–), CK (–), actin (–), vimentin (–) staining, and the Ki67 proliferation index was 70%. The pathology department reported the mass to be consistent with a diffuse large B cell lymphoma (centroblastic type). Cervical-thoracic-abdominopelvic CT was performed to determine the extent of the disease, and no masses, organomegaly, or enlarged lymph nodes were detected. Bone marrow aspiration and biopsy did not show bone marrow involvement. The patient received chemotherapy consisted of R-CHOP and was administered with six cycles. After chemotherapy, radiotherapy was given at a total dose of 40 Gy as 2 Gy per fraction. The strength of the bilateral lower extremity muscle groups showed daily improvement and the patient was able to walk normally with two courses of chemotherapy, after approximately six weeks. The patient remains in remission without clinical or radiological relapse under follow up after nearly 3 years.

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Objective: The neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) as inflammatory biomarkers have emerged as prognostic factors for patients with cancer.

infiltration by large atypical lymphoid cells with prominent nucleoli and a coarse chromatin structure. On immunohistochemical examination, neoplastic cells showed; CD20 (+, diffuse), CD3 (–), MPO (–), Tdt (–), CD1a (–), S100 (–), ALK (–), CD68 (–), CK (–), actin (–), vimentin (–) staining, and the Ki67 proliferation index was 70%. The pathology department reported the mass to be consistent with a diffuse large B cell lymphoma (centroblastic type). Cervical-thoracic-abdominopelvic CT was performed to determine the extent of the disease, and no masses, organomegaly, or enlarged lymph nodes were detected. Bone marrow aspiration and biopsy did not show bone marrow involvement. The patient received chemotherapy consisted of R-CHOP and was administered with six cycles. After chemotherapy, radiotherapy was given at a total dose of 40 Gy as 2 Gy per fraction. The strength of the bilateral lower extremity muscle groups showed daily improvement and the patient was able to walk normally with two courses of chemotherapy, after approximately six weeks. The patient remains in remission without clinical or radiological relapse under follow up after nearly 3 years.

Conclusion: The differential diagnosis of patients who present with a spinal mass should be made carefully. It must be considered that, although rarely, DLBCLs can present as massive disease-causing spinal compression, and that clinically significant improvement can be achieved by timely and effective treatment. In patients who present with spinal compression, early decompression, particularly by means of surgery, is of great importance. Considering that spinal DLBCL is a malignant disease, appropriate treatment approaches play a vital role in achieving neurological recovery, longer survival times, and better life quality.

https://doi.org/10.1016/j.htct.2020.09.085

PP 24

Comparison of 68ga-psma and 18f-fdg pet/ct uptake in different lymphoma

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Objective: Few reports have documented the uptake of radiolabeled Prostate-Specific Membrane Antigen (PSMA) in lymphomas.[1,2] It is not known how PSMA uptake varies among various histological subtypes and how it correlates with 18F-FDG uptake in lymphomas. This study aimed to compare 68Ga-PSMA and 18F-FDG in different lymphoma subtypes.

Methodology: Nine randomly selected patients with biopsy-proven lymphoma with a median age 43 (32–70) years, 5 female – were submitted to whole-body 18F-FDG and 68Ga – PSMA PET/CT (time interval: 1–6 days between procedures). Lymphoma subtypes included: nodular-sclerosis Hodgkin's lymphoma (HL; 2 patients); diffuse large B-cell lymphoma (DLBCL; 1); marginal-zone lymphoma (2); MALT lymphoma (ML; 1); follicular lymphoma (FL; 1); lymphoplasmacytic lymphoma (1); and B-cell non-Hodgkin's lymphoma, unspecified (BCNHL-U; 1). Eight patients were under initial staging and 1 (HL) with disease relapse after treatment. Two experienced nuclear physicians analyzed the images by consensus. The intensity of tracer uptake was visually classified as marked, moderate or mild. The affected sites (lymph node chains, spleen, diffuse bone marrow involvement and non-lymphatic focal lesions) were counted in both sets of images and their respective maximum SUV (SUVmax) were measured.

Results: PSMA PET/CT was positive in all patients except for one with ML. FDG PET/CT was positive in all patients. At visual analyses, FDG uptake was higher than PSMA uptake in all patients, except for one patient with BCNHL-U (both tracers with similar low-intensity uptake). The intensity of FDG and PSMA uptake was respectively classified as marked in 3/9 and 0/8 patients, moderate in 4/9 and 1/8 and mild in 2/9 and 7/8. One patient (FL) presented a "mismatch" uptake pattern with different parts of an extensive lesion presenting predominant uptake of PSMA or FDG. Brain infiltration in one patient (DLBCL) was more easily identified on PSMA than on FDG images. FDG detected a total of 58/58 and PSMA 43/58 affected sites in all patients with a median SUVmax of respectively 5.4 (2.0–31.1) and 2.8 (1.3–5.4), $p < 0.0001$. The median SUVs of the 43 lesions with uptake of both tracers was respectively 5.5 (2.0–28.9) and 2.8 (1.3–5.4) for FDG and PSMA, $p < 0.0001$.

Conclusion: Distinct lymphoma subtypes present PSMA uptake, with less intensity than FDG uptake. Although PSMA uptake is usually mild, several lymphoma subtypes might cause false-positive results in PSMA PET/CT performed to assess prostate cancer.

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https://doi.org/10.1016/j.htct.2020.09.086

PP 25

Prognostic value of pre-treatment neutrophil-lymphocyte and platelet-lymphocyte ratio in diffuse large B-cell lymphoma: a single-center experience

G. Dagci[1], M. Guzel Mastanzade[1], M. Ozbalak[2], D. Ozluk[2], T. Tiryaki[2], I. Yonal Hindilerden[2], M. Yenerel[2], M. Nalcaci[2], S. Kalayoglu Besisik[2,*]

[1] *Istanbul University School of Medicine Department of Internal Medicine, İstanbul, Turkey*
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Objective: The neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) as inflammatory biomarkers have emerged as prognostic factors for patients with cancer.

We aimed to explore the association between the NLR/PLR and prognosis in diffuse large B-cell lymphoma (DLBCL).

Methodology: The study was carried out retrospectively. A systematic search of the hospital database regarding DLBCL patients was performed between April 2004 and March 2019. Completely accessible data were included in the study.

Results: Overall, 122 patients included in the study. There were 64 males and 58 females. At the time of diagnosis, the mean age was 51.3 ± 14.3 years, whereas 26 (21.3%) were under 40 years, 26 (21.3%) between 40–49 years, 35 (28.7%) between 50-59 years, and 35 (28.7%) were over 60 years old. Approximately 50% were at an advanced stage. At the time of diagnosis, the mean NLR was 3.8 with an absolute neutrophil count of 4852.4/μL (0.600–16.000/μL), and the absolute lymphocyte count of 1757.9/μL (0.100–15.000/μL). The mean PLR was 213.6, with a mean platelet count of 250,000/μL (range 260,000–715,000/μL). ROC analysis gave the cut-off point for PLR as >152.86, and NLR >3.05. All patients (90.2%) received R-CHOP based therapy. The median follow-up time was 69 months (range 3–244). During the follow-up period, 8.2% of patients died. Patients with high NLR levels showed more frequent B symptoms ($p = 0.034$). Patients with high PLR levels had a statistically significant lower overall survival (OS) and progression-free survival (PFS) ($p = 0.012$ and $p = 0.004$, respectively). In patients with high NLR levels, the OS rate proved to be shorter, but this finding has not achieved a statistical significance. However, PFS was statistically significantly shorter ($p = 0.022$). In the multivariate analysis of PLR and clinical factors in terms of non-progressive survival, age, IPI score, and high PLR level are independent risk factors for non-progressive survival ($p = 0.013$, $p = 0.039$ and $p = 0.031$, respectively). In multivariate analysis of NLR and clinical factors, age and IPI score are independent risk factors for non-progressive survival ($p = 0.026$ and $p = 0.046$, respectively).

Conclusion: This study demonstrated that elevated pretreatment PLR was significantly associated with poor prognosis in DLBCL patients. PLR could be helpful as a potential prognostic biomarker to guide clinical decision-making and select individualized treatment strategies for DLBCL patients.

https://doi.org/10.1016/j.htct.2020.09.087

PP 26

Two diseases in a single lymph node: nodular lymphocyte predominant hodgkin lymphoma and kaposi's sarcoma

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Objective: Kaposi's Sarcoma (KS) is the most common low-grade mesenchymal angioproliferative disease seen in patients infected with the human immunodeficiency virus (HIV). Lymph node involvement is rare in classical KS, but it is common in endemic and epidemic (AIDS-related) KS. Kaposi's sarcoma-associated herpesvirus (KSHV), also known as human herpesvirus type 8(HHV8), was first described in HIV-associated KS. Nodular lymphocyte predominant Hodgkin Lymphoma (NLPHL)is a rare lymphoma with an incidence of 0.1 to 0.2/100,000/y. Significant histological feature is the presence of CD20 (+) CD15 (–) CD30 (–) variants in a nodular infiltration lymphocyte pattern of Reed-Sternberg cells. The coexistence of Hodgkin's disease (HD) and KS is a rare condition.

Case report: A 41-year-old male patient presented to the hematology outpatient clinic with painless swelling in the left armpit. There were no B symptoms at the patient's presentation. He had a history of RAI due to hyperthyroidism in 2004 and using 100 mcg of Levothyroxine. He also had a history of 7 packs/year of cigarette (exsmoker) and alcohol use as a social drinker. On physical examination, a well-demarcated, flip, painless lymphadenomegaly (LAM) was detected in the left axillary region, and hepatosplenomegaly (HSM) was not spresent. The laboratory results were as follows: wbc: 8300 UL; 15.1 g/dL, lymphoyte: 1450 mm^3, plt: 197,000 UL, albumin: 4.5 g/L, calcium: 10.9 mg/dL, ldh: 156 U/L, uric acid: 6.5 mg/dL. The serological tests were negative, other biochemical parameters were normal. The peripheral smear of the patient was evaluated as normal morphology. An cxcisional lymph node biopsy was taken from the left axilla. The pathology result was interpreted as nodular lymphocyte predominant Hodgkin's lymphoma (NLP) classical type and Kaposi's sarcoma with diffuse HHV-8 positivity. Bone marrow biopsy revealed no Kaposi's or Hodgkin's lymphoma infiltration. PET-CT imaging was performed for lymphoma staging. Lymphoproliferative disease involvement was observed at the left axilla level 2, 3 in bilateral, cervial, left infraclavicular, retropectoral area and along the medial line of the spleen. It was evaluated as stage II S. No additional lesion was detected in the patient evaluated by dermatology for Kaposi's sarcoma. Gastroscopy and colonoscopy were performed for gastrointestinal tract involvement and evaluated with biopsy. Helicobacter Pylori was observed in gastroscopy and eradication treatment was given. No pathological finding was seen in colonoscopy. By evaluating as early-stage NLP Hodgkin's Lymphoma, the patient was initiated on radiotherapy.

Methodology: Except for the need for an impaired immune system for the development of KS, it is thought that the relationship of KS with HD may be related to common pathogenic mechanisms instead of a direct causal relationship.

Results: Recently, HD and KS development has been associated with EBV and HHV-8, respectively. Although there are cases of KS and classical HD coexistence in the same lymph node, the coexistence of KS and NLPHL subtype in the same lymph node is quite rare.

Conclusion: Although KS is most commonly associated with immunodeficiency due to HIV infection or other causes of immunosuppression, it was not associated with any immunodeficiency status in our case. Due to the fact that KS and NLPHL were present in the same lymph node as two separate primers and were not immunosuppressed, we presented our

We aimed to explore the association between the NLR/PLR and prognosis in diffuse large B-cell lymphoma (DLBCL).

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PP 26

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case below. It was also unusual for KS to have primary lymph node involvement without cutaneous involvement.

https://doi.org/10.1016/j.htct.2020.09.088

PP 27

Extranodal marginal zone lymphoma of the ocular adnexa

A. Gül, O. Aydın*, E. Kelkitli, H. Atay, M. Turgut

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Objective: Ocular manifestations of non-Hodgkin lymphoma are rare, and the diagnosis can be delayed because of nonspecific symptoms and a tendency to mimic the appearance of other ocular diseases. Suspicious presentations will require confirmation of the lymphoma through surgical biopsy. The aim of this study was to present an ocular non-Hodgkin marginal zone lymphoma without systemic involvement, which was successfully managed with external beam radiation.

Case report: A 77-year-old female developed redness and swelling in the right eye which was initially treated as a nodular episcleritis and applied to our outpatient clinic. When the situation did not resolve, a subsequent biopsy diagnosed a low-grade non-Hodgkin marginal zone lymphoma. Systemic involvement was not detected in the images performed. Magnetic resonance imaging did not demonstrate any uveal or orbital extension and no intraocular involvement was noted. The lesion was treated with 30 Gy external beam radiation for a total of 10 days, resulting in significant tumor regression. Six month after the radiotherapy, the tumor has not recurred, and there has been no systemic involvement.

Conclusion: It is not unusual for ocular adnexa lymphomas to masquerade as another clinical entity, sometimes making the initial diagnosis challenging. A biopsy to rule out malignancy should be considered. We wanted to present this case because it is a rare case.

https://doi.org/10.1016/j.htct.2020.09.090

PP 28

Alk (–) anaplastic large cell lymphoma diagnosed by tongue root biopsy: case report

F. Yilmaz[1,*], M. Albayrak[1], M. Tiglioglu[1], M. Aras[1], S. Maral[1], A. Yildiz[2], U. Malkan[1]

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[2] *Hitit University Erol Olçok Training and Research Hospital, Department of Hematology, Ankara, Turkey*

Objective: Anaplastic large cell lymphoma(ALCL) which was described in 1985, is rare subtype among non-hodgkin lymphomas with rate of 2%. ALCL is located' mature T and NK neoplasms' group in 2016 WHO' mature lymphoid, histiocytic and dendritic neoplasms' classification. Besides ALCL subdivided into anaplastic lymphoma kinase (ALK) negative (–), ALK positive (+), primary cutaneous, group of associated with breast implant. CD30 and ALK are key molecules at pathology, diagnosis, treatment of ALCL. ALK (+) ALCL has a better prognosis than ALK (–) ALCL. Peripheral and mediastinal-abdominal lymphadenopathies (LAP), appears in more than half of patients. Approximately 60% of patients have extranodal involvement. The most common extranodal involvement sites are; skin, bone, liver, lung, spleen, bone marrow and soft tissue. Rare involvement occurs in the central nervous system and gastrointestinal tract. We wanted to our patient with ALK (–) ALCL diagnosed with tongue root biopsy in order to contribute to the literature.

Case report: It was learned that a-60-year old female patient applied to the otolaryngology department with the complaint of swelling in the neck, and in her detailed examination, tonsillectomy and tongue root biopsy was performed due to suspicious mass. The patient direct to us on the reporting of tongue root biopsy pathology as ALK(–) ALCL. PET-CT was taken for staging. As a result of PET-CT: left submandibular 15 mm × 8 mm LAP (SUVmax: 4.15), right submandibular 14 mm × 10 mm LAP (SUVmax: 6.32), left jugular 27 mm × 37 LAP (SUVmax: 15.91), left deep servical 11 mm × 8 mm (SUVmax: 10.35), left supraclavicular 13 mm × 10 mm (SUVmax: 15.08) was detected and there was no involvement in bone marrow biopsy. The patient was considered stage ll ALK (–) ALCL. A total of 6 cure of CHOEP (cyclophosphamide 100 mg/day, vincristine 2 mg/day, adriamycin 85 mg/day,etoposide 150 mg/day and methlylprednisole 100 mg/day) were planned. In the evaluation after 6 cure chemotherapy:the patient with complete remmision was followed up.

Conclusion: Although ALCL is rare, it is a disease that needs to be diagnosed and treated quickly due to its clinical course. Although skin, bone, liver, lung, spleen, bone marrow and soft tissue involvement are common, it should be kept in mind that it can be seen rare cases such as central nervous system, gastrointestinal system and tongue root as that our case. Protocols containing anthracycline such as CHOP/CHOEP (cyclophosphamide, doxorubucin, vincristine, prednisone/cyclophosphamide, doxorubucin, vincristine, etoposide, prednisone) form the basis of treatment. Non-CHOP induction strategies:ifosfamide, carboplatin, etoposide (ICE), autologous stem cell transplant/allogeneic stem cell transplant after ICE plus intrathecal methotrexate. Despite this protocols and new treatment agents (pralatrexate, ibrutinib, etc.) early diagnosis is very important at ALCL.

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PP 28

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Objective: Anaplastic large cell lymphoma(ALCL) which was described in 1985, is rare subtype among non-hodgkin lymphomas with rate of 2%. ALCL is located' mature T and NK neoplasms' group in 2016 WHO' mature lymphoid, histiocytic and dendritic neoplasms' classification. Besides ALCL subdivided into anaplastic lymphoma kinase (ALK) negative (–), ALK positive (+), primary cutaneous, group of associated with breast implant. CD30 and ALK are key molecules at pathology, diagnosis, treatment of ALCL. ALK (+) ALCL has a better prognosis than ALK (–) ALCL. Peripheral and mediastinal-abdominal lymphadenopathies (LAP), appears in more than half of patients. Approximately 60% of patients have extranodal involvement. The most common extranodal involvement sites are; skin, bone, liver, lung, spleen, bone marrow and soft tissue. Rare involvement occurs in the central nervous system and gastrointestinal tract. We wanted to our patient with ALK (–) ALCL diagnosed with tongue root biopsy in order to contribute to the literature.

Case report: It was learned that a-60-year old female patient applied to the otolaryngology department with the complaint of swelling in the neck, and in her detailed examination, tonsillectomy and tongue root biopsy was performed due to suspicious mass. The patient direct to us on the reporting of tongue root biopsy pathology as ALK(–) ALCL. PET-CT was taken for staging. As a result of PET-CT: left submandibular 15 mm × 8 mm LAP (SUVmax: 4.15), right submandibular 14 mm × 10 mm LAP (SUVmax: 6.32), left jugular 27 mm × 37 LAP (SUVmax: 15.91), left deep servical 11 mm × 8 mm (SUVmax: 10.35), left supraclavicular 13 mm × 10 mm (SUVmax: 15.08) was detected and there was no involvement in bone marrow biopsy. The patient was considered stage ll ALK (–) ALCL. A total of 6 cure of CHOEP (cyclophosphamide 100 mg/day, vincristine 2 mg/day, adriamycin 85 mg/day,etoposide 150 mg/day and methlylprednisole 100 mg/day) were planned. In the evaluation after 6 cure chemotherapy:the patient with complete remmision was followed up.

Conclusion: Although ALCL is rare, it is a disease that needs to be diagnosed and treated quickly due to its clinical course. Although skin, bone, liver, lung, spleen, bone marrow and soft tissue involvement are common, it should be kept in mind that it can be seen rare cases such as central nervous system, gastrointestinal system and tongue root as that our case. Protocols containing anthracycline such as CHOP/CHOEP (cyclophosphamide, doxorubucin, vincristine, prednisone/cyclophosphamide, doxorubucin, vincristine, etoposide, prednisone) form the basis of treatment. Non-CHOP induction strategies:ifosfamide, carboplatin, etoposide (ICE), autologous stem cell transplant/allogeneic stem cell transplant after ICE plus intrathecal methotrexate. Despite this protocols and new treatment agents (pralatrexate, ibrutinib, etc.) early diagnosis is very important at ALCL.

https://doi.org/10.1016/j.htct.2020.09.091

PP 29

Polatuzumab based chemoimmunotherapy showing complete response in a patient of r/r diffuse large b-cell lymphoma

U. Atas*, E. Vural, U. Iltar, O. Yucel, O. Salim, L. Undar

Akdeniz University Faculty of Medicine, Department of Hematology, Antalya, Turkey

Objective: Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma and it is curable in approximately half of cases with current therapy. However, some of the patients require 3 or more line of therapy. Optimal management for patients who experience two or more relapses of DLBCL is unknown. New treatment options are needed and are being investigated. One of them, polatuzumab vedotin (PV) is a monoclonal antibody that targets CD-79B. We would like to talk about a relapse refractory (R/R)-DLBCL patient who had received 4 previous line of therapy with a follow-up time of about 15 years and showed complete response to PV based chemoimmunotherapy.

Case report: The patient, 47 years old male was diagnosed with stage-IE DBBHL after orchiectomy in 2006 and received 6 cycles of R-CHOP chemoimmunotherapy. After the patient followed up for 8 years in complete remission, isolated central nervous system relapse confirmed by biopsy in 2014. A protocol including 3 cycles of high-dose methotrexate and cytosine arabinoside was applied to the patient. Since the patient failed mobilization with chemotherapy + granulocyte colony stimulating factor (G-CSF) and plerixafor + G-CSF, the treatment of the patient was completed with cranial radiotherapy. The patient followed in remission then developed a second relapse with an abdominal bulky mass that invaded the bladder, ureter and rectum in 2018. Relapse was demonstrated by a biopsy. Although more than 50% response was observed after 3 cycles of gemcitabine-oxaliplatin plus rituximab, there was a loss of response after 6 cycles. Radiation therapy was applied in 2019 and then ibrutinib was used. After radiation therapy and 3 months of ibrutinib treatment, the patient continued to be treated with ibrutinib with a response rate of more than 50%. In the 7th month of treatment a disease progression developed, and the patient was included in the Polatuzumab vedotin (1.8 mg/kg) + Bendamustin (90 mg/m^2) + Rituximab (375 mg/m^2) (Pola-BR) early access program in August 2019. After 3 cycles of PV based chemoimmunotherapy with complete response, the treatment of the patient was completed to 6 cycles in January 2020. Then, lenalidomide was started for maintenance therapy. The patient is still asymptomatic and being followed in remission.

Results: The general recommendation in relapse patients is autologous stem cell transplant (ASCT) after rescue chemotherapy. For patients with second or later relapse, relapse after ASCT and chemoresistant disease, prognosis is poor. The treatment options at this stage include if appropriate, allogeneic stem cell transplantation, monoclonal antibodies such as obinituzumab and PV, oral agents such as ibrutinib and lenalidomide, and CAR-T cell treatments. In June 2019, the FDA granted accelerated approval to polatuzumab vedotin with BR for the treatment of adults with RR-DBBHL who received a minimum of two rows of treatment. A trial that randomly assigned 80 transplant-ineligible patients to bendamustine plus rituximab (BR) versus BR plus PV reported that PV based treatment arm achieved superior outcomes. In our case with recurrent intraabdominal bulky disease, despite the 4th order treatment, dramatic response was obtained with Pola-BR.

https://doi.org/10.1016/j.htct.2020.09.092

MYELOMA

PP 30

Isatuximab plus carfilzomib and dexamethasone vs. carfilzomib and dexamethasone in relapsed/refractory multiple myeloma (ikema): interim analysis of a phase 3, randomized, open-label study

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Objective: To demonstrate benefit of adding Isatuximab (Isa) to (Kd) vs. Kd in relapsed/refractory multiple myeloma (RRMM).

Methodology: In this Phase-3 study (NCT03275285), patients with RRMM and 1–3 prior lines of therapy were randomized 3:2 and stratified by number of prior lines and R-ISS to receive Isa-Kd or Kd. Isa-Kd arm received Isa (10 mg/kg IV) weekly for 4 weeks, then every 2 weeks. Both arms received K (20 mg/m^2 days 1–2, 56 mg/m^2 thereafter) twice-weekly for 3 of 4 weeks, and d (20 mg) twice-weekly. Treatment continued until disease progression or unacceptable adverse events (AE). Primary objective: increase in PFS of Isa- Kd vs. Kd, determined by an Independent Response Committee (IRC). Comparison between arms conducted through log-rank testing. Key secondary objectives: overall response rate (ORR), rate of very good partial response (VGPR) or better, complete response (CR) rate, MRD negativity-rate (10^5 by NGS), and

PP 29

Polatuzumab based chemoimmunotherapy showing complete response in a patient of r/r diffuse large b-cell lymphoma

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MYELOMA

PP 30

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overall survival (OS). Key secondary endpoints tested with a closed test procedure. Safety data included treatment emergent adverse events (TEAE), hematological, and biochemistry results for all patients. Interim efficacy analysis is planned once 65% of total expected PFS events are observed.

Results: 302 patients (Isa-Kd: 179, Kd: 123) were randomized. Median age 64 (33–90) years; R-ISS I, II, III was 25.8%, 59.6%, 7.9% respectively; 44%, 33% and 23% had 1, 2 and ≥3 prior lines respectively; 90% and 78% had prior proteasome inhibitor and IMiD respectively; 24% had high-risk cytogenetics. At a median follow-up of 20.7 months and with 103 PFS events per IRC, median PFS was not reached for Isa-Kd vs. 19.15 months Kd; HR 0.531 (99% CI 0.318–0.889), one-sided $p = 0.0007$. Thus, the pre-specified efficacy boundary ($p = 0.005$) was crossed. PFS benefit was consistent across subgroups. ORR (≥PR) was 86.6% Isa-Kd vs. 82.9% Kd, one-sided $p = 0.1930$. ≥VGPR rate was 72.6% Isa-Kd vs. 56.1% Kd, $p = 0.0011$. CR rate was 39.7% Isa-Kd vs. 27.6% Kd. MRD negativity-rate (10–5) in ITT was 29.6% (53/179) Isa-Kd vs. 13.0% (16/123) Kd, descriptive $p = 0.0004$. OS was immature (events 17.3% Isa-Kd vs. 20.3% Kd). 52.0% Isa-Kd vs. 30.9% Kd pts remain on treatment. Main reasons for treatment discontinuation were disease progression (29.1% Isa-Kd vs. 39.8% Kd) and AEs (8.4% Isa-Kd vs. 13.8% Kd). Grade ≥3 TEAEs were observed in 76.8% Isa-Kd vs. 67.2% Kd. Treatment-emergent SAEs (59.3% vs. 57.4%) and fatal TEAEs were similar in Isa-Kd and Kd (3.4% vs. 3.3%,) and Infusion reactions were reported in 45.8% (0.6% grade 3–4) Isa- Kd and 3.3% (0% grade 3–4) Kd. Grade ≥3 respiratory infections (grouping): 32.2% Isa-Kd vs. 23.8% Kd. Grade ≥3 cardiac failure (grouping): 4.0% Isa-Kd vs. 4.1% Kd. As per lab results, grade 3–4 thrombocytopenia and neutropenia were reported in 29.9% Isa-Kd vs. 23.8% Kd and 19.2% Isa-Kd vs. 7.4% Kd, respectively.

Conclusion: Addition of Isa to Kd provided superior, statistically-significant improvement in PFS with clinically meaningful improvement in depth of response. Isa-Kd was well tolerated with manageable safety and favourable benefit-risk profile, and represents a possible new standard of care treatment in patients with relapsed MM. Data first presented at EHA 2020 virtual meeting, June 11–21st. Study sponsored by Sanofi.

https://doi.org/10.1016/j.htct.2020.09.093

PP 31

Relapse of multiple myeloma presenting as extramedullary plasmacytoma surrounding the aorta: a rare case report

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Objective: Extramedullary plasmacytoma (EMP) defines soft tissue tumors that are characterized by plasma cell infiltration and develop secondary to hematogenous spread, in an anatomical site distant from the bone marrow (usually liver, skin, central nervous system, pleura, kidneys, lymph nodes, and pancreas) (3,4). The prevalence of EMP in MM patients is approximately 6–8% at diagnosis and approaches 10–30% during the course of the disease. Here, we present a case of relapsed MM concomitant with a large EMP surrounding the aorta, which is an extremely rare pattern of involvement.

Case report: A 66-year-old male patient presented to our clinic with back pain and weakness in the legs. The patient had been diagnosed with IgG kappa multiple myeloma six years ago. In the initial diagnosis, he had been evaluated as an ISS stage-II, transplant eligible based on clinical and laboratory findings. He had received monthly zoledronic acid, two courses of VAD and two courses of VD regimens. Subsequent to complete response, he had undergone aHSCT with high-dose melphalan for the purpose of consolidation. The patient had achieved complete remission under follow-up after aHSCT. The disease had relapsed approximately 4 years after the first aHSCT, and the patient had undergone another aHSCT with high-dose chemotherapy after a VCD chemotherapy regimen, and had been in complete remission under follow-up. He presented with the complaints stated above 18 months after the second transplantation. On physical examination, bilateral lower extremities showed weakness and impaired sensation. Spinal vertebrae were examined with MRI in consideration of the history of MM. On MRI examination, there were diffuse lytic lesions involving all spinal segments and the sternum, and a soft tissue lesion that involved the aorta-vascular structures in the retrocrural space at the level of T7-L1 and extended to the spinal canal and involved the spinal cord at the level of T8-10. An imaging-guided trucut biopsy was taken from the mass and the diagnosis was confirmed as plasma cell myeloma based on histopathological and immunohistochemical findings. Although the patient underwent 2 courses of Len-Dex, and subsequently, 2 courses of VRD, there was no reduction in the size of the plasmacytoma, and the patient was considered non-responsive. As a more aggressive regimen, a combination of VDT-PACE was administered. A very good partial response was obtained after two courses. The patient was not suitable for allogeneic HSCT because of poor performance status. The patient and his relatives were consulted, and it was decided to continue the treatment with chemotherapy agents.

Conclusion: In conclusion, EMPs, although infrequently, are encountered during the course of multiple myeloma and its relapse. EMPs can be found in very rare localizations. Symptoms vary depending on the anatomical localization of the masses or the dysfunctions that result from the direct mass effect or organ involvement. In this regard, radiological, laboratory, and histopathological evaluation of massive lesions during follow-up is important. Particularly, MRI can be effective as an imaging method in the diagnosis and close follow-up of patients with symptoms associated with extramedullary plasmacytomas.

https://doi.org/10.1016/j.htct.2020.09.094

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PP 31

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https://doi.org/10.1016/j.htct.2020.09.094

PP 32

A rare subtype of poems syndrome: IGG4 subtype

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Objective: There is very limited data concerning the relationship between POEMS syndrome and IgG4-related disease.

Case report: A 40 year-old male patient presented with a 3 month history of progressive weakness and numbness in his lower extremities, impotence, diarrhea and weight loss. Complete blood count was as follows: WBC: 7.3×10^9/L, Hgb: 16.5 g/L, platelet 543×10^9/L. Liver enzymes, renal function, electrolytes and routine urine examination were normal. Ig G level was 14.5 g/dL (normal: 7–16 g/L). Serum immunofixation electrophoresis showed IgG λ monoclonality. Endocrine laborotory tests showed hipergonadotropic hipogonadism. Echocardiography showed pericardial effusion. Abdominal USG showed hepatomegaly and splenomegaly measuring 200 mm and 174 mm on longitudunal axis, respectively. On contrast enhanced MRİ, a 6 cm × 3.5 cm mass showing bone destruction was detected in the left sacral ala extending into the pelvis. PET CT scan demonstrated high FDG uptake (SUVmax: 10.5) for the sacral mass lesion. Based on these findings, a diagnosis of POEMS Syndrome was considered. Funduscopic examination showed no papiloedema. Vascular endothelial growth factor (VEGF) was very high (>700 pg/mL, normal: <96 pg/mL). Trucut biopsy of the mass lesion consisted of a nonneoplastic fibrous tissue and a dense infiltrate of mature plasmacytes with dense eosinophilic cytoplasm and eccentrically placed nuclei. Also, perivascular accumulation of sclerotic collagen like substance was noted. On immunohistochemical staining, neoplastic cells showed diffuse positivity for Ig G and Ig G4. Neoplastic cells were CD138(+), κ(−), λ(+), CD38(+), CD30 (−), ALK(−), CD20(−), CD10(−), CD23(−), CD45(−), CD56(−), CD57(−). Bone marrow biopsy showed a 3% monoclonal λ(+) plasma cell infiltration. Diagnosis of POEMS syndrome was confirmed. Taking into consideration high IgG4 expression in the neoplastic mass, IgG4 levels in serum was checked and found to be high 6.34 g/L (normal <1.35 g/L).

Methodology: POEMS syndrome and IgG4 related diseases show similarities including organomegaly and systemic organ damage. Polyneuropathy and bone lesions associated with IgG4 related diseases has not been reported. PET/CT detects bone lesions and lymph nodes in patients with suspected POEMS syndrome. In IgG4 related disease on the other hand, PET/CT identifies multiple lymph node enlargements/organomegaly with normal metabolic activity.

Results: Our patient had an osteosclerotic mass lesion demostrated by PET/CT and histopathological examination. Our patient had high serum IgG4 level and showed IgG4 plasmacyte tissue infiltration, yet her plasmacytes were shown to be monoclonal by bone marrow immunohistochemical staining and serum immunofixation electrophoresis. Therefore, final diagnosis was POEMS syndrome but not IgG4 related disease.

Conclusion: We propose this patient has a subtype of POEMS syndrome because he showed high serum IgG4 levels and a monoclonal IgG4 plasmacyte tissue infiltration. Monoclonal hyperglobinemia is not a feature of IgG4 related disease. It is not clear whether IgG4-positive plasma cell tissue infiltration and elevated serum IgG4 concentrations are origins or outcomes of IgG4 related diseases. To our knowledge, this is the second presumed case of POEMS syndrome-IgG4 subtype. Further research and collecting more cases are essential. We suggest every suspected POEMS patient should be tested for their serum IgG4 concentration.

https://doi.org/10.1016/j.htct.2020.09.095

PP 33

Monoclonal gammopathy of undertemined significance and solitary plasmacytoma: progression factors in population of gomel region in belarus

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Objective: To define progression factors of MGUS and SP in population of Gomel region in Belarus.

Case report: Solitary plasmacytoma (SP) and monoclonal gammopathy of undetermined significance (MGUS) are characterized by the presence of less than 10% of tumor cells in the bone marrow and the absence of CRAB criteria. Both diseases have a high risk of progression to multiple myeloma due to certain factors.

Methodology: The study included 106 patients: MGUS ($n = 90$) and SP ($n = 16$) of Gomel region (Belarus) in 2017–2019. The average age was 60.5 years; female patients prevailed All patients underwent aspiration biopsy with IPT and FISH, trepanobiopsy of the ilium wing with immunohistochemical examination of the bone marrow. (Bone marrow aspirates IPT and FISH, and biopsies were obtained for cytological and histopathological evaluation of PC infiltration, including immunohistochemical). The determination of the ratio of light chains of immunoglobulins (kappa/lambda) in blood serum was carried out. Results were assessed after 3 years of observation. The signs of progression include the appearance of any one of the CRAB-criteria.

Results: There were no statistically significant differences between groups of patients with MGUS and SP according to signs (presence of tumor plasma cells, CD95+, CD200+, CD27+,

PP 32

A rare subtype of poems syndrome: IGG4 subtype

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Objective: There is very limited data concerning the relationship between POEMS syndrome and IgG4-related disease.

Case report: A 40 year-old male patient presented with a 3 month history of progressive weakness and numbness in his lower extremities, impotence, diarrhea and weight loss. Complete blood count was as follows: WBC: 7.3×10^9/L, Hgb: 16.5 g/L, platelet 543×10^9/L. Liver enzymes, renal function, electrolytes and routine urine examination were normal. Ig G level was 14.5 g/dL (normal: 7–16 g/L). Serum immunofixation electrophoresis showed IgG λ monoclonality. Endocrine laborotory tests showed hipergonadotropic hipogonadism. Echocardiography showed pericardial effusion. Abdominal USG showed hepatomegaly and splenomegaly measuring 200 mm and 174 mm on longitudunal axis, respectively. On contrast enhanced MRİ, a 6 cm × 3.5 cm mass showing bone destruction was detected in the left sacral ala extending into the pelvis. PET CT scan demonstrated high FDG uptake (SUVmax: 10.5) for the sacral mass lesion. Based on these findings, a diagnosis of POEMS Syndrome was considered. Funduscopic examination showed no papiloedema. Vascular endothelial growth factor (VEGF) was very high (>700 pg/mL, normal: <96 pg/mL). Trucut biopsy of the mass lesion consisted of a nonneoplastic fibrous tissue and a dense infiltrate of mature plasmacytes with dense eosinophilic cytoplasm and eccentrically placed nuclei. Also, perivascular accumulation of sclerotic collagen like substance was noted. On immunohistochemical staining, neoplastic cells showed diffuse positivity for Ig G and Ig G4. Neoplastic cells were CD138(+), κ(−), λ(+), CD38(+), CD30 (−), ALK(−), CD20(−), CD10(−), CD23(−), CD45(−), CD56(−), CD57(−). Bone marrow biopsy showed a 3% monoclonal λ(+) plasma cell infiltration. Diagnosis of POEMS syndrome was confirmed. Taking into consideration high IgG4 expression in the neoplastic mass, IgG4 levels in serum was checked and found to be high 6.34 g/L (normal <1.35 g/L).

Methodology: POEMS syndrome and IgG4 related diseases show similarities including organomegaly and systemic organ damage. Polyneuropathy and bone lesions associated with IgG4 related diseases has not been reported. PET/CT detects bone lesions and lymph nodes in patients with suspected POEMS syndrome. In IgG4 related disease on the other hand, PET/CT identifies multiple lymph node enlargements/organomegaly with normal metabolic activity.

Results: Our patient had an osteosclerotic mass lesion demostrated by PET/CT and histopathological examination. Our patient had high serum IgG4 level and showed IgG4 plasmacyte tissue infiltration, yet her plasmacytes were shown to be monoclonal by bone marrow immunohistochemical staining and serum immunofixation electrophoresis. Therefore, final diagnosis was POEMS syndrome but not IgG4 related disease.

Conclusion: We propose this patient has a subtype of POEMS syndrome because he showed high serum IgG4 levels and a monoclonal IgG4 plasmacyte tissue infiltration. Monoclonal hyperglobinemia is not a feature of IgG4 related disease. It is not clear whether IgG4-positive plasma cell tissue infiltration and elevated serum IgG4 concentrations are origins or outcomes of IgG4 related diseases. To our knowledge, this is the second presumed case of POEMS syndrome-IgG4 subtype. Further research and collecting more cases are essential. We suggest every suspected POEMS patient should be tested for their serum IgG4 concentration.

https://doi.org/10.1016/j.htct.2020.09.095

PP 33

Monoclonal gammopathy of undertemined significance and solitary plasmacytoma: progression factors in population of gomel region in belarus

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Objective: To define progression factors of MGUS and SP in population of Gomel region in Belarus.

Case report: Solitary plasmacytoma (SP) and monoclonal gammopathy of undetermined significance (MGUS) are characterized by the presence of less than 10% of tumor cells in the bone marrow and the absence of CRAB criteria. Both diseases have a high risk of progression to multiple myeloma due to certain factors.

Methodology: The study included 106 patients: MGUS ($n = 90$) and SP ($n = 16$) of Gomel region (Belarus) in 2017–2019. The average age was 60.5 years; female patients prevailed All patients underwent aspiration biopsy with IPT and FISH, trepanobiopsy of the ilium wing with immunohistochemical examination of the bone marrow. (Bone marrow aspirates IPT and FISH, and biopsies were obtained for cytological and histopathological evaluation of PC infiltration, including immunohistochemical). The determination of the ratio of light chains of immunoglobulins (kappa/lambda) in blood serum was carried out. Results were assessed after 3 years of observation. The signs of progression include the appearance of any one of the CRAB-criteria.

Results: There were no statistically significant differences between groups of patients with MGUS and SP according to signs (presence of tumor plasma cells, CD95+, CD200+, CD27+,

CD56+, IHC of CD138+ plasma cells, presence of M-protein in bone marrow) (Fisher p ranged from 0.292 to 0.73). An aberrant phenotype or the presence of clonal plasma cells <10% in SP patients was detected in 31%. According to the secretion of immunoglobulins: with MGUS, IgG secretion (53.3%) was most common, with SP, we observed non-secretion variant (37.5%), IgG secretion (31.5%). During the observation period, disease progression into MM was recorded in 18.8% in SP and in 16% MGUS patients. Disease progression in SP patients was associated with the presence of cytogenetic changes (the presence of del13) in combination with IHC of CD138+ >10%, an abnormal ratio of κ/λ chains. High expression of CD27+ was observed. In one patient with SP (iliac plasmacytoma), the disease transformed into MM within six months in the presence of risk factors: clonal plasma cells in the bone marrow −3.1%, CD56+ 93.1%, CD95+ 3.8% by IPT, del13, IHC CD138+ 20%. With MGUS, disease progression was associated with the presence of a combination of CD138+ >10% (76.5% vs. 23.6%; $p < 0.0001$), CD95+ <20% (44.0% vs. 71.4%; $p < 0,083$), CD56+ >20% according to IPT (27.3% vs. 78.0%; $p < 0.0001$), loss of CD27+ expression (66.7%), abnormal ratio κ/λ of chains $p < 0.001$.

Conclusion: Our study showed that a combination of such indicators as the presence of cytogenetic changes (in particular, the presence of del13), CD138+ cells >10% according to IHC, CD56+ >20%, CD95+ <20% according to IPT in combination with an abnormal ratio of κ/λ chains can have prognostic value in transformation into MM in both MGUS patients and SP patients.

https://doi.org/10.1016/j.htct.2020.09.096

PP 34

Poems syndrome: a "multifaceted" entity of plasma cell disorder

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Objective: The objective of this study is to reveal patients with misdiagnosed POEMS syndrome in the group of patients with polyneuropathy and to stratify the right form of the plasma cell disease. POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes) is a rare paraneoplastic disorder caused by plasma cell proliferative disease. The exact incidence of POEMS syndrome is unknown as diagnosis of POEMS syndrome is prolonged and complicated due to variety and non-specific symptoms. In accordance to some sources the incidence of POEMS syndrome is 0.3 per 100,000, however the disease rate may be higher due to missed diagnosis. POEMS syndrome is a plasma cell disorder and the medications used for the treatment are similar to multiple myeloma treatment regimens. However this is a distinct entity with disease process nuances, that's why the selection of the right medication could be crucial for the wellness and survival of patient with POEMS syndrome.

Case report: The first case of POEMS syndrome is diagnosed in Armenia in 2019. The rate of plasma cell disorders that is mainly presented with multiple myeloma is 1.3 per 100,000 in Armenia. In the last decade there is a tendency of increasing of multiple myeloma cases in Armenia. This fact is associated with the improvement of diagnostic methods. The first reported patient with POEMS syndrome is a young men suffering of severe pain in the legs. He was diagnosed with chronic demyelinating polyneuropathy and treated with plasmapheresis and immunoglobulin for 6 months. No efficacy was observed. The progressive neuropathy and new symptoms such as edema, shortness of breath caused patients' disability and his admission to intensive care department. The CT scan, USD examination, bone marrow biopsy, echocardiography, serum protein electrophoresis, CBC, blood chemistry were performed. The examination results were not consistent with multiple myeloma disease, monoclonal gammapathy of undetermined significance (MGUS) and chronic inflammatory demyelinating polyneuropathy (CIDP). The deviations that were revealed during analysis were compared with POEMS syndrome diagnostic criteria and made the diagnosis of POEMS syndrome.

Methodology: 13 patients not responding to the standard treatment protocols for polyneuropathy and 4 patients not corresponding with classic multiple myeloma criteria were included in this study. The spectrum of standard examinations included bone marrow biopsy, immune fixation electrophoresis, CT scan, echocardiography, CBC, Blood chemistry, Interleukin 6 and Interleukin 12 levels detection.

Results: The results were promising. In 3 patients treated for polyneuropathy, not responding to treatment and taking morphine due to severe pain the blood electrophoresis revealed low quantity of monoclonal immunoglobulin (M-spike) with Lamda component detected by immune fixation and the CT show sclerotic lesions in the bones. 2 patients with uncommon myeloma symptoms such as specific pulmonary impairment show high level of Interleukin 6 and Interleukin 12, that can cause the pulmonary hypertension.

Conclusion: The new examinations must to be involved in the list of obligatory analysis for neurology disease. The spectrum of analyses (diagnostic criteria) adopted for plasma cell disorder have to be extended including echocardiography and analyses of interleukin 6 and interleukin 12 for the right diagnosis and target therapy.

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PP 34

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Conclusion: The new examinations must to be involved in the list of obligatory analysis for neurology disease. The spectrum of analyses (diagnostic criteria) adopted for plasma cell disorder have to be extended including echocardiography and analyses of interleukin 6 and interleukin 12 for the right diagnosis and target therapy.

https://doi.org/10.1016/j.htct.2020.09.097

PP 35

Pomalidomide-dexamethasone in the management of heavily pretreated multiple myeloma

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Objective: Pomalidomide is a new generation IMID, with a very good compliance, thanks to oral administration, which can be used also in heavily pretreated patients, in a domestic setting.

Case report: In this retrospective observational trial, it has been evaluated efficacy and tolerance of pomalidomide plus dexamethasone (PD) as salvage regimen in heavily pretreated patients with relapsed and refractory MM (rrMM), whose prognosis is particularly severe.

Methodology: 57 patients (31 M/26 F), with rrMM, median age at diagnosis 69 years (r. 52–86), and median age at start of treatment 76 years (r.56–90) treated with several lines of treatments (median 7, r. 2–11), every refractory to all the drugs previously received (also Bortezomib, Thalidomide and Lenalidomide), received Pomalidomide-Dexamethasone (Pomalidomide 4 mg for 21 days, Dexamethasone 40 mg days 1, 8, 15, 22, pegfilgrastim day +8) every 28 days, until progression. ISS was equally distributed, and cytogenetic at relapse was evaluable in 14 patients. All the patients had previously been treated with schedule containing bortezomib and IMIDs. 63% (36/57) had undergone at least to a single ASCT. All patients were relapsed and refractory to last therapies received before PD.

Results: Pomalidomide was well tolerated, with grade 3–4 transfusion-dependent anemia in 58% (33/57) of patients, 44% (23/57) grade 3–4 neutropenia (pegfilgrastim in primary prophylaxis was given, no hospitalization was required, no septic shocks were observed), 40% (23/57) grade 3–4 thrombocytopenia without hemorrhagic events and transfusion-dependence. No severe extra-hematologic toxicity was observed. According to IMWG, ORR1 (≥PR) was 47.3% (27/57: 5 CR, 11 VGPR, 7 PR, 4 MR), but, considering that we are evaluating a cohort of heavily pretreated patients, with poor prognosis, another parameter should be considered, ORR2 (≥SD), considering stable disease as a successful result in progressive MM. ORR2 was 77.1% (17 SD). These can be considered as impressive result in this subset of patients. Oral treatment gives a really good compliance, in frail and unfit patients, and response, when present, is always really fast (median time to response: 2 months (r.1–6)), median OS from diagnosis was 94 months (range 21–234), median OS from start of pomalidomide was 9 months (range 1–25). Nine patients have surprisingly achieved a notable response (3 VGPR, 4 PR, 2 MR) after failure of novel agents (i.e. Carfilzomib, Daratumumab and Pomalidomide).

Conclusion: Pomalidomide-dexamethasone has shown significant efficacy and a very good compliance, thanks to oral administration, in a particularly severe setting of heavily pretreated patients, relapsed and refractory to all available therapeutic resources, also after failure of novel agents.

https://doi.org/10.1016/j.htct.2020.09.098

PP 36

Carfilzomib-lenalidomide-dexamethasone in the management of lenalidomide-refractory multiple myeloma

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Objective: Carfilzomib is an epoxyketone proteasome inhibitor of second generation, proved to be effective and safe in relapsed and refractory Multiple Myeloma (rrMM), in combination with dexamethasone or lenalidomide and dexamethasone.

Case report: In this retrospective observational trial, it has been evaluated efficacy and safety of carfilzomib, in combination with lenalidomide-dexamethasone (KRD) as salvage regimen in patients with rrMM, refractory to lenalidomide, where lenalidomide-based regimens have no proven efficacy.

Methodology: 41 patients (23 M/18 F), with rrMM, median age at diagnosis 63.7 years (r. 43–82), median age at start of treatment 67 years (r. 48–84) previously treated with several lines of treatments (median 3, r. 2–11), underwent to KRD regimen (ASPIRE trial schedule) for a median treatment cycles of 8 (r 2–18). ISS was equally distributed, and all patients had previously been treated with bortezomib and IMIDs, and were refractory to this agents. 61% (19/31) of them had undergone at least to a single ASCT.

Results: According to IMWG criteria, after a median follow-up of 9 months (r. 2–18), ORR was 68.2% (28/41: 9 CR, 12 VGPR, 7 PR) with 5 progressive diseases (PD) and 8 patients in stable disease (SD): this can be considered as an impressive result in this subset of rrMM patients, refractory to lenalidomide. In particular, for 11 patients, KRD was, after having achieved at least a PR, a bridge to second/third autologous SCT. Median time to response was 1.3 months (r.1–4), median OS from diagnosis was 62 months (r. 9–170), median OS from start of Carfilzomib was 11 months (r. 2–18). Carfilzomib was well tolerated, with grade 2 anemia in 39%(16/41) of patients, successfully managed by ESAs, without necessity of blood transfusions; 29% (12/41) grade 3–4 neutropenia (pegfilgrastim in primary prophylaxis was given, no ospedalization was required, no septic shocks were observed); 34% (14/41) grade 2, 21% (9/41) grade 3 and 12% (5/41) grade 4 thrombocytopenia,

PP 35

Pomalidomide-dexamethasone in the management of heavily pretreated multiple myeloma

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Conclusion: Pomalidomide-dexamethasone has shown significant efficacy and a very good compliance, thanks to oral administration, in a particularly severe setting of heavily pretreated patients, relapsed and refractory to all available therapeutic resources, also after failure of novel agents.

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PP 36

Carfilzomib-lenalidomide-dexamethasone in the management of lenalidomide-refractory multiple myeloma

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Results: According to IMWG criteria, after a median follow-up of 9 months (r. 2–18), ORR was 68.2% (28/41: 9 CR, 12 VGPR, 7 PR) with 5 progressive diseases (PD) and 8 patients in stable disease (SD): this can be considered as an impressive result in this subset of rrMM patients, refractory to lenalidomide. In particular, for 11 patients, KRD was, after having achieved at least a PR, a bridge to second/third autologous SCT. Median time to response was 1.3 months (r.1–4), median OS from diagnosis was 62 months (r. 9–170), median OS from start of Carfilzomib was 11 months (r. 2–18). Carfilzomib was well tolerated, with grade 2 anemia in 39%(16/41) of patients, successfully managed by ESAs, without necessity of blood transfusions; 29% (12/41) grade 3–4 neutropenia (pegfilgrastim in primary prophylaxis was given, no ospedalization was required, no septic shocks were observed); 34% (14/41) grade 2, 21% (9/41) grade 3 and 12% (5/41) grade 4 thrombocytopenia,

without hemorrhagic events and transfusion-dependency. Moreover, it was observed pneumonia in 39% (16/41) of patients, treated by common antibiotic drugs and always solved. A cardiac monitoring was performed for all patients: hypertension (grade 2–3) in 34% (14/41) of patients; fatigue in 39% (16/31) of patients.

Conclusion: Carfilzomib-Lenalidomide-Dexamethasone has shown significant efficacy in a particularly severe setting of patients, relapsed and refractory to all available therapeutic resources, also lenalidomide, and it could be considered as a bridge to a second autologous or allogenic SCT.

https://doi.org/10.1016/j.htct.2020.09.099

PP 37

The relationship of hepcidin, soluble transferrine receptor, growth differentiation factor-15 and anemia in multiple myeloma

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Objective: Multiple myeloma is a malignant disease of clonal plasma cells and anemia takes part in most of the patients. Although it is similar to the anemia of chronic disease with many parameters, the exact mechanism has not been clarified. Hepcidin, Growth differentiation factor-15 (GDF-15), soluble transferrin receptor (sTfR) have been investigated in many forms of anemia, especially in chronic diseases and cancers. However, there are few studies investigating their role in anemia in myeloma. In this project, we aimed to determine the relationship between hepcidin, sTfR and GDF-15 levels in multiple myeloma patients and their clinical features such as anemia parameters and disease stage.

Methodology: This study was approved by Duzce University Faculty of Medicine Non-Invasive Ethics Committee with the decision dated 20.01.2015 and numbered 2015/110 and supported by Düzce University Department of Scientific Research Projects with Project number 2015.04.03.336. Multiple myeloma patients who were diagnosed at our hematology clinic were evaluated for the study. Among these newly diagnosed patients, those who received erythrocyte or whole blood transfusion, iron, B12 or folic acid treatment within the last month were excluded and total 28 patients were enrolled. A control group of 28 people was formed from the volunteers without any disease and fasting blood samples were taken from all participants. After reaching the targeted number of patients and control groups, serum hepcidin, sTfR and GDF-15 levels were obtained from these preserved samples by ELISA method.

Results: Although myeloma patients had significantly lower Hb and Hct levels compared to the control group (median Hb 9.95 vs. 13.40 g/dL and median Hct 30.35% vs. 40.00%, $p < 0.001$), none of the GDF-15, hepcidin and sTfR levels showed a significant difference between the myeloma and control groups. Among multiple myeloma patients, we found that the anemic subgroup had significantly lower hepcidin levels than the non-anemic subgroup ($p = 0.043$) but GDF-15 or sTfR levels were not different ($p > 0.05$). When the correlations were examined, GDF-15, hepcidin and sTfR levels showed correlation with each other, while GDF15 was positively correlated with creatinine and sTfR levels were positively correlated with many parameters such as LDH, CRP, ferritin, albumin, creatinine, Hb and ISS stage. None of the levels of GDF-15, hepcidin and sTfR had a significant effect on survival.

Conclusion: Our findings suggested that mediators of chronic inflammation may play an important role in myeloma anemia but there is not always a clear interaction as in chronic disease anemia, there may be mechanisms that include partial response deficiencies and accommodate variable responses according to the characteristics of the patient groups.

https://doi.org/10.1016/j.htct.2020.09.100

OTHER DISEASES

PP 38

Serum & salivary ferritin levels in iron deficiency anemia is there is a difference?

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Objective: Iron deficiency anemia (IDA) is one of the most important nutritional deficiencies in Egypt. The assessment of serum ferritin has been the gold standard method in the detection of this disease But, this involves the drawing of venous blood, which is invasive and is sometimes physically and psychologically traumatic to the patients, and sometimes it is difficult to withdraw blood from hidden veins. This study is done to estimate and correlate the serum ferritin levels & saliva of patients with IDA. Thus, assessing the effectiveness of saliva as an alternative non-invasive diagnostic tool. This study is done to estimate, compare and correlate the Ferritin level in serum & saliva of iron deficiency anemia patients, to determine whether saliva can be used as a predictive marker to monitor the iron levels in iron deficiency anemia.

Methodology: 60 patients with iron deficiency anemia and 20 healthy subjects as control were chosen for the study. Quantitative estimation of serum and salivary ferritin was performed by solid-phase ELISA, hemoglobin levels were also estimated to confirm the anemic status of the patient.

Results: Increased salivary ferritin level in patients with iron deficiency anemia and negative significant correlation between the salivary ferritin, salivary/serum ferritin ratio, and serum hemoglobin and a significant negative correlation between serum and salivary ferritin.

Conclusion: Salivary ferritin is a noninvasive method for the detection of IDA with a good predictive impact.

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without hemorrhagic events and transfusion-dependency. Moreover, it was observed pneumonia in 39% (16/41) of patients, treated by common antibiotic drugs and always solved. A cardiac monitoring was performed for all patients: hypertension (grade 2–3) in 34% (14/41) of patients; fatigue in 39% (16/31) of patients.

Conclusion: Carfilzomib-Lenalidomide-Dexamethasone has shown significant efficacy in a particularly severe setting of patients, relapsed and refractory to all available therapeutic resources, also lenalidomide, and it could be considered as a bridge to a second autologous or allogenic SCT.

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PP 37

The relationship of hepcidin, soluble transferrine receptor, growth differentiation factor-15 and anemia in multiple myeloma

B. Onec[1,*], D. Köş[2], G. Altun[2], M. Sungur[3]

[1] *Department of Hematology, Duzce School of Medicine, Duzce, Turkey*
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PP 39

Hepcidin level changes in type 2 diabetes

A. Gawaly*, F. Atyia

Tanta University, Tanta, Egypt

Objective: Background: Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion or insulin action, or both. Diabetes and its complications have become a major public health problem in the world and its prevention has become a public health priority. Hepcidin, a 25-amino-acid antimicrobial peptide, is the central regulator of iron homeostasis. Under normal circumstances, hepcidin expression and subsequent release into plasma prevents further absorption of iron from the duodenal enterocytes by preventing the efflux of iron by ferroportin channels, hence reduced amounts of iron delivery via transferrin to hepatocytes. In response to iron loading, hepcidin expression increased to prevent the further uptake of iron. Conversely, during iron deficiency, hepcidin expression decreased. Aim of the Study: Was to assess the possible changes of serum hepcidin that may occur in patients with type 2 diabetes. Objectives: Was to evaluate changes of serum hepcidin level in type 2 diabetes, assess possible relationships of serum hepcidin, iron status, hepcidin: Ferritin ratio and HOMA-IR in type 2 diabetes patients.

Methodology: This study consisted of randomized eighty subjects divided into four groups: Group 1: Included 20 patients with impaired glucose tolerance (pre-diabetes), Group 2: Included 20 patients with controlled diabetes, Group 3: 20 patients with uncontrolled diabetes, Group 4: Included 20 healthy volunteers.

Results: : Hepcidin: Ferritin ratio was statistically high in impaired glucose tolerance and low in uncontrolled diabetes with (p-value <0.001*) and normal in controlled diabetes and healthy volunteers. A significant negative correlation between hepcidin: ferritin ratio and HOMA-IR in impaired glucose tolerance with (p-value = 0.009*) was found.

Conclusion: Serum hepcidin affected by multiple factors so cannot be used for screening of type 2 diabetes. But hepcidin: Ferritin ratio could be a novel marker for early screening of patients with type 2 diabetes.

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PP 40

Chemotherapy delivering port-a-cath migration into the heart: a case report

A. Omar[1,*], O. Bheleel[1], A. Abushaala[1], L. Sabei[2], A. Rakha[1]

[1] *Tripoli University Hospital, Tripoli, Libya*
[2] *University Of Tripoli, Tripoli, Libya*

Objective: Chronically diseased patients who require long-term therapy through central venous access, a totally implanted central venous port systems are used. Such beneficial devises have life-threatening complications.

Case report: We report a 45-year-old Libyan female diagnosed with poorly differentiated gastric adenocarcinoma, underwent total gastrictomy with eso-jujenal anastomosis with port-a-cath placement to deliver chemotherapy. At the fourth cycle of chemotherapy, unfavourable event occurred; the catheter dislodged and migrated to the right cardiac chambers, which was successful removed by local anaesthesia with loop-snare technique via the right femoral vein.

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Results: The port-a-cath was successful removed by local anaesthesia with loop-snare technique via the right femoral vein and the patient preference to complement the chemotherapy cycles through peripheral line after psychological trauma she experianced of the dislodgment and empolization of the port-a-cath.

Conclusion: Port-a-cath is beneficial devise has serious complications. To avoid dislodgment, displacement, and empolization developing of the port-a-cath is needed.

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PP 41

Reactive lymphocytes in blood film of a covid-19 iraqi patient: a case report

A. Al-Ani

Hematology, Department of Pathology, Medical College, University of Anbar, Ramadi, Iraq

Objective: Coronavirus disease 2019 (COVID-19) is a novel highly infectious disease with variable laboratory parameters changes. The disease is highly contagious and any delay in the diagnosis leads to an increased possibility of its spread. This study explores the use of blood film as a cheap, rapid and feasible laboratory test in the disease diagnosis. In low medical resources countries, this can be a crucial diagnostic method.

Case report: A 51-year-old Iraqi male had investigations done by Istishari Medical – private – Laboratory. He was diagnosed with COVID-19, of a moderate severity. The CBC showed normal hemoglobin of 15.71 g/dL (packed cell volume, PCV of 49.4%), WCC of 7.4×10^9/L, neutrophils of 5.3×10^9/L (71.7%), lymphocytes of 1.0×10^9 (14.1%), monocytes and platelets count 125×10^9/L. Serum ferritin of 664.0 μg/L (NR: 30.0–400.0), CRP of 59.0 mg/L (NR: <5.0) and D-Dimer of 0.27 mg/ml (NR: up to 0.5). The biochemical changes for the liver and renal functions expressed mild changes. Stained peripheral blood smear showed presence of many characteristic large atypical lymphocytes, constituting about 43% of the all lymphocytes (14.5% of the WCC). The most common subtype seen in the patient's blood film displayed a distinctive abundant pale blue cytoplasm, sometimes confined to its irregular margins which

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indented by 'hug' the surrounding RBC. The nucleus exhibits loosely condensed chromatin with inconspicuous nucleoli. Less frequently, lymphoplasmacytoid lymphocyte was noticed in the stained blood smear. These cells showed ample pale blue unevenly stained cytoplasm with paranuclear of which contains eccentric nucleus with condensed chromatin.

Methodology: In this study, a peripheral blood smear of a COVID-19 patient was examined for the presence of abnormal leukocytes morphological changes.

Results: The blood film showed presence of atypical lymphocytes constituting about 43% of all lymphocytes (14.5% of the white cell count). This case report of COVID-19 patient represents an unusual feature of coronavirus family infections other than severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Conclusion: This study shows that the presence of reactive lymphocytes in the patient's blood film can be a pivotal finding in the diagnosis of COVID-19. Additionally, it emphasized the importance of blood film examination as an essential hematological test for COVID-19.

https://doi.org/10.1016/j.htct.2020.09.104

PP 42

A study of hematological disease prevalence in covid-19 pandemic: a single center experience

V. Gursoy

Department of Hematology, Bursa Yuksek Ihtisas Education and Training Hospital, University of Health Sciences, Bursa, Turkey

Objective: In the present study we aimed to investigate the prevalence of hematological conditions and patient characteristics among a patient population diagnosed with the COVID-19 infection at our hospital during the COVID-19 pandemic.

Methodology: Our study enrolled patients older than 18 years of age who were diagnosed with COVID-19 infection by physical examination and various studies and managed as inpatients at our hospital designated as a pandemic hospital within a two-month period between 15 March 2020 and 15 May 2020. The patients' age and sex distributions, contact status, comorbidities, primary hematological disorder, polymerase chain reaction (PCR) smear tests, computerized tomographic findings, need for intensive care, treatments regimens, total length of clinic stay, and rates of discharge and mortality were retrospectively reviewed.

Results: We reviewed the medical records of a total of 1928 patients who were admitted to pandemic clinics with the diagnosis of PCR-positive COVID-19 or suspected COVID-19 during the prespecified two-month period. Among these patients, 963 (49.9%) were male, and 965 (50.1%) were female. Their mean age was 51.3 ± 21.4 (min–max: 18–99) years. Eleven (0.57%) patients had a hematological condition and were thus consulted with the hematology department. They consisted of 3 females and 8 males with a mean age of 64.7 ± 18.7 (min–max: 22–89) years. A review of their diagnoses identified 4 patients with chronic lymphocytic leukemia (CLL), 2 patients with acute myeloid leukemia (AML), 1 patient myelodysplastic syndrome (MDS), 1 patient with non-Hodgkin lymphoma (NHL), 1 patient with chronic immune thrombocytopenia (ITP), 1 patient with polycytemia vera (PV), and 1 patient with thalassemia intermedia. While 4 patients had not taken any treatment for a hematological condition prior to the COVID-19 infection, 2 patients had taken azacitidine, 1 patient hydroxyurea, 1 patient chlorambucil, 1 patient R-FC (rituximab- fludarabine, cyclophosphamide), 1 patient R-Benda (rituximab-bendamustine), and 1 patient CHOP (Cyclophosphamide, Vincristine, Doxorubicin, Prednisolone). Three patients had a history of contact with COVID-19. While all patients had pulmonary involvement on a thoracic computerized tomography, three of them had mild involvement. Four patients needed intensive care. Seven (64%) patients had at least one comorbidity such as diabetes, hypertension, or coronary artery disease. All patients were treated with hydroxychloroquine, azithromycin, and enoxoparine. Four patients showing signs of disease progression were administered favipirapir while a patient received IVIG and another one received plasma therapy. The mean length of hospital stay was 12.7 days (min–max 2–27). Three of 11 patients died.

Conclusion: "COVID-19" and the "pandemic" it has caused, every detail of which we have still not understood, is a significant global problem from every aspects. Alongside of particularly the elderly, the patient group with hematological conditions that are immunosuppressed due to conditions themselves or their treatment regimens are at particular risk of infection by the COVID-19 pandemic. Our study have shown that the prevalence of hematological conditions is about 0.5% among patients infected by COVID-19. Patients with hematological conditions taking utmost care of isolation measures, protecting themselves, having strong family support, and being accustomed to the isolation process make a significant contribution to such a low prevalence.

https://doi.org/10.1016/j.htct.2020.09.105

PP 43

A case of malignant peritoneal mesothelioma as a rare cause of autoimmune haemolytic anaemia

I. Whybrow Huppatz*, V. Singh

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Objective: Nearly half of the cases of autoimmune haemolytic anaemia (AIHA) are associated with an underlying disorder that leads to immune dysregulation, and malignancies is one of them. Although AIHA is reported in patients with a wide range of haematological malignancies, most frequently in Chronic Lymphocytic Leukameia and Non-Hodgkin Lymphoma, only 1–2% are associated with solid organ malignancy. This case report highlights malignant peritoneal mesothelioma as a rare cause of autoimmune haemolytic anaemia.

Case report: We report a case of a twenty-nine year old female who initially presented to her general practitioner with a six month history of symptoms suggestive of irritable

indented by 'hug' the surrounding RBC. The nucleus exhibits loosely condensed chromatin with inconspicuous nucleoli. Less frequently, lymphoplasmacytoid lymphocyte was noticed in the stained blood smear. These cells showed ample pale blue unevenly stained cytoplasm with paranuclear of which contains eccentric nucleus with condensed chromatin.

Methodology: In this study, a peripheral blood smear of a COVID-19 patient was examined for the presence of abnormal leukocytes morphological changes.

Results: The blood film showed presence of atypical lymphocytes constituting about 43% of all lymphocytes (14.5% of the white cell count). This case report of COVID-19 patient represents an unusual feature of coronavirus family infections other than severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Conclusion: This study shows that the presence of reactive lymphocytes in the patient's blood film can be a pivotal finding in the diagnosis of COVID-19. Additionally, it emphasized the importance of blood film examination as an essential hematological test for COVID-19.

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PP 42

A study of hematological disease prevalence in covid-19 pandemic: a single center experience

V. Gursoy

Department of Hematology, Bursa Yuksek Ihtisas Education and Training Hospital, University of Health Sciences, Bursa, Turkey

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Case report: We report a case of a twenty-nine year old female who initially presented to her general practitioner with a six month history of symptoms suggestive of irritable

bowel syndrome. Her blood count identified a significant anaemia (haemoglobin 53 g/L) and thrombocytosis (platelets 1260×10^9/L), and was thus referred to haematology clinic. She was diagnosed with IgG-C3d AIHA. The patient was started on prednisolone 1 mg/kg with a good initial response. To investigate the underlying cause, a whole body CT scan was performed, which identified significant abdominal ascites. Serum CA-125 was raised at 6715U/mL (range 0–35) and paracentesis revealed an LDH of 1203 SU suggesting underlying malignancy, but no malignant cells were found on the ascitic fluid cytology. The patient went on to have a PET scan, which confirmed FDG avid serosal disease, with update in the liver, omentum and peritoneum. Diagnostic laparotomy revealed widespread nodules on all serosal surfaces, and the biopsy confirmed a diagnosis of peritoneal epithelioid malignant mesothelioma. Whilst the patient had her workup with the oncology team, her AIHA became refractory to steroid treatment, and was commenced on Rituximab at 375 mg/m^2 weekly infusions. The patient did not respond to 4 doses of Rituximab, and continued to require regular transfusion support. She eventually started chemotherapy for the mesothelioma, which reduced the briskness of haemolysis, and reduced transfusion requirements; although haemolysis did not completely cease.

Conclusion: To our knowledge, this is the third case of AIHA with malignant peritoneal mesothelioma reported in literature. There is currently no established treatment for AIHA associated with solid organ malignancy. This case highlights the poor response to standard treatments, and only a partial response to the definitive treatment for the underlying malignancy.

https://doi.org/10.1016/j.htct.2020.09.106

PP 44

Erdheim–Chester disease: a single center experience

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Objective: Erdheim-Chester disease (ECD) is a rare histiocytosis which has typical findings including central diabetes insipidus, restrictive pericarditis, perinephric fibrosis, and sclerotic bone lesions. ECD is primarily a disease of middle-aged adults, with a mean age of 46 years at diagnosis in the United States (range, 20–74 and 56 years in the French cohort (range, 29–86). The exact incidence is unknown due the lack of population-based mandatory reporting to national registries.

Case report: Patient-1 Patient-2 Patient-3 Patient-4 Patient-5 Sex Male Male Female Female Male Age at compilation 32 32 51 65 41 Age at diagnosis 28 29 48 64 37 Follow up from disease onset, mo 59 45 40 12 44 Constitional symptoms – – – – + Skeletal involvement + + + + + Extraskletal involvement + + – + + Cardiac involvement Coronary involvement – – – – – Pericardial involvement + – – – – Right atrial pseudotumor – – – – – Valvulopaty – – – – – Large vessel involvement – – – – – CNS involvement Central DI + – – + – SerebellarSyndrome – – – – – Extra–axial mass – + – – – Hypophyseal involvement – – – – Pulmonary involvement + – – – – Orbital involvement – – – – + Cutaneous involvement (xanthelasma) – – – – + Retroperitoneal involvement – – – – – Adrenal infiltration – – – – – Paranasal sinüs involvement – – – – – Maxillary involvement – – – – – Treatment + + + + + Peg IFN-α/IFN-α + – + + + Radiotherapy – – + – – Corticosteroids – – – – + Other – + – – +

Methodology: Data of five patients were retrospectively analyzed in our center. The mean age of the patients was 41.2 years (28–64 years) at the time of diagnosis. The mean follow-up period was 40 months (12–59 months).

Results: The patients were mostly diagnosed with the bone. The most commonly involved organ was the bone, followed by the central nervous system (CNS), heart, lung, periorbita, and skin, respectively. While bone involvement was observed in all patients, non-skeletal involvement was observed in 4 patients. Diabetes insipidus was detected in 2 patients. Patients received different treatments depending on the type of involvement and extent of the disease. Four patients received treatment with Peg-IFN, and one patient received radiotherapy due to the progression of the disease. Following excision of the mass, no recurrence was observed in one patient, and the patient was under follow-up without treatment. One of the patients was diagnosed with the disease before the first-line treatment with vemurafenib, therefore, a combination of vinblastine and methylprednisolone was used. However, a full response could not be achieved. IFN was used as the second-line treatment, and the patient was under follow-up with stable conditions. No patient passed away during the follow-up.

Conclusion: Of our patients, 60% were male, similar to the general epidemiological data. However, the mean age of our patients, who were American and French, were low. Evaluation of the expression levels of BRAFV600E was performed for three patients, but the results were negative. This may be due to the fact that one patient had overlapping entities with LCH and could not be evaluated with a method as sensitive as ddPCR, which is one of the most recent sequencing techniques. Although skeletal involvement was present in all patients, the absence of extra-axial involvement, such as life-threatening retroperitoneal involvement and adrenal involvement, was remarkable. Although the patients were BRAF V600E mutation negative and this made the conversion to vemurafenib therapy difficult, patients were followed up without progression during the conventional Peg-IFN therapy. Clinical profile and treatment approach algorithms of ECD

bowel syndrome. Her blood count identified a significant anaemia (haemoglobin 53 g/L) and thrombocytosis (platelets 1260×10^9/L), and was thus referred to haematology clinic. She was diagnosed with IgG-C3d AIHA. The patient was started on prednisolone 1 mg/kg with a good initial response. To investigate the underlying cause, a whole body CT scan was performed, which identified significant abdominal ascites. Serum CA-125 was raised at 6715U/mL (range 0–35) and paracentesis revealed an LDH of 1203 SU suggesting underlying malignancy, but no malignant cells were found on the ascitic fluid cytology. The patient went on to have a PET scan, which confirmed FDG avid serosal disease, with update in the liver, omentum and peritoneum. Diagnostic laparotomy revealed widespread nodules on all serosal surfaces, and the biopsy confirmed a diagnosis of peritoneal epithelioid malignant mesothelioma. Whilst the patient had her workup with the oncology team, her AIHA became refractory to steroid treatment, and was commenced on Rituximab at 375 mg/m^2 weekly infusions. The patient did not respond to 4 doses of Rituximab, and continued to require regular transfusion support. She eventually started chemotherapy for the mesothelioma, which reduced the briskness of haemolysis, and reduced transfusion requirements; although haemolysis did not completely cease.

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patients in Turkey should be created with longer follow-up and multi-center data collection.

https://doi.org/10.1016/j.htct.2020.09.107

PP 45

Acute brucellosis presenting as leukocytoclastic vasculitis

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Objective: Brucellosis is a zoonotic disease caused by Brucella spp. bacteria that is transmitted to humans through contact with animal products and body fluids of animals. It is a multisystemic disease associated with variable clinical symptoms. Although cutaneous symptoms can rarely be encountered at presentation and during the course of the disease, the occurrence of cutaneous vasculitis is extremely rare. Here, we present a case that presented with purpuric eruptions and was diagnosed with brucellosis-induced leukocytoclastic vasculitis.

Case report: A 62-year-old female presented to our clinic with fatigue, tiredness, and eruptions on the anterior aspects of both legs that had persisted for two weeks. On physical examination, there were diffuse, non-palpable maculopapular eruptions on the anterior surfaces of both tibias. Detailed patient history revealed complaints of myalgia and arthralgia, lumbar pain, fatigue, and eruptions that had persisted for approximately one month. The patient was a farmer and worked in animal husbandry. Laboratory tests were as follows; hemoglobin level, 12.3 g/dL (range, 12–16 g/dL); white blood cell count, 5.92×10^9/L (range, 4–10×10^9/L); platelet count, 115×10^9/L (range, 150–400×10^9/L); lactate dehydrogenase, 240 IU/L (range, 120–246 IU/L); total bilirubin, 0.8 mg/dL (range, 0–1.1 mg/dL); creatinine, 1.23 mg/dL (range, 0.6–1.2 mg/dL); alanine aminotransferase, 12 U/L (range, <31 U/L); erythrocyte sedimentation rate, 86 mm/h (range, 0–15 mm/h); C-reactive protein, 26.3 mg/L (range, <5); prothrombin time (PT), normal; and activated partial thromboplastin time (aPTT), normal. HBsAg was negative, Anti-HCV was negative, Anti-HIV was negative, anti-nuclear antibody (ANA) was negative, rheumatoid factor was 19 IU/ML (range, 0–15), p-ANCA and c-ANCA were negative. Rose Bengal test performed due to clinical suspicion was positive. Brucella standard tube agglutination (STA) test was performed twice and was positive at a titer of 1/1280. A skin biopsy was taken from the purpuric lesions on the anterior aspect of the tibia. On histological examination; vascular structures in the dermis showed diffuse inflammation and neutrophilic and lymphocytic infiltration. On immunofluorescence examination; IgA: (–), IgM: (–), IgG: (–), C3: (–) and the results were consistent with leukocytoclastic vasculitis. Leukocytoclastic vasculitis could not be explained by medication use or infective endocarditis, and cryoglobulin tests were negative. The clinical picture was considered to be induced by acute brucellosis. The patient was started on rifampicin (600 mg/day PO), doxycycline (100 mg PO, q 12 h) as brucellosis treatment. Vasculitic lesions showed significant improvement after two weeks of follow-up. Complete recovery was achieved with 6 weeks of antimicrobial treatment for brucellosis and Brucella SAT titres declined to 1:40 after the treatment.

Conclusion: Brucellosis is associated with a wide variety of cutaneous symptoms. Various cutaneous lesions such as maculopapular lesions, papules, petechia, purpura, and papulonodular lesions can be observed. Cutaneous symptoms encountered at presentation or during the course of the disease, particularly vasculitic eruptions, are extremely rare. Further, these eruptions can sometimes resemble subcutaneous bleeding induced by a hemostatic defect. However, in regions where brucellosis is endemic, such as Turkey, brucellosis should certainly be considered in the differential diagnosis when vasculitis is unexplained and classic brucellosis symptoms are concomitant.

https://doi.org/10.1016/j.htct.2020.09.108

PP 46

The frequency of anemia in the elderly patient population in Van Province, Turkey. A cross-sectional study

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Objective: Anemia is a common health problem among elderly patients and its prevalence increases with aging. Although it used to be considered as a natural consequence of aging in the past, many current studies indicate that anemia reflects a deterioration of health status and leads to unfavorable consequences if not treated. This study aims to determine the prevalence and morphological distribution of anemia among elderly patients who presented to the hospital during a certain time period.

Methodology: Hemogram parameters of all patients aged 60 or older who attended our hospital for any reason between April 2018 and October 2018 was reviewed. Anemia was defined according to the criteria by the World Health Organization (WHO), as a hemoglobin level lower than 12 g/dL in females and 13 g/dL in males. Cases of anemia were classified based on the mean corpuscular volume (MCV) results of the patients as microcytic, normocytic, or macrocytic. The prevalence and morphological classification of anemia were examined with respect to age and gender.

Results: Of 1192 total patients, 608 (51%) were female. The majority of the patients were in the 60–70-year range, with a rate of 60.3% (718). Mean age was 69.70 ± 7.55 years in females and 69.8 ± 7.15 in males, with no significant difference ($p = 0.680$). Anemia was detected in 340 patients (28.5%) in total. The rate of anemia was 24.8% in females and 32.4% in males, and the prevalence of anemia was significantly different between genders ($p = 0.004$). Mean hemoglobin level was found as 13 ± 1.89 g/dL in females

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Objective: Brucellosis is a zoonotic disease caused by Brucella spp. bacteria that is transmitted to humans through contact with animal products and body fluids of animals. It is a multisystemic disease associated with variable clinical symptoms. Although cutaneous symptoms can rarely be encountered at presentation and during the course of the disease, the occurrence of cutaneous vasculitis is extremely rare. Here, we present a case that presented with purpuric eruptions and was diagnosed with brucellosis-induced leukocytoclastic vasculitis.

Case report: A 62-year-old female presented to our clinic with fatigue, tiredness, and eruptions on the anterior aspects of both legs that had persisted for two weeks. On physical examination, there were diffuse, non-palpable maculopapular eruptions on the anterior surfaces of both tibias. Detailed patient history revealed complaints of myalgia and arthralgia, lumbar pain, fatigue, and eruptions that had persisted for approximately one month. The patient was a farmer and worked in animal husbandry. Laboratory tests were as follows; hemoglobin level, 12.3 g/dL (range, 12–16 g/dL); white blood cell count, 5.92×10^9/L (range, 4–10×10^9/L); platelet count, 115×10^9/L (range, 150–400×10^9/L); lactate dehydrogenase, 240 IU/L (range, 120–246 IU/L); total bilirubin, 0.8 mg/dL (range, 0–1.1 mg/dL); creatinine, 1.23 mg/dL (range, 0.6–1.2 mg/dL); alanine aminotransferase, 12 U/L (range, <31 U/L); erythrocyte sedimentation rate, 86 mm/h (range, 0–15 mm/h); C-reactive protein, 26.3 mg/L (range, <5); prothrombin time (PT), normal; and activated partial thromboplastin time (aPTT), normal. HBsAg was negative, Anti-HCV was negative, Anti-HIV was negative, anti-nuclear antibody (ANA) was negative, rheumatoid factor was 19 IU/ML (range, 0–15), p-ANCA and c-ANCA were negative. Rose Bengal test performed due to clinical suspicion was positive. Brucella standard tube agglutination (STA) test was performed twice and was positive at a titer of 1/1280. A skin biopsy was taken from the purpuric lesions on the anterior aspect of the tibia. On histological examination; vascular structures in the dermis showed diffuse inflammation and neutrophilic and lymphocytic infiltration. On immunofluorescence examination; IgA: (–), IgM: (–), IgG: (–), C3: (–) and the results were consistent with leukocytoclastic vasculitis. Leukocytoclastic vasculitis could not be explained by medication use or infective endocarditis, and cryoglobulin tests were negative. The clinical picture was considered to be induced by acute brucellosis. The patient was started on rifampicin (600 mg/day PO), doxycycline (100 mg PO, q 12 h) as brucellosis treatment. Vasculitic lesions showed significant improvement after two weeks of follow-up. Complete recovery was achieved with 6 weeks of antimicrobial treatment for brucellosis and Brucella SAT titres declined to 1:40 after the treatment.

Conclusion: Brucellosis is associated with a wide variety of cutaneous symptoms. Various cutaneous lesions such as maculopapular lesions, papules, petechia, purpura, and papulonodular lesions can be observed. Cutaneous symptoms encountered at presentation or during the course of the disease, particularly vasculitic eruptions, are extremely rare. Further, these eruptions can sometimes resemble subcutaneous bleeding induced by a hemostatic defect. However, in regions where brucellosis is endemic, such as Turkey, brucellosis should certainly be considered in the differential diagnosis when vasculitis is unexplained and classic brucellosis symptoms are concomitant.

https://doi.org/10.1016/j.htct.2020.09.108

PP 46

The frequency of anemia in the elderly patient population in Van Province, Turkey. A cross-sectional study

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Objective: Anemia is a common health problem among elderly patients and its prevalence increases with aging. Although it used to be considered as a natural consequence of aging in the past, many current studies indicate that anemia reflects a deterioration of health status and leads to unfavorable consequences if not treated. This study aims to determine the prevalence and morphological distribution of anemia among elderly patients who presented to the hospital during a certain time period.

Methodology: Hemogram parameters of all patients aged 60 or older who attended our hospital for any reason between April 2018 and October 2018 was reviewed. Anemia was defined according to the criteria by the World Health Organization (WHO), as a hemoglobin level lower than 12 g/dL in females and 13 g/dL in males. Cases of anemia were classified based on the mean corpuscular volume (MCV) results of the patients as microcytic, normocytic, or macrocytic. The prevalence and morphological classification of anemia were examined with respect to age and gender.

Results: Of 1192 total patients, 608 (51%) were female. The majority of the patients were in the 60–70-year range, with a rate of 60.3% (718). Mean age was 69.70 ± 7.55 years in females and 69.8 ± 7.15 in males, with no significant difference ($p = 0.680$). Anemia was detected in 340 patients (28.5%) in total. The rate of anemia was 24.8% in females and 32.4% in males, and the prevalence of anemia was significantly different between genders ($p = 0.004$). Mean hemoglobin level was found as 13 ± 1.89 g/dL in females

patients in Turkey should be created with longer follow-up and multi-center data collection.

https://doi.org/10.1016/j.htct.2020.09.107

PP 45

Acute brucellosis presenting as leukocytoclastic vasculitis

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Objective: Brucellosis is a zoonotic disease caused by Brucella spp. bacteria that is transmitted to humans through contact with animal products and body fluids of animals. It is a multisystemic disease associated with variable clinical symptoms. Although cutaneous symptoms can rarely be encountered at presentation and during the course of the disease, the occurrence of cutaneous vasculitis is extremely rare. Here, we present a case that presented with purpuric eruptions and was diagnosed with brucellosis-induced leukocytoclastic vasculitis.

Case report: A 62-year-old female presented to our clinic with fatigue, tiredness, and eruptions on the anterior aspects of both legs that had persisted for two weeks. On physical examination, there were diffuse, non-palpable maculopapular eruptions on the anterior surfaces of both tibias. Detailed patient history revealed complaints of myalgia and arthralgia, lumbar pain, fatigue, and eruptions that had persisted for approximately one month. The patient was a farmer and worked in animal husbandry. Laboratory tests were as follows; hemoglobin level, 12.3 g/dL (range, 12–16 g/dL); white blood cell count, 5.92×10^9/L (range, 4–10×10^9/L); platelet count, 115×10^9/L (range, 150–400×10^9/L); lactate dehydrogenase, 240 IU/L (range, 120–246 IU/L); total bilirubin, 0.8 mg/dL (range, 0–1.1 mg/dL); creatinine, 1.23 mg/dL (range, 0.6–1.2 mg/dL); alanine aminotransferase, 12 U/L (range, <31 U/L); erythrocyte sedimentation rate, 86 mm/h (range, 0–15 mm/h); C-reactive protein, 26.3 mg/L (range, <5); prothrombin time (PT), normal; and activated partial thromboplastin time (aPTT), normal. HBsAg was negative, Anti-HCV was negative, Anti-HIV was negative, anti-nuclear antibody (ANA) was negative, rheumatoid factor was 19 IU/ML (range, 0–15), p-ANCA and c-ANCA were negative. Rose Bengal test performed due to clinical suspicion was positive. Brucella standard tube agglutination (STA) test was performed twice and was positive at a titer of 1/1280. A skin biopsy was taken from the purpuric lesions on the anterior aspect of the tibia. On histological examination; vascular structures in the dermis showed diffuse inflammation and neutrophilic and lymphocytic infiltration. On immunofluorescence examination; IgA: (–), IgM: (–), IgG: (–), C3: (–) and the results were consistent with leukocytoclastic vasculitis. Leukocytoclastic vasculitis could not be explained by medication use or infective endocarditis, and cryoglobulin tests were negative. The clinical picture was considered to be induced by acute brucellosis. The patient was started on rifampicin (600 mg/day PO), doxycycline (100 mg PO, q 12 h) as brucellosis treatment. Vasculitic lesions showed significant improvement after two weeks of follow-up. Complete recovery was achieved with 6 weeks of antimicrobial treatment for brucellosis and Brucella SAT titres declined to 1:40 after the treatment.

Conclusion: Brucellosis is associated with a wide variety of cutaneous symptoms. Various cutaneous lesions such as maculopapular lesions, papules, petechia, purpura, and papulonodular lesions can be observed. Cutaneous symptoms encountered at presentation or during the course of the disease, particularly vasculitic eruptions, are extremely rare. Further, these eruptions can sometimes resemble subcutaneous bleeding induced by a hemostatic defect. However, in regions where brucellosis is endemic, such as Turkey, brucellosis should certainly be considered in the differential diagnosis when vasculitis is unexplained and classic brucellosis symptoms are concomitant.

https://doi.org/10.1016/j.htct.2020.09.108

PP 46

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Objective: Anemia is a common health problem among elderly patients and its prevalence increases with aging. Although it used to be considered as a natural consequence of aging in the past, many current studies indicate that anemia reflects a deterioration of health status and leads to unfavorable consequences if not treated. This study aims to determine the prevalence and morphological distribution of anemia among elderly patients who presented to the hospital during a certain time period.

Methodology: Hemogram parameters of all patients aged 60 or older who attended our hospital for any reason between April 2018 and October 2018 was reviewed. Anemia was defined according to the criteria by the World Health Organization (WHO), as a hemoglobin level lower than 12 g/dL in females and 13 g/dL in males. Cases of anemia were classified based on the mean corpuscular volume (MCV) results of the patients as microcytic, normocytic, or macrocytic. The prevalence and morphological classification of anemia were examined with respect to age and gender.

Results: Of 1192 total patients, 608 (51%) were female. The majority of the patients were in the 60–70-year range, with a rate of 60.3% (718). Mean age was 69.70 ± 7.55 years in females and 69.8 ± 7.15 in males, with no significant difference ($p = 0.680$). Anemia was detected in 340 patients (28.5%) in total. The rate of anemia was 24.8% in females and 32.4% in males, and the prevalence of anemia was significantly different between genders ($p = 0.004$). Mean hemoglobin level was found as 13 ± 1.89 g/dL in females

and as 13.7 ± 2.24 g/dL in males, with a significant difference between genders ($p = 0.001$). Mean MCV was higher in males than in females with a significant difference (84.98 ± 6.32 vs. 87.15 ± 7.28 fl, $p = 0.001$). According to morphological classification; 66 patients (19.4%) had microcytic anemia, 245 (72.1%) had normocytic anemia, and 29 (8.5%) had macrocytic anemia. Distribution of anemia across age groups revealed 169 (23.5%) patients with anemia in the 60–70-years age group, with a significant difference between genders (69 [18.2%] vs. 100 [29.6%], $p = 0.001$). The prevalence of anemia was different between genders in both the 60–70-years and ≥81 years groups; however, these differences were not statistically significant (respectively, 52 [14.6%] vs. 66 [18.5%], $p = 0.426$ and 30 [25.6%] vs. 23 [19.7%], $p = 0.295$).

Conclusion: In daily practice, determining the prevalence of anemia in the elderly patient group and, if possible, its distribution according to etiologic factors, may provide practical knowledge regarding the approach to be adopted towards patients in a certain region. In our study, the prevalence of anemia in patients aged 60 or older, and the distribution of anemia based on morphological classification were determined. The major limitation of this study is that etiologic distribution could not be revealed. However, we think that our study still provides important insight and awareness regarding the elderly anemic patient population in our region. It will contribute to the studies that will be conducted in the same region.

https://doi.org/10.1016/j.htct.2020.09.109

PLATELET DISEASES

PP 47

Effect of helicobacter pylori infection on the first-line treatment outcomes in patients with immune thrombocytopenic purpura

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Objective: In immune thrombocytopenic purpura (ITP) patients, studies in the literature have generally focused on the effects of the eradication of Helicobacter pylori (H. pylori) infection on increasing the platelet count in ITP patients, and the effect of H. pylori positivity on the response to conventional first-line treatment is not clear. This study aims to determine whether or not the response to the first-line treatment is affected by the states of H. Pylori-positivity and -negativity in ITP patients.

Methodology: The diagnosis of ITP was confirmed according to the Consensus Report on the Investigation and Management of Primary ITP. Untreated adult newly diagnosed or chronic ITP patients were included. H. Pylori-positive and -negative patients were categorized into two groups. Fecal antigen testing was used for the diagnosis of H. pylori infection in all patients. Patients who had received eradication therapy for H. Pylori infection were excluded from the study. The bleeding symptoms were evaluated according to the International Working Group (IWG) bleeding scale. Demographic data of the patients at diagnosis, presence, and severity of bleeding, initial platelet count, administered treatments, treatment response rates, and post-treatment platelet count were inspected.

Results: Of 119 total patients, 66 (55.5%) were female, 32 (26.9%) were H. pylori-positive, 87 (73.1%) were H. pylori-negative. H. pylori-positive and H. pylori-negative groups were not significantly different in terms of age ($p = 0.127$), gender ($p = 0.078$), diagnosis status ($p = 0.094$) and the distribution of bleeding symptoms ($p = 0.712$). The most common treatment was standard-dose steroid in both groups (62.5% vs. 68.9%, $p = 0.524$). Rates of complete response, partial response, no response were comparable for the two groups (respectively, 75% vs. 73.6%, and 18.8% vs. 19.5%, and 6.2% vs. 6.9%), and there was no significant difference between the groups ($p = 0.283$).

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https://doi.org/10.1016/j.htct.2020.09.110

PP 48

Safety of caplacizumab in patients without documented severe adamts13 deficiency during the hercules study

S. Besisik[1,*], J. De La Rubia[2], F. Peyvandi[3], M. Scully[4], S. Cataland[5], P. Coppo[6], J. A. Kremer Hovinga[7], P. Knoebl[8], A. Metjian[9], K. Pavenski[10], H. De Winter[11], R. De Passos Sousa[12], F. Callewaert[13]

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Objective: To describe the safety of caplacizumab in patients enrolled in HERCULES for whom the diagnosis of aTTP was not confirmed based on documented severe ADAMTS13 deficiency.

Methodology: In HERCULES (NCT02553317), ADAMTS13 was measured at study baseline (following initial TPE), weekly following cessation of daily TPE during the treatment period, and twice during the follow-up period. Data from patients for whom the diagnosis of aTTP was not confirmed based on documented ADAMTS13 levels <10% were extracted and analyzed descriptively for efficacy and safety outcomes, with a focus on bleeding events.

Results: Overall, 7 patients in the placebo group (9.6%) and 13 patients in the caplacizumab group (18.1%) had a baseline ADAMTS13 ≥10%; of these, 4 and 9 patients, respectively, had a prior medical history of aTTP and/or ADAMTS13 values <10% at other time points during the study. This left 3 patients in the placebo group and 4 patients in the caplacizumab group for whom the diagnosis of aTTP could not be confirmed based on subsequent ADAMTS13 values or prior medical history, suggesting a diagnosis other than aTTP. Baseline ADAMTS13 levels were >60% for all patients and remained well above 10% throughout the study period. Possible alternative diagnoses included pancreatitis-induced TTP in 2 patients. One patient was reported as having 'thrombotic microangiopathy' and discontinued study drug treatment after 4 days (but continued daily TPE). The fourth patient had a report of 'megaloblastic anemia' and 'general adenopathies' and was withdrawn from the study due to a 'non-TTP diagnosis' after 2 days. The patients who continued daily TPE achieved a platelet count of $>150 \times 10^9$/L. Two patients experienced a moderate bleeding-related serious adverse event (SAE), 1 case of 'gastric ulcer hemorrhage' (considered unlikely related to study drug and recovered without intervention) and 1 case of epistaxis that led to study drug discontinuation (considered possibly related to study drug and recovered without intervention). Other mild bleeding-related non-serious adverse events (AEs) were reported in 1 patient: gingival bleeding (possibly related), ecchymosis (possibly related), and rectal hemorrhage (not/unlikely related). All events recovered spontaneously without intervention. Two other non-bleeding related SAEs were reported in 2 patients, both considered unrelated to study drug: 1 case of bacteremia and 1 case of cardiac tamponade.

Conclusion: The experience of caplacizumab in patients with a suspected non-aTTP diagnosis to date is limited, and so no definite conclusion can be drawn. Bleeding-related AEs were reported in 3 of the 4 patients; however, the type, nature and manageability of these events appear similar to those reported in the other patients in the study. Data first presented at American Society of Hematology annual meeting, December 7–10, 2019. Study sponsored by Sanofi.

https://doi.org/10.1016/j.htct.2020.09.111

PP 49

Caplacizumab induces fast and durable platelet count responses with improved time to complete remission and recurrence-free survival in patients with acquired thrombotic thrombocytopenic purpura

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[12] *Sanofi, Lisbon, Portugal*

Objective: To characterize the durability of platelet count responses in the HERCULES trial.

PP 48

Safety of caplacizumab in patients without documented severe adamts13 deficiency during the hercules study

S. Besisik[1,*], J. De La Rubia[2], F. Peyvandi[3], M. Scully[4], S. Cataland[5], P. Coppo[6], J. A. Kremer Hovinga[7], P. Knoebl[8], A. Metjian[9], K. Pavenski[10], H. De Winter[11], R. De Passos Sousa[12], F. Callewaert[13]

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Results: Overall, 7 patients in the placebo group (9.6%) and 13 patients in the caplacizumab group (18.1%) had a baseline ADAMTS13 ≥10%; of these, 4 and 9 patients, respectively, had a prior medical history of aTTP and/or ADAMTS13 values <10% at other time points during the study. This left 3 patients in the placebo group and 4 patients in the caplacizumab group for whom the diagnosis of aTTP could not be confirmed based on subsequent ADAMTS13 values or prior medical history, suggesting a diagnosis other than aTTP. Baseline ADAMTS13 levels were >60% for all patients and remained well above 10% throughout the study period. Possible alternative diagnoses included pancreatitis-induced TTP in 2 patients. One patient was reported as having 'thrombotic microangiopathy' and discontinued study drug treatment after 4 days (but continued daily TPE). The fourth patient had a report of 'megaloblastic anemia' and 'general adenopathies' and was withdrawn from the study due to a 'non-TTP diagnosis' after 2 days. The patients who continued daily TPE achieved a platelet count of $>150 \times 10^9$/L. Two patients experienced a moderate bleeding-related serious adverse event (SAE), 1 case of 'gastric ulcer hemorrhage' (considered unlikely related to study drug and recovered without intervention) and 1 case of epistaxis that led to study drug discontinuation (considered possibly related to study drug and recovered without intervention). Other mild bleeding-related non-serious adverse events (AEs) were reported in 1 patient: gingival bleeding (possibly related), ecchymosis (possibly related), and rectal hemorrhage (not/unlikely related). All events recovered spontaneously without intervention. Two other non-bleeding related SAEs were reported in 2 patients, both considered unrelated to study drug: 1 case of bacteremia and 1 case of cardiac tamponade.

Conclusion: The experience of caplacizumab in patients with a suspected non-aTTP diagnosis to date is limited, and so no definite conclusion can be drawn. Bleeding-related AEs were reported in 3 of the 4 patients; however, the type, nature and manageability of these events appear similar to those reported in the other patients in the study. Data first presented at American Society of Hematology annual meeting, December 7–10, 2019. Study sponsored by Sanofi.

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PP 49

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L. Kaynar[1,*], P. Coppo[2], M. Scully[3], J. De La Rubia[4], F. Peyvandi[5], S. Cataland[6], J. A. Kremer Hovinga[7], P. Knoebl[8], K. Pavenski[9], J. Minkue Mi Edou[10], F. Callewaert[11], R. De Passos Sousa[12]

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[12] *Sanofi, Lisbon, Portugal*

Objective: To characterize the durability of platelet count responses in the HERCULES trial.

Methodology: In this post hoc analysis of the HERCULES (NCT02553317) intent-to-treat population (caplacizumab, $n=72$; placebo, $n=73$), we identified patients with a fast platelet count response (i.e., ≤3 days vs. >3 days) and described the exacerbation rate by treatment group. Time to durable platelet count response (defined as time to last daily TPE during the overall treatment period), time to complete remission (defined as platelet count $>150 \times 10^9$/L and lactate dehydrogenase <1.5 × the upper limit of normal for >30 days after cessation of daily TPE), and recurrence-free survival (absence of exacerbation or relapse during the overall study period) were calculated.

Results: More than half of the patients in the HERCULES trial achieved an initial platelet count normalization within 3 days (caplacizumab, 56/72 [78%]; placebo, 43/73 [59%]). In patients with a fast platelet count response (ie, ≤3 days), the exacerbation rate was 3.6% (2/56) with caplacizumab and 44.2% (19/43) with placebo, suggesting that the rapid platelet count response was sustained with caplacizumab, whereas almost half of the fast responders in the placebo group subsequently exacerbated. In patients with time to platelet count response >3 days, the exacerbation rate was 6.7% (1/15) with caplacizumab and 30.0% (9/30) with placebo, confirming the durable response with caplacizumab. The exacerbation rate among placebo patients with platelet response >3 days remained high but was numerically lower compared with fast responders. Of the patients who experienced exacerbations, 90% (2/3 in the caplacizumab group and 26/28 in the placebo group) switched to open-label caplacizumab, which may have favored the outcomes of placebo patients. Despite this bias, the median (95% CI) time to durable response was 4.5 (4.4–4.6) days with caplacizumab and 10.5 (6.5–14.5) days with placebo; accordingly, the median (95% CI) time to complete remission was shorter in the caplacizumab group (40.0 [37.7–41.1] days) compared with placebo (44.2 [42.0–48.2] days). The analysis of overall recurrence-free survival during the entire study period demonstrated an early and sustained benefit for caplacizumab over placebo, mainly driven by significant reduction in exacerbations during the study drug treatment period. The effect was sustained, despite six relapses in the caplacizumab group in the follow-up period in patients with unresolved underlying autoimmune disease activity.

Conclusion: Caplacizumab demonstrated a faster and sustained platelet count response compared with the placebo group, in which many fast responders subsequently had an exacerbation. Fast platelet count responses with caplacizumab were maintained and translated into clinically relevant improvements in time to complete remission and overall recurrence-free survival. Data first presented at EHA 2020 virtual meeting, June 11–21st. Study sponsored by Sanofi.

https://doi.org/10.1016/j.htct.2020.09.112

STEM CELL TRANSPLANT

PP 50

Transplant in aplastic anemia using combined G-CSF primed blood and bone marrow stem cells – a retrospective analysis

N. Ali, A. Butt*, B. Altaf, S. Adil, U. Shaikh

Aga Khan University Hospital, Karachi, Pakistan

Objective: Aplastic anemia is characterized by diminished or absent hematopoietic precursors in the bone marrow, most often due to injury to the pluripotent stem cell. In Pakistan, Aplastic Anemia is not uncommon and allogeneic hematopoietic stem cell transplant remains the only curative option in these patients. We aim to determine the transplant outcome of combined, G-CSF primed blood and bone marrow grafts in adult and pediatric patients with aplastic anemia.

Methodology: We retrospectively collected data of all transplant procedures performed from 2004–2019 at Aga Khan University Karachi, Pakistan. Variables analyzed included type of transplants, age, gender, type of stem cells used, conditioning regimens and overall survival for patients undergoing transplant in aplastic anemia.

Results: A total of 351 transplants were performed during the study period. Out of these, 239 were allogeneic transplants whereas 112 were autologous procedures. There were 254 males and 97 females. The main indications for allogeneic stem cell transplant were aplastic anemia (70), acute leukemia (58) and beta thalassemia major(40). Out of 70 patients with aplastic anemia, 52 were males and 18 were females. 38.6% percent of patients were from pediatric age group. The median age ± SD was 17.5 ± 9.4 years (range: 2–43 years). Cyclophosphamide/ATG was used as a conditioning regimen in 67 patients, while ATG/cyclophosphamide/fludarabine was used in 2. Haploidentical transplant was done in 1 patient. Twenty seven percent of patients underwent sex-mismatched procedures. In 52 patients, a combination of GCSF primed blood and bone marrow stem cells were used. The mean CD34 count was 5.2 × 10/kg. GVHD prophylaxis was done with cyclosporine and methotrexate. All patients received standard infection prophylaxis. Engraftment was achieved in 75% of patients. The median day of myeloid engraftment was 15 (range 10–22 days). Chronic GVHD was present in 3 patients while 4 had acute GVHD. The overall survival was 71.2% (median duration of 80 months). The causes of mortality included gram-negative sepsis (5), graft versus host disease (4), graft failure (4), disseminated fungal infection (2), intracranial bleed (2), bleeding diathesis (2) and transplant associated microangiopathy (1).

Conclusion: Combination of blood and bone marrow stem cells results in early engraftment with decreased frequency of GVHD in aplastic anemia. The overall survival was comparable to international literature.

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PP 51

Comparison of single and double autologous stem cell transplantation in multiple myeloma patients

U. Malkan[1,*], H. Demiroglu[2], Y. Buyukasik[2], A. Karatas[2], E. Aladag[2], H. Goker[2]

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[2] *Hacettepe University, Department of Hematology, Ankara, Turkey*

Objective: Multiple myeloma (MM) is the second most common hematological malignancy and autologous stem cell transplantation (ASCT) is one of the standard treatment of choice for eligible MM patients. The role of double ASCT as a treatment in patients with MM and its superiority over single ASCT are still a matter of discussion. Herein, we aimed to analyze MM patients at our center and compare the clinical outcomes of single and double ASCT patients.

Methodology: This study has been designed retrospectively. The patients who were diagnosed as multiple myeloma and had undergone ASCT in Hacettepe Hematology Department between the years 2003–2020 were evaluated.

Results: Disease assessment after ASCT stable or progressive disease, partial remission, very good partial or complete remission in single and double ASCT groups were 62/44/105 and 8/4/5, respectively, p: 0.22. Among the double transplanted patients, five of them were transplanted within 1 year after the first transplant. The median duration between the first and second transplant was 1322 (414–4242) days in double ASCT patients. OS duration of the single and double transplanted groups were 4011 ± 266 versus 3526 ± 326 days, respectively, p: 0.33. There was no statistically significant difference between OS durations of single and double ASCT patients. Only 4 patients had died from TRM in single ASCT group, whereas no patients had died from TRM in double ASCT group. Progression free survival durations of the single and double transplanted groups were 2344 ± 228 versus 685 ± 120 days, respectively, p: 0.22. There was no statistically significant difference between PFS durations of single and double ASCT patients. The factors that are related with the OS of double ASCT patients were analyzed. In univariate analysis, serum calcium levels and IgA type M protein were found to be related with OS of double ASCT patients (p: 0.09 and p: 0.06, respectively); however this relationship was not found in multivariate analysis. In univariate analysis, serum uric acid levels and beta-2 microglobulin were found to be related with PFS of double ASCT patients (p: 0.04 and p: 0.07, respectively); however this relationship was not found in multivariate analysis.

Conclusion: ASCT remains to be one of the main treatment options in MM. Many studies tried to find the best way of this procedure to maximize the benefit for the patients. Given the survival benefits observed with ASCT, trials have evaluated the use of additional intensive chemotherapy followed by a second ASCT. The recent general opinion among clinicians is that a second ASCT tends to be a feasible and rational treatment choice, particularly in patients with high risk MM. In the present study, it has been demonstrated that there seems to be no benefit with double ASCT in MM patients in terms of disease response rates and PFS and OS durations over single ASCT. Our study points out that the double ASCT treatment option in MM may not be effective as suggested, especially in the era of novel MM drugs. Further prospective larger studies are needed to clarify the role of double ASCT especially in high risk MM.

https://doi.org/10.1016/j.htct.2020.09.114

PP 52

Are the hemoglobin values different after sex-mismatched allogeneic stem cell transplantation?

S. Izmir Guner[1,*], M. Yanmaz[2]

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[2] *Memorial Sısli Hospital,Clinic of Medical Oncology, Istanbul, Turkey*

Objective: Allogenic hematopoietic stem cell transplant (HSCT) is used as a curative treatment approach in many hematological diseases. Allogenic HKHN made for nearly 30 years bone marrow microenvironment and stroma after transplantation are known to protect the recipient identity. It is well known that if sex mismatch allogeneic HSCT is performed from multipar women to men, graft-versus-host disease frequency and therefore transplant related mortality is increased. Inborn difference and its change after transplant in hemoglobin (Hb) levels between male and female did not draw attention on a scientific basis. The aim of this study to analyze Hb and red cell distribution width (RDW) changes after mismatch allogeneic HSCT.

Case report: 18–72 years old 62 cases with acute leukemia were included in this study, between 2016–2019. All of them underwent allogeneic HSCT with used conditioning regimens like myeloablative or non-myeloablative or RIC (reduced-intensity conditioning) and were in the first complete remission.

Methodology: The patients were divided into four groups according to the transmitter and gender compliance, as well as demographic features; MM (male to male), MF (male to female), FF (female to female) FM (female to male). Hemoglobin and red cell distribution (RDW) interval differences were evaluated before and after transplantation.

Results: There was no significant difference between groups in terms of age and performance status. The mean Hb level was significantly increased in all patients from 9.16 g/dL to 12.34 g/dL ($p < 0.0001$) after transplantation. The average RDW before transplantation was 16.60% after transplantation was 15.57%. When the mean Hb values at 12 months were compared with post-transplant, it was found to be 12.79 g/dL and 12.99 g/dL in male recipients and female recipients respectively. While mean values of male recipients were 15.78% and 15.02% in the MM group and FM group, it was observed that female recipients were 13.43% and 15.13% in the FF group and in the MF group, respectively. While the male recipient

PP 51

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therefore male stromal structure was terminated with >12 g/dL Hb values at 12 months, the mean value in female recipients was <12 g/dL. Male allogeneic HSCT recipients are more fortunate than women in this respect but in the study, no significant difference was found between women who have male donors and gender-matched sex in hemoglobin elevation.

Conclusion: In our study, no significant difference was found between women who have male donors and gender-matched sex in hemoglobin elevation. Finally, we think that in patients with both male and female donors, it can be concluded that the recipient's hemoglobin value may be higher by choosing a male donor.

https://doi.org/10.1016/j.htct.2020.09.115

PP 53

Experience of istanbul faculty of medicine bone marrow bank: periodical activity documentation

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[1] *Department of Medical Biology, Istanbul University, Istanbul Medical School, İstanbul, Turkey*
[2] *Department of Internal Medicine Hematology, Istanbul Faculty of Medicine, İstanbul, Turkey*

Objective: Unrelated stem cell transplant (SCT) is an option for patients who have no available related donor, and a transplant is the best treatment modality for them. We aimed to document our bone marrow bank activity to define the proficiency and unmet requirement.

Methodology: We retrospectively screened the medical records from electronic files. The data from 2016 until 2019 were collected. The statistical analysis of the patients who presented for stem cell transplant, and of the healthy donors for demographic features, stem cell counts, stem cell sources, diagnosis, survival, GVHD, CMV, and HLA matches were performed using the SPSS 21.0.

Results: A total of 640 patient and donor pairs enrolled in the study. Most of the patients were adults ($n = 359$). Patients' mean age was 26.77 ± 21.06 years (range 0–74), and donor's 31.9 ± 9.6 years (range 24–75). The gender distribution was as male to female 377/263 for patients and 333/304 for the donors. The primary (43%) SCT indication was acute leukemia. Preference of stem cell sources was as follows; peripheral blood ($n = 450$; pediatric/adult: 137/313), bone marrow ($n = 161$; pediatric/adult: 130/31), and cord blood ($n = 8$; pediatric/adult: 8/0). In 21 cases, donor leukocytes were provided (pediatric/adult: 6/15). The total HLA tissue group compatibility between the patient and the donor was *10/10 in 47.8% of cases, *9/10 in 51.3% cases, and *8/10, *5/6, *6/8 in 9% of cases. The survival analysis showed no statistical difference between 10/10 and 9/10 HLA matched transplants. The sex match between patient and donor and the stem cell source has no significant effect on GVHD development ($p > 0.005$ and p: 0.226, respectively).

Conclusion: The outcome of SCT is effected mainly by HLA tissue compatibility, age, sex, and blood group match. Istanbul Bone Marrow Bank, with the HLA tissue typing laboratory, works internationally and provides stem cells since 1999 for SCT. With the collaboration of SCT centers, donor and stem cell source selection, and transfer is getting faster. The SCT outcome information is also a modulating factor to improve the quality of work. We, therefore, periodically document our activity and pursue to find a solution for getting better.

https://doi.org/10.1016/j.htct.2020.09.116

TRANSFUSION MEDICINE AND APHERESIS

PP 54

Therapeutic plasma exchange in gastric signet ring cell carcinoma presenting as microangiopathic hemolytic anemia: a rare case report

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Objective: Cancer-associated microangiopathic hemolytic anemia (MAHA) is a rare but serious condition that is encountered in patients diagnosed with a malignancy. We describe a case of signet-ring cell carcinoma with a very rare presentation, namely a laboratory and clinical picture of MAHA, who demonstrated an effective thrombocyte level in response to therapeutic plasma exchange (TPE) therapy that was administered during the diagnostic period.

Case report: A 42-year-old male patient was referred to our hospital by an external center due to the complaint of recurrent epistaxis in the recent days, leukocytosis, anemia, and thrombocytopenia detected in his complete blood count. Hemogram data included the following; hemoglobin, 8.2 g/dL; white blood cells, 12.9×10^9/L; platelet count, 25×10^9/L; mean corpuscular volume (MCV), 82 fl. Laboratory data included the following: lactate dehydrogenase (LDH), 2826 IU/L; total bilirubin, 4.7 mg/dL; indirect bilirubin, 3.4 mg/dL; and a negative result on the direct antiglobulin test (Coombs). Vitamin-B12, folic acid, serum iron, and total iron-binding capacity levels, transferrin saturation, and thyroid function tests were normal. Peripheral blood smear showed fragmented erythrocytes (schistocyte), findings of erythrodysplasia, polychromasia, poikilocytosis, and in some areas, normoblasts and reticulocytosis. Reticulocyte percentage was nearly 14%. The patient was suspected of having MAHA based on these clinical, laboratory, and peripheral smear morphologic findings. Further tests were conducted in order to determine the etiology, primarily, TTP. A serum sample was collected to determine plasma ADAMTS-13 activity and therapeutic plasma exchange (TPE) was started as a treatment. Bone marrow aspiration (BMA) and biopsy (BMB) performed to examine bone marrow infiltration by hematologic and nonhematologic malignancies did not determine malignant cell infiltration. Serologies for viral infections autoantibodies were negative. A cervical-

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Case report: A 42-year-old male patient was referred to our hospital by an external center due to the complaint of recurrent epistaxis in the recent days, leukocytosis, anemia, and thrombocytopenia detected in his complete blood count. Hemogram data included the following; hemoglobin, 8.2 g/dL; white blood cells, 12.9×10^9/L; platelet count, 25×10^9/L; mean corpuscular volume (MCV), 82 fl. Laboratory data included the following: lactate dehydrogenase (LDH), 2826 IU/L; total bilirubin, 4.7 mg/dL; indirect bilirubin, 3.4 mg/dL; and a negative result on the direct antiglobulin test (Coombs). Vitamin-B12, folic acid, serum iron, and total iron-binding capacity levels, transferrin saturation, and thyroid function tests were normal. Peripheral blood smear showed fragmented erythrocytes (schistocyte), findings of erythrodysplasia, polychromasia, poikilocytosis, and in some areas, normoblasts and reticulocytosis. Reticulocyte percentage was nearly 14%. The patient was suspected of having MAHA based on these clinical, laboratory, and peripheral smear morphologic findings. Further tests were conducted in order to determine the etiology, primarily, TTP. A serum sample was collected to determine plasma ADAMTS-13 activity and therapeutic plasma exchange (TPE) was started as a treatment. Bone marrow aspiration (BMA) and biopsy (BMB) performed to examine bone marrow infiltration by hematologic and nonhematologic malignancies did not determine malignant cell infiltration. Serologies for viral infections autoantibodies were negative. A cervical-

therefore male stromal structure was terminated with >12 g/dL Hb values at 12 months, the mean value in female recipients was <12 g/dL. Male allogeneic HSCT recipients are more fortunate than women in this respect but in the study, no significant difference was found between women who have male donors and gender-matched sex in hemoglobin elevation.

Conclusion: In our study, no significant difference was found between women who have male donors and gender-matched sex in hemoglobin elevation. Finally, we think that in patients with both male and female donors, it can be concluded that the recipient's hemoglobin value may be higher by choosing a male donor.

https://doi.org/10.1016/j.htct.2020.09.115

PP 53

Experience of istanbul faculty of medicine bone marrow bank: periodical activity documentation

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Objective: Unrelated stem cell transplant (SCT) is an option for patients who have no available related donor, and a transplant is the best treatment modality for them. We aimed to document our bone marrow bank activity to define the proficiency and unmet requirement.

Methodology: We retrospectively screened the medical records from electronic files. The data from 2016 until 2019 were collected. The statistical analysis of the patients who presented for stem cell transplant, and of the healthy donors for demographic features, stem cell counts, stem cell sources, diagnosis, survival, GVHD, CMV, and HLA matches were performed using the SPSS 21.0.

Results: A total of 640 patient and donor pairs enrolled in the study. Most of the patients were adults ($n = 359$). Patients' mean age was 26.77 ± 21.06 years (range 0–74), and donor's 31.9 ± 9.6 years (range 24–75). The gender distribution was as male to female 377/263 for patients and 333/304 for the donors. The primary (43%) SCT indication was acute leukemia. Preference of stem cell sources was as follows; peripheral blood ($n = 450$; pediatric/adult: 137/313), bone marrow ($n = 161$; pediatric/adult: 130/31), and cord blood ($n = 8$; pediatric/adult: 8/0). In 21 cases, donor leukocytes were provided (pediatric/adult: 6/15). The total HLA tissue group compatibility between the patient and the donor was *10/10 in 47.8% of cases, *9/10 in 51.3% cases, and *8/10, *5/6, *6/8 in 9% of cases. The survival analysis showed no statistical difference between 10/10 and 9/10 HLA matched transplants. The sex match between patient and donor and the stem cell source has no significant effect on GVHD development ($p > 0.005$ and p: 0.226, respectively).

Conclusion: The outcome of SCT is effected mainly by HLA tissue compatibility, age, sex, and blood group match. Istanbul Bone Marrow Bank, with the HLA tissue typing laboratory, works internationally and provides stem cells since 1999 for SCT. With the collaboration of SCT centers, donor and stem cell source selection, and transfer is getting faster. The SCT outcome information is also a modulating factor to improve the quality of work. We, therefore, periodically document our activity and pursue to find a solution for getting better.

https://doi.org/10.1016/j.htct.2020.09.116

TRANSFUSION MEDICINE AND APHERESIS

PP 54

Therapeutic plasma exchange in gastric signet ring cell carcinoma presenting as microangiopathic hemolytic anemia: a rare case report

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[2] *Department of Pathology, Faculty of Medicine, Yüzüncü Yıl University, Van, Turkey*

Objective: Cancer-associated microangiopathic hemolytic anemia (MAHA) is a rare but serious condition that is encountered in patients diagnosed with a malignancy. We describe a case of signet-ring cell carcinoma with a very rare presentation, namely a laboratory and clinical picture of MAHA, who demonstrated an effective thrombocyte level in response to therapeutic plasma exchange (TPE) therapy that was administered during the diagnostic period.

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thoracic-full abdominal computed tomography (CT) scan was performed in order to detect malignancies. On abdominal CT, 1 to 2 lymphadenopathies of 15 × 12 mm in the peripancreatic and perigastric area and pathological wall thickening (2.5 cm) at the level of the gastric corpus were detected. Gastroduodenoscopy revealed an edematous, partly ulcerated lesion protruding from the mucosa that extended to the angularis from the gastric cardia. Gastric tissue biopsy report indicated poorly differentiated adenocarcinoma (signet-ring cell predominant). The case was accepted as MAHA secondary to gastric carcinoma (ADAMTS-13 activity tested earlier was within normal limits at 84%). While waiting for the results of the biopsy and the other tests, the patient underwent 14 sessions of TPE in total. Following TPE, platelet count increased from 25×10^9/L up to 162×10^9/L, fragmented erythrocyte rate in peripheral smear decreased more than 75% and other laboratory findings of hemolysis (LDH, bilirubin, etc.) significantly decreased. The patient was transferred to the medical oncology clinic for the chemotherapeutic treatment of the primary gastric carcinoma.

Conclusion: Malignancy-associated MAHA is generally linked to a poor prognosis and the optimal treatment is not known. However, there is evidence for the importance of promptly initiating an effective antineoplastic regimen and it is also noteworthy that administering therapeutic plasma exchange (TPE) therapy for the purpose of immunocomplex removal could be beneficial in patients with symptoms of bleeding and thrombosis.

https://doi.org/10.1016/j.htct.2020.09.117

PP 55

A signet ring cell carcinoma presented as refractory acquired thrombotic thrombocytopenic purpura

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Objective: Microangiopathic hemolytic anemia (MAHA) can be observed as a paraneoplastic syndrome (PS) in certain tumors. MAHA related signet ring cell carcinoma (SRCC) of an unknown origin is very infrequent. Herein we present a SRCC case presented with refractory acquired thrombotic thrombocytopenic purpura (TTP).

Case report: 35 years old men applied to emergency service with fatigue and headache on January 2020. In his anamnesis he had a history of alcoholic pancreatitis. His physical examination was normal except the neurological symptoms which are temporary loss of consciousness and disorientation. His laboratory tests resulted as white blood cell 9020/μL, hemoglobin 3.5 g/dL, platelet 18,000/μL, MCV 110.7 fl, urea 58 mg/dL, creatinine 0.84 mg/dL, AST 68 u/L, ALT 33 u/L, indirect bilirubin 1.88 mg/dL, LDH 2257 u/L, reticulocyte 0.1, haptoglobulin <8 mg/dL, INR 1.42, Prothrombin time 13.2, fibrinogen 184 mg/dL, coombs negative. He had consulted to our clinic with bicytopenia and hemolysis. Schistocytes, micro-spherocytes and thrombocytopenia were observed in his blood smear. Microangiopathic hemolytic anemia was present and he was considered as thrombotic thrombocytopenic purpura. Plasma exchange treatment was initiated however he was refractory to this treatment. He had epistaxis and blurred vision during the follow-up. Superficial hemorrhages on the edges of the optic disc and roth spots were detected. Pain had emerged in his right arm. Doppler ultrasonography revealed the occlusion of cephalic vein with non-recanalized thrombus in the subacute process from the antecubital level at the forearm level. Thorax and abdomen computerized tomography (CT) resulted as liver 220 cm, spleen 14 cm, minimal pleural effusion, thickening of minor curvature in stomach corpus with hepatogastric and paraceliac lymphadenopathy. As a result of CT endoscopic examination was planned. Bone marrow investigation by our clinic resulted as the metastasis of adenocarcinoma. Ulcerations and necrosis was observed by gastric endoscopy procedure. Biopsy was taken during endoscopic intervention which resulted as signet ring cell carcinoma. He was transferred to oncology clinic for his treatment. Unfortunately he died in one month after his transfer.

Conclusion: Only 40% of TTP cases have the complete pentad and in 75% of the cases there is a triad of microangiopathic hemolytic anemia, thrombocytopenia, and neurological findings. In our case there was no acute kidney failure, however all the other features favored TTP, and diagnosis was made without the kidney failure. MAHA may be seen as a PS in some tumors, especially gastric cancers. Tumor related MAHA is generally accompanied by bone marrow (BM) metastases. As a result, BM investigation may be used as the main diagnostic method to find the underlying cancer. Total plasma exchange is usually performed in the treatment of cancer-associated TTP, however fewer than 20% of the cases respond to plasma exchange. Likely, our case did not respond to plasma exchange treatment either. The clinical course of cases with tumor related MAHA is usually poor, and these cases are usually refractory to plasma exchange treatment. In conclusion, physicians should suspect a malignancy and BM involvement when faced with a case of refractory TTP.

https://doi.org/10.1016/j.htct.2020.09.118

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https://doi.org/10.1016/j.htct.2020.09.118

PEDIATRIK HEMATOLOGY
HEMATOLOGY – GENERAL

PP 56

Health-related quality of life for children with leukemia: child and parental perceptions

E. Ocak[1,*], A. Koca Yozgat[2], D. Kaçar[2], I. Ayrancı Sucaklı[1], N. Ozbek[2], O. Şükran Üneri[3], H. Yaralı[2]

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[2] *Ankara City Hospital Children's Hospital, Department of Pediatric Hematology, Ankara, Turkey*
[3] *Ankara City Hospital, Children's Hospital, Department of Child and Adolescent Psychiatry, Ankara, Turkey*

Objective: The importance of health-related quality of life (HRQoL) in patients with acute lymphoblastic leukemia (ALL) has increased in recent years. This study aimed to assess HRQoL in children with ALL, affecting factors, and the relationship between parent proxy-report and child self-report HRQoL.

Methodology: The study sample consisted of 2–12 years old children with ALL between November 2016 and May 2017 at the University of Health Sciences Ankara Child Health and Diseases Hematology and Oncology Training and Research Hospital, Department of Pediatric Hematology. Patients and their parents (both mother and father) were enrolled in this cross-sectional study. Turkish version of the Pediatric Quality of Life Inventory (PedsQoLTM) 3.0 Cancer Modules were used to determine HRQoL. Patients' diagnosis, risk group according to the ALL-IC BFM 2009 protocol [standard risk group (SR), intermediate-risk group (IR), high-risk group (HR)], treatment status, the period between the cessation of the chemotherapy to the study and total hospitalization period, was obtained from the patients' medical record. Demographic data regarding the information on parents' age, education level, employment status, monthly income, and chronic medical condition were noted. Cardiovascular diseases, cancer, asthma, diabetes mellitus, thyroid disorders, and psychiatric problems were classified as chronic medical conditions by the Centers for Disease Control.

Results: A total of 59 patients (52,5% male) with a mean age of 7.28 ± 2.67 years at study period and 4.02 ± 2.51 years at diagnosis were enrolled. 57 patients (96.6%) were pre-B ALL and two (3.4%) patients were T-ALL. According to the risk groups; 18 (30.5%) patients had SRG, 25 (42.4%) patients had MRG and 16 (27.1%) patients had HRG. There were not any significant differences between on-treatment and off-treatment groups, age at study period, age at diagnosis, gender. There was no significant relationship between total scores of PedsQL cancer module self-report and the leukemia or sociodemographic features. According to subscales of self-report form; nausea and operational anxiety scores differed significantly by the treatment status; communication score varied considerably by the total hospitalization period; pain and hurt, cognitive problems and perceived physical appearance scores differed significantly by maternal chronic disease status ($p < 0.05$). No significant relationship was found between the total scores of the PedsQoLTM-cancer module parent-proxy report (father) and leukemia or sociodemographic features. The presence of maternal chronic disease was significantly related to the total score of the PedsQLTM-cancer module parent-proxy report (mother) ($p < 0.05$). There was a moderate correlation between total scores of child and mother ($p < 0.05$, $r = 0.419$) but not with the father.

Conclusion: Children on-treatment had significant problems in nausea and procedural anxiety subscales; however, children who hospitalized more had fewer issues in the communication subscale. Also, children whose mother had chronic disease had poorer HRQoL regarding pain and hurt cognitive problems, and treatment anxiety. Given the importance of assessment and monitoring HRQoL in children with ALL, health professionals should be aware of how parents' chronic disease affects HRQoL. Psychosocial support should be provided to children and their parents, especially whose parents have a chronic illness.

https://doi.org/10.1016/j.htct.2020.09.119

PP 57

Rare infectious agents in children with hematological disease

Y. Akcabelen*, A. Koca Yozgat, Z. Guzelkucuk, O. Arman Bilir, M. Isik, D. Kacar, D. Gurlek Gokcebay, N. Yarali

Ministry of Health Ankara City Hospital, Ankara, Turkey

Objective: Infections are among the most important causes of mortality and morbidity in immunocompromised children. Although, the microbiological agents are usually opportunistic infections, sometimes rare infectious agents can also cause severe clinical conditions. Here, we present eight different microbial agents that can rarely cause infections in children with febrile neutropenia.

Case report: Case 1 is a 5-year-old girl with acute lymphoblastic leukemia (ALL) had a bloodstream infection during the reinduction therapy. Candida pelliculosa was detected in the blood culture taken from the port catheter. The catheter was removed and the patient was successfully treated with caspofungin. Case 2 is a 1-year-old girl with acute myeloblastic leukemia had a bloodstream infection during the first induction therapy. Cronobacter sakazakii was detected in peripheral blood culture. The patient was treated with cefepime and amikacin without port removal. Case 3 is a 5 month old girl with hemophagocytic lymphohistiocytosis had a pneumonia during the HLH 2004 protocol. Nocardia asteroides was detected in the bronchoalveolar lavage fluid. The patient was treated with trimethoprim-sulfamethoxazole and meropenem, however, she died of sepsis and multiple organ failure. Case 4 is a 2-year-old girl with ALL had a sepsis during the consolidation therapy. Candida tropicalis was detected in the port catheter and peripheral blood culture and renal abscess had developed. The patient was treated with broad spectrum antibiotics however she died sepsis and multiple

PEDIATRIK HEMATOLOGY
HEMATOLOGY – GENERAL

PP 56

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organ failure. Case 5 is a 9-year-old male with ALL had a bloodstream and port catheter infection after the first induction therapy. Herbaspirillum huttiense was detected in the blood culture taken from the port catheter. The patient was successfully treated with meropenem without port removal. Case 6 is a 10-year-old girl with ALL had a bloodstream and port catheter infection during the second induction therapy. Ralstonia pickettii was detected in the blood culture taken from the port catheter. The catheter was removed and the patient was successfully treated with piperacillin-tazobactam. Case 7 is a 7 month old male with Juvenile myelomonocytic leukemia had a bloodstream and port catheter infection in the neutropenic period. The patient was constantly inserting the port catheter into her mouth. Staphylococcus salivarius was detected in the blood culture taken from the port catheter. Then, 5 day after, Rothia mucilaginosa was detected in the peripheral blood culture. The patient was successfully treated with meropenem without port removal. Case 8 is a 9-year-old girl with ALL had a infective endocarditis and sepsis during the induction therapy. Magnusiomyces capitatus was detected in the peripheral blood culture. The patient was treated with fluconazole and amphotericin-B, but she died of multi-organ failure.

Conclusion: Many different microorganisms can cause infections in immune-compromised children as a result of primary disease or chemotherapy. Though empiric antibiotic therapy should be initiated early, the treatment should be revised according to the antibiogram and catheter should be removed as needed.

https://doi.org/10.1016/j.htct.2020.09.120

PP 58

Idiopathic hypereosinophilic syndrome associated pulmonary hypertension in a child

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Objective: Hypereosinophilic syndrom (HES) is defined by showing eosinophilic infiltration in any tissue or organ and increased eosinophils in peripheral blood. Other pathologies that cause eosinophil increase must be excluded. Pulmonary eosinophilic infiltration may have different symptoms and signs, but clinical presentation as PHT has not been shown in children.

Case report: A 6-month-old girl presented with dyspnea and hypoxia. A blood cell count and a morphological evaluation of a peripheral blood smear and confirmed hypereosinophilia (white blood cells 40,600/μL, eosinophils 18,900/μL, hemoglobin 10.3 g/dL, and platelets 425,000/μL). There was not any cellular morphological abnormalities in bone marrow aspiration examination. Pnomonia and parasites, allergic diseases, clonal abnormalities, cancer and vasculitis that might have caused HES were excluded. Echocardiogram showed 38 mmHg for pulmonary arterial pressure (PAP), suggesting pulmonary hypertension (PHT). After exclusion of other causes such as vasculitis, connective tissue diseases, bronchopulmonary displasia, congenital heart diseases, lung diseases, and chronic thromboembolic PHT. The patient was diagnosed with pulmonary arterial hypertension associated with idiopathic HES. Methylprednisolone treatment was started at 2 mg/kg/day. PHT and HES were both improved in the evaluation one month later.

Conclusion: Eosinophilic infiltration causes thickening and remodeling of the pulmonary artery intima and media, thereby causing pulmonary hypertension. Thus, PHT can be seen as HES clinical presentation. With corticosteroid therapy, HES and PHT clinical findings can be controlled.

https://doi.org/10.1016/j.htct.2020.09.121

PP 59

A rare variant of dyskeratosis congenita: RTEL1 defect

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[2] *Hacettepe University, Research Center for Fanconi Anemia and Other Inherited Bone Marrow Failure Syndromes, Ankara, Turkey*

Objective: Dyskeratosis congenita (DC) is a rare hereditary disorder characterized by bone marrow failure, malignancy predisposition and skin findings. As the disease progresses, patients may develop pulmonary fibrosis, esophageal stenosis, urethral stenosis and liver cirrhosis. Herein, we present a patient who was referred with a diagnosis Diamond Blackfan anemia and was diagnosed to have dyskeratosis congenita on whole exome sequencing (WES).

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Results: In dyskeratosis congenita cases where the disease does not follow classical presentation, the use of genetic

organ failure. Case 5 is a 9-year-old male with ALL had a bloodstream and port catheter infection after the first induction therapy. Herbaspirillum huttiense was detected in the blood culture taken from the port catheter. The patient was successfully treated with meropenem without port removal. Case 6 is a 10-year-old girl with ALL had a bloodstream and port catheter infection during the second induction therapy. Ralstonia pickettii was detected in the blood culture taken from the port catheter. The catheter was removed and the patient was successfully treated with piperacillin-tazobactam. Case 7 is a 7 month old male with Juvenile myelomonocytic leukemia had a bloodstream and port catheter infection in the neutropenic period. The patient was constantly inserting the port catheter into her mouth. Staphylococcus salivarius was detected in the blood culture taken from the port catheter. Then, 5 day after, Rothia mucilaginosa was detected in the peripheral blood culture. The patient was successfully treated with meropenem without port removal. Case 8 is a 9-year-old girl with ALL had a infective endocarditis and sepsis during the induction therapy. Magnusiomyces capitatus was detected in the peripheral blood culture. The patient was treated with fluconazole and amphotericin-B, but she died of multi-organ failure.

Conclusion: Many different microorganisms can cause infections in immune-compromised children as a result of primary disease or chemotherapy. Though empiric antibiotic therapy should be initiated early, the treatment should be revised according to the antibiogram and catheter should be removed as needed.

https://doi.org/10.1016/j.htct.2020.09.120

PP 58

Idiopathic hypereosinophilic syndrome associated pulmonary hypertension in a child

Y. Akcabelen*, T. Bayhan, G. Cinel, I. Ece, N. Ozbek

Ministry of Health Ankara City Hospital, Ankara, Turkey

Objective: Hypereosinophilic syndrom (HES) is defined by showing eosinophilic infiltration in any tissue or organ and increased eosinophils in peripheral blood. Other pathologies that cause eosinophil increase must be excluded. Pulmonary eosinophilic infiltration may have different symptoms and signs, but clinical presentation as PHT has not been shown in children.

Case report: A 6-month-old girl presented with dyspnea and hypoxia. A blood cell count and a morphological evaluation of a peripheral blood smear and confirmed hypereosinophilia (white blood cells 40,600/μL, eosinophils 18,900/μL, hemoglobin 10.3 g/dL, and platelets 425,000/μL). There was not any cellular morphological abnormalities in bone marrow aspiration examination. Pnomonia and parasites, allergic diseases, clonal abnormalities, cancer and vasculitis that might have caused HES were excluded. Echocardiogram showed 38 mmHg for pulmonary arterial pressure (PAP), suggesting pulmonary hypertension (PHT). After exclusion of other causes such as vasculitis, connective tissue diseases, bronchopulmonary displasia, congenital heart diseases, lung diseases, and chronic thromboembolic PHT. The patient was diagnosed with pulmonary arterial hypertension associated with idiopathic HES. Methylprednisolone treatment was started at 2 mg/kg/day. PHT and HES were both improved in the evaluation one month later.

Conclusion: Eosinophilic infiltration causes thickening and remodeling of the pulmonary artery intima and media, thereby causing pulmonary hypertension. Thus, PHT can be seen as HES clinical presentation. With corticosteroid therapy, HES and PHT clinical findings can be controlled.

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PP 59

A rare variant of dyskeratosis congenita: RTEL1 defect

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Results: In dyskeratosis congenita cases where the disease does not follow classical presentation, the use of genetic

testing confirms the diagnosis at an early stage and reduces morbidity and mortality due to the disease. WES is helpful to detect such cases.

Conclusion: Various genes such as DKC1, CTC1, RTEL1, TERF1, TINF2, TERC have been found to be responsible for DKC. RTEL1 is a DNA helicase necessary for telomere replication and stability. With the understanding of the molecular basis of the disease, patients with hematological findings at the time of diagnosis and those without skin findings were also identified. In our case, signs of bone marrow failure were observed primarily and no changes in nail dystrophy, leukoplakia and skin pigmentation and neurological findings were detected. In cases where the disease does not follow classical presentation, the use of genetic testing confirms the diagnosis at an early stage and reduces morbidity and mortality due to the disease. WES is helpful to detect such cases.

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PP 60

Acquired aplastic anemia in childhood: single-center experience

M. Bilici[1,*], R. Tuna[1], S. Sahin[1], Z. Karakas[1], A. Unuvar[1], S. Anak[2], D. Tugcu[1], S. Karaman[1]

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Case report: Nine patients who were diagnosed with acquired aplastic anemia over ten years were evaluated.

Methodology: The patients admitted to the Istanbul Medical Faculty Pediatric Hematology-Oncology Outpatient Clinic between 2000 and 2010 were diagnosed with acquired aplastic anemia (those who underwent BMT, IST, or both) were evaluated retrospectively on patient files and computer records.

Results: Nine patients were diagnosed with acquired aplastic anemia over ten years. 4 of them were girls, and 5 were boys. The average age was 10 (1–17 years). There was a history of hepatitis in 3 cases and a history of metamizole use in 1 case. As a treatment, six patients were treated with IST, and five patients were treated with BMT. ATG 40 mg/kg/day 4 days, cyclosporin 10 mg/kg/day (6 months), methylprednisolone 2 mg/kg/day (2 months) and G-CSF 5 μg/kg (2 months) as immunosuppressive therapy. Response to immunosuppressive therapy was received at an average of 3 months. Two of them were fully responsive. One patient was lost due to septic shock before the IST response was evaluated. BMT was performed in 5 cases, three of them were unresponsive to IST. In the follow-up, two cases are in remission, and three are lost due to sepsis. When evaluating our 5 cases with dead, two of them were very severe aplastic anemia, the symptoms of sepsis were present in their first admission, and they died before the treatment started. Two of them died due to the complication of BMT in the very early period. One case was admitted with perforated appendicitis while in remission after BMT and died due to septic shock.

Conclusion: Two primary treatment modalities are used to treat patients with severe aplastic anemia; IST and BMT. The first option is BMT with the matched sibling donor. If there is no suitable sibling, IST is started first, and a fully compatible donor is searched immediately. If there is no response to IST, an allogenic BMT must be applied in the presence of a suitable donor. Our mortality rate is high compared to the literature because of severe disease presentation; most of them were late admission to the hospital due to low socioeconomic level.

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HEMOSTASIS, THROMBOSIS, AND VASCULAR BIOLOGY

PP 61

The course of intracranial bleeding in the patient with immune thrombocytopenia

M. Babayev*, A. Ahmadova, K. Mehtiyeva, N. Babayeva

National Hematology and Transfusiology Center, Moscow, Russian Federation

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At the moment, the child's hematological and neurological status is quite satisfactory.

https://doi.org/10.1016/j.htct.2020.09.124

PP 62

The cause of very severe trombocytosis: iron deficiency anemia

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Objective: Platelet count above 450,000 mm^3 is defined as thrombocytosis. It is called mild thrombocytosis if the platelet count is between 700,000–900,000 mm^3, and severe thrombocytosis between 900,000–1,000,000 mm^3. If the platelet count is over 1,000,000 mm^3, it is considered as very severe thrombocytosis. In this case report; we have showed that iron deficiency can also lead to very severe thrombocytosis by presenting the case of very severe thrombocytosis developing in an adolescent female patient.

Case report: The 12-year-old girl was referred to our hospital for anemia (Hgb: 5.8 g/dL) by an external clinic she applied due to her headache in the morning for the past month. The patient's history and family history were unremarkable. Her physical examination revealed that her general condition was moderate-poor, skin was pale, conjunctiva was extremely pale, peak heart rate: 130–140/min, TA: 90/50 mm/Hg. Lymphadenopathy and hepatosplenomegaly were not detected. In the laboratory tests of the patient, the following findings were detected; the leukocytes count was: 14,900/mm^3, neutrophil count: 11.9/mm^3, Hgb: 4.8 g/dL, Hct: 20%, MCV: 53 fl, RBC: 3.7 milyon/uL, MCH: 12.9 pg (27–31), platelet count 2,629,000/mm^3. Peripheral smear of the patient was analyzed. In eritrocytes, a high degree of hypochromic microcytes were detected and 80% neutrophils, 2% monocytes, 18% lymphocytes, abundant platelets were seen. Serum iron: 6.7 uL/dL (50–120); iron binding capacity: 525 uL/dL (155–355); ferritin: 0 ng/mL; folate: 10.6 ng/mL (0.3–24) and vitamin B12: 437 ng/mL. There was no abnormality in other biochemical examinations. Iron replacement was started at a dose of 6 mg/kg/day considering iron deficiency anemia and related thrombocytosis. Abdominal ultrasonography was evaluated within normal limits according to age. Since the patient had tachycardia, appropriate cross erythrocyte transfusion was performed. Viral serologies and autoantibodies of the patient were evaluated as normal. The control hgb level was 7.9 g/dL and thrombocyte count was 1,875,000/mm^3 after transfusion. In the bone marrow aspiration assessment, the myeloid and erythroid series in the normocellular bone marrow were seen as normal, blasts were not seen, megakaryocytes were increased. The patient had hgb: 10.4 g/dL, platelet: 732,000/mm^3 in the clinical examination performed in the second week. She is under the oral +2 valence iron treatment and had no clinical problem in her follow-up examinations.

Methodology: Information was obtained from the patient file.

Results: In childhood, thrombocytosis usually occurs due to secondary causes and thrombocytosis regresses by controlling the causing disease. Thrombocytosis due to iron deficiency is mostly seen in infancy period.

Conclusion: The cause of thrombocytosis in iron deficiency is not fully understood. The fact that the increase in EPO stimulates TPO receptors (c-mpl) in iron deficiency is known to result in thrombocytosis. However, it is very important that children should be evaluated immediately for infection and iron deficiency before performing further examinations. Keywords: Thrombocytosis; iron deficiency; child.

https://doi.org/10.1016/j.htct.2020.09.125

LEUKEMIA/LYMPHOMA/HISTIOCYTE DISORDERS

PP 63

Immune markers are closely related to the remission achievement in childhood acute myeloid leukemia

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[1] *Federal State Budgetary Institution "N. N. Blokhin National Medical Research Center of Oncology" Of the Ministry of Health of the Russian Federation, Moscow, Russian Federation*
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Objective: Immunophenotyping of the blast population at the diagnosis of acute myeloid leukemia is a routine study that supplements the data obtained by morphological, cytochemical and cytogenetic studies of tumor cells. Currently, risk-stratification of children with acute myeloid leukemia (AML) is based on initial leukocytosis and genetic abnormalities. However, those genetic aberrations which effect the prognosis of childhood AML are found only in about 35% of cases. The search for reliable factors to clarify the stratification of patients into risk groups continues, and along with chromosomal and gene abnormalities, aberrations of the immunophenotype of tumor blasts are of interest. There are conflicting data on the effect of immunological factors on the prognosis of AML. Most of them were obtained by the analysis of AML in adults. It is of interest to analyze the effect of the immunophenotypic "portrait" of blast cells on the course of the disease. The achievement of complete remission (CR) is the main prognostic factor for AML in children.

Methodology: In our study, CR was achieved in 84 of 105 children with AML (80.0%) and achieving complete remission was very significant ($p = 0.000$) prognostic factor in assessing overall survival. We analyzed the influence of gender, age, FAB-variants and immunological markers on the probability of remission achievement. The effects of age, FAB-variants and gender were not significant, though boys achieved complete remission more rarely than girls ($p = 0.11$). We analyzed effect of the following immunological markers: CD7 ($n = 69$), CD117 ($n = 37$), CD34 ($n = 93$), CD13 ($n = 97$), CD33 ($n = 96$), CD20 ($n = 47$), CD19 ($n = 84$), CD9 ($n = 9$), CD38 ($n = 50$), HLA-DR ($n = 83$), CD11b

At the moment, the child's hematological and neurological status is quite satisfactory.

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PP 62

The cause of very severe trombocytosis: iron deficiency anemia

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Objective: Platelet count above 450,000 mm^3 is defined as thrombocytosis. It is called mild thrombocytosis if the platelet count is between 700,000–900,000 mm^3, and severe thrombocytosis between 900,000–1,000,000 mm^3. If the platelet count is over 1,000,000 mm^3, it is considered as very severe thrombocytosis. In this case report; we have showed that iron deficiency can also lead to very severe thrombocytosis by presenting the case of very severe thrombocytosis developing in an adolescent female patient.

Case report: The 12-year-old girl was referred to our hospital for anemia (Hgb: 5.8 g/dL) by an external clinic she applied due to her headache in the morning for the past month. The patient's history and family history were unremarkable. Her physical examination revealed that her general condition was moderate-poor, skin was pale, conjunctiva was extremely pale, peak heart rate: 130–140/min, TA: 90/50 mm/Hg. Lymphadenopathy and hepatosplenomegaly were not detected. In the laboratory tests of the patient, the following findings were detected; the leukocytes count was: 14,900/mm^3, neutrophil count: 11.9/mm^3, Hgb: 4.8 g/dL, Hct: 20%, MCV: 53 fl, RBC: 3.7 milyon/uL, MCH: 12.9 pg (27–31), platelet count 2,629,000/mm^3. Peripheral smear of the patient was analyzed. In eritrocytes, a high degree of hypochromic microcytes were detected and 80% neutrophils, 2% monocytes, 18% lymphocytes, abundant platelets were seen. Serum iron: 6.7 uL/dL (50–120); iron binding capacity: 525 uL/dL (155–355); ferritin: 0 ng/mL; folate: 10.6 ng/mL (0.3–24) and vitamin B12: 437 ng/mL. There was no abnormality in other biochemical examinations. Iron replacement was started at a dose of 6 mg/kg/day considering iron deficiency anemia and related thrombocytosis. Abdominal ultrasonography was evaluated within normal limits according to age. Since the patient had tachycardia, appropriate cross erythrocyte transfusion was performed. Viral serologies and autoantibodies of the patient were evaluated as normal. The control hgb level was 7.9 g/dL and thrombocyte count was 1,875,000/mm^3 after transfusion. In the bone marrow aspiration assessment, the myeloid and erythroid series in the normocellular bone marrow were seen as normal, blasts were not seen, megakaryocytes were increased. The patient had hgb: 10.4 g/dL, platelet: 732,000/mm^3 in the clinical examination performed in the second week. She is under the oral +2 valence iron treatment and had no clinical problem in her follow-up examinations.

Methodology: Information was obtained from the patient file.

Results: In childhood, thrombocytosis usually occurs due to secondary causes and thrombocytosis regresses by controlling the causing disease. Thrombocytosis due to iron deficiency is mostly seen in infancy period.

Conclusion: The cause of thrombocytosis in iron deficiency is not fully understood. The fact that the increase in EPO stimulates TPO receptors (c-mpl) in iron deficiency is known to result in thrombocytosis. However, it is very important that children should be evaluated immediately for infection and iron deficiency before performing further examinations. Keywords: Thrombocytosis; iron deficiency; child.

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($n=3$), CD64 ($n=59$), CD14 ($n=20$), CD5 ($n=51$), CD3 ($n=55$), CD56 ($n=52$), CD10 ($n=67$).

Results: Among them presence of CD33, CD19 and CD56 increased the probability of remission achievement ($p=0.005$; 0.025 and 0.049 respectively) while CD14 ($p=0.028$) had a negative effect on it. It is important to note that none of these markers had a significant effect on the overall survival.

Conclusion: In conclusion, search for new prognostic factors for AML in children continues, and aberrantly expressed immunophenotypic markers may become important for clinicians.

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PP 64

The course of toxic hepatitis at the stage of treatment consolidation acute leukemia in children

M. Babayev*, A. Ahmadova, K. Mehtiyeva, N. Babayeva

National Hematology and Transfusiology Center, Moscow, Russian Federation

Objective: Toxic hepatitis occupies a special place among the complications of chemotherapy in the treatment of patients with acute leukemia. The research work we have presented is devoted to studying the frequency of toxic hepatitis and the choice of treatment tactics for children who are at the stage of consolidating acute leukemia.

Methodology: The study group included 110 children from both sexes who reached complete remission after a course of induction. Patients were 9 months old up to 15 years. The treatment was carried out according to the Moscow-Berlin-2015 program, where the consolidation phase was composed of 3 courses of 8 weeks. The severity of toxic hepatitis was predetermined by its criteria.

Results: According to the data obtained, 81 patients had toxic hepatitis (73.6%). In mild form it was noted in 46 children (56.7%), in moderate severe in 31 (38.4%), and in severe in 4 children (4.9%).

Conclusion: In the mild form of hepatitis from the intravenous use of Essentiale forte and Riboxin against the background of ongoing chemotherapy, a positive effect was obtained. With moderate severity, intravenous administration of Adeomethionine preparations (Heptral/Legend) in combination with Aevit per os turned out to be more effective. In 4 patients, upon transition to a severe form in the last course of consolidation, along with these drugs, ursodeoxycholic acid (Ursobil) + enhanced detoxification therapy was prescribed, which led to a complete recovery. After the treatment of toxic hepatitis, all patients with moderate and severe form, for the purpose of prevention, was prescribed combination therapy with Ursobil + Aevit + Lipoic acid, which gave a long-term positive effect.

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PP 65

Klippel–Trenaunay syndrome associated with chronic myeloid leukemia

C. Coskun*, T. Aksu, F. Gumruk, S. Unal

Hacettepe University Center for Fanconi Anemia and Other Inherited Bone Marrow Failure Syndromes, Ankara, Turkey

Objective: Klippel–Trenaunay syndrome (KTS) has been associated with capillary, venous, lymphatic and soft tissue malformations, whether it predisposes to malignancy is not clear. We report a case of chronic myeloid leukemia (CML) with KTS. We report this case because of its rarity and need for long term follow-up.

Case report: A 14-year-old boy presented with a painless mass on his left groin which was extending to his knee. Physical examination revealed splenomegaly, limb length discrepancy, left lower extremity hypertrophy and capillary hemangiomas over the posterolateral skin of the left thigh. KTS was suspected and confirmed with heterozygous mutation (c1634A>C/p.Glu545Ala) at the PIK3CA gene. The patient consulted to the hematology due to hemorrhage complication of the surgery. Complete blood counts showed a hemoglobin level of 7.3 g/dL, white blood cell as 164×10^9/L, neutrophil 76.4×10^9/L and thrombocytes 104×10^9/L). The differential was metamyelocytes 20%, bands 4%, neutrophils 70%, eosinophils 4%, lymphocytes 2%, normoblast 4%, except circulating blasts. Bone marrow aspiration showed normocellular myeloid/erythroid ratio of 23:1, granulopoiesis with left shift, increased megakaryocytes seen with normal maturation and blasts were lower than 5%. RT-PCR from peripheral blood was positive for the BCR-ABL p210 transcript. Conventional karyotyping revealed a typical 46 XY, t(9,22)(q34;q11.2) without any additional cytogenetic abnormalities in all (20/20, 100%). Chronic phase CML (CML-CP) was diagnosed, and imatinib was initiated with a 300 mg/m^2 dose daily.

Results: To our knowledge there has been no description of an association between KTS syndrome and CML in the literature. We report this case because of its rarity.

Conclusion: Klippel–Trenaunay syndrome is a rare congenital malformation involving blood and lymph vessels and abnormal growth of soft and bone tissue. The exact cause of KTS is not clear, several genes and pathways have been identified in its pathogenesis. Remarkably, PIK3CA gene mutations have been detected in some cases of KTS. PIK3CA encodes for a subunit of the phosphoinositide 3-kinase enzyme, which is involved in cell proliferation and migration. The angiogenic gene VG5Q has also been implicated in KTS. We report the case of a 14 year-old boy with diagnosed KTS, who presented with a bleeding from the surgical region that was found to be a chronic myeloid leukemia. To our knowledge there has been no description of an association between KTS syndrome and CML. In the literature, there are cases where KTS is associated with Wilms tumor, neurofibromatosis and osteoblastoma, but no hematologic malignancy has been so far.

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PP 66

Multiple relapsed acute lymphoblastic leukemia with t(9;13) in a child

D. Gurlek Gokcebay*, Y. Akcabelen, A. Koca Yozgat, D. Kacar, O. Arman Bilir, M. Isik, I. Ok Bozkaya, N. Ozbek, N. Yarali

Ankara City Hospital, Ankara, Turkey

Objective: Acute lymphoblastic leukemia (ALL) is the most common form of childhood cancer. Patients with ALL are classified into genetic subtypes based on the occurrence of recurrent chromosomal abnormalities detected by karyotyping, fluorescent in situ hybridization (FISH), and/or polymerase chain reaction (PCR) amplification. Both the B-cell precursor and T-ALL comprise multiple subtypes defined by chromosomal alterations. The most known subtypes of ALL are t(12;21), t(1;19), t(9;22), iAMP21, hypo/hyperdiploidy and KMT2A rearrangements.

Case report: A 5-year-old boy was admitted to our hospital with fever and cough. His physical examination was normal, except hepatosplenomegaly. Complete blood count showed hemoglobin of 12.1 g/dL, white blood cell count of 198 $\times$ 10^9/L, and platelet count of 61 $\times$ 10^9/L. His peripheral blood and bone marrow aspiration smear showed L1-type lymphoblasts. He was diagnosed with B-precursor ALL without central nervous system (CNS) involvement, and ALL-IC BFM 2009 protocol was initiated. His bone marrow cytogenetic analysis revealed 46, XY with t (9;13). 33rd-day bone marrow showed >5% blasts, minimal residual disease (MRD) result by flow cytometry was 0.014%. He received a high-risk chemotherapy protocol, and hematopoietic stem cell transplantation (HSCT) was performed with total body irradiation conditioning from a matched unrelated donor. On the 130th day of the HSCT, he was readmitted to the hospital with testicular enlargement. Complete blood count showed a leukocyte count of 111x109/L with lymphoblasts. Orchiectomy was performed for testicular relapse, and REZ-BFM 2016 protocol and then blinatumomab was given. Thereafter, a second HSCT from another matched unrelated donor was performed. However, on the 83rd day of the second HSCT, bone marrow and CNS relapse occurred. He received weekly intrathecal chemotherapy and FLAG-IDA (fludarabine, high dose cytarabine, G-CSF, and idarubicin) protocol that continued with weekly oral methotrexate and daily 6-mercaptopurine and received 18 Gy cranial radiotherapy. Five months later, he admitted to hospital with generalized convulsion and isolated CNS involvement detected. He received intrathecal chemotherapy for six weeks with oral methotrexate and 6-mercaptopurine. However, two months later, he readmitted with headache and combined CNS and bone marrow involvement was detected and ETO-FLAG (fludarabine, high dose cytarabine, G-CSF, and etoposide) regimen was given. He is still followed-up at our clinic with invasive fungal infection and neutropeni.

Methodology: Herein, we present a child had t (9;13) with multi-relapsed ALL.

Results: In English literature, only one adult ALL case has been reported with t (9;13) and poor outcome. Nonrandom abnormalities of chromosome 9p, especially a breakpoint in 9p21-22, may occur in childhood ALL in association with a higher incidence of extramedullary relapse and treatment failure, as in our case.

Conclusion: Treatment of relapsed ALL still is a challenge and experimental trials may be considered for these patients.

https://doi.org/10.1016/j.htct.2020.09.129

PP 67

Occurence of acute myeloid leukemia after primary hepatic carcinoma in a patient who had liver transplantation

C. Coskun[1,*], S. Unal[2], A. Uner[3], T. Aksu[1], S. Aytac[1], B. Kuskonmaz[1], F. Gumruk[1]

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[2] *Hacettepe University, Research Center for Fanconi Anemia and Other Inherited Bone Marrow Failure Syndromes, Ankara, Turkey*
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Objective: Recent advances in disease-free survival rate following organ transplantation have led to an increased incidence of malignancies after transplantation. The most common malignancies after transplantation are solid tumors, including posttransplantation lymphoproliferative diseases, sarcomas and skin carcinomas. Acute leukemias are very rare after transplantation and the incidence of acute leukemia among solid organ recipients is 0.12–2.5%. Herein, we describe a case of AML-M7 after liver transplantation.

Case report: A 10 years-old girl was admitted to our hospital because of abdominal pain and abdominal mass. An abdominal ultrasound examination showed the solid mass lesion in right adrenal region and liver. With the pathology report, the patient was diagnosed with hepatocellular carcinoma. Chemotherapy was started and surgical mass excision was made. After recurrence, liver transplantation was performed from the father. Tacrolimus was started prophylactically. Approximately 5 years after liver transplantation, the patient was referred to hematology with fatigue and leg pain. Family history revealed that mother had breast cancer and her brother died at the age of 2.5 due to hepatoblastoma. She was pancytopenic and bone marrow aspiration and biopsy revealed acute myeloid leukemia with flow cytometry AML FAB M7 was diagnosed. AML BFM 2019 protocol was initiated. Cytogenetic and molecular work-up from bone marrow samples revealed only monosomy 7. Familial cancer susceptibility genes revealed p53 gene mutation and BRCA2 gene mutations. Hematopoietic stem cell transplantation was planned.

Results: Immunosuppressive treatments used after liver transplantation may have impact on secondary cancer development, additionally genetic familial risks in our patient may also have contributed to subsequent leukemia development.

Conclusion: The development of AML after liver transplantation is a relatively rare complication and several such cases of AML have been reported, previously. Immunosuppressive treatments used after liver transplantation may have impact on secondary cancer development, additionally

PP 66

Multiple relapsed acute lymphoblastic leukemia with t(9;13) in a child

D. Gurlek Gokcebay*, Y. Akcabelen, A. Koca Yozgat, D. Kacar, O. Arman Bilir, M. Isik, I. Ok Bozkaya, N. Ozbek, N. Yarali

Ankara City Hospital, Ankara, Turkey

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PP 68

Acute lymphoblastic leukemia with ebv infection and multiple chromosomal abnormalities in a child

D. Kacar*, A. Koca Yozgat, S. Sahin, Y. Akcabelen, F. Kurtipek, D. Gurlek Gokcebay, N. Yarali

Ankara City Hospital, Pediatric Hematology and Oncology Department, Ankara, Turkey

Objective: Acute lymphoblastic leukemia (ALL) is the most common type of cancer in childhood but its etiology is largely unexplained. Epstein Barr Virus (EBV) may play a role in the pathogenesis of ALL by integrating into the genome of precursor B cells, disturbing differentiation and proliferation control.

Case report: Two and a half year old boy admitted with fever. Physical examination findings were unremarkable. Laboratory investigations revealed a low hemoglobin level (9.7 g/dL), a low platelet count (31,000 cells/mm^3), a normal leukocyte count (7130 cells/mm^3) and also an elevated lactate dehydrogenase level (661 U/L). A peripheral blood (PB) examination revealed the presence of leukemic blasts of uncertain origin (51%). A bone marrow (BM) smear showed almost complete infiltration of L1 blasts (94%). Immunophenotyping was consistent with pre-B ALL. Conventional cytogenetic analysis of BM blasts revealed a mosaic karyotype with hypodiploidy (46,XY[7]/45,XY[3]/40-44,XY[2]). FISH analyses showed inversion 16 (20%), trisomy 7(12%). FISH analyses also detected elevated signals suggesting duplications or trisomies at IGH region of 14th chromosome, at ETV6 region of 12th chromosome and at AFF1 region of 4th chromosome. Before chemotherapy EBV DNA was 1563 IU/mL in PB. EBV viral capsid antigen (VCA) immunoglobulin (Ig) M was positive and EBV VCA Ig G was low suggesting a primary acute infection. At the end of induction the patient was in remission and EBV DNA could not be detected neither in BM nor in PB. Karyotype and FISH analyses were both normal. Maintenance treatment is going on without an EBV activation.

Methodology: Herein, we present a child with ALL who has EBV positivity and multiple chromosomal abnormalities.

Results: Since EBV was identified, it has been associated with a variety of diseases of hematological origin such as Burkitt's lymphoma, Hodgkin lymphoma, post-transplant lymphoproliferative disease, hemophagocytic lymphohistiocytosis (HLH) and etc. The same cell type in lymphoma and lymphocytic leukemia lead similar diseases with different clinical manifestations and stages sharing similar biological characteristics. It is reported that lymphocyte chromosome mutations or translocations caused by EBV infection can lead to oncogene activation resulting in the occurrence of lymphoma. In addition, chromosome abnormalities have been observed in EBV-associated HLH and chronic active EBV infection. Ahmed at al. screened 80 pediatric patients with leukemia and 20 healthy controls from Sudan, for the presence of EBV latent membrane protein 1 (LMP1) gene transcripts. Although there was no positivity in the control group, they found high ratios in leukemia group suggesting the role EBV in the etiology of pediatric leukemia. Guan et al. detected EBV DNA copies in BM of both pediatric and adult patients with ALL, AML and they also found higher ratios from healthy controls.

Conclusion: The child we presented herein has pre-B ALL with multiple chromosomal abnormalities detected by karyotype analysis combined with FISH. These anomalies and leukemia itself can be associated with active EBV infection. Studies with large sample sizes to elucidate the possible role of EBV infection in acute leukemias and associated chromosome aberrations are required.

https://doi.org/10.1016/j.htct.2020.09.131

PP 69

Hypercalcemia due to concomitant use of all trans retinoic acid and voriconazole

A. Koca Yozgat*, Y. Akçabelen, Y. Unal, N. Yaralı

Ankara City Hospital, Ankara, Turkey

Objective: Objective: All-trans-retinoic acid (ATRA) has been used in the treatment of acute promyelocytic leukemia (APL). Although the well-known side effects include retinoic acid syndrome and Sweet's syndrome, hypercalcemia associated with ATRA has rarely been reported. The metabolism of ATRA occurs through cytochrome p450 enzymes, and the azole antifungals are known to be potent inhibitors of the cytochrome p450 enzyme system. Here, we report a child who had severe hypercalcemia in the treatment of acute promyelocytic leukemia.

Case report: Case: A 8-years old boy presented with epistaxis and petechia. The patients' bone marrow aspiration and flow cytometry results were compatible with APL, and t (15;17) was positive. The treatment of AML BFM 2013 protocol and ATRA were initiated. After induction treatment, voriconazole treatment was started prophylactically. While the patient was receiving voriconazole and ATRA, hypercalcemia (Ca: 12.4 mg/dL) and hypertension (140/90 mm Hg) developed. Endocrine and nephrological evaluations of the patient were normal. After the voriconazole treatment was discontinued, hypercalcemia and hypertension improved and never recurred.

Conclusion: Discussion: Hypercalcemia associated with the treatment with ATRA has been described in the literature. The mechanisms of hypercalcemia due to ATRA include accelerated mineral resorption through increased osteoclastic activity, increased interleukin-6 levels that increase bone resorption, and increased parathyroid hormone-related protein. Hypercalcemia is due to the inhibition of ATRA metabolizing cytochrome p450 enzymes, by voriconazole. To decrease the incidence of this side-effect, the use of any medications that can inhibit the cytochrome P450 enzyme system during ATRA therapy is inappropriate unless mandatory.

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https://doi.org/10.1016/j.htct.2020.09.132

PP 70

Acute lymphoblastic leukemia in the context of constitutional mismatch repair deficiency syndrome: a case report

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Objective: B-cell precursor acute lymphoblastic leukemia (pre-B ALL) is the most common childhood cancer. Although most childhood B-ALL is sporadic, a subset occurs in children with pre-existing conditions that predispose to leukemogenesis.

Case report: Five and a half year old girl admitted with fever. There were multiple cafe au lait spots without axillary freckling, hepatosplenomegaly and cervical lymphadenopathy on physical examination. Family history elicited that her mother and father were first degree cousins and none of them but her little brother had multiple cafe au lait spots. Laboratory investigations revealed a low hemoglobin level (4.9 g/dL), a low platelet count (13,000 cells/mm^3) and a normal leukocyte count (6610 cells/mm^3). A peripheral blood (PB) examination revealed the presence of leukemic blasts of uncertain origin (30%). A bone marrow (BM) smear showed complete infiltration of L1 blasts. Immunophenotyping was consistent with pre-B ALL. Karyotype of BM blasts could not be analysed because of insufficient number of metaphase cells. FISH analyses showed trisomy 8. Accompanied with ALL IC BFM 2009 chemotherapy protocol, diagnostic work up directed to cancer predisposition syndromes proceeded. Next-generation sequencing (NGS) revealed a mutation in one of the CMMRD genes. The mutation was biallelic in PMS2 gene and according to American College of Medical Genetics and Genomics 2015 guidelines, it was an "uncertain clinical significance" mutation. At the end of induction she was in remission and karyotype and FISH analyses of BM were both normal. The patient experienced hepatosplenic candidiasis and lobar pneumonia during chemotherapy but no dose reduction was made. Follow-up for CMMRD and maintenance treatment of ALL is going on.

Methodology: We present a child with constitutional mismatch repair deficiency syndrome (CMMRD) related pre-B ALL.

Results: Although we do not know the exact karyotype of blasts in our case, at least they have trisomy 8. Trisomy of chromosome 8 is frequently reported in myeloid lineage disorders and also detected in lymphoid neoplasms as well as solid tumors, suggesting its role in neoplastic progression in general. Trisomy 8 is associated with poor prognosis in acute and chronic myeloid leukemias but prognostic significance of extra 8th chromosome in lymphoid malignancies is not reported widely. Trisomy 8 could represent an alternative mechanism for increasing c-myc gene dosage to achieve amplification of c-myc oncogene but mechanisms underlying the events need further study.

Conclusion: CMMRD syndrome is a rare disease and related malignancies need individualization of therapy and novel approaches to optimize care. The child presented herein is a unique case who has CMMRD syndrome phenotype with an "uncertain clinical significance" mutation in PMS2 gene and ALL with trisomy 8. To our knowledge, trisomy 8 has not been reported in ALL in the context of CMMRD syndrome.

https://doi.org/10.1016/j.htct.2020.09.133

RED BLOOD CELL DISORDERS

PP 71

Potential risk of subclinical iron deficiency anemia in misinterpretation of glycosylated hemoglobin a1c (hba1c): a case report

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Objective: Iron deficiency anemia (IDA) which is a global public health problem affecting both developing and developed countries, appears to be more common in diabetic patients compared to non-diabetic population. Gycosylated hemoglobin (HbA1c) which is widely considered as the primary target for glycemic control of diabetic patients, may be altered by certain condition including depletion of iron store with elevation of HbA1C concentrations independent of glycemia. However, reports of the clinical significance of iron deficiency on the glycosylated HbA1c levels have been inconsistent.

Case report: We report a case of 48-year-old diabetic patient with subclinical iron Deficiency, who was in a potential risk of receiving unneeded insulin injection because of false-high values of HbA1c.

Methodology: The false-high values of HbA1c (>7.0%) noticed earlier with the subclinical iron deficiency anemia (hemoglobin 12.7 g/dL, serum iron: 7.94 umol/L, ferritin: 7 ng/mL), then after with frank iron deficiency anemia (hemoglobin 10.1 g/dL, serum iron: 5.68 u, mol/L, ferritin: 5.9 ng/mL).

Results: Interestingly, this high value of HbA1c was subsequently fall (5.8%) simply on correcting the iron deficiency (Ferritin: 10.6 ng/mL) by receiving iron supplementation.

Conclusion: We emphasizes that iron deficiency with or without anemia must be corrected before any diagnostic or therapeutic decision is made based on HbA1c in order to prevent misclassification of diabetes with its hazardous consequences of incorrect treatment.

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Ankara City Hospital, Pediatric Hematology and Oncology Department, Ankara, Turkey

Objective: B-cell precursor acute lymphoblastic leukemia (pre-B ALL) is the most common childhood cancer. Although most childhood B-ALL is sporadic, a subset occurs in children with pre-existing conditions that predispose to leukemogenesis.

Case report: Five and a half year old girl admitted with fever. There were multiple cafe au lait spots without axillary freckling, hepatosplenomegaly and cervical lymphadenopathy on physical examination. Family history elicited that her mother and father were first degree cousins and none of them but her little brother had multiple cafe au lait spots. Laboratory investigations revealed a low hemoglobin level (4.9 g/dL), a low platelet count (13,000 cells/mm^3) and a normal leukocyte count (6610 cells/mm^3). A peripheral blood (PB) examination revealed the presence of leukemic blasts of uncertain origin (30%). A bone marrow (BM) smear showed complete infiltration of L1 blasts. Immunophenotyping was consistent with pre-B ALL. Karyotype of BM blasts could not be analysed because of insufficient number of metaphase cells. FISH analyses showed trisomy 8. Accompanied with ALL IC BFM 2009 chemotherapy protocol, diagnostic work up directed to cancer predisposition syndromes proceeded. Next-generation sequencing (NGS) revealed a mutation in one of the CMMRD genes. The mutation was biallelic in PMS2 gene and according to American College of Medical Genetics and Genomics 2015 guidelines, it was an "uncertain clinical significance" mutation. At the end of induction she was in remission and karyotype and FISH analyses of BM were both normal. The patient experienced hepatosplenic candidiasis and lobar pneumonia during chemotherapy but no dose reduction was made. Follow-up for CMMRD and maintenance treatment of ALL is going on.

Methodology: We present a child with constitutional mismatch repair deficiency syndrome (CMMRD) related pre-B ALL.

Results: Although we do not know the exact karyotype of blasts in our case, at least they have trisomy 8. Trisomy of chromosome 8 is frequently reported in myeloid lineage disorders and also detected in lymphoid neoplasms as well as solid tumors, suggesting its role in neoplastic progression in general. Trisomy 8 is associated with poor prognosis in acute and chronic myeloid leukemias but prognostic significance of extra 8th chromosome in lymphoid malignancies is not reported widely. Trisomy 8 could represent an alternative mechanism for increasing c-myc gene dosage to achieve amplification of c-myc oncogene but mechanisms underlying the events need further study.

Conclusion: CMMRD syndrome is a rare disease and related malignancies need individualization of therapy and novel approaches to optimize care. The child presented herein is a unique case who has CMMRD syndrome phenotype with an "uncertain clinical significance" mutation in PMS2 gene and ALL with trisomy 8. To our knowledge, trisomy 8 has not been reported in ALL in the context of CMMRD syndrome.

https://doi.org/10.1016/j.htct.2020.09.133

RED BLOOD CELL DISORDERS

PP 71

Potential risk of subclinical iron deficiency anemia in misinterpretation of glycosylated hemoglobin a1c (hba1c): a case report

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[2] *Department of Clinical Science, College of Pharmacy and Health Sciences, Ajman University, UAE, Ajman, United Arab Emirates*

Objective: Iron deficiency anemia (IDA) which is a global public health problem affecting both developing and developed countries, appears to be more common in diabetic patients compared to non-diabetic population. Gycosylated hemoglobin (HbA1c) which is widely considered as the primary target for glycemic control of diabetic patients, may be altered by certain condition including depletion of iron store with elevation of HbA1C concentrations independent of glycemia. However, reports of the clinical significance of iron deficiency on the glycosylated HbA1c levels have been inconsistent.

Case report: We report a case of 48-year-old diabetic patient with subclinical iron Deficiency, who was in a potential risk of receiving unneeded insulin injection because of false-high values of HbA1c.

Methodology: The false-high values of HbA1c (>7.0%) noticed earlier with the subclinical iron deficiency anemia (hemoglobin 12.7 g/dL, serum iron: 7.94 umol/L, ferritin: 7 ng/mL), then after with frank iron deficiency anemia (hemoglobin 10.1 g/dL, serum iron: 5.68 u, mol/L, ferritin: 5.9 ng/mL).

Results: Interestingly, this high value of HbA1c was subsequently fall (5.8%) simply on correcting the iron deficiency (Ferritin: 10.6 ng/mL) by receiving iron supplementation.

Conclusion: We emphasizes that iron deficiency with or without anemia must be corrected before any diagnostic or therapeutic decision is made based on HbA1c in order to prevent misclassification of diabetes with its hazardous consequences of incorrect treatment.

https://doi.org/10.1016/j.htct.2020.09.134

PP 72

Hematologic manifestations associated with deficiency of adenosine deaminase 2 and a novel ada2 variant

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Objective: Deficiency of Adenosine-deaminase 2 (DADA2) is an autoinflammatory, autosomal recessive disorder due to mutations in CECR1 gene. DADA2 is phenotypically extending beyond its classical features (fever, early-onset stroke, livedo reticularis and polyarteritis nodosa) to include various hematologic presentations and rarely manifests as pure red cell aplasia (PRCA). We report a novel mutation in CECR1 gene (ADA2), that results in DADA2 and presented with PRCA as a unique manifestation.

Case report: A 5-year-old female who presented with severe pallor, with no family or medical history of concern. Autoimmune hemolytic anemia (AIHA) was suspected due to positive DAT, so the child started intravenous immunoglobulin and steroids but with no response. Bone marrow aspirate/biopsy showed markedly reduced erythropoiesis consistent with PRCA. The child almost required blood transfusion on weekly basis. She has an HLA-matched sibling donor and started hematopoietic stem cell transplant (HSCT) process. Meanwhile, a whole exome sequencing (WES) was requested for final diagnosis.

Methodology: We obtained a sequence analysis of all protein coding genes in the patient's genome, coupled with Whole Exome Deletion/Duplication (CNV) Analysis. Also, we reviewed the literature for hematologic manifestations of DADA2.

Results: Whole Exome Plus identified a homozygous frameshift variant CECR1 c.714_738dup, p. (Ala247Glnfs*16). It duplicates 25 base-pairs and generates a frameshift, leading to a premature stop codon in exon 5 (of 10 total exons), at position 16 in a new reading frame that is predicted to cause a loss of normal protein function. To the best of our knowledge, this variant was not described in the medical literature or reported in disease-related variation databases. Interestingly, our patient did not show any features suggesting DADA2 nor congenital form of aplastic anemia as she presented solely with PRCA. We reviewed a total of 151 patients from 27 published reports for patients with DADA2 in which hematologic manifestations were part of their presentations. One hundred patients, (66%, Female $n=52$), median age 5 years, presented with hematologic manifestations. Different anemias (AIHA, Evans syndrome, PRCA, DBA like features) were the most frequent occurring in 51% of patients, followed by lymphopenia and organomegaly, (32% each). Of concern, PRCA was the main manifestation in 12 patients without typical features of DBA nor vasculitis. Four patients were successful on HSCT, 1 on anti-tumor necrosis factor (TNF), 2 failed on steroids and 2 failed on anti-TNF, while others are either maintained on blood transfusion, steroids, or monthly intravenous immunoglobulins. The treatment for DADA2 previously included steroids, thalidomide and tocilizumab that showed success but associated with severe adverse events. Recently, treatment with anti-TNF-agents is believed to be effective especially in cases of vasculitis due to a subtotal loss of ADA2 function. However, complete loss of function seen in hematologic disorders is not favoring TNF inhibitors. HSCT is the most definitive treatment, particularly, when reversal of cytopenias and immunodeficiency is aimed.

Conclusion: We report a novel ADA2 variant in child presented with PRCA. We emphasis on genetic testing for hematologic disorders that lacks a definitive etiology, as it might result in the best pharmacogenomic-based therapeutic strategies without the need of unnecessary interventions.

https://doi.org/10.1016/j.htct.2020.09.135

PP 73

Pyruvate kinase deficiency misdiagnosed as congenital dyserythropoietic anemia type i

A. Koca Yozgat*, A. Yazal Erdem, D. Kaçar, N. Özbek, N. Yaralı

Ankara City Hospital, Ankara, Turkey

Objective: Objective: Pyruvate kinase (PK) deficiency is the most common enzyme abnormality in the glycolytic pathway, which leads to an anemia secondary to decreased ATP synthesis. The disease exhibits autosomal recessive inheritance and is caused by mutations in the PKLR gene. The diagnosis of PK deficiency is based on the presence of clinical signs and symptoms of hemolytic anemia, evidence of extravascular hemolysis on laboratory findings, measurement of the PK activity or antigen levels and detection of mutations in the PKLR gene.

Methodology: Here, we describe two siblings with PK deficiency that was misdiagnosed as congenital dyserythropoietic anemia (CDA) type I.

Results: Cases: The siblings were referred to our hospital for the evaluation of the anemia when they were newborn. On physical examination, they both had an icteric appearance. Their PK, glucose-6-phosphate dehydrogenase and 5' nucleotidase enzyme activities, hemoglobin electrophoresis and osmotic fragility test were normal. Erythroid hyperactivity with many bi-multilobed erythroblasts, which raised the concern of CDA, was seen in bone marrow aspiration. Spongy appearance (Swiss cheese appearance) of heterochromatin in all normoblasts and expansion of the perinuclear areas and the extension of the cytoplasm towards the nucleus in some, were observed with electron microscopy. CDA panel by next generation sequencing showed no mutation. Though their PK enzyme levels were normal, the molecular study of PKLR gene, a homozygote variant c.1623G>C (p.Lys541Asn) in exon 12 was found in our patients.

Conclusion: Discussion: Pyruvate kinase deficiency is a rare cause of hemolytic anemia and given to the rarity and the clinical heterogeneity, the diagnosis of PK deficiency can be difficult, mostly in atypical forms. PK deficiency should be considered in the differential diagnosis of CDA. Instead of the enzyme activity, comprehensive genetic analysis is warranted

PP 72

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more effective diagnosis of patients with suspected CDA and congenital hemolytic anemia.

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SICKLE CELL DISEASE

PP 74

How to treat and manage covid19 in SCD patients

N. Verdiyeva*, T. Ibrahimova, A. Nasibova, V. Huseynov

Institute of Hematology and Tranffusiology, Saint Petersburg, Russian Federation

Objective: Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was first identified in December 2019 in Wuhan, China, and has resulted in an ongoing pandemic.

Case report: A 24-year-old man with a history of SCD (HbS/β0-thalassemia) on maintenance hydroxyurea therapy presented to our hospital, with a complaint of pain in the extremities and chest over two days. The patient with mild cough and high fever was hospitalized. Blood tests and lung CT were performed. Result of blood test show evidence of systemic hemolysis with a decrease in hemoglobin from 8.9 g/dL to 6.7 g/dL. His white blood cell count was $25.2 \times 10^3/\mu L$, CRP 243.21 mg/L. CT scans of the lungs showed a consolidated area where air bronchograms were observed in and around the medial segment of the middle part of the right lung and the posteriobasal segment of the lower part of both lungs, and an icy glass landscape was observed. Lung damage is 1–5% (grade I). His oxygen saturation SpO2 was normal (98%). The SARS-CoV-2 PCR nasopharyngeal swab testing was sent and returned negative on hospital day one after which the patient was started on antiviral and antibiotic for severe COVID-19 pneumonia. An improvement in blood counts was observed 4 days after starting treatment (WBC $16.93 \times 10^3/\mu L$, CRP 100.31 mg/L). On day ten, after normalization of all symptoms and blood values the patient was discharged home.

Methodology: In this study we selected 1 patient with SCD followed in Thalassemia Center of Azerbaijan.

Results: Given the higher likelihood of ACS it is possible that SCD patients are also at higher risk of such complications from COVID-19, particularly those with a history of pulmonary comorbidities. However, it is unclear if the SARS-CoV-2 pandemic will lead to increased rates of ACS for sickle cell patients. Still, hospitalized sickle cell patients should be monitored closely for development of ACS and if this occurs, exchange transfusion should be promptly initiated.

Conclusion: COVID-19 pneumonia as a cause of acute chest syndrome in an adult sickle cell patient. Patients with sickle cell disease (SCD) who are infected with COVID-19 may have a significant risk of developing acute chest syndrome (ACS), a potentially life-threatening complication. In this case we will present how manage COVID 19 in patient with SCD.

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STEM CELL TRANSPLANTATION

PP 75

High-dose methyl prednisolone in veno-occlusive disease

A. Akyay*, Y. Oncul

Inonu University School of Medicine, Malatya, Turkey

Objective: Veno-occlusive disease (VOD) is a serious complication of hematopoietic stem cell transplantation (HSCT). If it is not identified and treated earlier, mortality is high. Combination usage of high-dose methyl prednisolone (MPZ) and defibrotide in VOD treatment have been described in some studies. Here, we present a patient with VOD who responded well to high-dose MPZ.

Case report: 14-month-old girl, diagnosed with thalassemia major, received HSCT from her sibling donor with busulfan and cyclo-phosphamide conditioning. On day +11, the patient experienced painful hepatomegaly and elevated total bilirubin (2.25 mg/dL) with 7% weight gain from baseline and respiratory distress while under defibrotide prophylaxis. VOD was diagnosed according to the modified Seattle criteria. Fluid and salt restriction were performed, spironolactone was started, and defibrotide was continued. Due to lack of significant improvement in the patient condition after 4 days of defibrotide, HDM was started at dose of 250 mg/m^2 per dose every 12 h on day +15.

Methodology: A day after MPZ, the patient's condition started to improve. After six doses of methylprednisolone, the dose was reduced to 2 mg/kg. Then, the dose was reduced by decreasing to half-dose in three-day periods. The defibrotide was discontinued on day +36, and the patient was discharged on day +45. The patient is currently being followed problem-free after 2 years of transplantation with 100% donor chimerism.

Results: VOD treatment response with high-dose MPZ and defibrotide combination can be better than treatment response with defibrotide alone. The easier and cheaper supply of steroids also prevents the treatment delay. In a study, it was shown that receiving high-dose MPZ without defibrotide was also found to be effective in the VOD treatment. The mortality rate in patients with multiple organ failure symptoms in VOD is between 50% and 100%. However, mortality rate can be decreased by early detection of VOD symptoms such as of painful hepatomegaly, weight gain and ascites. This findings may develop before hyperbilirubinemia especially in pediatric patients. Knowing this is important for early diagnosis and treatment of VOD.

Conclusion: As a conclusion; high-dose MPZ was found to be an effective treatment in VOD even at a dose of 250 mg/m^2 per dose every 12 h in aour patient. High-dose MPZ might be an alternative treatment to defibrotide in early phase VOD. Further studies are needed on the efficacy and dosage of MPZ in VOD.

https://doi.org/10.1016/j.htct.2020.09.138

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SICKLE CELL DISEASE

PP 74

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Methodology: In this study we selected 1 patient with SCD followed in Thalassemia Center of Azerbaijan.

Results: Given the higher likelihood of ACS it is possible that SCD patients are also at higher risk of such complications from COVID-19, particularly those with a history of pulmonary comorbidities. However, it is unclear if the SARS-CoV-2 pandemic will lead to increased rates of ACS for sickle cell patients. Still, hospitalized sickle cell patients should be monitored closely for development of ACS and if this occurs, exchange transfusion should be promptly initiated.

Conclusion: COVID-19 pneumonia as a cause of acute chest syndrome in an adult sickle cell patient. Patients with sickle cell disease (SCD) who are infected with COVID-19 may have a significant risk of developing acute chest syndrome (ACS), a potentially life-threatening complication. In this case we will present how manage COVID 19 in patient with SCD.

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PP 75

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https://doi.org/10.1016/j.htct.2020.09.138

PP 76

Isolated extramedullary relapse after hematopoietic stem cell transplantation

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Objective: Isolated extramedullary (EM) relapse of acute leukemia is rare. It is more common in patients who undergo hematopoietic stem cell transplantation (HSCT) than patients receive chemotherapy alone. We aimed to describe the demographic and clinical features, and clinical outcomes of children diagnosed with isolated EM relapse after allogeneic HSCT.

Methodology: Between 2012 and 2020, patients aged <18 years and treated with the diagnosis of isolated EM relapse after HSCT at the Department of Pediatric Hematology and Oncology, Health Sciences University Ankara Pediatric Hematology-Oncology Training and Research Hospital were enrolled in our study. The demographic features, clinical manifestations, treatment, and prognosis were analyzed retrospectively.

Results: Eight patients with extramedullary relapse after allogeneic HSCT were evaluated. Two patients were female, and six patients were male. The mean age of the patients was 9.8 years (min–max value: 12/12–168/12years). The type of leukemia was precursor B acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), and chronic myeloid leukemia (CML) in four, two, and two patients respectively. One patient had mass in the left iliac fossa, 1 patient had multiple mass in the right femur distal and tibia, 2 patients had mass in the testis,1 patient had mass head of the femur,1 patient had mass left orbit, 1 patient had central nervous system relapse and mass in the right lateral of the nose, medial part of the sacrum, 1 patient had mass in kidney. All patients had a biopsy-proven histopathological diagnosis. The mean relapse time after HSCTwas 17.3 months (min–max duration; 3–48 months). The mean follow-up time was 41.7 months (min–max: 12–120 months). Four patients died during the follow-up period. One patient; developed severe febrile neutropenia, mucositis attacks, and acute pancreatitis with systemic chemotherapy. After 13 months, HSCT was performed from her other compatible sibling due to medullary relapse, and she is still in remission. Other one patient was treated with systemic chemotherapy and imatinib, donor lymphocyte infusion, and local radiotherapy and continued to be followed in remission. Two patients treated with systemic chemotherapy; however, they had recurrent relapses and still on systemic chemotherapy.

Conclusion: Isolated extramedullary relapse is mostly reported during AML, rarely during other myeloproliferative diseases (CML) and more often in male patients. In our study, male patients were predominant that was similar to the literature. Of interest, four patients with precursor B ALL had isolated EM. Although the survival rates were low in these patients, the mean follow-up time was 41.7 months.

https://doi.org/10.1016/j.htct.2020.09.139

ONCOLOGY
SOLID TUMORS

PP 77

Candida guillermondii onychomycosis involving fingernails in a breast cancer patient under decetaxel chemothrapy

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Objective: Onychomycosis has been shown to have a higher incidence in cancer patient. Nail toxicity is quite common side effect of anticancer agents, Taxotere© is a chemotherapeutic known to cause great incidence of nail change and has a role of subungual suppuration. We present a case of onychomycosis induced by Taxotere chemotherapy and proved by mycological tests.

Case report: We report on a 52 year-old female, with breast cancer admitted in our institution for onycholysis. Because of stage and histology of breast cancer neoadjuvant chemotherapy was initiated, patient received 8 cycles of taxotere and Adriamycin (AT), and she underwent a modified radical mastectomy. Three-month later, patient evidence of onycholysis developed, involving all the fingernails. We observed the following changes in nails of all the digits in both hands: onycholysis, dystrophy, oedema, and exudate.

Methodology: Nail scraping and purulent discharge were collected for culture and direct examination by KOH and chloral lactophenol for mycological examination, fungal identification was based on physical features of the colonies and biochemical tests (Auxacolor©).

Results: Physical features of the colonies and biochemical tests (Auxacolor©)revealed Candida guillermondii as sole etiologic agent of onychomycosis. This case details an onycholysis in cancer breast case successfully managed solely with amorolfine lacquer 5% for a minimal duration of 3 month.

Conclusion: Candidiasis is one of the commonest complications seen in immunosuppressed cancer patients, and Candida guillermondii is frequently isolated in onychomycosis. Early recognition and treatment of yeast onychomycosis with purulent discharge is important especially in immunocompressed patients.

https://doi.org/10.1016/j.htct.2020.09.140

PP 76

Isolated extramedullary relapse after hematopoietic stem cell transplantation

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PP 78

Pretreatment neutrophile lymphocyte ratio (NLR) may have a prognostic role in patients receiving pemetrexed treatment for advanced stage non small cell lung adenocarcinoma

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Objective: We aimed to investigate the prognostic effect of Neutrophil/Lymphocyte ratio (NLR) on overall survival (OS) and progression time (PFS) as an inflammatory marker in patients diagnosed with lung adenocarcinoma who started pemetrexed treatment after primary level platinum-based chemotherapy.

Methodology: Laboratory data before initiation of treatment was retrospectively analyzed in 63 patients who were admitted to our outpatient clinic with a diagnosis of lung adenocarcinoma between 2017 and 2020, and who were deemed appropriate to start pemetrexed treatment. NLR was calculated as "Neutrophil/Lymphocyte". The pre determined cut-off value for NLR was derived from meta-analysis results from the literature. The analysis of the relationship between NLR and survival and progression times was assessed. The normal distribution was evaluated by the Kolmogorov–Smirnov test. Continuous variables were expressed as mean and standard deviation displaying normal distribution, and as median and 95% confidence intervals if not displaying normal distribution. Statistical difference was considered as $p < 0.05$.

Results: The median age of diagnosis of patients included in the study was 60.62 (34–78) years; 63.5% (40) consisted of denovo metastatic patients. 50.8% of the patients consisted of patients who received radiotherapy before (32). Median pemetrexed duration of use was 4.01 months (95% CI 4.89–8.45). 68.3% (43) of the patients who received pemetrexed treatment progressed. Median PFS was 4.22 months (95% CI 3.51–8.35). At the end of the study follow up period, 68.3% (43) of the patients have died. Median OS was 5.49 months (95% CI 5.75–11.56). Clinical benefit rate was not significantly different between two study groups ($p = 0.09$. The death rate of those with NLR above 5 before receiving pemetrexed treatment was significantly higher (p: 0.012) while the median PFS and OS times were significantly shorter compared to patients with NLR lower than 5[PFS (median ± IQR): 2.07 ± 3.02 vs. 5.32 months ± 6.54; $p = 0.018$ and OS (median ± IQR): 2.79 months ± 3.52 vs. 6.29 months ± 8.32; $p < 0.004$; respectively].

Conclusion: In our study, we found that high NLR was an independent poor prognostic factors in patients receiving pemetrexed treatment as second line therapy for advanced stage lung adenocarcinoma. This simple parameter which is an established surrogate marker for systemic inflammatory response can prove to be useful in identifying high-risk patients and making individual treatment decisions.

https://doi.org/10.1016/j.htct.2020.09.141

PP 79

Systemic inflammatory markers as predictors of response to chemoradiotherapy in rectal cancer

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Objective: Both Neutrophil to Lymphocyte (NLR) and C-reactive protein to albumin (CAR) ratio are surrogate markers of host immune system's reaction against systemic inflammation generated by tumor microenvironment. Recent studies have reported the efficacy of host's reaction to systemic inflammation as a prognostic marker in various cancers. However, its association with tumor response to neoadjuvant chemoradiotheraoy treatment in rectal cancer has not been fully elucidated.

Methodology: Pretreatment NLR and CAR along with other clinical and serological markers were evaluated in 54 patients undergoing chemoradiotheray for rectal cancer from February 2019 to February 2020. The predictive significance of these markers were then determined by both univariate and multivariate logistical analysis. Predetermined cutoff values for NLR and CAR and serum CEA levels were used for response prediction

Results: Pretreatment low NLR (<2, $p < 0.01$), pretreatment low CAR (<0.025, $p = 0.01$) and lower CEA levels were significantly associated with both good pathological response and complete pathological response to chemoradiotherapy in univariate analysis. However, in multivariate Cox analysis although both NLR and CAR levels were found to be independent predictors for complete response to neoadjuvant therapy, NLR seemed to be a better predictor in terms of hazard ratio(HR) than the CAR (HR = 2.870 versus HR = 1.784). Patients with NLR < 2 had significantly better response to chemoradiotherapy and NLR was superior to other serum inflammatory markers for predicting response to neoadjuvant therapy.

Conclusion: Pretreatment NLR and CAR were significant predictors of complete pathological response to neoadjuvant chemoradiotherapy in rectal cancer patients. However, NLR is found to be a better discriminator for complete response to neoadjuvant chemoradşotherapy in patients with rectal cancer.

https://doi.org/10.1016/j.htct.2020.09.142

PP 78

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PP 79

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