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HEMATOLOGY TRANSFUSION AND CELL THERAPY

Hematology Specialist Association
18. National Congress

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HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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HEMATOLOGY,
TRANSFUSION AND
CELL THERAPY

ABHH®
Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular

Hematology Specialist Association

18. National Congress

Abstract Book

21-24 November 2024

HEMATOLOGY
SPECIALIST ASSOCIATION

Welcome Address

Dear Colleagues,

Our meeting, previously organized as “Çukurova Hematology Days” until 2020, has expanded beyond the Çukurova region due to increasing interest and participation from across Turkey, prompting a name update. Since 2021, we are delighted to present it as the “National Congress of the Hematology Specialization Society.”

The 18th National Congress of the Hematology Specialization Society will take place from November 21-24, 2024, at Sherwood Exclusive Lara in Antalya. The congress format is designed to highlight our young colleagues, who will lead discussions through topic presentations and case studies. Our esteemed senior experts will provide guidance, sharing their experience and wisdom. Thus, alongside our mission to cultivate the next generation of speakers, we are also thrilled to create a resource for post-graduate training for young professionals stepping into the field.

Another key feature of the event is that it enables physicians in our country to exchange knowledge on various treatments and compare approaches, enriching their therapeutic practices.

Kind regards,

Birol Güvenç

President of Hematology Specialist Association

Serdar Bedii Omay

President of Hematology Specialist Association

Hematology Specialist Association

President

Birol Güvenç

Vice President

Serdar Bedii Omay

Secretary General

Hüseyin Saffet Beköz

Board Members

Şebnem İzmir Güner

Fatih Erbey

Mahmut Bakır Koyuncu

Alpay Yeşilaltay

Executive Committee

Birol Güvenç

President of Hematology Specialist Association

Serdar Bedii Omay

Vice President of Hematology Specialist Association

Alpay Yeşilaltay

Congress Scientific Secreteriat

Local Organizing Committee

Hüseyin Saffet Beköz- Secretary General of Hematology Specialist Association
Şebnem İzmir Güner - Member of Hematology Specialist Association Board
Fatih Erbey - Member of Hematology Specialist Association Board
Mahmut Bakır Koyuncu - Member of Hematology Specialist Association Board
Şule Menziletoğlu Yıldız - Director of the School of Health Services, Çukurova University
Hüseyin Derya Dinçyürek - Mersin City Hospital

Abstract Reviewing Committee:

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Serdar Bedii Omay
Hüseyin Saffet Beköz
Rıdvan Ali

Faculty:

Abdullah Agit

Abdullah Karakuş

Abdülkadir Baştürk

Ahmet Emre Eşkazan

Ahmet Sarıcı

Ali Eser

Ali İhsan Gemici

Ali Turunç

Alpay Yeşilaltay

Anıl Tombak

Aslı Odabaşı

Aslıhan Sezgin

Atakan Turgutkaya

Ayfer Gedük

Aysun Gönderen

Aysun Şentürk Yıkılmaz

Ayşe Nur Akınel

Ayşe Tülin Tuğlular

Barbaros Şahin Karagün

Bengisu Ece Duman

Bengü Macit

Bengü Sezer

Berksoy Şahin

Birgül Öneç

Birol Güvenç

Birsen Sahip Yesiralioğlu

Bulut Sat

Burak Deveci

Burcu Altındağ Avcı

Büşra Tuğçe (Akman)Tonyalı

Can Özlü

Candaş Mumcu

Cem Selim

Cemaleddin Öztürk

Cenk Sunu

Ceren Dehri Bahşi

Claudio Cerchione

Cumali Yalçın

Damla Çağla Patır

Didar Yanardağ Açık

Dilek Özden Özlük

Düzgün Özatlı

Ebru Kavak Yavuz

Eldane Memmedova

Elif Aksoy

Elif Yıldız

Emel İşleyen Kaya

Emin Kansu

Emin Kaya

Engin Yola

Ennur Ramadan

Eray Arslan

Erman Öztürk

Esra Terzi Demirsoy

Esra Yıldızhan

Fahir Öztürk

Fatih Erbey

Fatma Arıkan

Fehmi Hindilerden

Ferda Can

Feride Aslanca

Funda Ceran

Gamze Tanrıöver

Gaye Kalacı Katayıfçı

Gökhan Demirci

Gökhan Pektaş

Gülsüm Özet

Güven Çetin

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Hande Oğul Sücüllü

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Hasan Göze

Hasan Kaya

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Hüseyin Avni Solgun

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Mahmut Bakır Koyuncu

Mahmut Yeral

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Mehmet Ali Uçar
Mehmet Bakırtaş
Mehmet Hilmi Doğu
Mehmet Sezgin Pepeler
Mehmet Sinan Dal
Meral Uluköylü Mengüç
Mesut Göçer
Metban Mastanzade
Metin Çil
Mihriban Yıldırım
Muhammed Murati
Murat Çınarsoy
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Nigar Abdullayeva
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Nurgül Karakaya
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Rıdvan Ali
Satı Betül Beydilli
Seda Yılmaz
Selami Süleymanoğlu
Selver Kurt
Semih Başcı
Serdar Bedii Omay
Serhat Çelik
Simten Dağdaş
Sinem Namdaroğlu
Songül Beskisiz Dönen
Süleyman Atay
Svetlana Chulkova
Şebnem İzmir Güner
Şehmus Ertop
Şerife Emre Ünsal
Şule Çalışkan Kamış
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Tansu Koparmal
Tayfur Toptaş
Tekin Aksu
Tuba Öztoprak
Turgay Ulaş
Ulvıyya Hasanzade
Utku Aygüneş
Vahap Okan
Veysel Erol
Yasin Kalpakçı
Yıldız İpek
Yusuf Hekimoğlus
Yusuf Ulusoy
Zafer Serenli Yeğen
Zahit Bolaman
Zekeriya Aksöz
Zeliha Yıldız Kandemir
Zeynep Tuğba Güven

Chairs and Speakers Biographies

Muzaffer Keklik

A. *Personal Information*

Prof. Muzaffer Keklik, MD, is the president of Erciyes University Hematology department and Bone Marrow Transplantation Center, in Kayseri, Turkey.

Her main areas of research interests focus on; hematological malignancies, bone marrow transplantation, therapeutic apheresis, lymphomas, leukemias and immunology.

She is member of Turkish Society for Apheresis, National Hematology Assocation, and Experimental Hematology. She has published more than 200 scientific articles in international and national journals, peer-reviewed papers, review articles, book chapters, congress abstracts and oral presentations.

A.1. Name Surname: Muzaffer KEKLIK

A.2. Date and place of birth: 23.11.1971

A.3. Foreign Languages: English

A.4. Place of Duty: Erciyes Üniversity Faculty of Medicine – Kayseri

A.5. Contact Information *(e-mail address/ phone)*: muzafferkeklik @yahoo.com, mkeklik@erciyes.edu.tr
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B. Education Information

B.1. Erciyes Üniversity Faculty of Medicine, Kayseri -1994

B.2. Erciyes Üniversity Faculty of Medicine, İnternal Medicine- 2001

B.3. Erciyes Üniversity Faculty of Medicine, Hematology- 2014

B.4. *Academic degrees:* Associated Professor- 2015 (İnternal Medicine- Hematology)
: Professor- 2023 (İnternal Medicine- Hematology)

C. Information About Work Experience:

C1.Yahyalı Hospital – Kayseri 2001-2004

C2. Private Hospitals: Hunat Hospital – Kayseri 2004-2007
Melikgazi Hospital-Kayseri 2008-2009
Tekden Hospital-Kayseri 2009-2010

C3. Nuh Naci Yazgan Chest Hospital- Kayseri 2010-2011

C4. Erciyes University faculty of Medicine Hematology- Kayseri 2011-2014

C5. Kayseri City Hospital: 2015-2019

C6. Erciyes University: 2019

Serdar Bedii Omay

He graduated from Ankara Science High School in 1976 and School of Medicine, Hacettepe University in 1985.

He completed his Internal Medicine residency in Ege University.

He achieved hematology residency and completed doctorate in MIE University, Japan between the years of 1990-1995.

He was awarded doctorate degree on molecular biology and leukemia signal conduction system.

He was initiated to Ege University after returning to home country and given the title of Professor in 2003.

He took office as Head of Hematology Department of Karadeniz Technical University in 2005 and Head of Internal Medicine Department in 2006.

He was assigned as founding chancellor of Mardin Artuklu University in 2008.

He was retired and took office as the director of Hematology Department in Emsey Hospital in 2015.

He currently provides service in Bone Marrow Transplantation Unit and Hematology Department of Emsey Hospital in Istanbul.

He published many national and international articles and has good command of the English and Japanese languages.

Gamze Tanriover

I was born in Izmir in 1976. After completing my undergraduate education at Hacettepe University Faculty of Science, Department of Biology, I completed my master's degree at Akdeniz University Faculty of Medicine, Department of Histology and Embryology. Following my master's degree, I won the scholarship of the Ministry of National Education and worked for 5 months at the University of Oslo, Department of Neurophysiology, on “Molecular mechanisms in embryonic brain development”. Subsequently, I stayed at the USA “Yale University Faculty of Medicine, Department of Neurosurgery, Neurovascular Genetics” for 2 years to do my PhD thesis with an integrated doctoral program. I became a University Associate Professor in 2012; in 2018, I was appointed to the position of Professor.

I am currently working as a faculty member at Akdeniz University Faculty of Medicine, Department of Histology and Embryology and Department of Medical Biotechnology.
75 publications I contributed to the literature; there are 2 international and 4 national book chapters.
President of the Turkish Histology and Embryology Association for 2 terms, Board Member of the Turkish Brain Research Association, Molecular Cancer Research Association, Turkish Electron Microscopy Association; Stem Cell and Cellular Therapies Association; Basic Oncology Association and; I am a member of the European Cancer Society.
Also, I am working on Tubitak Health Sciences Research Support Group. I have been serving as a Group Executive Board Member of Tubitak Health Sciences Research Support Group for 2 years. Between 2019 and 2022, I served as a Tubitak Health Sciences Research Support Group Advisory Board Member for 3 years. Since 2020, Tubitak Health Sciences Research Support Group; I continue to serve as a Call Program Advisory Board Member and Tubitak Mentoring Program Member.
I am training 4 doctoral students.
I speak English, I am married and the mother of a 16-year-old daughter.

Fatih Erbey

Professor Dr. M. Fatih Erbey graduated from Çukurova University School of Medicine in 1999. He completed his Pediatrics residency at Çukurova University School of Medicine in 2005, and his Pediatric Oncology training in 2009. He worked as an Observer Physician at the Pediatric Bone Marrow Transplantation Unit of Pittsburgh Children's Hospital, USA in 2007. He fulfilled his public service obligation at Van Women's and Children's Hospital in 2009-2010. He worked as a faculty member at the Pediatric Oncology and Bone Marrow Transplantation Unit of Ege University School of Medicine in 2011. He worked at the Pediatric Hematology/Oncology and Bone Marrow Transplantation Unit of Medicalpark Bahçelievler Hospital between 2011-2014, and at the Pediatric Hematology/Oncology and Bone Marrow Transplantation Unit of Acıbadem University School of Medicine between 2014-2018. He became an Associate Professor in 2013. Dr. M. Fatih Erbey has been working as a faculty member at Koç University School of Medicine since March 2019. He received the title of Professor in June 2022. He is currently working as a faculty member at Koç University School of Medicine, Pediatric Hematology/Oncology & Pediatric Bone Marrow Transplantation Unit.

Müzeyyen Aslaner AK

I was born in 1977 in Van-Erciş. I graduated from Dokuz Eylül University Faculty of Medicine in 2000. I completed my Internal Medicine specialization at Istanbul Training and Research Hospital in 2009. After working as an internal medicine specialist for three years, I completed my Hematology specialization at Zonguldak Bülent Ecevit University Faculty of Medicine, Department of Hematology between 2013-2016. I completed my compulsory subspecialty service in Hematology at Gaziantep Dr. Ersin Arslan Training and Research Hospital between 2016-2018. I worked at Ege University Faculty of Medicine, Department of Hematology, Bone Marrow Transplantation Unit for one year between 2018-2019. I have been working as an assistant professor at the Department of Hematology at Zonguldak Bülent Ecevit University, Faculty of Medicine, since December 2019, and as an associate professor of hematology since 2023.

Atakan Turgutkaya

Dr. Atakan Turgutkaya was born in Izmir/Türkiye in 1985. He attended Uludağ University Faculty of Medicine /Türkiye between the years of 2003-2009. He worked as a general practitioner at Batman Sason State Hospital. In 2011, he started his residency in internal medicine at Ege University Faculty of Medicine /Türkiye and graduated as an Internal Medicine Specialist in 2015. After the compulsory service at Kırklareli State Hospital, he started the hematology subspecialty at Aydın Adnan Menderes University/ Türkiye in 2016 and graduated as a hematology specialist in 2019. He worked at Aydın State Hospital between 2020 and 2022. Since February 2022, he has been working as an assistant professor and a lecturer at Aydın Adnan Menderes University Faculty of Medicine.

Hande Oğul Sücüllü

I was born in Istanbul in 1984.
I graduated from Yeditepe University Faculty of Medicine in 2009.
I was appointed as a general practitioner to the Bozkır district of Konya province through the government service obligation duty.
In 2012, I started working as an Internal Medicine resident doctor at Medipol University Hospital.
In 2017, I was appointed to Bozkır State Hospital as an internal medicine specialist through a government service obligation duty.

In October 2018, I started working as a Hematology fellowship doctor at Pamukkale University Hospital.
After completing my specialization, I started working as a Hematology specialist doctor at Batman Training and Research Hospital in March 2022, through the government service obligation duty.
After completing my government service obligation duty, I have been working as a Hematology Specialist at Batman Medical Point Hospital since January 2024.

Ali Zahit Bolaman

Name: A Zahit Bolaman
Birth Date and Place: 1959 Fatsa/Ordu Turkey

Education
Intermediate School: Fatsa Ortaokulu-Lisesi
High School: Ege University Medical School 1978-1984 İzmir

Academic Degree
Internist: Dicle University Medical School:1991-1992
Internist-Assistant Professor: Dicle University Medical School: 1992-1993
Haematolog: Dicle University Medical School:1993
Internal Medicine-Associate Professor: Dicle University Medical School:1993-1994.
Haemalolog and Internist, State Hospital Denizli
Internal Medicine Professor:Adnan Menderes University Medical School: 2000.

Position

1. Adnan Menderes University Chief of Internal Medicine (1999-2005, 2016-2021)
2. Chief of Haematology Department (1999-2007)

Registration to Association

1. Turkish Haematology Association
2. European Bone Marrow Transplantation
3. Turkish Internal Medicine Association
4. Geriatric Hematology Association

Reviewer

1. Turkish Journal Hematology (in addition 2001-2004 associate ed,)
2. Haema (The Journal of Hellenic Society of Haematology) (2001-2006)
3. Dicle Medical Journal (Reviewer) (2002)
4. Muğla Sıtkı Koçman Universitesi Dergisi (2015)
5. Adnan Menderes Üniversitesi Tıp Fakültesi Dergisi (Reviewer) (2000)
6. Aegean Medicine Journal (Reviewer) (2005)
7. Clinics of Turkey (Reviewer) (2004)

Adnan Menderes Üniversitesi Tıp Fakültesi Dergisi (Reviewer) (2001)

Publications
National publications: Overall 150 number (case report, original article, case report, review and letter)
International publications: More than 200 number (case report, original article, review and letter) in index medicus and web of science.
Announcements (national plus international): Overall 200 number

Books:
Immunology (Turkish)

Translation
Bone Marrow Transplantation Hand Book 2015
Hoffbrand's Hematology 2017

Translation of Chapter
Harrison of Internal Medicine 2013
Current Treatment 205, 2016
Hematology (eds Ekrem Müftüoğlu)

Main interest topics
Leukemias and Myelodysplastic syndromes
Lymphoma and Myelomas
Stem Cell Transplantation
Thrombocytopenias

Marital Status: Married and have two children

Adress:
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Adnan Menderes Üniversitesi
Tıp Fakültesi
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Anil Tombak

Prof. Dr. Anil Tombak, MD, was born on April 25, 1976. He graduated from Gazi Anatolian High School in 1994 and then from Çukurova University Medical Faculty in 2000. Subsequently, he was trained at Mersin University Medical Faculty, Internal Medicine Department, and after internal medicine specialization, he became a Fellow of Hematology at the same University. He became a hematologist in 2013 and now working at VM Medical Park Mersin Hospital, Mersin, Turkey. He has performed research in several fields, with over 50 publications in international journals and numerous papers at scientific conferences. He received several awards and is a member of the Turkish Society of Hematology. Dr. Tombak is married and has two children.

Funda Ceran

Speciality: Hematology
E-mail: ceranf@gmail.com
Address: Ankara Bilkent City Hospital Hematology Clinic
Phone: (312) 552 60 00

Education and Training Activities
M.D., Ege University Faculty of Medicine, Izmir, Turkey, 1997

Residency Graduation Thesis: The evaluation and importance of cardiac structure and functions in patients with rheumatoid arthritis
Fellowship Graduation Thesis: Clinical significance of CD87 (uPAR) expression in acute myeloblastic leukemia

Professional Experience
Professor, University of Health Sciences, 2023
Associated Professor, Ankara Numune Training and Research Hospital, Ankara, Turkey, 2017
Chief Assistant, Ankara Numune Training and Research Hospital, Ankara, Turkey, 2013-2019
Hematology Specialist, Ankara Numune Training and Research Hospital, Ankara, Turkey, 2007-2013
Fellowship, Hematology, Ankara Numune Training and Research Hospital, Ankara, Turkey, 2003-2007
Residency, Internal Medicine, Ankara Diskapi SSK Training and Research Hospital, Ankara, Turkey, 1998-2002

Languages
English – Turkish
Certification & Courses
Certificate of Bone Marrow Transplantation

Mehmet Bakirtaş

Personal Information
Name Surname: Mehmet BAKIRTAŞ
Academic Title: Associate Professor
Birth Date: 08.06.1986- Köyceğiz/ Turkey
Knowledge of foreign Languages: English, German
Duty Station: Tekirdağ İ.Fehmi Cumalıoğlu Cıty Hospital /Hematology Department
Tekirdağ/Turkey
E-mail adress: drbakirtas@hotmail.com/drbakirtas@gmail.com
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Educational Information
University/faculty graduated from: Black Sea Technical University, Faculty of Medicine, **2005-2011, 2011 Graduation**, **Medicine Doctor**
Akdeniz University/Faculty of Medicine/Department of Internal Medical Sciences/Department of Internal Medicine)- **Internal Medicine Research Assistant 28.02.2012-17.01.2017- / 17.01.2017 İnternal Medicine Specialist**
University of Health Sciences/Ankara Dr. Abdurrahman Yurtaslan Oncology Health Application and Research Center/ Department of Hematology, **Hematology Fellowship 12.12.2017-30.07.2021**
Republic of Turkey Ministry of Health Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital, Department of Hematology, **2021- still working /**

Equivalencies

1- European Hematology Association (EHA) Board Certificate 2020.

Tanju Atamer

He was born in Ayancık district of Sinop in 1948. He completed his primary and secondary education in Ayancik, Giresun, Kastamonu and Karabuk. He started his higher education at Istanbul University Istanbul Faculty of Medicine in 1966 and graduated in 1972.
In 1976, he completed his internal medicine specialty training and he became an Internal Medicine specialist with his thesis "The place of Vinca Rosea alkaloids in ITP treatment", and continued to work as a specialist doctor in the same clinic. Meanwhile, he completed his short-term military service in Etimesgut in the fall of 1975.
Between 1980 and 1981, he worked at the Hematology Clinic and Basic Sciences Departments of the University of Paris, Saint Antoine Faculty of Medicine (Prof. Dr. G. Duhamel) for 10 months and carried out studies on in vitro granulocyte-macrophage stem cell cultures in myeloproliferative diseases and acute myeloid leukemia. While continuing his studies in the hematology service of the same faculty, he also completed hematopathology courses (Dr. J. Stachowiak).
In 1982, he became an associate professor of Internal Medicine at Istanbul University, having passed the thesis "In vitro examination of granulopoiesis in Acute Myeloid Leukemia" and the colloquium exam. After that, he continued to work as a faculty member in the Hematology Department of the same clinic (Prof. Dr. Şeref Inceman) until his retirement.
In 1984, according to the Higher Education Institution law, he was appointed as the sole faculty member in the Department of Hematology of Dicle University for a half-year period in educational and teaching duties.
In 1988, he was appointed professor at Istanbul University. In 1991, he switched from full-time to partial status and continued to work. His studies in the field of hematology are on acute leukemias, myeloproliferative diseases, hematopathology, hemostasis disorders and paraproteinemias. In 2003, he chaired the Acute Leukemia Subcommittee of the Turkish Hematology Association.
He retired in 2011. He speaks foreign languages French and English. He is married and has two children.

Utku Aygüneş

Name, surname: Utku AYGÜNEŞ
Birth Place and date: Niğde 1984
Adress: Gürselpaşa Mah. 75364 Sk. Çiçekkent Sitesi C2 Blok Daire 6 Seyhan /Adana
Mobile phone number: 05062225522
e-mail: utkuayg@gmail.com

Education: Postgraduate

Degree	Department	Institute	Date
Degree	Medical School	İstanbul University	2002-2008
Specialization	Pediatrics	Cumhuriyet University	2009-2013
Sub-specialization	Pediatric Hematology-Oncology	Uludag University	2014-2017

Foreign language: English

Work Experience

Title	Work Place	Date
M.D.	Niğde Bağlama Health center	2008-2009
Research assistant	Pediatrics, Cumhuriyet University	2009-2013
Expert	Pediatrics, Sivas State Hospital	2013-2014
Research assistant	Uludag University Medical School, Pediatric Hematology and Oncology	2014-2017
Assistant Professor	Cumhuriyet University Medical School, Pediatric Hematology and Oncology	2017-2019
Expert	SBÜ T.C. Konya Training and Research Hospital, Pediatric Hematology and Oncology	2019-2020
Expert	Acıbadem Adana Hospital, Pediatric Hematology-Oncology and Stem Cell Transplantation Unit	2020-

My name is Utku Aygüneş. I was born in Niğde. I am married and have two children. I speak English fluently.

Birgül Öneç

Department of Hematology, Duzce University Faculty of Medicine, Duzce, Turkey

Birgül Öneç MD, has graduated from Ankara University Faculty of Medicine in 2002 and completed her internal medicine residency training at Ankara Numune Education and Research Hospital (2002-2009). She completed her hematology residency program at Dıskapı Yıldırım Beyazıt Education and Research Hospital in 2013. Dr. Öneç worked as Hematology Assistant Professor and Associate Professor at Department of Hematology, Duzce University Faculty of Medicine (2014-2023) and is still working at the same department as Proffesor since January 2024.

Cumali Yalçin

Doğum Tarihi ve Yeri: 15.09.1987/Ceyhan
Görev Yeri ve Ünvanı: Kütahya Şehir Hastanesi- Hematoloji Uzmanı
Mezun Olduğu Üniversite / Fakülte ve Mezuniyet Tarihi: İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi/2011
Uzmanlık eğitimini aldığı yer ve tarih: Kartal Dr. Lütfi Kırdar Eğitim ve Araştırma Hastanesi/İç hastalıkları Anabilim Dalı/ 2011-2016.
Çalıştığı kurumlar: Bitlis Devlet Hastanesi/2016-2020
Yandal uzmanlık eğitimini aldığı yer ve tarih: Bursa Uludağ Üniversitesi Tıp Fakültesi/İç hastalıkları Anabilimdalı/hematoloji Bilim Dalı- Yan Dal Araştırma Görevlisi

Yayınlar

1. C. Yalcin, V. Ozkocaman, I. E. Pinar, B. Orhan, O. Candar, T. G. Koca, M. N. Akyol, N. G. Ada, C. Ozakin, R. Ali et al., Evaluation of Using Empiric Glycopeptides in Accordance with the IDSA Guidelines in Hematologic Malignancy Patients with Febrile Neutropenia, MEDITERRANEAN JOURNAL OF HEMATOLOGY AND INFECTIOUS DISEASES, 2022, 2035-3006, 14, 6.
2. C. Ozlu, C. Yalcin. Effects of methane emissions on multiple myeloma-related mortality rates: A World Health Organization perspective, Medicine, 2024, 0025- 7974, 103, 15, 5.
3. T. Ersal, F. Ozkalemkas, V. Ozkocaman, M. Sezen, C. Yalcin, B. Orhan, O. Candar, S. Cubukcu & T. G. Koca et al., Two Cases of Kidney Transplant Recipients With Multiple Relapsing Pure Red Cell Aplasia Due to Parvovirus B19 Infection, Experimental and Clinical Transplantation, 2024, 1304-0855, 22, 1, 5.
4. T. ErsaL, V. Ozkocaman, C. Yalcin, B. Orhan, O. Candar, S. Cubukcu, T. G. Koca, F. C. Hunutlu & F. Ozkalemkas et al., The effect of cryopreservation on engraftment kinetics in fully matched allogeneic stem cell transplantation: Reallife data and literature review, Transfusion and Apheresis Science, 2023, 1473-0502, 62, 6, 7.
5. B. Orhan, V. Ozkocaman, C. Akdemir, T. Ersal, C. Yalcin, S. Cubukcu, P. Ambarcioglu, R. ALI & F. Ozkalemkas et al., Potential modifications of the Plasmic scoring system for predicting thrombotic thrombocytopenic purpura: Sometimes, less is more, International Journal of Laboratory Hematology, 2023, 1751-5521, 45, 5, 7.
6. I. E. Pinar, V. Ozkocaman, T. Ersal, M. E. Dagtekin, C. Yalcin, O. Candar, T. G. Koca, V. Gursoy & F. Ozkalemkas et al., The effect of the time from diagnosis to induction therapy on prognosis in patients with acute leukemia undergoing leukapheresis for symptomatic hyperleukocytosis, Therapeutic Apheresis and Dialysis, 2023, 1744-9979, 27, 4, 11.
7. Orhan B, Özkalemkaş F, Özkocaman V, et al. The Role of White Blood Cell Count in Perianal Pathologies: A Retrospective Analysis of Hematologic Malignancies. Mediterr J Hematol Infect Dis. 2022;14(1):e2022051.

Gökhan Pektaş

I was born in 1981 in the Bolvadin district of Afyonkarahisar. I completed my primary, secondary and high school education in Ankara. I graduated from Istanbul University Cerrahpaşa Faculty of Medicine in 2005. I did my compulsory service in Bingöl Karlıova in 2005. I worked as an assistant physician at Ankara Atatürk EAH Internal Medicine Clinic with the April 2006 TUS. In 2010, I worked as an Internal Medicine Specialist at Ankara Etlik Specialization Hospital due to my spouse status. When my spouse status ended, I was assigned to Erzurum Aşkale district within the scope of my compulsory service and shortly after, I started working as a Hematology assistant at Adnan Menderes University Hematology Department with YDUS. After graduating in December 2014, I was assigned to Elazığ ERH within the scope of my compulsory service. After my duty here, I started working as an Assistant Professor at Muğla Sıtkı Koçman University in 2019. I received the title of Associate Professor in 2021. I am currently continuing my academic duties in Muğla. I am married and the father of two sweet children, a girl and a boy, and I continue my military service.

Nurgul Karakaya

Current contact details:
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e-mail: nurgul_1990@hotmail.com
Date of Birth: Sep 30, 1990
Nationality: Turkish Republic

Education

January 2020 to June 2023: Izmir SBU Dr. Behcet Uz Pediatric Diseases and Pediatric Surgery Education and Research Hospital; Clinical Fellow in Pediatric Hematology and Oncology
September 2017/ May 2019: Aydin Adnan Menderes University Faculty of Medicine. Aydin, Turkey. Department of Pediatrics, Resident in Pediatrics
January 2015/ September 2017: Afyon Kocatepe University Faculty of Medicine. Afyon, Turkey. Department of Pediatrics, Resident in Pediatrics
September 2008 / June 2014: Afyon Kocatepe University Faculty of Medicine. Afyon, Turkey.

Work

From August 2023 to Now: Necip Fazil Government Hospital, Pediatric Hematology And Oncology Specialist

Aslihan Sezgin

Information
Date of birth: 01.01.1981
Current occupation: MD, New Century University Hematology and Bone Marrow Transplantation Unit
E-mail:A5L1HAN@hotmail.com
Phone number: +90536 9483729

Education

Ege University Medical Faculty (Graduation: 2005)
Istanbul Medeniyet University Göztepe Research And Training Hospital / Internal Medicine (Graduation: 2013)
Marmara University Medical Faculty / Hematology (Graduation: 2017)

Work Experience

Istanbul Medeniyet University Göztepe Research And Training Hospital / Internal Medicine (2009 - 2013)
Marmara University Medical Faculty /Hematology (2014-2017)
Ağrı Research And Training Hospital /Hematology (2017-2019)
Acıbadem Altunizade Hospital /Hematology and Bone Marrow Transplantation Unit (2019-2021)
New Century University /Hematology and Bone Marrow Transplantation Unit (2021-)

Publications

1. Prolonged QT dispersion in inflammatory bowel disease DOI: 10.3748/wjg.v19.i1.65
   Effects of Deeper Molecular Responses on Outcomes in Chronic Myeloid Leukemia Patients in Chronic Phase Treated With Imatinib Mesylate DOI: 10.1016/j.clml.2016.09.006
2. Preclinical Assessment of Efficacy and Safety Analysis of CAR-T Cells (ISIKOK-19) Targeting CD19-Expressing B-Cells for the First Turkish Academic Clinical Trial with Relapsed/Refractory ALL and NHL Patients DOI: 10.4274/tjh.galenos.2020.2020.0070
3. Splenectomy in İmmune Thrombocytopenia: A Retrospective Analysis of 25-Year Follow-up Data from a Tertiary Health Clinic DOI: 10.1007/s12288-021-01467-0
4. Preliminary Report of the Academic CAR-T (ISIKOK-19) Cell Clinical Trial in Turkey: Characterization of Product and Outcomes of Clinical Application DOI: 10.4274/tjh.galenos.2022.2022.0193
5. Efficacy and safety of eltrombopag in treatment-refractory primary immune thrombocytopenia: a retrospective study DOI: 10.1097/MBC.0000000000000380

Sub-investigator in

1. Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma DOI: 10.1056/NEJMoa1606038
2. MERGE: A Multinational, Multicenter Observational Registry for Myeloproliferative Neoplasms in Asia, including Middle East, Turkey, and Algeria DOI: 10.1002/cam4.3004

3. Evaluation of clinical characteristics of patients with paroxysmal nocturnal hemoglobinuria treated with eculizumab in Turkey: a multicenter retrospective analysis PMID: 34322292; PMCID: PMC8303018.
4. Real-life ruxolitinib experience in intermediate-risk myelofibrosis DOI: 10.5045/br.2021.2021101

Şehmus Ertop

Education. Dicle University Medicine Faculty(1976-1982)
Internal Medine Specilization. Dicle University Medicine Faculty (1984-1988)
Departrment of Hematology: Dicle University 1992
Hematology Specialist (1992-2024)-
(Still go on …)

Deparrment of Hematology: 1992- 1994 Dicle University
1994-2011 Ataturk Government Hospital _Zonguldak
2011-2024 Zonguldak Bulent Ecevit University
Orchid ID: 0000-0001-8771-7343
Corporate email: drsertop@beun.edu.tr
drsertop@yahoo.com

Selami Süleymanoğlu

Selami Süleymanoğlu was born in Malatya in 1967. He received his primary and high school education in Malatya. Between 1984-1990, he studied at GATA Faculty of Medicine. Afterwards, he worked as a warship doctor for 3 years. He became a pediatrician in 1997 and a pediatric cardiologist in 2001. He worked as a faculty member between 2003-2016. He retired in 2016. After 2016, it did not produce science, but became a consumer of science. Apart from medicine, he spends his daily life in thematic readings on philosophy, neuroscience, theoretical physics, literature, history, sociology, travel, ecology and space. He works as a doctor in a private hospital to earn money. He is married and has a daughter.

Aysun Gönderen

I was born in Kayseri, Turkey, in 1979. I completed my medical education at Istanbul University Cerrahpaşa Faculty of Medicine between 1998 and 2004. Following this, I specialized in internal medicine at Ankara Dışkapı Training and Research Hospital from 2005 to 2010. Subsequently, I pursued a subspecialty in haematology at Ankara Numune Training and Research Hospital between 2011 and 2015. Since 2016, I have been working as a haematology specialist at Kütahya Evliya Çelebi Training and Research Hospital and, for approximately a year, at Kütahya City Hospital. In addition, I have been working as an assistant professor at Kütahya Health Sciences University since 2016.

Ayfer Gedük

I was born in Tekirdağ in 1981. I graduated from Istanbul Faculty of Medicine in 2005. I received my hematology subspecialty from KOÜ Faculty of Medicine in 2015. I am currently working as an associate professor at Koü Faculty of Medicine, Department of Hematology.

Büşra Tugce Akman Tonyali

Name Surname:
Title: Internal Medicine Specialist
Date of Birth: 09.09.1989
Place of Birth: Ankara
Foreign Language: English
E-mail Address: akmantugce@hotmail.com

Education
Primary and secondary education
1996-2004 Yenimahalle Ataturk Primary School
2004-2007 Ankara Gazi Anatolian High School

Medical Education
2008-2014 Necmettin Erbakan University Meram Faculty of Medicine

Experiences
2014-2015 Zonguldak Eregli Community Health Center
2015-2019 Ankara Yildirim Beyazit University Internal Medicine Clinic
2019-2022 Ankara Baskent University Hematology Clinic
2023-… Şırnak State Hospital Hematology Clinic

Zekeriya Aksoz

Hello. I was born on January 1, 1984 in Maden/Elazig. After completing my primary, secondary and high school education in Elazig, my hometown, I graduated from the Faculty of Medicine at Firat University in 2004. After graduating in 2010, I completed my internal medicine training at Ankara Keçiören Training and Research Hospital and my hematology training at Atatürk University. I am married and have 2 sweety boys. I think it is a great privilege to be a hematologist.

Elif Aksoy

E-mail:*aksoyelif127@gmail.com*
Department: Hematology Clinic
Language: English
Education:

- Istanbul University Istanbul Faculty of Medicine 2009- 2015
- Istanbul University Istanbul Faculty of Medicine 2016- 2021
- Bakırkoy Dr. Sadi Konuk Training and Research Hospital 2022

Experience:

- Tekirdağ State Hospital, Physician at Emergency Department,2015-2015
- Istanbul University Istanbul Faculty of Medicine 2016- 2020 Physician at Internal Medicine 2016 - 2021
- Muş Bulanık State Hospital, Physician at Internal Medicine, 2021-2022

Research and Publications:

1. Safak S, **Aksoy E,** Dirim AB, Demir E, Garayeva N, Oto OA, Artan AS, Yazici H, Besisik S, Turkmen A. Successful treatment of a COVID-19 patient with thrombotic microangiopathy. Clin Kidney J. 2021 Jan 29;14(4):1287-1288.
2. Caliskan Y, Mirioglu S, Dirim AB, Ozluk Y, Yegit O, **Aksoy E,** Safak S, Guller N, Demir E, Artan AS, Oto OA, Besisik S, Yazici H, Turkmen A, Lentine KL. A comparison of methods of plasmapheresis for the treatment of late antibody-mediated rejection in kidney transplant recipients. Ther Apher Dial. 2022 Oct 6.
3. Ozbalak M, Kalayoglu Besisik S, Tor YB, Medetalibeyoglu A, Kose M, Senkal N, **Aksoy E**, Cagatay A, Erelel M, Gul A, Esen F, Simsek Yavuz S, Isoglu Alkac U, Tukek T. Initial complete blood count score and predicting disease progression in COVID-19 patients. Am J Blood Res. 2021 Feb 15;11(1):77-83.
4. Artan AS, Mirioğlu Ş, Üstemihan Z, **Aksoy E**, Dirim AB, Çavuş B, Oto ÖA, Çifçibaşı-Örmeci A, Beşışık F, Çalışkan Y, Öztürk S, Yazıcı H, Kaymakoğlu S, Türkmen A. Efficacy and Safety of Sofosbuvir and Ledipasvir for Hepatitis C in Kidney Transplant Recipients: A Single-center Retrospective Observational Study. Balkan Med J. 2023 Mar 24.
5. Tor YB, Ozbalak M, Kalayoglu-Besisik S, **Aksoy E**, Cagatay AA, Gul A, Erelel M, Senkal N, Medetalibeyoglu A, Kose M, Tukek T. Independent risk factors for COVID-19-associated coagulopathy. Eur Rev Med Pharmacol Sci. 2023 Aug; 27(16):7851-7860. doi: 10.26355/eurrev_202308_33440. PMID: 37667962.
6. Hindilerden, Fehmi; **Aksoy, Elif**; Ozturkmen, Asli Yuksel; Turker, Gamze; Gulturk, Emine; Hancer, Veysel Sabri; Mercan, Selda. Poisoning by butylated hydroxytoluene quinone methide acting as a superwarfarin: first reported case in humans. Blood Coagulation & Fibrinolysis.

Ali Eser

Ali Eser works as a hematology specialist and physician in charge of the bone marrow transplantation unit at Gaziantep Medical Point Hospital. He graduated from Uludağ University in 1990. He completed his internal medicine training at Istanbul Training and Research Hospital between 2000-2004 and became an internal medicine specialist in 2004. He received hematology training at Marmara University between 2010-2013 and became a hematology specialist in 2013. He then worked as an assistant professor at Çanakkale Onsekiz Mart University and Bezmialem Vakıf University, respectively. He completed his academic studies in the field of hematology in 2022 and received the title of Associate Professor. He has worked in bone marrow transplantation units of various hospitals for the last 6 years. He is currently the physician in charge of the bone marrow transplantation unit at Gaziantep Medical Point Hospital.

Cem Selim

I was born in Ankara on 31.03.1987. I completed my primary education at Çayırhan Cumhuriyet Primary School and Atıfbey Middle School between 1993-2001. I graduated from Ankara Atatürk Anatolian High School in 2005. I graduated from Eskişehir Osmangazi Faculty of Medicine in 2011. I worked as a gynecology and obstetrics assistant at Izmir Atatürk Hospital for 3 months between September and November in 2012 and left. Apart from these 3 months, I worked as a general practitioner at Çankırı Orta District Hospital from September 2011 to September 2013. I worked as an internal medicine assistant at Dışkapı Hospital between March 2013 and March 2018. After working as an internal medicine specialist at Çankırı State Hospital between March 2018 and September 2018, I completed my hematology training at Adnan Menderes Faculty of Medicine, Department of Hematology between 2018-2021. I worked at Şanlıurfa Mehmet Akif İnan Training and Research Hospital between 2021 and 2024. I am married with two children. My foreign languages are English and German. Original Versus Generic Lenalidomide in Patients with Relapsed Refractory Multiple Myeloma: Comparison of Efficacy and Adverse Events, Masquerading of COVID-19 Infection as Primary Mediastinal Large B-Cell Lymphoma, Use Of Gemtuzumab Ozogamicin In Relapsed Refractory Acute Myeloblastic Leukemia: Multi-Center Real Life Data FromTurkey, Clinical Characteristics and Outcomes of COVID-1 9 in Turkish Patients with Hematological Malignancies Acquired Hemophilia A In Adults: A Multicenter Study from Turkey, Pharmacological dose ascorbic

acid administration in relapsed refractory multiple myeloma patients, Role of Bradyrhizobium enterica in gastrointestinal graft-versus-host disease,The relationship between increased iron load and respiratory function tests in patients diagnosed with transfusion dependent thalassemia, Application the Beck Depression Test to Screen for Depressive Findings Before and After Treatment in Patients with Iron Deficiency Anemia and/or Vitamin D Deficiency, The relationship between immunologic system and ferritin levels in patients with transfusion dependent thalassemia: a retrospective single-center study. I am currently working as an assistant professor in the Department of Hematology at Konya Selçuk University, Faculty of Medicine.

Hatice Zeynep Dikici

Date Of Bırth: 01.01.1985
Bırthplace: Konya/Turkiye
Foreıgn Language: English
Adress: Ankara Ataturk Sanatoryum Education and Research Hospital,
Phone Number: 0505 622 70 87
E-Maıl: drzeynepdikici@hotmail.com

Education
1991-1996: Konya Gazi Mustafa Kemal Primary School
1996-2000: Konya Meram Anatolian High School
2000-2003: Konya Meram Science High School

Education

	University/Program	Date/Year
Degree in Medicine	Ankara University Faculty of Medicine	2003-2010
Resident - Internal Medicine	Ankara Numune Education and Research Hospital, Internal Medicine	2011-2016
Resident - Hematology	Necmettin Erbakan University Faculty of Medicine, Department of Hematology	2020- 2023

Exmployment

		Date/Year
Internship	Ankara Eryaman Emergency Health Services Station	2010-2011
Resident - Internal Medicine	Ankara Numune Education and Research Hospital, Internal Medicine	2011-2016
Internal Medicine MD	Ankara Numune Education and Research Hospital, Internal Medicine	2017-2019
Internal Medicine MD	Ankara Bilkent City Hospital	2019-2020
Resident - Hematology	Necmettin Erbakan University Faculty of Medicine, Department of Hematology	2020- 2023
Consultant Hematologist	Ankara Ataturk Sanatoryum Education and Research Hospital	2023- ongoing

Gaye Kalaci KatayifçI

Personal Information
Name Surname: Gaye KALACI KATAYIFÇI
Academic Title/Position: Subspecialty Residency Student
Workplace: Ankara Bilkent City Hospital Hematology Clinic
Phone Number: 05325677744
Email Address: gayekatayifci@gmail.com

Educational Background

Year	Department	Institution	Degree
2003-2009	Faculty of Medicine	Başkent University	Medical Doctor
2011-2015	Internal Medicine	Başkent University	Specialist
2021-	Hematology	Ankara Bilkent City Hospital	Subspecialty Resident

Professional Experience

Date Range	Institution	Position
2009	Esenler Health Group Presidency	General Practitioner
2011-2015	Başkent University	Internal Medicine Specialist
2015-2016	Çorum Sungurlu State Hospital	Internal Medicine Specialist (Mandatory Service)
2016-2021	Ankara Training and Research Hospital	Internal Medicine Specialist

Conferences and Courses

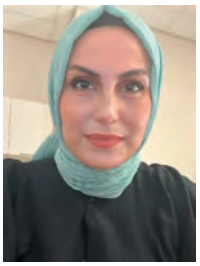
Conference Name	Attendance Date
6th Rare Hematologic Diseases	6/2023
7th Rare Hematologic Diseases	2/2024
4th Leukemia Lymphoma Myeloma Congress	5/2024
50th National Hematology Congress	10/2024

Poster presentations and Oral Presentations

Presentation Date	Venue	Type
2/2024	7th Rare Hematologic Diseases	Poster
2/2024	Turkish Hematology Association Podcast Presentation	Podcast Presentation
4/2024	Istanbul Hematology Days	Poster
5/2024	4th Leukemia Lymphoma Myeloma Congress	Oral Presentation
10/2024	50th National Hematology Congress	Poster

Ongoing Multicenter or Single-Center Studies
Study on evaluating transplant preparation regimens, donor information, post-transplant GVHD/chimerism/remission statuses of Türkök and haploidentical transplant patients treated at our clinic between 2019 and 2024.

Zeynep Tuğba Güven



Name and Surname Z	Zeynep Tuğba Güven
Academic title/position	Assoc. Prof.
Place of duty	Adana City Hospital Hematology Clinic
Phone number	+9 05383638130
Email address	drztkarabulutguven@gmail.com

Education Information:

2004-2010	Faculty of Medicine	Ankara Ufuk University Faculty of Medicine
2011-2015	Internal Medicine	Ankara Numune Training and Research Hospital Specialization
2017-2021	Hematology	Erciyes University Faculty of Medicine
2020-	Molecular Biology and Genetics	Molecular Biology and Genetics Erciyes University Gen-kök PhD

Associations:

—Turkish Hematology Association
—EHA (European Hematology Association)
—SOHO (Society of Hematologic Oncology)

Serhat Çelik

Serhat Çelik currently works at Yenimahalle Training and Research Hospital. Serhat is especially interested in malignant hematology, and genetics. His PhD education in molecular biology and genetic is still progress in resume. His hematology fellowship was completed at the Hematology Department of Erciyes University Faculty of Medicine. He completed the Turkish Society of Hematology acute leukemia master class. He is a field editor in national and international journals. He is currently chef editor at Journal of Current Hematology & Oncology Research.
Membership
Turkish Society of Hematology
European Hematology Association
Society of Hematologic Oncology

Emel Işleyen Kaya

Educational Information

Year	Department	Institution	Degree
2001-2007	Faculty of Medicine	Eskişehir Osmangazi University Faculty of Medicine	Bachelor's
2009-2013	Internal Medicine Residency	Başkent University Faculty of Medicine	Specialization
2019-2022	Hematology Subspecialty	Ankara Bilkent city Hospital HEmatology	Subspecialization

Professional Experience
List the institutions/organizations you have worked for in chronological order.

Date Range	Institution	Position
19/09/2007-05/06/2008	Iğdır Aralık Health Center	General Practitioner
06/06/2008-02/07/2009	Ankara Kazan Saray Health Clinic	General Practitioner
06/07/2009-29/11/2013	Başkent University Faculty of Medicine	Internal Medicine Resident
14/03/2014-24/04/2017	Ankara Elmadağ Dr. Hulusi Alataş State Hospital	Internal Medicine Specialist
25/04/2017-14/11/2018	Ankara Ulus State Hospital	Internal Medicine Specialist
15/11/2018-04/10/2019	Ankara Pursaklar State Hospital	Internal Medicine Specialist
04/10/2019	Ankara Bilkent City Hospital	Hematology Subspecialty Assistant
31/10/2022-Present	Ankara Bilkent City Hospital	Hematology Specialist

General Information on Clinical Research

Training/Certificate Name and Training Location	Date
Good clinical practices certificate - Ankara Bilkent City Hospital	18-19 June 2022
Advanced clinical practices certificate - Turkish Hematology Association	19-20 June 2021

Clinical Research	Date Range	Role
Ianalumab/VAY736. Study Code CVAY736Q12301: A phase 3, randomized, double-blind study comparing ianalumab with placebo in addition to eltrombopag in patients with primary immune thrombocytopenia who have an inadequate response to first-line steroid therapy or experience relapse after first-line steroid therapy	6/2023-Ongoing	Co-Investigator

BARBAROS ŞAHİN KARAGÜN

My name is Barbaros Şahin KARAGÜN. I was born in Gaziantep. My childhood was a joyful and exciting period when everything was possible and easily accessible. Due to my father's job, I had to be in different cities for a short time, but after completing high school at Gaziantep High School in Gaziantep, I came to Adana in 1992 to receive medical education. I completed my tiring and exhausting medical education at Çukurova University Faculty of Medicine in 1998.
After graduating, I worked as a general practitioner in the Hasanbeyli district of Osmaniye province. My life, which started with an exam, continued with an exam and as a result

of the TUS exam I passed, I started working as a research assistant in the Department of Child Health and Diseases at Çukurova University Faculty of Medicine. In 2005, I was first assigned to the Hassa district of Antakya as a Child Health and Diseases specialist. I worked here for 2 years. During this period, I completed my military service at Ağrı Military Hospital in Ağrı province.

After completing my military service, I was accepted to Çukurova University Faculty of Medicine, Department of Pediatric Hematology-Oncology and started working in 2008. After graduating in 2011 as a Pediatric Hematology-Oncologist, I started working at Sivas Numune Hospital.

In 2008, I started working at Acıbadem University Adana Acıbadem Hospital Bone Marrow Transplantation Center in order to learn and specialize in stem cell and bone marrow transplantation, which has been my greatest source of interest and connects me to this profession since the first moment I started working in the Pediatric Hematology-Oncology department. I worked at the Bone Marrow Transplantation Center for 10 years and took part in many Allogeneic Stem Cell Transplantations.

During this period, I completed my academic studies and became an associate professor in 2021. In 2022, I left the private sector and transferred back to the public hospital, namely Adana City Training and Research Hospital. In 2023, I was appointed to the academic staff at Adana Faculty of Medicine, University of Health Sciences.

While I continue my duties as a specialist doctor in the Department of Pediatric Hematology-Oncology at Adana City Training and Research Hospital, I am trying to fulfill the duty of being a father to my 3 children by having a family, which is the biggest and most beautiful responsibility of my life.

Ferda Can

Speciality: Hematology

Education and Training Activities

M.D., Ankara University Medical School, Ankara, 2009

Internal Medicine Specialist, Ankara University Medical School, Ankara, 2014

Hematology Specialist, Gazi University Medical School, Ankara, 2019

Professional Experience

Attending Physician

Ankara City Hospital, Ankara, Turkey, Hematology-present

Ankara Cubuk Halil Sıvgın Hospital, Ankara, Turkey, 2014-2015

Fellowship, Gazi University Medical School, Ankara, Turkey, 2015-2019

Residency, Ankara University Medical School Internal Medicine Department, Ankara, Turkey, 2009-2013

Languages

English Upper Level speaking and reading

Certification & Courses

20-21/3/2010 Young Internists Winter School, Ankara

09-10/12/2010 Occupational Professional Development Programme, Ankara University- Ankara

01-02/06/2011 Diagnosis and Treatment Approach in Liver Diseases With Acute Onset, Ankara

27/06/2014 Diabetes Experts Preceptorship Programme, Pittsburgh Univesity- Dublin

18/10/2014 Certificate of Suitability About Internal Medicine, Turkish Society of Internal Medicine Specialists

12-13/09/2015 Hematopoietic Stem Cell Transplant Course With Cases, Ankara

03/09/2016 Good Clinical Practice Certificate, TransCelerate Biopharma

24/01/2017 Good Clinical Practice Certificate, Firecrest

01/04/2017 Step-by-step Myelodysplastic Syndrome, Ankara

04/11/2017 Hematology Specialization Qualification Certificate, Turkish Society of Hematology

18-19/09/2018 Basic Education of Communication Skills in Medicine, Gazi University Medical School, Ankara

30/10/2018 Genetic Course For Hematologists, Antalya

06/01/2019 Good Biostatistics Applications Course, Ankara

27/11/2019 Hemophilia Academy, Ankara

01-29/09/2020 Rising Star Academy of Hemophilia (HeYY-A) 2020

25-26 May 2021 Clinical Research Association, Hematology Oncology Clinical Research Basic Training

2021-2022 Turkish Society of Hematology Acute Leukemias Master Class

25-26/11/2022 Ministry of Health of the Republic of Turkey Directorate General for European Union and Foreign Relations Project Cycle Management, National and International Funds Course

02/11/2023 49. National Hematology Association Congress Flow Cytometry Course

11 May 2024 Ministry of Health of the Republic of Turkey basic good clinical practice training

29 Oct 2024 50. National Hematology Association Congress Erich Frank-Orhan Ulutin Hemostasis Laboratory Course

Alphan Küpesiz

Upon completion of my primary, secondary, and high school education in Eskişehir, I proceeded to undertake my medical education at Akdeniz University Faculty of Medicine between 1986 and 1992. After completion of my one-year mandatory service in Muş Malazgirt, I resumed my studies at Akdeniz University, pursuing a specialisation in Pediatrics (1994-1999). Subsequently, upon completion of my Pediatric Haematology subspecialty in 2004, I assumed the role of academic staff, continuing my career at the university as a faculty member.

From 2005 to 2007, I was based at Michigan Children's Hospital, USA, where I conducted research in the field of pediatric hemostasis and thrombosis. I have been engaged in intensive research in the field of stem cell transplantation for the past 26 years. I currently serve as a professor and head of stem cell transplantation unit.

HEMATOLOGY, TRANSFUSION AND CELL THERAPY

www.htct.com.br

Speech Summaries

01

Z-EMATOLOGY IN TURKEY

Birol Güvenç

Çukurova Üniversitesi Tıp Fakültesi Hastanesi

In alignment with this vision, we are excited to introduce a new initiative: Z-Ematology. This concept is designed to bridge the gap between Generation Z and the evolving field of hematology. The new generation brings fresh perspectives and skills, especially in areas such as artificial intelligence, big data, telemedicine, and digital health technologies. Z-Ematology reflects our belief that adapting to these trends is essential for the future of hematology, and we are committed to integrating innovation into every aspect of the profession.

https://doi.org/10.1016/j.htct.2024.11.083

02

OPTIMIZATION OF IMID-BASED THERAPIES

Murat Çınarsoy

Şanlıurfa Mehmet Akif Inan Training And Research Hospital, Hematology Department

The word optimization, meaning "to achieve the best possible," is a branch of science called the science of the best. It has also created a field within the health care system, which is a complex system, called "medical optimization". Medical optimization is defined as "a person-centered approach to the safe and effective use of medicines to ensure that people achieve the best possible outcomes from treatment. In this context, what can be said on the basis of the treatment of myeloma and the use of IMIDs? Multiple myeloma is a disease of advanced age. Although there are classical findings such as anemia, bone disease, loss of renal function, hypercalcemia, a significant proportion of patients suffer from sleep disorders, anxiety and depression, pain, malnutrition, which are not less common than classical signs and symptoms and lead to serious deterioration in the patient's quality of life. Due to the advanced age of most patients, polypharmacy, defined as the use of 4 or more drugs, can reach 80% in multiple myeloma patients, while inappropriate drug complications can reach 50%. Treatment compliance was 68% and treatment discontinuation rate was 36%. In this case, it is clear that multiple myeloma treatment optimization cannot be achieved by considering multiple myeloma treatment only as applying the appropriate drug combination.In order to ensure the optimization of IMID-based therapies, it is necessary to take a broad perspective. This perspective should include the correct selection of the patient to be treated with IMID, the development and implementation of IMID forms that will increase patient compliance, the use of techniques to predict the development of resistance, side effect management during treatment, preventing the increase in disease burden with appropriate maneuvers by following the disease burden after treatment, and drug-free follow-up. It is recommended to avoid thalidomide in the presence of peripheral neuropathy, to prefer other agents instead of lenalidomide in the presence of renal function loss, and to avoid pomalidomide in patients with COPD. Nex-20, a once-monthly subcutaneous formulation of lenalidomide, is expected to be an important breakthrough in improving patient compliance. Prediction of which patients will develop resistance will be very useful in order to have the best treatment outcomes.Calculation of miRNA risk scores, measurement of lenalidomide metabolite levels in urine, measurement of cereblon levels in blood, or immunohistochemical detection of cereblon levels are some of the methods currently being tried to predict disease resistance. Patients who develop anemia should be treated with erythropoietin, skin reactions should be treated with steroids and antihistamines, diarrhea should be treated with loperamide and colestyramine, and in general, the drug should be discontinued and the same dose or a lower dose should be insisted upon. An important part of treatment is maintenance therapy with lenalidomide. Drug discontinuation is the best possible treatment outcome. In the IFM-2009, GEM2014MAIN and MASTER trials, patients receiving lenalidomide for a fixed duration stopped the drug with MRD monitoring and had prolonged PFS.

https://doi.org/10.1016/j.htct.2024.11.084

03

ATYPICAL HEMOLYTIC UREMIC SYNDROME DIAGNOSIS AND TREATMENT

Atakan Turgutkaya

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Atypical hemolytic uremic syndrome (aHUS), more commonly known as complement-related HUS is a kind of thrombotic microangiopathy (TMA) characterized by inherited pathogenic variants in complement genes or acquired autoantibodies against complement factors, predominantly involving kidney [1]. Activation of the alternative complement pathway (AP), which occurs due to dysfunction in complement regulatory proteins or, less commonly, activation of mutations in the complement proteins themselves, constitutes the pathogenesis of aHUS and enables endothelial damage [2]. It may also present as secondary aHUS triggered by COVID-19, Shiga toxin-producing Escherichia coli, or other identifiable conditions [1]. As a triad for the diagnosis of aHUS; thrombocytopenia, microangiopathic hemolytic anemia (MAHA), and acute kidney injury are used, however, there is no universally accepted diagnostic criterion and it is considered inadequate because it is established without even histological findings in the kidney [1]. Complement factor H (CFH), complement factor I (CFI), membrane cofactor protein (MCP, CD46), thrombomodulin, complement factor B (CFB), and complement 3(C3) mutations are the mutations that play a dominant role in the pathogenesis of aHUS [2,3]. In 30% to 40% of patients who respond to complement inhibition, these mutations are not detectable or have genetic variants of unknown significance [2]. In a patient presenting with TMA findings, thrombotic thrombocytopenic purpura (TTP) must be excluded by showing that ADAMTS13 activity is above 10%. Short-acting C5 blockade (eculizumab) should be initiated without delay in those with ADMTS13 levels above 10% and those with severe oliguric acute renal failure [1]. Stool sampling should be done in individuals with diarrhea to detect Shiga toxin and/or microorganisms that produce Shiga toxin. Ravulizumab is a long-acting C5 inhibitor that is considered safe and effective in both treatment-naive adult and pediatric patients and in pediatric patients who have previously received complement inhibition [4]. Ravulizumab's half-life is four times longer than eculizumab (~51.8 days vs. ~11 days) and offers a reduced dosing frequency of up to 4-8 weeks instead of every 2-3 weeks [5]. All patients receiving complement inhibitors should be included in the vaccination program for Neisseria meningitis, Streptococcus pneumonia, and Haemophilus influenza type b, and early signs of infection should be carefully monitored and necessary parenteral antibiotic therapy should be started without delay. Although plasma exchange (PEX) treatment can provide partial benefit, especially in those with CFH, C3, and thrombomodulin gene variants, it has now been replaced by complement inhibitors where available. PEX treatment response is insufficient in CFI variants and does not provide additional benefits to complement inhibitors in MCP (CD46) deficiency [6]. Kidney transplantation treatment is associated with a high risk of recurrence, especially in patients with CFH mutations. However, the post-transplant relapse rate decreased with eculizumab treatment[7]. Iptacopan is an orally available, highly potent proximal complement inhibitor that specifically binds to CFB, the primary driver of the disease, thereby inhibiting AP [8]. Other treatments are being investigated, including alternative pathway-blocking agents and lectin pathway inhibitors.

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04

INNOVATIONS IN AL AMYLOIDOSIS MANAGEMENT

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Introduction: Immunoglobulin light chain (AL) amyloidosis is the most common type of systemic amyloidosis. AL amyloidosis is considered a plasma cell disorder caused by generally small and slowly proliferating clone of plasma cells in bone marrow that produces nonfunctional immunoglobulins. **Diagnosis:** Considering diagnosis of systemic amyloidosis is to evaluate for the presence of monoclonal paraprotein with electrophoresis and immunofixation of both serum and urine, serum kappa and lambda free light chain (FLC) levels, 24-hour urine protein. If testing confirms presence of a monoclonal immunoglobulin or abnormal FLC ratio, then tissue biopsy necessary for diagnosis should be performed. If amyloid is detected in the biopsy, the type of amyloid must be determined for a complete diagnosis. **Staging:** The most frequently used staging system is the Mayo 2012 model, which assigns a score of 1 for troponin T (≥0.025 μg/L), N-terminal probrain natriuretic peptide (NT-pro BNP; ≥1800ng/L) or BNP ≥400 ng/L, and a difference in serum FLCs (dFLC ≥180 mg/Land is believed to be superior at identifying very high risk individuals (1). An alternative model with high prediction performance is the European 2015 modification of the Mayo 2004 model assigning a score of 1 for troponin T (≥0.035 μg/L), NT-proBNP (≥ 332ng/L) and for stage 3 patients uses the absence or presence of ≥1800 ng/L criteria for IIIA, IIIB designation, respectively (2). Induction Therapy for Newly Diagnosed AL Amyloidosis: Many clinical studies investigated the role of bortezomib-based regimens, which were eventually accepted as the standart of care, the most commonly used regimen is combination of CyBorD. With the completion of the phase III Andromeda trial, the treatment paradigm has started to the addition of daratumumab together with CyBorD in the upfront setting. For patients who are eligible for autologous stem cell transplantation (ASCT), recommended beginning with induction therapy with daratumumab-CyBorD for two to four cycles and then evaluate the response. In patients who achieve a hematological very good partial response (VGPR) or better, forego ASCT and associated treatment-related morbidity and mortality in favor of completion of daratumumab-CyborD induction, followed by daratumumab maintenance for a total of 2 years. **Autologous Stem Cell Transplantation:**

Lack of consensus on optimal use of ASCT in patients with AL amyloidosis. A randomized phase II study involving 91 patients comparing high-dose intravenous melphalan (HDM) followed by ASCT with a course of oral melphalan 10 mg/m^2 given once daily and dexamethasone 40 mg given once daily for the first 4 days of a 28 day cycle for up to 18 cycles. At a median follow-up of 3 years, median overal survival (OS) in the HDM arm was significantly worse than those taking high dose melphalan and dexamethasone (22.2 versus 56 months). Clinical studies using modern induction regimens and strict selection criteria emphasize an improved outlook on early survival outcomes in transplantation. . The HOVON104 study evaluated ASCT after four cycles of bortezomib-based induction in 50 patients reported an estimated 3-year OS in the 86% and 72% cardiac response rate in evaluable patients at 2 years.

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05

CAR-T CELL THERAPY IN LYMPHOMAS: EXPANSİON OF INDICATIONS AND NEW APPROACHES

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CAR-T (chimeric antigen receptor T-cell) therapy represents a revolutionary advance in treating hematologic cancers, offering promising outcomes for lymphoma patients, especially those with relapsed or refractory disease. Initially approved for diffuse large B-cell lymphoma (DLBCL), CAR-T therapy is expanding to address a broader range of lymphomas, including other B-cell and T-cell subtypes. As CAR-T technology evolves, researchers are exploring innovative delivery strategies and engineering methods to enhance efficacy and address the unique challenges of treating different lymphoma types. CAR-T cell therapy works by genetically modifying a patient's T cells to express a receptor targeting specific cancer cell antigens. In B-cell lymphomas, CD19 has proven an effective target, with CAR-T therapies such as axicabtagene ciloleucel and tisagenlecleucel demonstrating remarkable responses. Recent studies reveal high remission rates in DLBCL, mantle cell lymphoma, and follicular lymphoma when using CD19-targeted CAR-T therapy, even in patients who have exhausted other treatment options. The success of these therapies has catalyzed research into additional lymphoma subtypes and new antigen targets, allowing CAR-T cell therapy to benefit an expanding patient population (Denlinger et al., 2022). One notable development is the investigation of CAR-T cell therapy in T-cell lymphomas. T-cell lymphomas pose unique challenges due to their antigen overlap with healthy T cells, leading to risks like T-cell fratricide, where CAR-T cells inadvertently destroy each other. To address this, researchers are designing CAR-T cells targeting less common antigens, such as CD30, which is often overexpressed in Hodgkin lymphoma and some T-cell lymphomas, but not in normal T cells. CD30-directed CAR-T therapies have shown early success in clinical trials, offering hope for relapsed Hodgkin lymphoma patients who lack other viable options (Brudno et al., 2024, Ramos et al., 2020). Localized CAR-T cell therapy is another emerging strategy, particularly for lymphomas affecting the central nervous system (CNS). CNS lymphomas present an additional barrier because CAR-T cells administered intravenously may struggle to cross the blood-brain barrier (BBB) and reach tumor cells. Direct intrathecal CAR-T administration, which bypasses the BBB, has shown promising early results for CNS lymphoma, providing high CAR-T cell concentrations directly within the CNS and improving patient outcomes. This approach may reduce systemic side effects like cytokine release syndrome (CRS) and neurotoxicity, although localized neurotoxicity remains a concern (Sagnella et al., 2022). Engineering advancements are also helping address antigen escape, where cancer cells evade CAR-T cells by losing the targeted antigen. Dual-target CAR-T cells can recognize multiple antigens, reducing the risk of relapse due to antigen loss. For example, dual CD19/CD22 CAR-T therapies are being studied for their ability to sustain long-term remission by targeting two markers common to B-cell lymphomas, thus enhancing durability and reducing escape mutations. Also combining CAR-T with immune checkpoint inhibitors improve CAR-T cell efficacy. (Roddie et al., 2023). In summary, CAR-T cell therapy has transformed the lymphoma treatment landscape, extending beyond DLBCL to address Hodgkin lymphoma, follicular lymphoma, and other challenging subtypes. As new approaches evolve—such as local delivery for CNS lymphoma, dual-target CAR-T constructs, and novel T-cell lymphoma strategies—CAR-T therapy's role continues to expand, offering new hope to patients with previously untreatable lymphomas. Continued innovation will be crucial for refining CAR-T technology, overcoming barriers, and realizing its full potential across diverse lymphoma types.

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06

PROFESSOR DOCTOR SEREF INCEMAN'S BIOGRAPHY AND LEGACY

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Dr Inceman was born in Istanbul in 1919. He completed his primary education at Galatasaray High School (1940). He graduated from Istanbul University Faculty of Medicine (1940-1946). After graduation, he started his residency at the Internal Medicine Clinic (Capa) of the same faculty. He completed his military service in Erzincan (1949-1950). He worked in the clinic of Professor Jean Bernard, who conducted studies on leukemia and immunohematology at the University of Paris (1950-1951). in 1951, he stayed with Professor Swen Moeschlin at the Internal Medicine Clinic of the University of Zurich, Switzerland for a month. He was promoted to Associate Professor in 1956 and to Professor in 1966. Between 1963 and 1986, he directed the Hematology Department and served as its chairman. He was one of the founding members of THD in 1967 and was its first president. His research interest in the

field of hematology are mainly focused on hemostasis disorders. His studies on platelet adhesion and aggregation have been referred to in numerous foreign researches. He has conducted studies on some hereditary or acquired coagulation disorders, leukemias, some anemias, and plasma cell dyscrasias. He is one of the four Turkish hematologists that Wintrobe included in the book "Hematology, The Flowering of a Science: A Story of Inspiration and Effort". He has shown the recognition and diagnostic methods of many hemostasis disorders in our country with his Turkish publications. Prof. Dr. Inceman's followers became Prof. Dr. Y. Tangun, Prof. Dr. Y. Pekcelen, Prof. Dr. T. Atamer and Prof. Dr D. Sargin. He retired in 1986. He succumbed to colon cancer in 1994. He was a good listener, a serious and kind gentleman. He paid attention to details, closely followed contemporary information.

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07

SICKLE CELL DISEASE UPDATE: NEW TREATMENTS

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Sickle-cell disease is the most common genetic blood disorder, causing blockage of the circulation and resulting painful vaso-occlusive episodes, acute chest syndrome, stroke, chronic anemia, and multiorgan failure, with increased mortality. Three novel medications have been approved in the past five years: L-glutamine in 2017, and voxelotor and crizanlizumab in 2019. L-glutamine treatment was linked to a reduction in the rate of RBC transfusions as well as a decrease in hospitalizations, pain crises, and the period between the first and second crises. By raising adenosine triphosphate and lowering 2,3-diphosphoglycerate, a glycolytic red blood cell intermediate, mitapivat, an oral pyruvate kinase activator, also has therapeutic potential. Crizanlizumab, a P-selectin inhibitor, reduces the grade of inflammation by lowering the adhesion between the endothelium and leukocytes, sickled red blood cells, platelets, and endothelial cells. Crizanlizumab is associated with a decrease in the requirement for opiate use as well as a decrease in the number of pain crises and the time until the first crisis. Adverse effects include infusion reactions, headache, nausea, and insurance difficulty. Voxelotor increases hemoglobin levels and affinity for oxygen, preventing HbS polymerization, and lowering hemolysis indicators in the process and was associated with lower hemolysis indicators and higher hemoglobin. Insurance denial and adverse effects like headache, rash, and diarrhea were obstacles to using Voxelotor. None of these therapies, however, are curative. There are efficient cell-based treatments including red blood cell exchange, and hematopoietic stem cell transplantation is the only treatment that can cure the disease. Gene editing has shown promise in the treatment of β-thalassemias and sickle cell disease.

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08

PNH TREATMENT: TREATMENTS OF TODAY AND TOMORROW

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Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired blood disorder characterized by chronic destruction of red blood cells (hemolytic anemia) and blood clots (thrombosis).[1] PNH can occur at any age, although it is most often diagnosed in young adulthood. the only cure for paroxysmal nocturnal hemoglobinuria (PNH) is an allogeneic hematopoietic stem cell transplantation.[2] Stem cell transplantation is associated with high mortality and it is reserved for severe cases of PNH with aplastic anemia or transformation to leukemia, both of which are life-threatening complications. Other treatment strategies include complement mediators that inhibit components of the complement system. Several monoclonal antibodies (ie, eculizumab, ravulizumab, crovalimab) that target the C5 complement component have been approved for treatment of PNH by the US Food and Drug Administration (FDA).[3,4] A monoclonal antibody that inhibits C3, pegcetacoplan, has also been approved for treatment of PNH. Pegcetacoplan is a C3 inhibitor that is administered subcutaneously, twice weekly, and is capable of blocking both intravascular and extravascular hemolysis.[5] Iptacopan, an oral inhibitor of factor B (a component of the alternative complement pathway) was approved by the FDA in 2023. It is indicated as monotherapy for PNH.[6] Danicopan, a selective inhibitor of complement factor D, was approved by the FDA in 2024 for patients who experience clinically significant extravascular hemolysis, as an add-on to C5 inhibitor therapy (eg, eculizumab, ravulizumab).[7] Additional treatment strategies are focused on managing the symptoms and complications of PNH. Depending on the anemia symptoms they experience, patients with PNH may receive supportive treatments, such as blood transfusion, iron replacement therapy, growth factors, and erythropoeitin. Steroids may also be used only for short-term use in symptomatic extravascular hemolysis. [8,9] Treatment with anticoagulants, including heparin and coumarin derivatives, may reduce the risk of thrombosis.[1] Supplementation with folate, iron, and vitamin B12 can be used to support increased erythropoiesis in the bone marrow.

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09

NOVEL TARGETS AND THERAPIES IN MULTIPLE MYELOMA

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Multiple Myeloma (MM) is the second most frequent cancer and constitutes 10 % of hematological malignancies. Median age at onset is older than 65 years old.Despite significant improvement has been gained for management of the

diasease in the last decades cure has not been achieved. Clinicial use of monoclonal antibodies targeting cluster of differentiation (CD) 38 or signaling lymphocye activation molecular family 7 (SLAMF7) combined with immunomodulatory drugs and preoteosome inhibitors lead to prolonged progression free survival in a group of relapsed refractory MM (RR MM) patients. High risk disease forms such as extramedullary involvement, advanced stage or poor cytogenetic features still suffer decreased survival. Novel immunotherapies targeting B cell maturation antigen (BCMA), G protein- coupled receptor family C group 5 member D (GPRC5D), Fc receptor homolog 5 (FcRH5), CD138, CD 48, CD 56 and CD74 as well as cellular therapies such as chimeric antigen receptor (CAR) T / CAR NK cells therapies has been emerging. Daratumumab, elotuzumab and isotuxumab are approved monoclonal antibodies that have been in clinical use since 2015. Thereafter Belantamab mafodotin,AMG 224 and MEDI 2228 are the examples of antibody- drug conjugates with the approval of Belantamab after 4 lines of therapy in relapsed refractory MM. Teclistamab and elranatamab are the approved bispesific antibodies targeting BCMA on MM cells and CD3 on T lymphocytes. They both showed overall response rate exceeding 60 % in RRMM. Cytokin release syndrome was observed in two thirds of patients but were mostly low grade. Bispesifics showed objective responses on patients with prior antiBCMA targeted and CAR-T directed therapies. Two CAR T cell therapies has been approved in MM up to date. Idecabtagene vicleucel (ide-cel) and ciltacabtagene autocel (cilta-cel) are anti BCMA autologous CAR T cell products that have FDA approvals in RRMM. Both agents improved progression free survival compared to standard regimens. Allogeneic anti BCMA CAR T cells can also be an option in a near future based on earlier phase trials. Along with approved novel agents investigational studies for earlier lines of therapy and newer agents are emerging.Minimal residual disease (MRD) negativity is an emerging term for depth of response giving the possibility of cure and novel agents promise better MRD negativity as well as disease control.

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10

NOVEL MAINTENANCE THERAPIES IN ACUTE MYELOID LEUKEMIA: PROLONGING REMISSION AND IMPROVING OUTCOMES

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Maintenance therapy, defined as the administration of less intensive treatment following initial intensive induction and consolidation chemotherapy, has shown promise in enhancing long-term outcomes for AML patients. Allogeneic stem cell transplantation (HSCT) improves disease-free survival (DFS) in patients with AML who are suitable for transplantation. However, not all patients are suitable for transplantation. From past to present, maintenance treatment for AML has evolved from chemotherapy to immune modulatory and targeted therapies. In the early studies, low-intensity chemotherapy was used in different combinations in maintenance treatment of AML, but it could not be shown to increase overall survival. In general, novel maintenance therapy includes HMAs, the combination of HMAs with other agents, and targeted therapies. HOVON97 trial showed that azacitidine maintenance after CR/CRi after intensive chemotherapy is feasible and significantly improves DFS. The most important trial regarding HMA care is the QUAZAR AML-001 trial. CC-486 (oral azacitidine) resulted in an improvement in OS compared with placebo at approximately 12 months of follow-up. In AML 342 trial, azacitidine/venetoclax maintenance therapy was tolerable and improved RFS in AML patients not eligible to HSCT. The SORAML study demonstrated improved EFS in the sorafenib arm in adult patients with AML regardless of FLT3 status (3-year EFS: 40% vs 22%), but there was no difference in OS. The phase III ADMIRAL trial led to the approval of gilteritinib as monotherapy in adult patients with relapsed or refractory FLT3-ITD/tyrosine kinase domain-mutated AML In a long-term follow-up (37 months) of the trial, continued gilteritinib therapy preserved the superior OS. In the QuANTUM First trial, the addition of quizartinib to intensive chemotherapy followed by maintenance in patients with FLT3-ITD AML improved RFS and OS. In the phase I study, ivosidenib (n=60) or enasidenib (n=91) was added to intensive chemotherapy and continued as a maintenance agent until relapse, toxicity, or HSCT. Twelve-month OS was 75% in both groups. A phase I study of posttransplantation enasidenib (scheduled for 1 year) in 19 patients with IDH2 mutations) showed 2-year PFS and OS to be 69% and 74%, respectively. In conclusion, maintenance treatment with HMAs with or without venetoclax is recommended for intermediate and adverse-risk AML patients. Corresponding inhibitor therapies can be used in patients with targetable mutations such as FLT3 and IDH.

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11

ADVANCES IN THALASSEMIA MANAGEMENT AND CHELATION THERAPY

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Autosomal recessive thalassemias are a heterogeneous group of diseases characterized by hypochromic microcytic anemia, which develops as a result of defective synthesis of one or more of the hemoglobin (Hb) chains. It occurs when the Hb chain or chains are produced in small numbers or not at all. In other words, while the production of beta chains is insufficient, the production of alpha chains causes alpha thalassemia. Approximately 3 babies in every 1000 births in the world are affected by severe beta chain disorders, and approximately 350,000 new babies with the disease are born each year. Even under modern treatment conditions, severe clinical complications may develop in the clinical follow-up of patients. In recent years, the introduction of oral chelators and the ability to determine organ iron load with non-

invasive methods have played a very important role in improving the prognosis of patients with thalassemia. Today, the only and definitive treatment option for cases with beta thalassemia major is hematopoietic stem cell transplantation. After myeloablative conditioning treatment, allogeneic stem cell transplantation from an HLA-compatible sibling donor is considered the treatment of choice. However, for patients who do not have a suitable donor, the risk of mortality and morbidity, especially in transplants from unrelated or haploidentical donors, creates anxiety. Therefore, in recent years, alternative gene therapy strategies have been studied that aim to correct the defective β-globin gene by transferring a normal β-globin gene or replacing the defective gene with homologous recombination. RNA-based treatment approaches, known as RNA Therapies, are also being investigated in the treatment of thalassemia. These treatments target the genetic mutations that cause thalassemia and aim to correct faulty RNA production. In addition to regular blood transfusions applied to improve the quality of life of patients, Iron Chelators are among the new drugs and treatment approaches in thalassemia patients. Iron binders used as part of thalassemia treatment help to remove iron accumulated in the body due to continuous blood transfusions. The most commonly used iron binders today include deferoxamine, deferasirox, and deferiprone. These drugs help prevent iron accumulation from causing damage to organs. New drugs used other than chelators Hydroxyurea: Although hydroxyurea is usually used to treat sickle cell anemia, it is also being investigated in the treatment of thalassemia. This drug can relieve anemia symptoms by increasing hemoglobin production. In some thalassemia patients, hydroxyurea treatment can reduce the frequency of blood transfusions. Luspatercept: Luspatercept is a biologic drug that reduces the need for blood transfusions by increasing the production of red blood cells. This drug can improve the quality of life of patients by regulating the production of blood cells. Ferroportin Modulators: Ferroportin is a protein that plays an important role in iron transport in the body. New treatment strategies aim to reduce iron imbalance and excessive iron accumulation by modulating ferroportin. This treatment is among the future treatment options for controlling iron overload in thalassemia patients. Epoetin Alfa and Epoetin Beta: Epoetin alfa and epoetin beta are analogs of the hormone erythropoietin (EPO). These drugs may improve anemia management and reduce the frequency of blood transfusions in some thalassemia patients. Conclusion: Future treatment options include alternative treatment approaches such as genetic therapies, biologics, and bone marrow transplantation. Clinical studies are constantly being conducted on new treatment methods, which aim to further improve patients' response to treatment. These new drugs and treatment options used in the treatment of thalassemia aim to improve patients' quality of life and manage the symptoms of the disease. However, each patient's response to treatment may vary, so the treatment plan should be individualized for each patient. More research is needed on the effectiveness and safety of new treatment approaches.

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12

PRECISION MEDICINE IN CLL: TREATMENT BASED ON MOLECULAR PROFILES

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Chronic Lymphocytic Leukemia (CLL) is a genetically and clinically heterogeneous disease, characterized by a wide range of genetic mutations and chromosomal abnormalities that contribute to its variable clinical course and response to treatment. This heterogeneity makes CLL a complex disease to manage, with genetic factors playing a crucial role in prognosis and treatment decisions. Approximately 80% of patients with CLL have at least one of the chromosomal abnormalities: del(13q), del(11q), del(17p), or trisomy 12. The most commonly used genetic tests are FISH (Fluorescence In Situ Hybridization) and next-generation sequencing (NGS). Conventional cytogenetics is not preferred in CLL due to its lower sensitivity for detecting smaller chromosomal abnormalities and subtle genetic mutations. FISH is highly effective at detecting specific chromosomal abnormalities, such as del(13q), del(11q), del(17p), or trisomy 12, while NGS provides a detailed analysis of molecular mutations, including those in genes like TP53, NOTCH1 and SF3B1. The immunoglobulin heavy chain variable region (IGHV) mutation status plays a critical role in prognosis. IGHV mutation status is typically assessed using Sanger sequencing or NGS. The prognostic significance of the chromosomal abnormalities and mutations described above in CLL is well-established(Gaidano& Rossi, 2017; Hallek et al.,2021). Multiple studies have shown that del(17p), TP53 mutations, and/or unmutated IGHV status are associated with poor prognosis in CLL. In addition to poor survival outcomes, these factors also carry a high risk of poor response to initial chemoimmunotherapy and earlier relapse after achieving remission(Eichhorst et al.,2021; Mato et al.,2022; Tausch et al.,2020). Currently, treatment guidelines for CLL include prognostic evaluations and treatment planning based on these three mutation statuses(Eichhorst et al.,2021; Eichhorst et al.,2024; Hampel & Parikh,2022) NOTCH1 mutations have been identified as potential biomarkers of resistance to anti-CD20 monoclonal antibodies, such as rituximab and ofatumumab, in CLL, with further clinical validation needed to confirm their role and assess the efficacy of obinutuzumab in overcoming this resistance(Estenfelder et al., 2016). While other mutations, such as NOTCH1, are being investigated, they are not yet ready for widespread use in clinical practice or treatment decision-making. In CLL, the use of measurable (previously referred to as ''minimal'') residual disease (MRD) is still largely limited to clinical trials. MRD is commonly used as a marker of treatment efficacy. Flow cytometry, PCR, and NGS are the primary methods employed to detect MRD. The threshold for MRD detection remains a subject of debate. The current international consensus defines "undetectable" MRD as U-MRD4, though some studies report data at MRD5 or lower levels. Currently, MRD is associated with disease prognosis and is utilized to adjust the duration of treatment. However, it is still unclear whether therapeutic decisions based on

MRD will consistently provide clinical benefits or be sufficient to challenge established treatment strategies for CLL(Fisher et al.,2023; Wierda et al.,2021; Yang et al,2021). Complex karyotype (CK) in CLL is defined by at least three numerical or structural abnormalities in two or more metaphases within the same clone. CK is linked to advanced disease, unmutated IGHV, TP53 mutations, adverse FISH abnormalities, and telomere dysfunction. Even within the CK subgroup, heterogeneity exists in the number and type of aberrations. While CK is a significant prognostic marker, its predictive value and role in treatment remain uncertain. (Chatzikonstantinou et al., 2021). Advances in understanding epigenetics in CLL, including DNA methylation and microRNAs, may lead to targeted therapies(Zhang et al., 2024). In conclusion, CLL's genetic and epigenetic landscape is complex, with numerous chromosomal abnormalities and molecular mutations playing a critical role in disease progression, prognosis, and treatment outcomes. Ongoing studies into genetic biomarkers and MRD monitoring continue to refine our understanding of the disease, thereby providing the foundation for more individualized and potentially more effective treatment approaches in the future.

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13

NEW GENERATION BTK INHIBITORS AND RESISTANCE IN CLL TREATMENT

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Chronic lymphocytic leukemia (CLL) is an indolent lymphoproliferative malignancy characterized by monoclonal B lymphocytosis. BCR signaling plays a critical role in B cell development and survival. Bruton Tyrosine Kinase inhibitors (BTKi) disrupt the BCR signaling pathway by inactivation of BTK, leading to inhibition of proliferation and survival of CLL cells. There are two classes of BTK inhibitors, covalent and non-covalent. İbrutinif is the first approved covalent BTKi (cBTKi) of its class. The second-generation cBTKi (acalabrutinib and zanubrutinib) were designed to increase selectivity against BTK and reduce off-target toxicity. Continuous therapy with BTKi contributes to the acquisition of secondary resistance leading to clinical relapse. Pirtobrutinib, a noncovalent BTKi (ncBTKi), represents a novel class of BTKi developed to improve effectiveness and overcome acquired resistance to cBTKi. Mutations in BTK, particularly in the c481s region, and mutations in the PLCG2 region are considered the predominant mechanism of BTKi resistance in patients with CLL. Pirtobrutinib, retains kinase inhibition even in the presence of a BTK C481 mutation and demonstrates high specificity for BTK, with minimal off-target effects. The toxicity profiles of BTKis are closely linked to their kinase-binding patterns, including both on-target inhibition of BTK and variable off-target inhibition of other kinases, such as interleukin-2-inducible T-cell kinase (ITK), tyrosine kinase expressed in hepatocellular carcinoma (TEC), and epidermal growth factor receptor (EGFR) family kinases. AEs such as cardiac arrhythmias, bleeding, diarrhea, arthralgia, hypertension and infection are the primary reasons for ibrutinib discontinuation. Optimal management of AEs is crucial to achieving good outcomes and maintaining quality of life.

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14

THE HYPOXIA INDUCIBLE FACTOR (HIF) PATHWAY IN AML: THERAPEUTIC TARGETING

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The increase in levels of the hormone erythropoietin, which leads to increased production of red blood cells in response to hypoxia, was a physiological response known in the early 20th century. However, the mechanism of the cellular reaction to hypoxia was unknown. William G. Kaelin Jr., Peter J. Ratcliffe, and Gregg L. Semenza received the 2019 Nobel Prize in Physiology and Medicine for their contributions to this field. HIFs have been identified as transcription factors that function in response to hypoxia. When oxygen levels are low, the HIF protein complex is protected from degradation and accumulates in the nucleus, where it connects with the aryl hydrocarbon receptor nuclear translocator (ARNT/HIF1-β) and binds to specific DNA sequences (HREs) in hypoxia-regulated genes. At normal oxygen levels, HIF-1α is rapidly degraded by the proteasome. Oxygen regulates the degradation process by adding hydroxyl groups (OH) to HIF-1α. The VHL protein can then recognize HIF and form a complex that leads to its degradation in an oxygen-dependent manner (1,2). It is known that there are 3 types of HIF: HIF-1, HIF-2, and HIF-3. Hypoxia activates all three HIFs, with HIF-3 acting as a regulator by suppressing the gene expression of HIF-1 and HIF-2. All three HIFs consist of two subunits, α and β. The β subunit is consistently expressed in the nucleus, independent of oxygen levels, whereas the α subunit exhibits differential responses to hypoxia and normoxia, serving as the primary site for HIF-1 in tumorigenesis. To date, three isoforms of the HIF α-subunit have been identified; these are HIF-1α, -2α, and -3α. In particular, HIF-1α is the most extensively studied isoform and is generally expressed in human cells. HIF-2α is expressed only in specific tissues and cell types, such as the lung, kidney, and liver. HIF-3α is mainly expressed in heart, kidney, and lung epithelial cells. Two genes, ARNT1 and ARNT2, encode HIF-1β subunits. HIF1A, EPAS1, and HIF3A encode the HIF1/2/3α proteins, respectively. HIF-1a has been detected in high amounts in many types of cancer and is known to regulate the expression of over 100 genes.It has an effect on gene categories related to angiogenesis, energy metabolism, invasion and metastasis, proliferation and apoptosis-related proteins, immune evasion, and drug resistance, which are important steps in tumor homeostasis (3).This makes the HIF pathway a targetable focus in cancer treatment. Studies have shown that there is an increase in HIF-1α and HIF-2α expression in

AML and that suppression of HIF-1α induces apoptosis (4-5). It has also been shown that hypoxic environment and HIF pathway play an important role in the long-term survival of leukemic stem cells in the bone marrow. However, there are also studies showing that HIF-1α deficiency causes AML to progress more rapidly (6).Therefore, these findings indicate that the role of HIF-1α should be considered carefully in practical applications depending on specific conditions. Pre- and post-clinical studies targeting the HIF pathway are ongoing. The HIF pathway appears promising as a new therapeutic target.

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TARGETED THERAPIES IN AML: CURRENT AND FUTURE TRENDS

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Acute Myeloid Leukemia (AML) encompasses several subtypes defined by distinct cytogenetic and molecular characteristics, which complicates treatment and necessitates therapies that can target multiple pathways. Despite advancements, there remains a significant need for molecular treatments that can achieve long-term remissions and potentially cure this heterogeneous disease. In the past 5 to 6 years, the FDA has approved several targeted therapies for both newly diagnosed and relapsed/refractory AML. These novel therapeutics, along with others currently being investigated, have shown promising activity against AML and have improved outcomes for many patients. This presentation will explore various molecular mechanisms that contribute to the pathogenesis of AML and review current research into how these mechanisms are being targeted in treatment strategiesA **Approved Drugs:** Since the 1970s, the classical therapy for AML has consisted of cytarabine combined with an anthracycline (daunorubicin or idarubicin), famously known as the "7 + 3" regimen. The small-molecule FDA-approved drugs for AML over the last decade include IDH inhibitors (olutasidenib, ivosidenib, enasidenib), FLT3 inhibitors (gilteritinib, midostaurin), BCL-2 inhibitor (venetoclax), hypomethylating agents (azacitidine, decitabine), and CPX-351 (liposomal cytarabine and daunorubicin). **Non-Approved Drugs:** Several FLT3 inhibitors, such as sorafenib and quizartinib, have undergone clinical trials for acute myeloid leukemia (AML). However, the FDA did not approve these drugs due to various concerns regarding the trial data. Recent reports from 2021 highlighted an oxoindoline-based selective FLT3 inhibitor as a potential candidate for treating FLT3-ITD-positive AML, a condition associated with a poor prognosis. Additionally, a first-in-class hydrazide-based HDAC inhibitor was reported in 2022, and a promising CDK9 inhibitor for AML treatment was identified in 2021. Rearrangements of the KMT2A (MLL1) gene occur in up to 10% of acute leukemias. Moreover, the TP53 tumor suppressor gene is often inactivated in cancers due to loss-of-function mutations or missense mutations in the DNA-binding domain, occurring in nearly 50% of cases. Targeting mutant p53 to restore its function could provide a promising avenue for new therapeutics. APR-246 is a compound designed to reactivate mutant p53. **Conclusions:** While this presentation does not cover all targeted agents, many promising options are available. A continuous and dedicated focus on understanding the fundamentals of molecular genetics and epigenetics, along with ongoing monitoring of clonal evolution before and after treatment with these targeted therapies, could lead to innovative changes in treatment strategies. This may ultimately provide the most beneficial outcomes for patients of all ages.

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HEMOPHILIA: ADVANCES IN TREATMENTS

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Introduction: Hemophilia is an X-linked recessive disorder. It is divided into two different subtypes; hemophilia A (HA) and B (HB), which result from the deficiency or complete absence of clotting factors VIII (FVIII) and IX (FIX) respectively. Current management of HA and HB includes prophylactic factor replacement[1]. Neutralising antibodies, as inhibitors, can develop against the infused factor and that can complicate the management of hemophilia patients. If inhibitors develop, immune tolerance induction can potentially promote tolerance to exogenous FVIII or FIX, and bypassing agents (BPAs) such as recombinant factor VIIa (rFVIIa) and activated prothrombin complex concentrates (aPCC) can be used to circumvent factor use. Inhibitor development impacts negatively upon quality of life and treatment compliance, highlighting the need for improved therapies. Several novel pharmacological therapies developed for hemophilia aim to rebalance the clotting cascade. These therapies utilise a range of different mechanisms, namely: the extension of the circulating half-life of standard recombinant factors; the mimicking of factor VIII cofactor activity; rebalancing of coagulation through targeting of natural anticoagulants such as antithrombin and tissue factor pathway inhibitor; and inducing the production of endogenous factors with gene therapy. **Discussion:** Extended half–life products involves fusing FVIII or FIX to a protein with a long half-life. Albumin and the constant region (Fc) of IgG have long plasma half-lives as they bind to the neonatal Fc receptor, which is critical for the endogenous recycling of both IgG and albumin. Another method is PEGylation, where one or more PEG chains are covalently linked to rFVIII or rFIX. PEG chains interfere with the recombinant factors binding to their clearance receptors, thereby prolonging circulating half-life. Emicizumab, a recombinant humanised bispecific IgG antibody, mimics the cofactor function of the missing FVIII in HA. It simultaneously binds activated FIX (FIXa) and factor X (FX), bringing them into spatial proximity to promote FIXa-catalysed FX activation, thereby restoring haemostasis. Fitusiran, a novel therapy applicable to both HA and HB, consists of the amino acid,

N-Acetyl- galactosamine, the ligand of the hepatic asialo-glycoprotein receptors, conjugated to a synthetic siRNA. It targets and degrades a region of the SERPINC1 gene mRNA, preventing antithrombin production and enhancing thrombin generation. Antithrombin is a potent anticoagulant which inactivates FIXa, activated factor X (FXa) and activated factor II (FIIa/thrombin). Therefore, fitusiran can correct the coagulation imbalance and prevent the bleeding phenotype. Concizumab is an IgG4 monoclonal antibody targeting tissue factor pathway inhibitor (TFPI). It presents an alternative therapy for HA and HB patients, both with and without inhibitors. TFPI is a coagulation inhibitor. It limits coagulation during the initiation of the coagulation cascade through inhibition of the tissue factor-activated factor VII (TF-FVIIa) complex and through FXa inhibition. Gene therapy presents a novel and effective treatment modality for hemophilia, potentially bypassing complications of other therapies. Gene therapy regimens consist of single infusions of a viral vector, which result in transduction of a gene coding for the deficient factor into patient hepatocytes. Current gene therapy regimens for hemophilia predominantly utilise adeno-associated virus (AAV) vectors to deliver the required gene. **Conclusion:** Current factor replacement poses numerous issues, resulting in poor adherence and reduced QoL. Inhibitor development presents a key limitation to factor replacement. EHL products, emicizumab, fitusiran, and concizumab (summarised in appear effective in patients with and without inhibitors, and their longer half-lives enable less frequent injections.

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OPTIMIZATION OF FIXED DURATION TREATMENT OPTIONS IN CHRONIC LYMPHOCYTIC LEUKEMIA: CURRENT DATA AND FUTURE DIRECTIONS

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Introduction of Bruton tyrosine kinase inhibitors (BTKi) and B-cell lymphoma 2 (Bcl-2) antagonists changed the historical approach to chronic lymphocytic leukemia (CLL). Fixed-duration, targeted combination of these novel agents have replaced chemoimmunotherapy and have become preferred treatment options. Benefit of treating asymptomatic early stage disease is yet to be shown and indications for treatment are still mostly guided by International Working Group for CLL (iwCLL) 2018 recommendations. However; risk stratification has also come to question as genetic studies such as 17p/TP53 mutations, IGHV mutation status showed better risk analysis following chemoimmunoterapy (CIT) era. BTKi and Bcl-2 inhibitors also led to investigations on duration of treatment (fixed duration versus continuous) and best combination that provides most overall survival (OS) and progression-free survival (PFS) benefit. Since most CLL patients are elderly, comorbidities limit treatment options and these comorbidities correlate with shorter OS. Prior studies have shown that young and fit patients benefited from first line CIT such as fludarabine, cyclophosphamide, rituximab (FCR) and FCR provided long term remissions in previously untreated patients. Advent of BTKi and venetoclax offered a better treatment option for older population with high Cumulative Illness Rating Scale (CIRS) with fewer side effects although negative impact of comorbidities persisted.[3] In recent years, trials such as CLL14 have included patients with CIRS>6 and low creatinine clearence and showed the FD obinituzumab plus venetoclax combination was superior and provided longer PFS compared with to obinituzumab plus chlorambucil (median, 76.2 vs 36.4 months; hazard ratio [HR], 0.40; 95% confidence interval [CI], 0.31-0.52; $P < .0001$). Treatment with FD ibrutinib plus venetoclax in older patients also provided better responses. PFS was significantly longer for ibrutinib-venetoclax compared to chlorambucil-obinutuzumab (hazard ratio, 0.216; 95% confidence interval [CI], 0.131 to 0.357; $P<0.001$). PFS remained higher including patients 65 years of age or older or with a CIRS >6.These studies have provided basis for the approval of FD ibrutinib plus venetoclax combinations and showed clear benefit compared with historical CIT. FD treatments versus continuous ibrutinib became the focus of recent trials as well as determination of optimal duration for any treatment. Although continuous ibrutinib is the treatment of choice, trials have shown increased PFS and OS with FD treatments. With ibrutinib and venetoclax combination 36 −month overall survival (OS) was >95% regardless of high-risk features. Following recent trials, minimal residual disease (MRD) status as well as its incorporation into treatment duration emerged as a marker to guide CLL treatment. Subgroup analysis of trials have reported better PFS in patients with MRD negativity. Recently MRD guided treatment was shown to be effective and re-initiation of treatment with ibrutinib plus venetoclax was able to achive MRD negativity following discontinuation of treatment. Trials with ibrutinib and next generation BTKi and venetoclax are expected to incorporate MRD to further expand its role as an independent risk factor for long term survival. MRD tailored treatments in clinical practice may allow for discontinuation of treatment and also predict relapse. Appropriate method to determine MRD status requires further data from trials.

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OPTIMISATION OF THERAPEUTIC APPROACHES FOR HIGH-RISK ALL SUBTYPES

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There are actually several subtypes of acute lymphoblastic leukemia (ALL), some of which are especially difficult to manage. The high risk ALL subtypes included in this overview are neonatal ALL, KMT2A rearrangement, Philadelphia chromosome-positive (Ph+), Philadelphia-like (Ph-like), and Early T-cell precursor (ETP). Ph+ ALL: Tyrosine kinase inhibitors

(TKIs), such as imatinib, dasatinib, and nilotinib, constitute a part of the the main treatment for Ph+ ALL, which is characterized by the BCR-ABL1 fusion gene. Chemotherapy and/or steroids are frequently utilized in combination with TKIs. ABL001 provides a new method of ABL inhibition, although ponatinib works well against T315I mutations. Ph-like ALL: This type of ALL frequently contains CRLF2 rearrangements and ABL-class fusions, but it lacks the BCR-ABL1 fusion yet shares a comparable gene expression profile.(Jain & Abraham, 2020) For CRLF2-rearranged cases, JAK inhibitors like as ruxolitinib show promise, although conventional TKIs might work well for ABL-class fusions. KMT2A Rearranged ALL: KMT2A rearrangements are frequent in infant ALL and have an undesirable prognosis. (Richard-Carpentier vd., 2021)By targeting protein interactions and epigenetic changes, DOT1L and menin inhibitors,(Candoni & Coppola, 2024) such as SNDX-5613, are becoming potential therapeutic options. ETP ALL: A rare and aggressive type of T-cell ALL, ETP ALL can be identified by certain genetic changes and immunophenotypic markers.(Onishi vd., 2023) JAK inhibitors and Venetoclax, a BCL-2 inhibitor, are being studied as potential therapies for the dysregulated IL-7 and BCL-2 receptor pathways. Infant ALL: Challenges with infant ALL include an underdeveloped immune system and high frequency of KMT2A rearrangements. To improve those results, epigenetic modifiers and improved immunotherapeutic strategies, such as CAR T-cell therapy, are being researched. To sum it up, understanding the particular characteristics each high-risk ALL subtype is critical to designing personalised treatments. To overcome the difficulties presented by drug resistance and immune system infancy, ongoing research and clinical trials are important.

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IMMUNOTHERAPY IN ALL: MONOCLONAL ANTIBODIES AND BEYOND

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In acute lymphoblastic leukemia (ALL) patients, overall survival is around 90% in childhood, whereas 5-year overall survival (OS) is less than 45% in adults. For eligible patients, allo-HCT remains the standard treatment, while immunotherapies are drawing attention in studies aimed at developing alternative treatment regimens. The most popular immunotherapies include bispecific antibodies (BsAbs), antibody-drug conjugates, CAR T-cell, and CAR NK cell therapies, which aim to target cancer cells using the patient's immune system. Blinatumomab is a bispecific T-cell-engaging (BiTE) antibody. It is designed to include binding regions that target two different antigens simultaneously. By binding to CD19 on B-ALL cells and CD3 on T cells, it activates T cells, leading to the polyclonal expansion of cytotoxic T cells, T cell activation, and the release of cytokines and cytotoxic granules, which cause the lysis of CD19+ lymphoblasts. Initially approved by the FDA in 2014 for the treatment of Ph(-) relapsed/refractory B-ALL, it has since received FDA approval for consolidation therapy in patients with MRD-positive disease as well as for MRD-independent consolidation therapy. Hematologic side effects are similar to those of standard chemotherapy, while non-hematologic side effects include cytokine release syndrome and neurological events, which are relatively manageable due to prophylactic measures and its short half-life. In the Alcantara study, it was shown that sustainable responses were achieved in patients with Ph(+) R/R ALL, despite the low number of patients enrolled in the study. Inotuzumab is an antibody-drug conjugate that consists of calicheamicin, a DNA-binding cytotoxic antibiotic, covalently linked to an anti-CD22 IgG4 mAb. In 2017, it received FDA approval after monotherapy with inotuzumab showed superiority over standard chemotherapy for relapsed/refractory CD22(+) B-ALL. The most common grade ≥3 side effects are hematologic and liver-related, including 11% VOD, which is mostly seen after sequential allo-HSCT. It is recommended for patients without known liver disease. To reduce VOD risk, it is advised to administer only up to two cycles of inotuzumab before SCT and avoid double alkylators in conditioning regimens. Inotuzumab monotherapy has shown high CR and MRD negativity rates when combined with low-intensity chemotherapy in elderly patients in first-line treatment, but it is still not approved by the FDA and EMA. Cell-based therapy, despite side effects limiting CAR T-cell, has shown remarkable efficacy in r/r B-ALL with CD19-targeted therapy, such as tisagenlecleucel (tisa-cel) for patients ≤25 years and brexucabtagene autoleucel for adults. Side effects include cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome (ICANS), and B-cell aplasia. For relapsed/refractory T-cell leukemia, CD5-CART, CD7-CART, and NS7CAR studies are ongoing. Although experimental, CAR-NK therapies using NK cells, which are isolated from peripheral blood and do not pose a GVHD risk, hold promise with fewer side effects, reduced relapse, and prolonged survival. Studies on immune checkpoint inhibitors in combination with other immunotherapies may be significant for B-ALL, while combinations of BCL-2 and BCL-XL inhibitors with chemotherapy may be important for T-ALL, which currently lacks antibody therapy. While challenges persist in treating T-ALL and Ph-like ALL, immunotherapy and cellular therapies continue to be significant for B-ALL treatment, with ongoing research into the optimal combinations and integration stages into therapy.

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CAR-T CELL THERAPY IN ACUTE LEUKEMIAS

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Acute leukemias, particularly acute lymphoblastic leukemia (ALL) and, to a lesser extent, acute myeloid leukemia (AML), remain among the most challenging hematologic

malignancies due to high mortality rates and limited treatment options. In this context, Chimeric Antigen Receptor T (CAR-T) cell therapy has emerged as a promising approach for patients with refractory or relapsed disease. CAR-T cells are generated by genetically engineering the patient's T cells to express synthetic receptors targeting specific tumor-associated antigens. In ALL, CD19-targeted CAR-T cell therapies have demonstrated complete remission (CR) rates of 70–90%. For AML, ongoing research is exploring alternative targets. Clinical Studies and Outcomes ELIANA Trial The ELIANA trial, the largest global multicenter study of CD19-targeted CAR-T therapy, focused on pediatric and young adult ALL patients Tisagenlecleucel was infused into 75 ALL patients and evaluated for efficacy. The overall remission rate at 3 months was 81%, and all patients who responded to treatment were found to be negative for minimal residual disease by flow cytometry. Event-free survival and overall survival rates were 73% and 90% at 6 months and 50% and 76% at 12 months, respectively. Median duration of remission was not achieved. Tisagenlecleucel persisted in the blood for up to 20 months. Grade 3 or 4 adverse events thought to be related to tisagenlecleucel occurred in 73% of patients. Cytokine release syndrome occurred in 77% of patients, 48% of whom received tocilizumab. Neurological events occurred in 40% of patients and were managed with supportive care, and no brain edema was reported. ZUMA-3 Trial The ZUMA-3 an international, multicentre, single-arm, open-label study evaluating the efficacy and safety of the autologous anti-CD19 CAR-T-cell therapy KTE-X19 in adult patients with relapsed or refractory B-precursor acute lymphoblastic leukaemia. KTE-X19 was administered to 55 (77%) patients. At a median follow-up of 16.4 months (13.8-19.6), 39 patients (71%; 95% CI 57-82, p<0.0001) had CR or CRi and 31 (56%) achieved CR. Median duration of remission was 12.8 months (95% CI 8.7 - not estimable), median relapse-free survival was 11.6 months (2.7-15.5) and median overall survival was 18.2 months (15.9 - not estimable). Among responders, median overall survival was not reached and 38 (97%) patients had MRD negativity. Ten (18%) patients received allo-SCT consolidation after KTE-X19 infusion. The most common adverse events of grade 3 or higher were anemia (27 [49%] patients) and pyrexia (20 [36%] patients). 14 (25%) patients had grade 3 or higher infections. Two grade 5 KTE-X19-related events occurred (cerebral herniation and septic shock). Grade 3 or higher cytokine release syndrome occurred in 13 (24%) patients, and grade 3 or higher neurologic events occurred in 14 (25%) patients. AML Target Studies AML poses unique challenges due to its heterogeneous cell populations. Early-phase studies of CD33-targeted CAR-T cells have shown promising tumor burden reductions in specific patient cohorts. However, these studies are still in the clinical validation phase. Future Perspectives Next-generation CAR-T cell designs aim to enhance target specificity and minimize adverse effects, improving the therapy's safety and efficacy profile. Allogeneic CAR-T platforms and universal CAR-T cell technologies are also under development, potentially increasing accessibility for a broader range of patients. In conclusion, CAR-T cell therapy represents a transformative step in personalized treatment strategies for acute leukemias. Continued advancements in clinical trials and translational research will further unlock the potential of this innovative approach in hematology.

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PRECISION MEDICINE IN MULTIPLE MYELOM

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Precision medicine, an approach tailored to individual patient characteristics and disease profiles, has become increasingly important in the treatment of multiple myeloma (MM). Conventional MM treatment often yields variable results because the biological and clinical course of MM is heterogeneous. One of the main strategies in precision medicine for MM is genetic profiling. Certain genetic mutations such as t(4;14), t (14;16) and del(17p) are associated with a higher risk of aggressive disease. In addition, copy number alterations involving the long arm of chromosome 1 (1q) predict worse survival. In addition to cytogenetics, differential gene expression profile (GEP) signatures are independent prognostic factors for both PFS and OS, thus providing an additional method to identify high risk. By identifying these markers early, clinicians can classify patients into risk categories and tailor treatment accordingly. High-risk patients may receive more intensive treatments, while standard-risk patients may benefit from less aggressive regimens that preserve quality of life. Targeted therapies are another critical component of precision medicine in MM. Unlike conventional chemotherapy, which affects both cancerous and healthy cells, targeted therapies are designed to act specifically on the molecular pathways that drive MM cell growth. Drugs such as proteasome inhibitors, immunomodulatory agents and monoclonal antibodies are designed to attack key mechanisms in MM cells. For example, proteasome inhibitors disrupt protein excretion pathways in cancer cells, leading to cell death, while monoclonal antibodies can mark MM cells for immune destruction. These therapies offer more effective and tolerable treatment options when matched to patients whose disease characteristics are compatible with the drug's mechanism. CAR-T cell therapy and bispecific antibodies are promising options for relapsed/refractory MM and offer significant disease reduction for patients with limited options. Precision medicine also plays a role in monitoring minimal residual disease (MRD), which refers to the small number of cancer cells that can remain after treatment and potentially cause relapse. Multiparameter flow cytometry (MFC) and next-generation sequencing (NGS) are the most common and standardised methods. Whole body MRI and PET/CT provide better assessment for extramedullary disease. Patients with MRD-negative status generally have better long-term outcomes, so precision medicine approaches can tailor treatment to MRD status, aiming for complete eradication of disease in patients with evidence of remaining cancer cells. Finally, clinical trials are essential to develop precision medicine in MM. Studies focused on biomarker-driven therapies and novel agents give

patients access to cutting-edge treatments that may be more effective for specific disease profiles. As genomic data and biomarker research progress, trials are increasingly focused on matching patients with therapies based on individual molecular characteristics, increasing the likelihood of a favourable outcome. AI is supporting precision medicine in MM by improving diagnostic accuracy, risk stratification and treatment matching, potentially transforming personalised oncology care. Overall, precision medicine in MM, supported by AI insights, aims to optimise treatment efficacy, promote longer-lasting remission and improve quality of life by tailoring therapies to each patient's unique disease profile.

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SUPPORTIVE CARE AND QUALITY OF LIFE IN MDS: ESSENTIAL MANAGEMENT STRATEGIES

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Supportive care is critical for patients with Myelodysplastic Syndromes (MDS), aiming to enhance quality of life (QoL) amidst this chronic, hematologic disorder. MDS management focuses on alleviating symptoms of ineffective hematopoiesis and preventing complications like infections and cardiovascular disease. Managing Anemia and Transfusion Dependence: Anemia is prevalent in MDS, often requiring blood transfusions. However, frequent transfusions can lead to iron overload, risking damage to organs like the heart and liver. Iron chelation therapy mitigates this risk by reducing iron buildup, crucial for transfusion-dependent patients. Erythropoiesis-stimulating agents (ESAs) are effective in lower-risk MDS patients, reducing transfusion needs, while the recent COMMANDS Trial highlights luspatercept as an alternative to epoetin alfa, showing promising results in managing anemia and improving QoL. Addressing Thrombocytopenia and Bleeding Risks: Patients with MDS frequently experience thrombocytopenia, which increases bleeding risk. Thrombopoietin receptor agonists, like eltrombopag and romiplostim, aid platelet production, though long-term safety and efficacy require further research. For severe cases, prophylactic platelet transfusions are essential, with tailored transfusion thresholds improving patient outcomes. In addition, antifibrinolytic agents, such as tranexamic acid, are used adjunctively to manage bleeding. Infection Prophylaxis: Due to compromised immunity, MDS patients face high infection risks. Antimicrobial prophylaxis and vaccinations against common pathogens are critical. Prophylactic measures are especially relevant for patients with neutropenia, where antibiotics, antifungals, and antivirals provide protection. Vaccinations further support infection prevention, although immune responses in MDS patients may require adjustments. Nutritional and Metabolic Support: Malnutrition is common in MDS and correlates with poor prognosis. Regular nutritional assessments help address deficiencies, and supplements, particularly of B vitamins and folate, are beneficial in sustaining hematopoiesis. Recent findings suggest vitamin C's potential in supporting hematologic function through DNA demethylation, though optimal dosages are still under study. Cardiovascular and metabolic complications are also common, emphasizing lifestyle modifications and careful management of comorbidities like hypertension and diabetes. Psychological and Palliative Care: Chronic symptoms and disease progression often lead to depression and anxiety among MDS patients. Psychosocial support, including therapy and support groups, can significantly enhance emotional resilience. For those in advanced stages, palliative care, emphasizing dignity and comfort, is essential. Pain management and non-pharmacological approaches for symptoms like fatigue help improve end-of-life quality. Role of Technology and Geriatric Assessments: Telemedicine offers a means for remote monitoring, enhancing access to care for elderly or immobile patients. Geriatric assessments guide treatment decisions, balancing efficacy and tolerance, especially in older patients who may face higher treatment-related risks. In conclusion, MDS supportive care integrates various strategies, from anemia management to infection control, tailored for physical, emotional, and psychosocial well-being. Multidisciplinary approaches and emerging tools like telemedicine continue to improve outcomes, underscoring supportive care's pivotal role in MDS management.

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HARMONIZATION OF TREATMENT APPROACHES: DRAWING INSPIRATION FROM PEDIATRIC TREATMENTS IN ADULT ACUTE LYMPHOBLASTIC LEUKEMIA THERAPY

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Age, genetic characteristics, comorbidities, and minimal residual disease determine prognosis in patients with Acute Lymphoblastic Leukemia (ALL). Advanced age, the presence of adverse genetic markers and reduced treatment intensity typically lead to poorer outcomes, with disease-free survival and remission rates decreasing with age. In adult patients, disease remission rates are around 35%. In recent years, there has been a growing focus on applying treatment protocols developed for pediatric age groups to adult ALL patients. In pediatric ALL protocols, the main factor that enhances treatment success is the dose intensity. These protocols involve higher doses and more frequent dosing intervals of L-asparaginase, vincristine, methotrexate and steroids compared to adult ALL protocols. In recent years, it has been shown that treatment regimens applied to young adult/adolescent ALL patients have an independent impact on outcomes. Various retrospective studies have shown that complete response rates in the 15-20 age group were similar between adult and

pediatric protocols, but disease-free survival was significantly higher with pediatric protocols. There is no consensus about age range for the young adult/adolescent group. In some protocols, these protocols can be applied up to the age of 35 to 50 years. Rather than age, the intensity of chemotherapy can be determined according to patients' comorbidities and performance status. Current guidelines recommend pediatric-based chemotherapy protocols for young adult/adolescent patients with no comorbidities. These protocols include CALGB 10403, DFCI Protocol 00-01 and PETHEMA ALL-96. According to the prospective study results using the CALGB 10403 protocol, for ALL patients aged 17-39 years, the median event-free survival (EFS) was 78.1 months (historical control: 30 months); the 3-year EFS was 59%; and the median overall survival (OS) was not reached. The estimated 3-year OS was 73%, with a low treatment-related mortality rate of 3%. In a study by the Dana-Farber Cancer Institute (DFCI) group in adult ALL patients aged 18-50 using pediatric-based chemotherapy protocols, 85% of patients achieved complete remission (CR) after one month of intensive induction therapy. With a median follow-up of 4.5 years, the 4-year disease-free survival (DFS) for patients who achieved CR was 69%, and the 4-year OS was 67%. In the PETHEMA group's data for ALL patients aged 15-30 treated with a pediatric-based chemotherapy protocol, the CR rate was 98%. The 6-year EFS and OS were 61% and 69%, respectively. Other protocols recommended for ALL patients under 65 include the dose-adjusted CALGB 8811 Larson, MRC UKALLXII/ECOG 2993, GRAALL-2005, dose-adjusted HyperCVAD, USC/MSKCC ALL regimen based on the CCG-1882 regimen and the Linker 4-drug regimen. Studies using these protocols, CR rates were reported between 85% and 95%. Median survival was 36 months, with 3-year OS ranging from 50% to 70%, and 5-year OS ranging from 30% to 40%. Chemotherapy-related mortality is reported at approximately 5%. In conclusion, pediatric-based chemotherapy protocols offer higher CR rates compared to low-intensity treatments. Despite the lack of a significant increase in treatment-related mortality, the advantage of prolonged OS means that pediatric-based chemotherapy should be applied to all eligible adult ALL patients, whenever appropriate.

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ONGOING CLINICAL TRIALS IN MULTIPLE MYELOMA

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a) BCMA-Targeted Therapies: I. CAR-T Cell Therapies: 1- KarMMa-3 Trial: This is a multicenter, randomized, open-label, Phase 3 study comparing the efficacy and safety of ide-cel versus standard regimens in subjects with R/R multiple myeloma. Ide-cel therapy significantly prolonged progression-free survival and improved response as compared with standard regimens. 2- CARTITUDE-4 Trial: The purpose of this study is to compare the efficacy of ciltacabtagene autoleucel (cilta-cel) with standard therapy, either PVd or DPd. A single cilta-cel infusion resulted in a lower risk of disease progression or death than standard care in lenalidomide-refractory patients. II. Bispesific Antibodies: 1- MajesTEC-1 Trial: The purpose of this study is to evaluate the efficacy of teclistamab at the recommended Phase 2 dose. Teclistamab resulted in a high rate of deep and durable response in patients with triple-class–exposed relapsed or refractory multiple myeloma. 2- MagnetisMM-3 Trial: The purpose of the study is to evaluate whether single-agent Elranatamab can provide clinical benefit in participants with R/R multiple myeloma. Elranatamab induced deep and durable responses with a manageable safety profile. III. Drug-Antibody Conjugates: 1- DREAMM-7 Trial: This is a Phase 3, randomized, open-label study designed to evaluate safety and efficacy of belantamab mafodotin in combination with bortezomib/dexamethasone (Arm A) versus daratumumab in combination with bortezomib/dexamethasone (Arm B). BVd therapy conferred a significant benefit with respect to progression-free survival among patients who had R/R multiple myeloma after at least one line of therapy. b) Selinexor Combinations: 1- Updated Results Of Boston Trial By Prior Therapies: Stratified subgroup data from longer follow-up in the BOSTON trial confirm the PFS benefit of SVd over Vd in patients. 2- STOMP Trial: This study will independently assess the efficacy and safety of 11 combination therapies in 12 arms, in dose-escalation/-evaluation and expansion phases, for the treatment of patients with R/R multiple myeloma and newly diagnosed multiple myeloma. X–containing regimens are potent and achieve durable responses with numerically higher overall response and clinical benefit rates, as well as median progression free survival c) Venetoclax Combinations: 1- CANOVA Trial: A study designed tocompare progression-free survival (PFS) in participants with t (11;14)-positive MM treated with venetoclax in combination with dexamethasone versus pomalidomide in combination with dexamethasone. Patients with $BCL2^{high}$ or gain(1q) had numerically improved clinical efficacy with VenDex versus PomDex. d) CELMoDs (Cereblon E3 Ligase Modulation Drugs): 1- CC-92480-MM-001 Trial: This is an open-label, multi-center, international, Phase 1/2 study to assess the safety, PK and efficacy of mezigdomide monotherapy and in combination with dexamethasone in subjects with relapsed and refractory multiple myeloma (RRMM). The all-oral combination of mezigdomide plus dexamethasone showed promising efficacy in patients with heavily pretreated multiple myeloma, with treatment-related adverse events consisting mainly of myelotoxic effects. 2- CC-220-MM-001 Trial: This is a multicenter, multi-country, open-label, Phase 1b/2a dose-escalation study. Iberdomide plus dexamethasone was generally safe and showed meaningful clinical activity in heavily pretreated patients with multiple myeloma, including in disease that was refractory to immunomodulatory drugs.

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MONOCLONAL ANTIBODIES

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Obinutuzumab, an anti CD-20 monoclonal antibody, can be used in combination with venetoclax, ibrutinib or acalabrutinib in CLL patients with newly diagnosed or relaps patient's treatment indications. Another anti CD-20 monoclonal antibody, rituximab, has been used in combination with bendamustine, FC in del 17p/tp53 negative, ig H mutated patients in previous years. In addition, rituximab is currently used in combination with venetoclax. Chimeric antigen receptor T cells The CD19-directed chimeric antigen receptor (CAR)-T cell therapy lisocabtagene maraleucel (liso-cel) is an option for fit patients with relapsed or refractory CLL/SLL after two or more lines of systemic therapy, including a BTK inhibitor and a BCL2 inhibitor (venetoclax). This population has few therapeutic alternatives, and low-quality evidence suggests that liso-cel may produce sustained remissions in a subset. However, treatment is associated with substantial toxicity, and the manufacturing process is complex and expensive. As such, the decision to proceed with CAR-T cell therapy is individualized and highly dependent on an estimation of complication risk and the needs and wishes of the patient. CAR-T cells are genetically modified ex vivo, expanded in a production facility, and then infused back into the patient as therapy. Prior to reinfusion, patients receive a lymphodepleting chemotherapy preparative/conditioning regimen (ie, fludarabine plus cyclophosphamide). Trials have allowed for additional "bridging" therapy for disease control during the manufacturing process. Hematopoietic cell transplantation (HCT) Patients with CLL are generally older adults with a median age greater than 70 years, and due to the relatively benign course of the disease in the majority of patients, only selected patients are candidates for intensive treatments such as HCT. The determination of transplant eligibility should be made based on a risk-benefit assessment and the needs and wishes of the patient. HCT may also be appropriate for young patients with relapsed or refractory CLL already exposed to a BTK inhibitor and venetoclax. İnvestıgatıonal Therapies Most commonly, there is no better therapy to offer a patient than enrollment in a well-designed, scientifically valid, peer-reviewed clinical trial especially in relapsed/refractory patients. Additional information and instructions for referring a patient to an appropriate research center can be obtained from the United States National Institutes of Health. Many agents are under active investigation. These include novel agents (eg, additional noncovalent Bruton tyrosine kinase [BTK] inhibitors, BTK degraders), combinations of agents already used in CLL, and agents approved for other diseases. We await the results of these studies before incorporating medications not approved for CLL. Specifically, lenalidomide should not be used for patients with CLL outside of a clinical trial. While initial studies reported moderate activity for lenalidomide, some studies have been terminated due to toxicity concerns and excess deaths. We also do not use the anti-CD52 monoclonal antibody alemtuzumab for patients with CLL. While partial responses may be seen in approximately one-third of patients, use is limited by toxicities that include infusion-related side effects, myelosuppression, and infections

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ANTI-CD38 MONOCLONAL ANTIBODIES: TRANSFORMING MULTIPLE MYELOMA TREATMENT

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Introduction: Multiple myeloma (MM) is a neoplasm defined by the clonal proliferation of malignant plasma cells (PC) within the bone marrow (BM). Multiple myeloma (MM) originates from the asymptomatic proliferation of pre-malignant plasma cells, categorized as monoclonal gammopathy of undetermined significance (MGUS) and smoldering myeloma (SMM). Patients with MGUS exhibit low serum M-protein levels (< 3 g/dL) and monoclonal plasma cells in bone marrow (< 10%), while patients with SMM demonstrate elevated serum M-protein levels (≥ 3 g/dL) and/or plasma cells in the bone marrow (≥ 10%). Conversely, the diagnosis of multiple myeloma necessitates the identification of end-organ damage correlated with the presence of serum M-spike and/or monoclonal plasma cells in the bone marrow. **CD38 structure and functions:** This protein is a type II transmembrane glycoprotein encoded on chromosome 4 (4p15.32) and comprises three domains: a 21-amino acid intracellular domain (N-terminus), an alpha-helix transmembrane domain, and a 256-amino acid extracellular domain (C-terminus). This extracellular domain exhibits multifunctional enzymatic activity. CD38, originally characterized as an ADP-ribosyl cyclase, catalyzes the cyclization of nicotinamide adenine dinucleotide (NAD) to cyclic ADP-ribose (cADPR). **CD38 expression in multiple myeloma:** It is essential to emphasize the role of CD38 in multiple myeloma, one of the most thoroughly researched CD38-related conditions. Numerous studies have demonstrated significant and elevated CD38 expression on malignant plasma cells in bone marrow samples of multiple myeloma patients. CD38, a glycoprotein, interacts with CD31, which is co-expressed on multiple myeloma cells, and plays a role in several cellular processes. These encompass T cell activation and proliferation, B cell differentiation, and the chemotaxis of neutrophils and monocytes. Furthermore, as an ectoenzyme, CD38 regulates intracellular NAD + levels, which are essential for sustaining low glycolytic activity that facilitates cell proliferation and survival (Morandi et al., 2018). Under varying pH settings, CD38 facilitates the transformation of NAD + into adenosine (ADO), a mediator of calcium signaling that enhances tumor survival and immune evasion. Alongside CD38, several ectoenzymes including CD39, CD73, and CD203a contribute to the extracellular synthesis of adenosine (ADO), with their concentrations indicating disease progression. Furthermore, CD38 functions as a metabolic sensor

through its interaction with osteoclasts (OCs) during adult skeletal remodeling. Osteoclasts, essential for bone remodeling, are influenced by CD38 inhibition, which not only impedes bone resorption but also reinstates T-cell functionality, thus preventing the advancement of bone disease. **Treatment with anti-CD38 monoclonal antibodies:** The increase of CD38 on cancer cells and its role in cancer progression has prompted researchers to create various monoclonal antibodies (mAbs) that target CD38. Commercially available CD38 monoclonal antibodies for multiple myeloma treatment include daratumumab. Additional novel drugs are currently in clinical trials, including MOR202 (Felzartamab) (completely human), TAK079 (Mezagitamab) (fully human), FTL004 (humanized Ig1), SAR442085 (totally human engineered), and TNB-738 (entirely human). Their anticancer efficacy relies on Fc-dependent immunological effector mechanisms and immunomodulatory actions that eradicate CD38 regulatory T cells, hence reinstating T-cell and NK-cell-mediated antitumor immune responses.

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EXPANSION OF INDICATIONS FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): CURRENT STATUS AND FUTURE DIRECTIONS

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Hematopoietic Stem Cell Transplantation (HSCT) is examined under 3 headings. 1. Autologous bone marrow transplantation 2. Syngeneic bone marrow transplantation 3. Allogeneic bone marrow transplantation (myeloablative, nonmyeloablative) a. Sibling b. Unrelated c. Haploidentical Bone marrow, peripheral stem cell and cord blood are used as stem cell sources. Autologous stem cell transplantation It is based on the principle of being able to apply much higher doses of chemotherapy to patients and overcoming the bone marrow damage that will occur in the meantime by means of stem cells obtained from the patient himself. Therefore, the sensitivity of the tumor to chemotherapy and the dose-response relationship are of great importance in the success of the treatment. Autologous stem cell transplantation (ASCT) is an important treatment option in the treatment of hematological malignancies such as multiple myeloma and lymphoma. While it finds a place in the first-line treatment of multiple myeloma, it is a very important treatment approach in chemosensitive relapse disease in diffuse large B-cell lymphomas. The place of ASCT in acute leukemias is controversial and other No significant superiority has been shown to treatment options. ASCT has also been used in some solid organ tumors other than M. myeloma and lymphomas. With the introduction of high-dose chemotherapy in the nineties, it has been shown that survival rates of 30% can be achieved even in patients with negative prognostic factors in germ cell tumors. It has been determined that autologous stem cell transplantation increases survival in childhood cancers such as medulloblastoma, soft tissue sarcoma, osteosarcoma, Ewing sarcoma, and retinoblastoma. Allogeneic stem cell transplantation HSCT is a treatment modality with a potential curative effect in many malignant and benign diseases. The use of a reduced-intensity conditioning regimen has also enabled transplantation in elderly patients. Developments in transplantation technology, advances in preventive and supportive treatments have led to positive developments in early and late-term outcomes of transplantation. Donors can be categorized as HLA-compatible sibling or other family donors and unrelated donors. A well-matched unrelated donor requires a 10/10 or 8/8 match in high-resolution class 1 (HLA-A,B,C) and class 2 (HLA-DRB1, -DQB1) antigen assessment. If there is at least 1 incompatibility at the antigen or allele level in HLA A,B,C or DR, an incompatible unrelated donor is mentioned. A haplo-idetic donor is defined as at least 1 haplotype among family members being genetically identical to the patient. Its most important advantage is that it is easier and faster to find a donor for many patients. The fact that graft versus host disease (GvHD) events are more common and the relative chance of relapse is a significant disadvantage. It can be successfully applied especially in malignant diseases such as acute myeloid and lymphoblastic leukemias, relapsed refractory lymphomas, relapsed refractory multiple myeloma and also in thalassemia, sickle cell anemia, immune deficiencies and autoimmune diseases.

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MANAGEMENT OF INHIBITORS IN HEMOPHILIA

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Introduction: The improved understanding of Acute Myeloid Leukemia (AML) pathobiology has led to significant advances in treatment options. AML is a highly heterogeneous disease, with clinical, morphological, cytogenetic, and molecular variability, which is crucial for developing targeted therapies within different subgroups. The "7+3" regimen (7 days of cytarabine and 3 days of daunorubicin) remains the standard, but its long-term efficacy is limited, with remission rates below 40% in younger, fit patients. In contrast, for older patients or those unsuitable for intensive chemotherapy, median survival is approximately 9 months, and 5-year survival rates are under 10%. Treatment strategies are typically tailored, with intensive chemotherapy preferred for younger/fit patients, and low-intensity therapies for older/unfit patients. This section reviews emerging targeted treatment options. **Antibody-Drug Conjugates (ADCs):** Gemtuzumab ozogamicin (GO), a CD33-targeted ADC combined with high-dose cytarabine, has increased survival rates from 50% to 75-80%. IMGN779, a novel anti-CD33 ADC, is highly effective against AML cells, including those with adverse molecular abnormalities, and its sensitivity is correlated with CD33

expression levels. AVE9633, another anti-CD33-maytansin conjugate, has shown promising results in Phase I trials with relapsed/refractory AML patients. Targeting CD123 with ADCs and exploring NK cell therapies offer hope for AML with measurable residual disease (MRD) or high-risk forms. **Bispecific T-Cell Engagers (BiTEs):** Bispecific T-cell engagers (BiTEs), such as AMG330 and AMG673, redirect T-cells or NK cells to AML cells, yielding a 20-30% response rate, though they are associated with significant side effects like cytokine release syndrome. These therapies may benefit MRD-positive AML patients in remission. T-cell immunotherapies, including flotetuzumab (FLZ), enhance T-cell activation and MHC-independent killing of AML cells, showing promise in overcoming chemotherapy resistance. **Checkpoint Inhibitors:** Immune checkpoint inhibitors targeting PD-1/PD-L1 are being explored in AML and Myelodysplastic Syndromes (MDS). Preclinical studies suggest potential benefits, but challenges remain in identifying biomarkers and optimizing combination therapies. Magrolimab, an anti-CD47 monoclonal antibody, has shown a 71% response rate and 45% complete remission (CR) when combined with azacitidine in TP53-mutant AML. **CAR-T Cell Therapies:** The success of CAR-T cell therapies in hematologic cancers has sparked interest in applying this approach to AML. Preclinical studies show that CAR-T cells targeting AML surface proteins, such as CD33 and CD123, can effectively eliminate AML cells. However, off-target toxicity due to antigen expression on healthy stem cells remains a concern. **NK Cell-Based Therapies:** Natural killer (NK) cells are being explored as an alternative to allogeneic cell therapies. NK cells can recognize and kill AML cells without causing graft-versus-host disease or cytokine release syndrome, offering a potentially safer treatment approach. **Conclusion:** In conclusion, with accumulating data, new treatment standards are being developed for AML, particularly for younger and older patients, including induction, consolidation, hematopoietic stem cell transplantation (HSCT), and maintenance therapy.

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ADVANCES IN THE ASSESSMENT OF MINIMAL RESIDUAL DISEASE (MRD) IN ALL

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General Information: A “positive” or “negative” MRD test result indicates whether measurable disease is detected above certain thresholds that may vary by test and laboratory. It is important to recognize that a negative MRD result does not necessarily indicate eradication of disease, but rather represents disease below the test threshold in the tested sample, and patients may still experience relapse. **MRD Methods:** ELN identifies multiparametric flow cytometry (MFC) and quantitative polymerase chain reaction (qPCR) among useful methods suitable for detecting MRD. Recently, innovative techniques such as digital PCR (dPCR), next-generation sequencing (NGS), and next-generation flow cytometry (NGF) have also been applied in the detection of MRD. **MRD in ALL:** In the study by Yilmaz et al., it was seen that earlier MRD negativity in Ph(-) B-ALL was associated with higher survival. The best results were obtained with Flow Cytometry MRD negativity after the 1st cycle (i.e. CR time). The 3-year relapse rate in early MRD negativity was still approximately 25%. Short NJ et al investigated the effect of CMR in Ph (+) B ALL. In 85 Ph+ ALL patients who were treated with Hyper-CVAD plus TKI and did not undergo HSCT in CR1, the median OS was 127 months in the group achieving CMR; OS was 38 months in those without CMR (P=0.009). CMR at 3 months was seen as the only prognostic factor for OS. In the study by Sasaki K et al. evaluating the effect of TKI selection on achieving 3-month CMR; 84 Ph+ ALL patients were treated with Hyper-CVAD plus TKI and CMR was achieved at 3 months. 5-year OS was found to be 84% with ponatinib. 5-year OS was found to be 60-65% with other TKIs. Ponatinib treatment was the only prognostic factor for PFS or OS. Ghobadi A et al found no benefit from allogeneic SCT in patients with Ph+ ALL who achieved CMR. Short NJ et al. compared the correlation and prognostic impact of NGS MRD and MFC MRD in Ph(-) ALL. NGS MRD (-) 5-year OS: 90%; NGS MRD (+) 5-year OS: 61%; MFC MRD (-) NGS MRD (+) 5-year OS: 62% were seen. 46% of the MFC MRD (-) group was NGS MRD (+). Blinatumomab for MRD in B-Cell ALL showed MRD negativity rate = 78% after 1 cycle in BLAST Study. Pulsipher MA et al viewed pretransplantation NGS MRD status as prognostic in pediatric ALL. Prospective follow-up for posttransplantation MRD was superior with NGS. Liang EC et al assessed NGS MRD up to 1 year after SCT for 139 patients after allogeneic SCT. Muffly L et al evaluated the correlation of NGS MRD with Peripheral Blood and Bone Marrow. Strong correlation (r=0.87; P<0.0001) was seen between PB and BM NGS MRD. MRD was detected in PB in 100% of those who relapsed after SCT and in 85% of those who relapsed after CAR T. Pulsipher MA et al. study, MRD assessment after CAR T Cell for ALL was considered prognostic. NGS-detectable MRD after tisagenlecleucel was independently predictive of EFS and OS in multivariate analysis. Short NJ et al evaluated the effect of NGS MRD for IG/TR in Ph+ ALL. The study enrolled adults with Ph+ ALL receiving first-line therapy. Disagreements between MRD assessment by PCR and MRD assessment by NGS are relatively common. RT-PCR for BCR::ABL1 is not prognostic in patients who achieve NGS MRD negativity. Ph+ ALL patients who achieve NGS MRD negativity have good outcomes regardless of PCR response. Flow cytometry in T-ALL has been validated in T ALL, including ETP. Good agreement between bone marrow and peripheral blood. NGS has not been validated in T ALL because the cells have not yet undergone a TCR rearrangement. **MRD Follow-up Periods:** In first-line ALL, MRD from bone marrow should be measured after the end of induction, during early consolidation (after approximately 3 months of therapy), and then approximately every 3 months for at least 3 years (5 years for patients with Ph-positive ALL in first remission who do not undergo HSCT). In patients undergoing HSCT, MRD should be assessed immediately before HSCT; serial MRD measurements should be performed after HSCT (approximately every 3 months).”

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CHANGING IMAGE OF TKIS: ORIGINAL, BIOSIMILAR AND GENERIC OPTIONS

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BCR-ABL is a 210 kDa protein that is required for the proliferation of CML-specific myeloid cells and has sustained kinase activity. Kinase activity provides uncontrolled signal transduction related to cell proliferation, apoptosis and adhesion. Although there are many tyrosine kinase enzymes, imatinib is especially effective on ABL, c-kit and PDGF-R-dependent tyrosine kinases. The advantage of TKI is that it inhibits more than one receptor and therefore the possibility of signaling is increased. Another advantage is that these compounds offer ease of use to patients since they are used orally. In general, TKIs are well tolerated in clinical practice compared to the toxicity of cytostatic drugs. Side effects are usually mild (grade 2 and lower) and occur early in treatment. Due to the emergence of imatinib resistance and intolerance, second generation TKIs were developed (Dasatinib, Nilotinib and Bosutinib). In nonclinical models, they are 30 to 300 times more potent than Imatinib and can inhibit most imatinib-resistant BCR-ABL mutations. Patients with the T315I mutation respond only to treatment with the third-generation TKI Ponatinib. The crystal form of a drug's active ingredient may cause differences in solubility, stability, density, melting point, processability. The original imatinib is produced in b-crystalline form, generics are mostly in crystalline form and have been observed to be less stable at room temperature than the b-form. Several in vitro and in vivo studies comparing the pharmacological properties of the reference molecule and generics have proven that both forms are equivalent. The high financial burden of these treatments can be a serious problem for both patients and patients. With the emergence of generic imatinib, the reimbursement policies of many countries have changed and generic drugs have become an alternative treatment option for CML patients. In addition to their possible positive effects, there are concerns about these drugs, including bioequivalence, efficiency, effectiveness, safety, tolerability, adherence, permanence and healthcare costs, due to the use of generic imatinib in healthcare systems. In many countries other than the USA and in Turkey, CML patients can access more than one generic imatinib, and this competitive environment generally results in significant cost reductions. In general, the efficacy and safety profiles of generic and original imatinib were found to be similar in almost all studies. In light of these results, it is possible to say that generic drugs have a generally manageable toxicity profile and are not inferior to the original molecule in terms of effectiveness. Two pharmaceutical equivalent or pharmaceutical alternative drugs containing the same active ingredient in the same molar dose are considered bioequivalent if their bioavailability (rate and degree of absorption) is within predetermined acceptance limits. Generic pharmaceutical products are placed on the market if they are therapeutically equivalent to the reference product containing the same active substance in the same molar dose. Considering the data in the literature, both in vitro and in vivo studies have shown that generic drugs are comparable to the original imatinib in terms of bioequivalence and bioavailability. In most studies, generic drugs have shown similar results in terms of efficacy and safety, both in newly diagnosed patients and after switching from the original.

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OPTIMIZATION OF TKI SELECTION IN CML: BALANCING EFFICACY, SAFETY, AND PATIENT PREFERENCES

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The long-term results from key studies such as ENESTnd, DASISION, and BFORE have helped guide first-line treatment decisions in chronic myeloid leukemia (CML). These studies compare the efficacy of different TKIs, including imatinib, dasatinib, and nilotinib, showing the potential benefits of second-generation TKIs in achieving deeper and faster molecular responses. Early molecular response (EMR) is a crucial prognostic factor, as patients who achieve EMR are more likely to have better long-term outcomes. Risk scores such as Sokal, EUTOS, and ELTS play a role in determining the appropriate first-line TKI, with higher-risk patients potentially benefiting from second-generation TKIs due to their more aggressive nature. Second-generation TKIs, including nilotinib, dasatinib, and bosutinib, offer enhanced potency over imatinib but come with distinct safety profiles. Nilotinib has demonstrated superior efficacy in terms of molecular response, but it is associated with cardiovascular risks, including QT prolongation. Dasatinib, while effective in achieving rapid molecular responses, can lead to pulmonary complications like pleural effusion. Bosutinib, which is less commonly used, has a more favorable gastrointestinal side effect profile but may have less activity in some resistant CML cases. Management of cardiovascular, pulmonary, and metabolic side effects is crucial in selecting the appropriate TKI for each patient, particularly for those at higher risk of cardiovascular or pulmonary issues. TKI resistance, primarily due to BCR-ABL1 kinase domain mutations, presents a challenge in CML treatment. Mutations such as T315I are particularly problematic as they confer resistance to most TKIs. Ponatinib, a third-line treatment, is highly effective against T315I and other mutations, but it carries significant cardiovascular risks, necessitating careful monitoring. Asciminib, a newer drug that targets BCR-ABL1 through allosteric inhibition, offers a promising alternative for patients with resistance to other TKIs, as it bypasses common mutations like T315I and is associated with a different side-effect profile. Off-target inhibition of kinases by TKIs is a significant contributor to their side-effect profiles. For instance, nilotinib has been linked to glucose metabolism disturbances, leading to hyperglycemia, whereas dasatinib may cause pulmonary hypertension due to PDGFR inhibition.

Understanding these molecular mechanisms helps in managing side effects and improving patient outcomes. Monitoring for these adverse effects and adjusting treatment accordingly is essential to minimize long-term toxicity while maintaining treatment efficacy. The concept of TFR, where patients discontinue TKI therapy after achieving sustained molecular remission, is gaining ground. Studies such as EURO-SKI, ENESTfreedom, and DASFREE have demonstrated that certain patients can safely stop treatment without relapse, provided they remain MRD-negative. Selecting the right candidates for TFR is critical, and patients must be closely monitored for minimal residual disease (MRD). Even after discontinuation, immunological changes and potential relapse mechanisms must be carefully tracked. In special populations such as pregnant women, pediatric patients, and the elderly, TKI therapy requires careful consideration. TKIs are contraindicated in pregnancy due to potential teratogenic effects, and fertility preservation options should be discussed with male patients. In pediatric CML patients, concerns about growth and development arise, and TKI dosing must be adjusted for optimal treatment without affecting growth. Elderly patients or those with comorbidities may require lower doses and closer monitoring to minimize toxicity while ensuring adequate therapeutic effects. This summary highlights key aspects of TKI therapy in CML, including treatment selection, resistance mechanisms, side effects, treatment discontinuation strategies, and considerations for special populations. Each of these factors plays a significant role in optimizing treatment and improving patient outcomes.

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THE EVOLVING ROLE OF PROTEASOME INHIBITORS IN CANCER TREATMENT

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Recent developments in tumor immunology have led to a shift from chemotherapy to targeted therapy, focusing on blocking the pathways that drive cancer. An important aspect of this approach is the personalization of treatment, as the same cancer can present different immunopathologies in different individuals. Genetic mutations or variations in gene expression serve as determinants for identifying molecules that should be targeted in treatment. This has given rise to the concept of personalized therapy. One of the key therapeutic pathways is the proteasome system. This system is essentially a circular enzyme system that helps eliminate substances that may pose a threat to the cell. Its primary role is to process and degrade intracellular antigens and present them to CD8 T lymphocytes, in conjunction with the Major Histocompatibility Complex (MHC I) and Class II genes. The proteasome system carries out this function with the help of the endoplasmic reticulum (ER) and autophagy. Proteins that are continuously produced in the body are corrected within the ER if they misfold, in order to prevent potential antigenic properties. If the amount of misfolded proteins in the ER increases, it overwhelms the ER's capacity, resulting in a condition known as ER stress. In this case, the misfolded proteins are sent to the proteasome system for degradation, or alternatively, the autophagic pathway is activated through the enzyme Beclin to eliminate these faulty proteins. These mechanisms are essential for maintaining cellular integrity and survival. This survival strategy applies not only to healthy cells but also to cancer cells. In fact, proteasome inhibition is increasingly being used in the treatment of various cancers, including Multiple Myeloma. When the proteasome system is inhibited, cancer cells are unable to eliminate toxic or misfolded substances, leading them toward apoptosis. Proteasome inhibition can occur at different levels within the body and is not limited to the nucleus. Different proteasomes are responsible for degrading different substances. Thus, rather than aiming to completely eliminate the proteasome system, future cancer treatments are focusing on the selective inhibition of specific proteasomes. Research is ongoing in this direction, with the goal of developing more targeted and effective therapies for cancer.

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IMPROVING TREATMENT OPTIONS IN POLYCYTHEMIA VERA: FROM INTERFERON TO NEW AGENTS

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Polycythemia Vera (PV) is a chronic myeloproliferative neoplasm characterized by the overproduction of red blood cells, often accompanied by increased white blood cells and platelets. The disease is primarily driven by mutations in the Janus kinase 2 (JAK2) gene, specifically the JAK2 V617F mutation, which is present in approximately 95% of patients. The clinical presentation of PV includes a range of symptoms that significantly impact the quality of life (QoL) of affected individuals. Common symptoms include fatigue, pruritus, headaches, and visual disturbances, which are often attributed to the hyper viscosity of the blood resulting from increased red blood cell mass. The diagnosis of PV is based on the World Health Organization (WHO) criteria, which include elevated hemoglobin or hematocrit levels, the presence of the JAK2 mutation, and evidence of bone marrow hypercellularity. Diagnostic challenges may arise due to overlapping features with other myeloproliferative neoplasms, necessitating comprehensive blood evaluations and sometimes bone marrow biopsies. The disease is associated with a significant risk of thrombotic events, including stroke and myocardial infarction, which can occur in up to 26% of patients. Furthermore, the risk of transformation to more severe forms of hematological malignancies, such as acute myeloid leukemia (AML) or myelofibrosis, is notable, with studies indicating a

transformation rate of approximately 10% over a 20-year period. Management of PV focuses on reducing the risk of thrombotic complications and alleviating symptoms. Phlebotomy is often the first-line treatment to reduce hematocrit levels, particularly in patients with high thrombotic risk. In cases where phlebotomy is insufficient or not tolerated, cytoreductive therapies, such as hydroxyurea, are commonly employed. However, approximately 25% of patients may experience inadequate responses or unacceptable side effects from hydroxyurea, necessitating alternative treatments. Ruxolitinib, a JAK2 inhibitor, has emerged as a promising option for patients who do not respond adequately to conventional therapies, demonstrating efficacy in reducing splenomegaly and symptom burden. In conclusion, PV is a complex hematological disorder with significant clinical implications. Early diagnosis and appropriate management are crucial to mitigate the risks associated with the disease. Ongoing research into novel therapeutic agents and treatment strategies continues to enhance our understanding and management of this condition, ultimately aiming to improve patient outcomes and QoL.

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TREATMENT OF MYELOFIBROSIS: PRESENT AND FUTURE

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Primary myelofibrosis (PMF) is a myeloproliferative neoplasm characterised by stem cell-derived clonal myeloproliferation often, but not always, accompanied by JAK2, CALR or MPL mutations. It is associated with bone marrow reticulin/collagen fibrosis, abnormal inflammatory cytokine expression, anaemia, hepatosplenomegaly, extramedullary haematopoiesis (EMH), constitutional symptoms, cachexia, risk of leukaemic transformation and shortened survival. Somatic mutations in MPN are classified as ‘driver’ and ‘other’ mutations. Driver mutations are JAK2, CALR and MPL, other mutations are ASXL1, SRSF2, U2AF1, IDH1/2, SF3B1, TET-2, DNMTA3A. SRSF2, ASXL1, and U2AF1-Q157 mutations indicate poor prognosis in PMF. RAS/CBL mutations predict resistance to ruxolitinib treatment. Type 1/like CALR mutation is associated with better survival. The hallmark of MF is the disruption of the JAK/STAT signalling pathway. **TREATMENT** In the treatment approach, allogeneic stem cell transplantation (ASCT) should first be positioned as a priority option. Then, treatment should be planned according to risk stratification for the control of anaemia and improvement of splenomegaly and related symptoms. The recommended treatment strategy is what we call risk-adaptive treatment, which is treatment according to risk groups and symptoms/symptoms. The general approach is observation in low-risk asymptomatic patients, treatment selection according to symptoms (constitutional findings, splenomegaly, anaemia) in the medium and low risk group, stem cell transplant-based treatment in the high risk group. If additional risk factors are present in the intermediate risk group, ASCT should be considered as an alternative and a patient-based approach should be taken as basis. In the absence of symptomatic splenomegaly, non-JAK inhibitor drugs may be preferred as first-line treatment for anaemia. Androgens, prednisone (can be used in addition to androgen therapy or alone), danazol, thymodomide, lenalidomide, erythropoiesis-stimulating agents (ESAs) can be used. Although luspatercept is approved for the treatment of anaemia associated with beta thalassaemia and low/intermediate risk MDS, it has been largely ineffective in MF patients. Response rates to each of these drugs range between 15-25%. In the 2nd step, JAK inhibitors, especially momelotinib and pacritinib, can be considered. These drugs exhibit erythropoietic activity as well as favourable effects on splenomegaly and systemic symptoms. Among the available JAKi, Momelotinib shows activity against all three major complications in MF, including anaemia, splenomegaly and constitutional symptoms. Ruxolitinib (RUX) is the first oral JAK1-2 inhibitor. It received FDA approval in 2011. Long-term data from the COMFORT-I/II studies showed a 30 per cent mortality reduction in intermediate-2/high-risk patients compared to the control group. COMFORT-I and II analyses found that a reduction in spleen size with ruxolitinib treatment correlated with longer survival. Fedratinib (FEDR) received FDA approval in 2019. In the JAKARTA study, FEDR was reported to significantly prolong patients' prognosis compared with placebo. Fedratinib is a treatment option for the treatment of symptoms and splenomegaly or for patients who are resistant or intolerant to ruxolitinib. It includes a warning regarding the potential risk of serious encephalopathy, including Wernicke's encephalopathy. Pacritinib is a selective JAK 2 inhibitor. It received FDA approval in 2022 in moderate-to-high patients. Momelotinib received FDA approval in 2023. JAK1, JAK2 and ACVR1 inhibitor; targets symptoms, splenomegaly and anaemia. The new therapies, complementary or independent with JAK inhibitors, aim to improve patients' responses and quality of life, going beyond current treatment limitations with a focus on improving anaemia, thrombocytopenia and fibrosis, with an impact on overall survival. One future combination appears to be Pelabresib + Ruxolitinib. In the MANIFEST II study, the $_{SVR35}$ response at week 24 was significantly higher in patients assigned to pelabresib+ruxolitinib compared to ruxolitinib alone (66% vs. 35%). At Week 24, at least one degree of improvement in bone marrow fibrosis was seen in 24.2% of patients who received ruxolitinib alone and 38.5% of patients who received pelabresib+ruxolitinib.In conclusion, PELA+RUX shows the potential to improve the four key features of MF with a significant reduction in splenomegaly, improvement in symptom score, improvement in anaemia and reduction in bone marrow (BM) fibrosis at Week 24.

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CAR-T CELL THERAPY IN CLL

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The treatment paradigm for chronic lymphocytic leukemia (CLL) has shifted dramatically with the FDA approval of lisocabtagene maraleucel (liso-cel) in March 2024. This marks a historic moment as it introduces the first CAR T-cell therapy for CLL, providing renewed hope to patients who have exhausted conventional treatment options. CAR T-cell therapy represents a remarkable advancement in personalized medicine and immunotherapy. By engineering a patient's own T-cells to target and destroy cancer cells, this innovative approach has demonstrated significant potential. Among CLL patients who undergo this therapy, approximately 25% achieve sustained remission lasting six years or longer, raising the possibility of a curative outcome in select cases. Achieving this milestone, however, has been fraught with challenges. Response rates to CAR T-cell therapy in CLL have traditionally been lower than those seen in other hematologic malignancies. Despite these hurdles, recent clinical trials have produced encouraging results, with overall response rates exceeding 75% in some studies, particularly when the therapy is combined with agents such as ibrutinib. A key distinction of CAR T-cell therapy lies in its one-time treatment model, in stark contrast to the ongoing management required by traditional therapies. While adverse effects, including cytokine release syndrome and neurotoxicity, remain significant concerns, these risks are increasingly well-managed with modern protocols. The transformative potential of this therapy outweighs these challenges for many patients. Looking to the future, ongoing research aims to enhance the efficacy and accessibility of CAR T-cell therapy. Scientists are focused on understanding why some patients respond more favorably than others and are exploring strategies to overcome resistance. The approval of liso-cel signals not just the addition of a new therapy, but a paradigm shift in the treatment of CLL. This pivotal advancement extends beyond a new treatment option. It signifies hope for patients who previously had limited choices, offering the possibility of durable remission and, in some cases, even a cure. With liso-cel, the fight against CLL enters a new era, one defined by innovation, resilience, and optimism.

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HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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Oral Abstracts

Adult Hematology Abstract Categories

Acute Leukemias
OP 1

PHARMACOVİGİLANCE OF DRUG-INDUCED LEUKEMİA: A DESCRİPTİVE STUDY OF FDA ADVERSE EVENT REPORTİNG SYSTEM FROM 1969-2024

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Background: Drug-induced leukemia is a recognized adverse drug reaction associated with specific classes of medications. This study aims to quantify the frequency of leukemia-related adverse drug reactions and identify the medications most implicated as potential causes in the FDA Adverse Event Reporting System (FAERS). **Methods:** Leukemia-related adverse events were analyzed from the FAERS database spanning the period from 1969 to June 30, 2024. The search terms included various leukemia subtypes, such as “acute myeloid leukemia” (AML), “acute lymphoblastic leukemia” (ALL), “chronic myeloid leukemia” (CML), “chronic eosinophilic leukemia” (CEL), “chronic myelomonocytic leukemia” (CMML), “chronic lymphocytic leukemia” (CLL), and “hairy cell leukemia” (HCL). Cases were categorized by generic drug names, and the number of FAERS reports associating specific drugs with leukemia as an adverse event was determined. Descriptive statistics were applied to analyze the frequency, distribution, and outcomes of the reported cases. **Results:** Between 1969 and June 30, 2024, FAERS recorded a total of 29,153,222 adverse events, of which 26,758 (0.0009%) were linked to leukemia. Of these cases, 11,947 (31.9%) resulted in death. AML was the most frequently reported leukemia subtype, accounting for 14,490 cases, followed by CML with 4410 cases and CLL with 4,276 cases. The age distribution indicated that AML was predominantly reported among adults, with 4,777 cases (32.97%) occurring in individuals aged 18-64 years and 4,877 cases (33.66%) in those aged 65-85 years. Notably, the medications most frequently associated with leukemia were those primarily used in its treatment, including cyclophosphamide, lenalidomide, and imatinib mesylate. **Conclusion:** Medications commonly employed in the treatment of leukemia were frequently reported in FAERS due to concerns regarding their ineffectiveness rather than their expected therapeutic benefits. This highlights the critical need for continuous pharmacovigilance to ensure the efficacy and safety of these therapeutic agents.

Keywords: advers events, leukemia, pharmacovigilance, drug ineffectiveness, drug-induced leukemia.

Table 1 – Distribution of cases by age range

Age	Leukemia Subtype						
	AML (n,%)	ALL (n,%)	CML (n,%)	CEL (n,%)	CMML (n,%)	CLL (n,%)	HCL (n,%)
0-1 Month	8 (0,06)	2 (0,07)					
2 Months-2 Years	96 (0,66)	74 (2,73)	6 (0,14)		4 (0,63)	2 (0,05)	
3-11 Years	363 (2,51)	293 (10,80)	36 (0,82)		9 (1,43)	2 (0,05)	
12-17 Years	305 (2,10)	220 (8,11)	60 (1,36)		6 (0,95)	5 (0,12)	
18-64 Years	4.777 (32,97)	964 (35,53)	1.935 (43,88)	13 (68,42)	181 (28,68)	1.155 (27,01)	93 (42,47)
65-85 Years	4.877 (33,66)	469 (17,29)	798 (18,10)	3 (15,79)	262 (41,52)	1.449 (33,89)	54 (24,66)
More than 85 Years	188 (1,30)	11 (0,41)	44 (1)	1 (5,26)	10 (1,58)	87 (2,03)	2 (0,91)
Not Specified	3.876 (26,75)	680 (25,06)	1.531 (34,72)	2 (10,53)	159 (25,20)	1.576 (36,86)	70 (31,96)
Totals	**14.490 (100)**	**2.713 (100)**	**4.410 (100)**	**19 (100)**	**631 (100)**	**4.276 (100)**	**219 (100)**

Table 2 – Patient Numbers and Mortality Rates by Leukemia Subtypes

Leukemia subtype	n	%	Total
AML	7.929	54.7	14.490
ALL	1.015	37.4	2.713
CML	1.472	33.3	4.410
CEL	3	15.7	19
CMML	245	38.8	631
CLL	1.261	29.4	4.276
HCL	22	10	219

Table 3 – The most frequently reported agents with their generic names

Drugs (in order of frequency)	Leukemia Subtype						
	AML	ALL	CML	CEL	CMML	CLL	HCL
Most frequent	Cyclophosphamide	Lenalidomide	Imatinib Mesylate	Imatinib Mesylate	Cyclophosphamide	Ibrutinib	Cladribine
2nd	Azacitidine	Cyclophosphamide	Nilotinib	Yellow fever vaccine	Azacitidine	Venetoclax	Adalimumab
3rd	Etoposide	Dexamethasone	Dasatinib	Hepatit A vaccine	Prednisone	Rituximab	Rituximab
4rd	Venetoclax	Methotrexate	Ponatinib	Lenalidomide	Lenalidomide	Cyclophosphamide	Cyclosporine
5rd	Lenalidomide	Blinatumomab	Cyclophosphamide	Bleomycin	Mycophenolate Mofetil	Lenalidomide	Infliximab

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Adult Hematology Abstract Categories

Coagulation Diseases
OP 02

MANAGEMENT OF BLEEDING IN A PATIENT WITH ACQUIRED HAEMOPHILIA A: A CASE REPORT

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Objective: Acquired haemophilia A (AHA) is a blood clotting disorder caused by the presence of autoantibodies that interfere with the function of factor VIII, often called factor VIII inhibitor (1). It has a prevalence of about one per million per year. Acquired haemophilia A is usually associated with autoimmune diseases, malignancies, skin disorders, drug interactions, and the postpartum period, and as many as 50% of cases have unknown causes (2). Bleeding often occurs under the skin (purpura/ecchymosis) and in soft tissues, and rarely in the joints (haemarthroses) (3). The presence of Factor VIII inhibitors causes a disruption in the intrinsic coagulation pathway, leading to prolongation of the activated partial thromboplastin time (APTT) parameter, which does not improve after mixing test, and has low Factor VIII activity (2). The management of patients with AHA aims to control bleeding and its complications and to eradicate factor VIII inhibitors. Immunosuppressive agents are usually used to eradicate factor inhibitors. In this study, we report a case of acquired haemophilia A presenting with spontaneous unprovoked bruising and discuss the approach to diagnosis and how to alert the clinician to suspect this potentially rare but devastating disease. **Case report:** A 67-year-old man presented to the emergency department with bruising on his left hand and right leg for approximately 10 days. The patient had no history of trauma. He had a history of hypertension and chronic obstructive pulmonary disease. Approximately 2 months prior to presentation, he had complained of bruising on his arms after taking medication (etodolac, ampicillin-sulbactam) (Figure 1). There had been no bleeding after the cholecystectomy. Physical examination revealed an anteroposterior diffuse haematoma extending from the right inguinal to the popliteal area and a haematoma on the dorsal aspect of the left hand (Figure 2). Other systemic examinations were normal. All laboratory results showed the initial complete blood count; normochromic anaemia, normal platelet count and prolonged activated partial thromboplastin time (APTT) with normal prothrombin time (PT). Liver and renal function tests were within normal limits. The test results showed very low factor VIII activity with normal von Willlebrand factor and fibrinogen levels (factor VIII activity: <0.4%). There was no improvement in the mixing test. The factor VIII inhibitor level was 96 Bethesda Units (BU). Workup for connective tissue disease and malignancy screening were otherwise negative. The patient's USG showed a $21 \times 20 \times 65$ mm haematoma in the muscle planes of the right thigh, which was drained by interventional radiology. The patient was then admitted to the haematology clinic and started on methylprednisolone at 1 mg/kg/day. However, recombinant factor VIIa followed by activated prothrombin complex concentrate was administered to the patient whose bleeding could not be controlled. In addition, the patient whose bleeding could not be controlled received three sessions of plasmapheresis every other day. After three weeks of steroid treatment, cyclophosphamide was added due to lack of response and treatment was continued for approximately 5 weeks. Factor 8 activity returned to normal after approximately two months and no inhibitor was detected after this period. **Conclusion:** Acquired haemophilia A (AHA) is a rare condition in which the body produces autoantibodies against factor VIII (1). Approximately half of cases are associated with a disease, and the others are idiopathic. The most commonly reported associations are autoimmune diseases, solid organ and lymphoproliferative malignancies, skin disorders, medications and pregnancy (2).Patients usually present with subcutaneous and mucocutaneous bleeding, followed by muscular, gastrointestinal, genitourinary and retroperitoneal bleeding (4). Our patient above presented with both subcutaneous and intramuscular haematomas.The first suspicion of this condition is usually based on a coagulation profile. This may show an isolated prolonged APTT ratio in a patient with unexplained bleeding. The platelet count will usually be normal. An isolated prolonged apTT raises two possibilities; either an absolute deficiency of intrinsic pathway coagulation factors, or the presence of antibodies or inhibitors to these factors (5). The BU test is performed to quantify the inhibitor titer and confirm the diagnosis. The stronger the inhibitor, the higher the BU (6). In general, a titer greater than 5 BU indicates a high titer inhibitor. Our patient had a reported inhibitor titer of 96 BU.Bypassing agents such as active recombinant factor VII have shown good results in stopping bleeding, while immunosuppressive drugs such as corticosteroids,

cytotoxic agents (cyclophosphamide, cyclosporine) and rituximab (anti-CD-20 monoclonal antibody) are often used to eradicate inhibitors (7).Our patient, who presented with diffuse bleeding in the right leg and left hand, was also difficult to treat due to high factor inhibitor level and was hospitalised for approximately one month.In conclusion, AHA should be recognised and treated rapidly, as delays in diagnosis can have serious consequences. In our patient, AHA was diagnosed rapidly and treatment and bleeding control were effective.

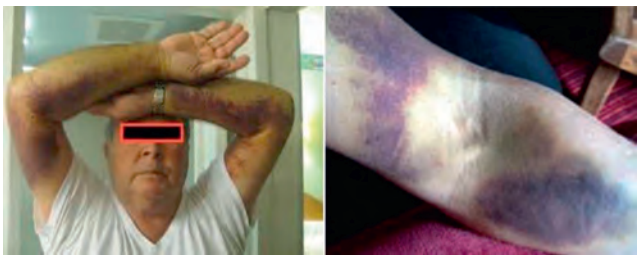

Figure 1: Ecchymosis on the forearms of both arms

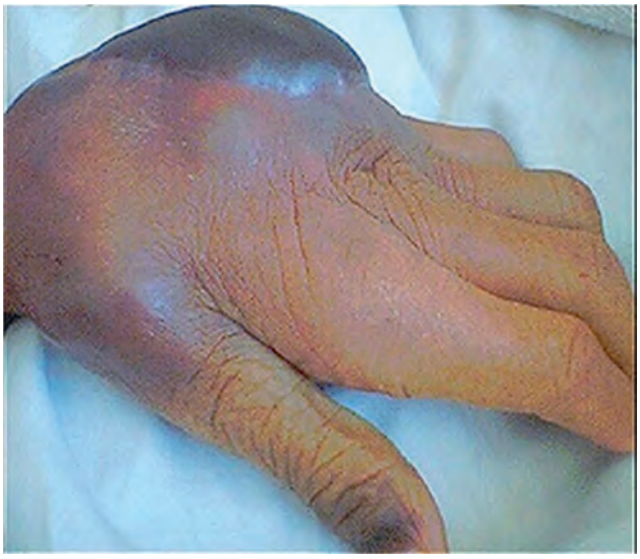

Figure 2:Ecchymosis on the dorsal left hand

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OP 03

NEWLY DIAGNOSED HEREDITARY FACTOR V DEFICIENCY IN A PATIENT PRESENTING WITH DEEP VEIN THROMBOSIS: A Rare Case

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Objective: Factor V (FV) is a crucial regulator of hemostasis, functioning as both a procoagulant and an anticoagulant glycoprotein within the coagulation cascade. In plasma, FV exists as an inactive precursor, which is activated by thrombin or factor Xa into its procoagulant form, FVa, contributing to the formation of the prothrombinase complex. Additionally, FV isoforms generated via alternative splicing, notably FV-short, exhibit anticoagulant properties by interacting with tissue factor pathway inhibitor-alpha (TFPIα), thus playing a role in regulating blood coagulation. Factor V deficiency is a rare condition characterized by a bleeding tendency, with a prevalence of approximately 1:1,000,000 in the general population. Clinical presentations can range from mild mucosal bleeding to severe hemorrhagic events. However, in rare cases, thrombotic complications may also occur, highlighting the heterogeneous clinical spectrum of FV deficiency. In this case report, we will discuss a patient who presented with deep vein thrombosis (DVT) and was diagnosed with FV deficiency. **Case report:** A 43-year-old female presented to the emergency department of Dicle University Hospital on July 21, 2024, with complaints of pain and swelling in her left leg. Physical examination and lower extremity venous Doppler ultrasonography revealed an echogenic thrombus within the distal iliac, femoral, popliteal, and proximal deep crural veins, leading to a diagnosis of deep vein thrombosis (DVT). Initial coagulation tests showed prolonged prothrombin time (PT) of 246 seconds, INR of 2.21, and activated partial thromboplastin time (APTT) of 38.2 seconds, with PT being more significantly prolonged. The complete blood count was normal. The patient was admitted to the cardiovascular surgery clinic for thrombolytic therapy and underwent thrombectomy and thrombolysis. Anticoagulant therapy with bemiparin sodium (HIBOR) was initiated. Due to abnormal coagulation tests, hematology consultation was requested. Further investigations showed normal lupus anticoagulant levels (1.16). Factor assays revealed a Factor V level of <6% (normal: 70-120%), while other factor levels were within normal limits. Anticardiolipin IgM and IgG were negative, and homocysteine was normal. APC resistance was measured at 0.64 seconds (normal: 0.91-1.19). Both Factor V Leiden and Factor II mutations were homozygous normal. Antithrombin III activity, as well as Protein C and S levels, were normal. ANA and anti-dsDNA tests were negative. A repeat Factor V level confirmed it remained <6%. The patient had no history of bleeding episodes and had not experienced bleeding complications during previous childbirths or minor surgeries. This case highlights the rare identification of Factor V deficiency in a patient presenting with deep vein thrombosis, an uncommon association, illustrating the complexity and variable clinical manifestations of Factor V deficiency. **Dıscussıon:** Factor V deficiency is a rare coagulopathy, typically characterized by a bleeding tendency, with an incidence of approximately 1:1,000,000 in the general population. The disease is inherited in an autosomal recessive manner and is caused by various mutations in the FV gene. As FV plays a critical role in both procoagulant and anticoagulant pathways, its deficiency usually manifests with symptoms such as mucosal bleeding, postoperative hemorrhage, and menorrhagia. However, paradoxically, some patients with FV deficiency have been reported to develop thrombotic events. In this patient, who presented with complaints of deep vein thrombosis, the absence of a bleeding history and lack of hemorrhagic complications during past surgical procedures highlights the

heterogeneous clinical presentation of FV deficiency. This supports the hypothesis that FV deficiency, due to its dual roles, may predispose not only to bleeding but also to thrombosis. Although the relationship between FV deficiency and thrombosis has not been fully elucidated, some potential mechanisms have been suggested. First, reduced TFPIα levels in patients with FV deficiency may disrupt the hemostatic balance, increasing the risk of thrombosis. Additionally, APC resistance observed in these patients could explain the hypercoagulability associated with FV deficiency. **Conclusion:** This case is significant in that it highlights the diagnosis of a rare Factor V deficiency in a patient presenting with deep vein thrombosis. While FV deficiency is typically characterized by a bleeding tendency, the predominance of a thrombotic complication in this case underscores the heterogeneous clinical course of this disorder and the challenges in its management. Although the development of thrombosis in patients with FV deficiency is rare, such cases emphasize the complexity of hemostatic balance and the necessity for individualized treatment approaches. Further case reports and a better understanding of the underlying mechanisms may lead to the development of more effective strategies for managing patients with FV deficiency.

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Adult Hematology Abstract Categories

Lymphoma
OP 04

EVALUATION OF THE IMPACT OF DEMOGRAPHIC DATA AND CLINICOPATHOLOGICAL RISK FACTORS ON TREATMENT RESPONSE AND SURVIVAL IN PATIENTS WITH PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA: A SINGLE-CENTER EXPERIENCE

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Objective: Primary central nervous system lymphoma (PCNSL) is a large B-cell lymphoma originating from specific regions such as the brain, spinal cord, and leptomeninges (1). The pathophysiology of PCNSL is not fully understood, but alterations in genes involved in the binding of immunoglobulins and B-cell receptors expressed in the central nervous system (CNS) and in NF-κB signaling are thought to play a central role (2,3). Other factors, such as T cells, macrophages/microglia, endothelial cells, chemokines, and interleukins, may also have important roles. The presenting symptoms of patients vary depending on the affected regions of the CNS (4). Standard treatment includes methotrexate-based polychemotherapy followed by age-adapted cytotoxic therapies and autologous stem cell transplantation (HDC-ASCT) (5,6). For patients ineligible for or unwilling to undergo transplantation, whole-brain radiotherapy (WBRT) or single-agent therapy may be used for consolidation (7). Personalized treatments, primary radiotherapy, or supportive care are options for patients with insufficient performance for treatment (8). Despite these treatments, 15-25% of patients do not respond to chemotherapy, and 25-50% relapse after an initial response. Although recurrence rates are higher in elderly patients, the prognosis of relapsed patients is poor, regardless of age (9). There is a need for further research to identify diagnostic biomarkers, develop more effective and less neurotoxic treatments, improve drug penetration into the CNS, and explore immunotherapies and adaptive cell therapies. **Methodology:** In this study, we aimed to evaluate the treatment responses and survival of patients with primary central nervous system lymphoma treated and followed at the Çukurova University Medical Oncology Clinic, based on their demographic data and clinicopathological risk factors. We reviewed the medical records of all lymphoma patients treated at our hospital, and 26 patients with central nervous system lymphoma were included in the study. We assessed the patients' age, gender, comorbidities, diagnosis dates, tumor locations, presenting symptoms, etiopathological factors, laboratory values, including baseline B2-microglobulin, IPI, and MSKCC scores at presentation. Pathology reports were evaluated for c-myc, Bcl-2, Bcl-6, and Ki-67 immunohistochemical markers, and FISH results, if available. The primary treatment options, treatment initiation dates, number of treatment cycles, best response, and its date were recorded. We also evaluated the radiotherapies received in addition to systemic chemotherapy. Disease progression, the date of progression, second-line treatments in case of progression, responses, and any autologous transplantation or maintenance therapies were documented. Survival outcomes, including progression-free survival and overall survival, were analyzed in relation to clinicopathological risk factors. **Results:** A total of 26 patients, 13 (50%) female and 13 (50%) male, were included in the study. The mean age was 56 (min 26- max 90). The most common comorbidity was hypertension. Regarding tumor localization, 8 patients had frontal lobe involvement, the most frequent site. The most common presenting symptoms were headache and seizures. At diagnosis, all patients required steroids, and 11 patients required antiepileptic drugs, while only 2 patients did not. Histopathological verification was performed in all patients, with all cases reported as diffuse large B-cell lymphoma. Only 1 patient had a history of hepatitis C as an etiological factor. Based on MSKCC scores at diagnosis, 8 patients were high-risk (score 3), 8 were intermediate-risk (score 2), and 8 were low-risk (score 1). Immunohistochemical analysis showed that c-myc was overexpressed in 10 patients (above 40%). Bcl-2 was positive in 12 patients, and Bcl-6 was positive in 19 patients. Five patients were triple expressors, and five were double expressors. Ki-67 ranged from 25 to 100, with 21 patients showing Ki-67 levels above 70% and 3 patients with levels above 95%. Pre-treatment laboratory tests revealed normal albumin levels in only 4 patients, while the majority had hypoalbuminemia. LDH levels were above the upper limit in

16 patients, and 3 patients had levels three times the normal limit. Inflammatory markers, including CRP and ESR, were elevated in 17 patients. The most commonly used first-line treatments were high-dose methotrexate with rituximab in 6 patients, methotrexate-rituximab-temozolomide (MTR) in 4 patients, and the MATRix protocol (methotrexate, cytarabine, thiotepa) in 3 patients. Radiotherapy, including whole-brain irradiation, was administered in 8 patients during or after first-line treatment. Ki-67 reached statistical significance when evaluating overall survival and progression-free survival with clinicopathological risk factors. No statistical significance was found for other pathological and clinical laboratory values. **Conclusion:** CNS lymphoma is a rare type of cancer that develops in central nervous system (CNS). PCNSL comprises ~4% of all primary CNS tumors. There are only about 1,500 new cases of CNS lymphoma diagnosed in each year. It occurs most often in people over 50, with the average age of diagnosis being 65. In our study, the average age of our patients was younger than the literature, and our average age was 56. It's slightly more common in men. People with HIV or AIDS and other immunodeficiencies are more likely to receive a CNS lymphoma diagnosis. Symptoms depend on where your tumor is located. A tumor is a mass of cancer cells. For instance, CNS lymphoma likely won't cause symptoms if the tumor's located in the membrane covering your brain and spinal cord. In contrast, a tumor near one or both eyes often causes vision changes. If the mass occurs near the area of your brain that controls movement, you could have weakness or coordination changes. Symptoms of CNS lymphoma may include: nause and vomiting, hearing loss, weakness in arms, legs or face, weakness affectşng one side of body, headaches, confusion, seizures. The most common reasons for admission of the patients included in our study were headache, unilateral weakness in the body and seizure. The brain parenchyma is the most common location. In our study, similar to the literature, the location of the tumors in all our patients was the brain parenchyma. Our study's findings were consistent with the literature regarding histology. However, we did not demonstrate a correlation between high-risk factors such as elevated LDH, performance scores, and double or triple expression with survival outcomes. Nevertheless, we confirmed the prognostic and predictive importance of Ki-67, in line with the literature. The lack of statistical significance for other prognostic factors may

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OP 05

RICHTER TRANSFORMATION OF CLL DISEASE: A CASE REPORT WITH CENTRAL NERVOUS SYSTEM INVOLVEMENT

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Objective: Richter transformation (Richter syndrome) is defined as the transformation of chronic lymphocytic leukaemia (CLL) into an aggressive lymphoma. Richter transformation is estimated to occur with a rate of 5-10% (1). In this article, we aimed to present a case of Richter transformation with central nervous system (CNS) involvement. **Case report:** In 2018, a 64-year-old woman who presented with lymphocytosis underwent flow cytometry examination and was diagnosed with chronic lymphocytic leukaemia (CLL). 6 cycles of Rituximab + Bendomustine treatment was administered. In 2024, the patient was admitted to the neurosurgery outpatient clinic with complaints of balance disorder, slowing of speech and facial slippage, and lesions were detected in the periventricular area at the level of basal ganglia in the brain (Figure 1). CSF examination did not reveal any findings in favour of lymphoma. A biopsy was taken from the intracranial mass. The biopsy result was reported as high-grade B- cell lymphoma. Transition from CHL to lymphoma was evaluated as Richter transformation. On PET CT examination, a 13*11 mm hyperdense lesion at the level of the left basal nucleus nucleus lentiformis, showing intense hyper metabolic activity compared to the surrounding parenchyma, showed central nervous system involvement of lymphoma. The patient was interned to the BMT ward and MATRIX protocol containing high-dose Ara-C and high-dose methotrexate with high CNS transmission was applied for a total of 3 cycles. Control brain imaging showed regression of the mass lesion observed in the previous examination. **Conclusion:** Central nervous system (CNS) infiltration is rare in Richter syndrome (RS). It has only been discussed at the case level (2). Various symptoms including headache, convulsions, diplopia, ataxia, facial paralysis and cognitive dysfunction are observed in these patients (3). In our patient, neurological findings including balance disorder, slowing of speech and facial slipping were observed. Central nervous system involvement was diagnosed by brain biopsy. When the literature is analysed, CNS involvement in these patients is very rare and usually demonstrated by CSF analysis. In a few patients, the diagnosis was made by brain biopsy as in our patient (3). In the literature, no optimal treatment has been reported in patients with Richter transformation with CNS involvement. Negative results have been shown despite treatments including high dose Methotrexate and Rituximab (1,2,3). In our case, successful results were obtained with MATRIX -C protocol including high dose Ara-C and high dose methotrexate. As a result of this treatment, regression was observed in control brain imaging. CONCLUSION: Richter transformation with CNS involvement is a rare but life-threatening condition. Close follow-up in the course of CLL, early diagnosis and initiation of appropriate chemotherapy may be life-saving. References: 1. PRONELLO, Edoardo, et al. Richter's syndrome of the central nervous system. Canadian Journal of Neurological Sciences, 2021, 48.6: 889-892. 2. Xu L, Song J Ch, Xiu H S, and et al. Richter's syndrome of the central nervous system diagnosed concurrently with chronic lymphocytic leukaemia: A case report and literature review. Medicine (Baltimore). 2018 Oct;97(41): e12701. 3. Nakanishi T, Ito T, Fujita Sh, etal. Refractory Chronic Lymphocytic Leukemia with Central Nervous System Involvement: A Case Report with Literature Review. J Blood Med. 2020; 11: 487–502.Figure 1: Intracranial mass appearance on computed tomography of the brain (marked with red colour)

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Adult Hematology Abstract Categories

Myeloma
OP 06

A TALE OF THE CRUMBLING AMYLOID WALL: BREAKING THROUGH LIVER STIFFNESS IN AL AMYLOIDOSIS

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Objective: Systemic AL amyloidosis is characterized by the deposition of misfolded amyloid fibrils in tissues, produced by clonal plasma cells. Daratumumab, a human IgG kappa-type monoclonal anti-CD38 antibody, is expressed on the surface of plasma cells, hematopoietic stem cells, regulatory T and B cells, monocytes, and dendritic cells. Due to this broad range of activity, daratumumab is thought to improve organ responses in AL amyloidosis through direct effects on tumor cells and via immunomodulatory mechanisms, providing additional therapeutic benefits. FibroScan, a noninvasive method for measuring liver stiffness, is routinely used today in the diagnosis and follow-up of chronic liver diseases. One condition that increases tissue stiffness is the accumulation of amyloid deposits in tissues. Various studies suggest that it can be useful in diagnosis when tested for this purpose. We aim to present two cases demonstrating that FibroScan can be a valuable tool not only in diagnosis but also in monitoring the progression of the disease. **Case report:** Case 1 A 53-year-old male patient was referred to our clinic after an incidental finding of M protein (2 g/dl) on serum protein electrophoresis requested at the Neurology Clinic, where he was being followed for epilepsy. An IgG lambda-type paraproteinemia was documented by immunofixation electrophoresis. His tongue was slightly noticeably enlarged. With suspicion of AL amyloidosis abdominal fat aspiration was performed, which revealed amyloid existence by Congo red stain positivity. He has no other organ involvement symptoms and signs but the liver was greater than normal size being 17 cm in the mid-clavicular line. The serum alkaline phosphatase (ALP) level was within normal limits. The liver elastography (FibroScan) result was 9 kPa, consistent with moderate scarring. He was monitored without intervention. Three years later when he developed peripheral neuropathy-related symptoms, AL amyloidosis management was decided. The liver size was similar and serum ALP level was still normal but the FibroScan result changed to severe scarring as being 9.1 kPa. Case 2 A 60-year-old female patient presented with a 20 kg weight loss over one year and chest pain. Imaging revealed diffuse infiltrates in the lungs. A bronchoscopy biopsy was consistent with AL amyloidosis. The patient had parenchymal lung involvement, anemia (Hb 9.7 g/dL), and an interventricular septal diameter (IVSD) of 1.5 cm. She was classified as Mayo 2012 stage 1 and Palladini renal stage 1. At diagnosis, her ALP level was 308 IU/L (laboratory upper limit: 130 IU/L) and her Fibroscan result was 51.2 kPa. The patient was started on daratumumab, bortezomib, cyclophosphamide, and dexamethasone therapy. After 18 months of monthly daratumumab treatment, follow-up measurements showed an ALP of 221 IU/L and a Fibroscan of 9.1 kPa. During the same period, hematological response was assessed as a very good partial response (dFLC: 19.6 mg/L), and NT-pro BNP decreased from 1558 to 512 pg/ml **Conclusion:** In the first case, liver stiffness measurements remained nearly stable over two years with a slight increase during clinical progression. In the second case, despite stage I cardiac and renal involvement, liver stiffness was very high and showed a striking reduction after treatment. Thus, liver stiffness may be an occult sign of liver involvement and may provide insights for monitoring disease progression

https://doi.org/10.1016/j.htct.2024.11.007

OP 07

A SINGLE-CENTER REAL-LIFE EXPERIENCE WITH FIRST-LINE DARATUMUMAB, BORTEZOMIB, CYCLOPHOSPHAMIDE, AND DEXAMETHASONE (DARA-VCD) IN AL AMYLOIDOSIS

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Case Report: Systemic amyloidosis results from the production of misfolded immunoglobulin light chains by monoclonal CD38 + plasma cells. These misfolded light chains form amyloid fibrils, which accumulate in various tissues and cause organ damage. Following the results of the Phase 3 ANDROMEDA study, where the addition of daratumumab, an anti-CD38 agent, to first-line treatment showed favorable outcomes, Dara-VCD has become a standard first-line therapy. In this study, we compared the outcomes of patients with AL amyloidosis who were treated with first-line Dara-VCD in our clinic to those treated with other triplet regimens. **Methodology:** Patient's data with AL amyloidosis followed between 2010 and 2024 were retrospectively reviewed from the institution's database. Two groups were established patients treated with Dara-VCD and those without Dara. The clinical characteristics and response criteria were compared using SPSS 21. **Results:** A total of 52 patients were included in the study, with a mean age of 60 ± 10 years for the entire group. There was no statistically significant difference in the demographic distribution between the groups ($p = 0.003$). The median follow-up period was 32 months (1-114 months). In 27 (51.9%) patients, cardiac involvement was present, and 26

(50%) had renal involvement. The stages of these involvements are summarized in Table 1. In the group treated without Dara, the triplet regimens were VCD (n=30), VRD (n=3), and VMP (n=2). Mortality was significantly lower in the Dara-VCD group. When evaluating responses, progression was only in 1 (9%) patient in the Dara group, whereas in 8 (32%) in the without Dara group. The overall survival was not statistically significant between the two groups (log-rank p=0.394). (Figure 1). **Conclusion:** We used Dara after Health Authority approval and reimbursement in our country. So, we get the opportunity to compare Dara-added VCD effectiveness to VCD or VRD as a real-life analysis. Dara-VCD resulted in a significantly lower rate of progression and mortality compared to those without Dara. The follow-up duration was shorter for comment on overall survival. Additionally, 10 patients without the Dara group, did receive daratumumab with VCD (n=5), or with other agents (n=5)). With this study, we documented from a real-life experience addition of daratumumab to the VCD regimen in first-line treatment reduces mortality and progression in AL amyloidosis.

Table 1 – Patient Characteristics

	Dara-VCD (n=17)	Other Triplet Regimens (n=35)	P-value
Age (mean ± std)	65±6	57±11	**0,003**
Gender (F/M)	10 (%58.8)/7 (%41.2)	14 (%40)/21 (%60)	0,202
Median follow-up (months)	15(1-68)	36 (1-114)	0,108
ECOG performance score >2	7 (%43.8)	11 (%33.3)	0,273
Mayo 2012 Staging System			0,954
Stage 1	6 (%37.5)	10 (%29.4)	
Stage 2	3 (%18.8)	7 (%20.6)	
Stage 3	5 (%31,3)	12 (%35,3)	
Stage 4	2 (%12.5)	5 (%14.7)	
Palladini et al. Staging System			0,166
Stage 1	7 (%43.8)	18 (%51,4)	
Stage 2	7 (%43.8)	7 (%20)	
Stage 3	2 (%12.5)	10 (%28,6)	
dFLC (mg/L)	106,5 (4-1945)	95 (0-2425)	0,624
hs Pro BNP (median)	1769 (25-30117)	1184 (17-25113)	0,4
eGFR (mL/min)	71 (2-106)	85 (9-124)	0,264
ASCT	3 (%17,6)	12 (%34,3)	0,214
Mortality	3 (%17,6)	18 (%51,4)	**0,02**
Treatment Response (Hematologic)			**0,042**
VGPR and above	8 (%72,7)	7 (%28)	
SD	2 (%18,2)	10 (%40)	
Progression	1 (9,1)	8 (%32)	

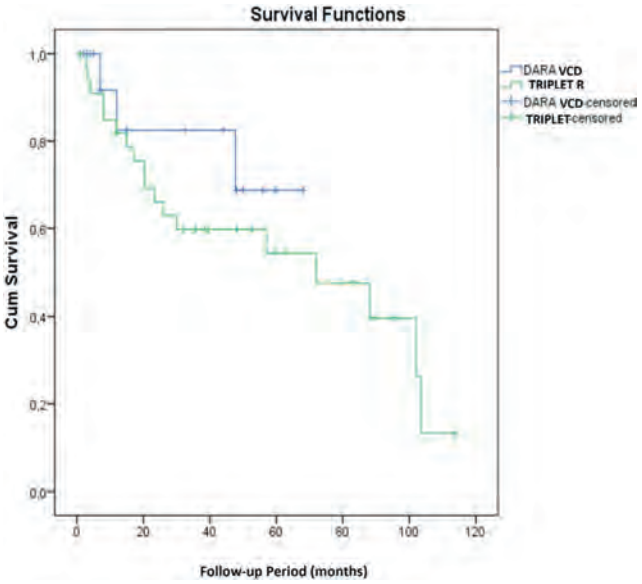

Figure 1: Overall Survival in Dara-VCD and without-Dara Triplet Treatment Groups

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OP 08

FROM MULTIPLE MYELOMA TO ACUTE MYELOID LEUKEMIA

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Objective: Multiple myeloma (MM) and acute myeloid leukemia (AML) are malignant clonal diseases of cells in different lineages. Only 79 cases of the two diseases occurring together have been reported in Pubmed in the last 10 years. However, simultaneous occurrence of MM and AML on presentation in chemotherapy-naive patients is rare, with only a 25 cases reported in the literature so far. [(1)]This case presents our experience with a patient who was diagnosed with AML shortly after the diagnosis of MM. **Case report:** A 57-year old male patient was referred to hematology due to pancytopenia. Serum immunofixation confirming monoclonal gammopathy of IgG kappa was detected. ß-2 microglobulin was found as 3,56 mg/dL. All routine tests required for MM diagnosis and follow-up were performed. (table 1) Bone marrow biopsy showed 40% plasma cell infiltration stained with CD38, CD138 and kappa. PET/CT scan revealed lytic lesions in the bones. t(4;14) was found positive in fluorescence in situ hybridization analysis. Bortezomib, lenalidomide, dexamethasone (VRD) regimen was started. After 4 cycles of VRD, the patient was hospitalized due to febrile neutropenia and severe dyspnea. Pulmonary embolism and pneumonic infiltration were not detected in thorax CT. However; bilateral septal edema and pleural effusion up to 3,5 cm were detected. Pleural fluid sampling was performed. No infectious agent was detected in exudative effusion. 3,25% myeloid blasts, 1,99% plasma cells were found by flow cytometry of pleural fluid. (figure 1) A bone marrow biopsy was performed again due to blasts in the pleural fluid results. Biopsy showed 40% myeloid blasts (CD117 and CD34) and 18% plasma cells in the bone marrow parenchyma. (figure 2) We decided to treat the patient with 7+3 induction chemotherapy (Idarubicin and cytarabine) with daratumumab and dexamethasone (Dara-d). After induction and one course of dara-d, bone marrow biopsy was performed again to evaluate response. The patient could not achieve remission and died due to acute respiratory failure. **Results Conclusion:** Multiple myeloma (MM) and acute myeloid leukemia (AML) may usually develop in the same patient but they are generally seen in MM patients receiving chemotherapy and in due course of treatment AML develops. (2) Presence of AML with MM in a shortly after treatment begins is an extremely rare occurrence. Concurrent diagnosis of these two hematological malignancies yields a poor prognosis. (3)References:(1) Jamal I, Shuchismita S, Choudhary V. Twin Malignancy of Acute Myeloid Leukemia and Multiple Myeloma in a Chemotherapy-Naïve Patient: A Rare Occurrence. J Lab Physicians. 2022 Oct 20;15(2):306-310. doi: 10.1055/s-0042-1757588. PMID: 37599817; PMCID: PMC10437150.(2) Parapia L, Abbott CR, Masters G, Roberts BE. Simultaneous pre

sentation of acute myelomonocytic leukaemia and multiple myeloma. Acta Haematol 1982;68(02):153–156 (3) Annino L, Martino P, Barsotti P, Serra P, MArinozzi V, Mandelli F. Multiple myeloma and acute myelomonocytic leukemia: simultaneous occurrence without previous chemotherapy. Acta Haematol 1980;64:195–200

Table 1 – Laboratory and bone marrow biopsy findings of the patient at the time of diagnosis

Laboratory tests	Results	Normal Value
Hemoglobin	8,00 g/dL	12,1 - 16,6
Total leukocyte count	2,51 × $10^3/\mu$L	3,46 - 10,04
Platelets	76 × $10^3/\mu$L	172-380
Creatinine	0,86 mg/dL	0,7 - 1,2
Serum immunoglobulin G	57,82 g/L	7-16
ß-2 microglobulin	3,56 mg/dl	-
Serum kappa free light chain	243	17-37
Serum lambda free light chain	10,8	9-21
Bone marrow plasma cell percentage	%35-40	

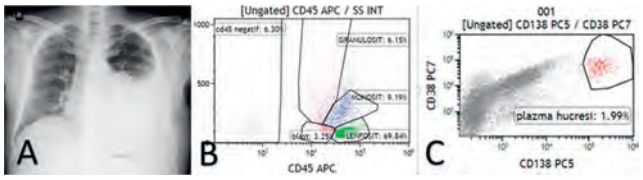

Figure 1: (A) Chest X-ray showed pleural effusion. (B) Pleural fluid was positive for myeloid blasts. (C) Plasma cell persentage of pleural fluid.

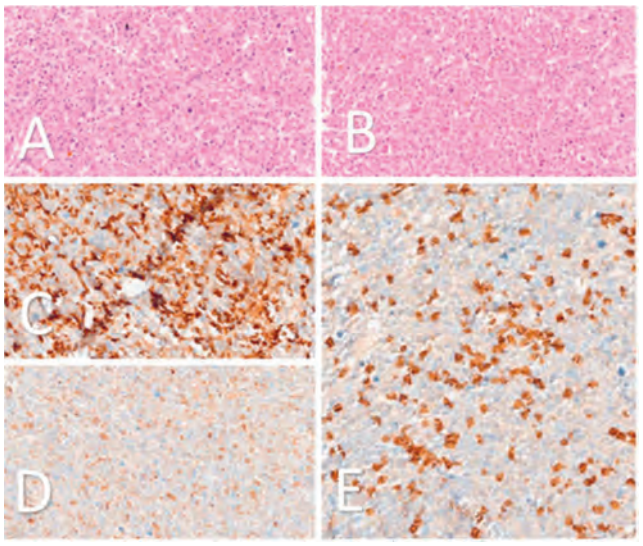

Figure 2: (A) Bone marrow biopsy, H & E stain × 40. The bone marrow is hypercellular. (B) Bone marrow biopsy, H & E stain × 40, The number of normal hematopoietic elements is markedly increased, the infiltrate consists of plasma vcells and blasts. (C) Approximately 40% CD34 staining in the bone marrow parenchyma. (D) CD117 staining cells are 18% of the mrrow. (E) Number of cells stained with CD138, 18% of parenchyma.

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OP 09

CASE REPORT: SIMULTANEOUS OCCURRENCE OF PLASMA AND B CELL MALIGNANCY

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Objective: Multiple myeloma (MM) and chronic lymphocytic leukemia (CLL) are two distinct hematological malignancies thought to arise at different stages of the B cell maturation pathway. Here, we aimed to present our approach to such a patient. **Case report:** A 59-year-old male patient was examined for hematuria in 2019, lymphocytosis was detected, and flow cytometry (FC) was performed. The result was found to be compatible with CLL. The patient was evaluated as Binet A, Rai 0 at the diagnosis, and was followed without treatment. In the fourth year of treatment-free follow-up, the patient developed severe B symptoms and widespread lymphadenopathies (LAP), splenomegaly (size 15.5 cm) on imaging, and shortened lymphocyte doubling time, so bone marrow aspiration biopsy (BMAB), FC and cytogenetic tests were performed. The patient had a CLL immunophenotype score of 1 in flow cytometry, and cytogenetics showed negative 17p del and TP53 mutations. In BMAB, 80% atypical morphology and immunohistochemical (IHI) examination showed small lymphoid cells with CD19(+), CD20(+), CD23(+), and CD5(+) staining. The patient was evaluated as Binet B, Rai 2, and got 6 cycles of Chemoimmunotherapy (Rituximab, Fludarabine, Cyclophosphamide). After treatment, B's symptoms regressed, and LAP and splenomegaly returned to normal. The patient developed neutropenia requiring granulocyte colony-stimulating factor (G-CSF) during follow-up, therefore, the patient underwent repeat BMAB. In the result, plasma cells with intense kappa positive staining were observed, and in the IHI examination, the CD38 and 138 positivity rates were evaluated as 20%. The patient, who did not have hypercalcemia, renal dysfunction, anemia, bone lesions, and extramedullary involvement, was assessed as MGUS, neutropenia resolved spontaneously during follow-up, and it was decided to follow the patient at three-month intervals without treatment. **Conclusion:** MM and CLL were rare in the same patient, and there is limited information regarding clinical outcomes and management. The clonal relationship between them is controversial.

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OP 10

THE PROGNOSTIC ROLE OF WHOLE BLOOD VISCOSITY AND BONE MARROW FIBROSIS IN PREDICTING SURVIVAL OUTCOMES IN NEW DIAGNOSIS MULTIPLE MYELOMA PATIENTS

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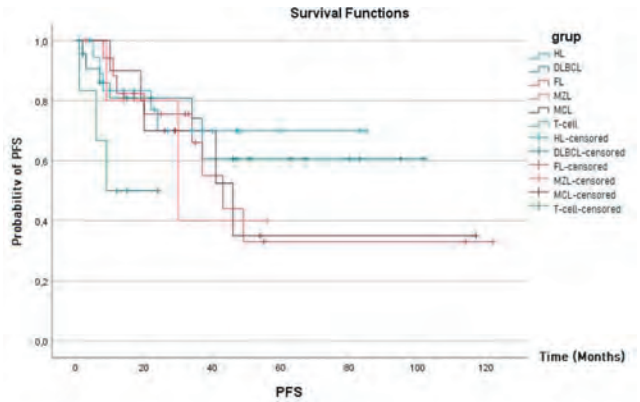
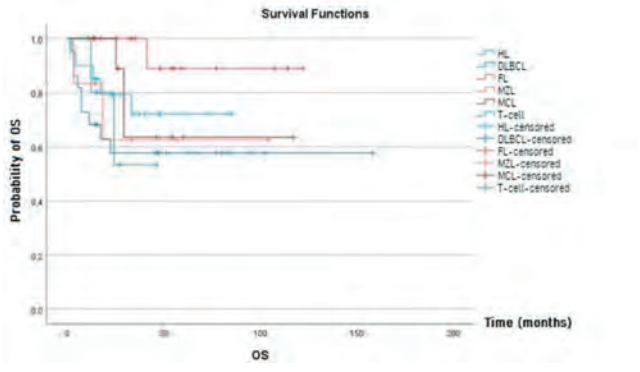
Objective: This study aimed to evaluate the prognostic role of whole blood viscosity and bone marrow fibrosis in predicting survival outcomes and relationships with prognostic predictors, such as international scorin system albumin levels, beta2-microglobulin, total protein, albumin and lactate dehydrogenase in newly diagnosed multıple myeloma patients. **Case report:** Methodology We retrospectively evaluated 108 patients diagnosed with multıple myeloma between 2015-2022. Whole blood viscosity was calculated using the Simone formula, incorporating the haematocrit and total protein values. Bone marrow fibrosis was graded as mild (2), significant (3), or advanced. Comparisons of grade 0-3 bone narrow fibrosis and high-low calculated whole blood viscosity groups in terms of overall survival were conducted using the Kaplan-Meier survival curve and log-rank test. **Results:** The median follow-up period was 16 months, and 57.4% of patients died during follow-up. The median overall survival was 26 months. The calculated whole blood viscosity (c-WBV) value predicted mortality with 88.7% sensitivity and 45.7% specificity. Patients with a high c-WBV (≥17.14 208 mPa-s) had significantly lower one- and two-year survival rates than those with a low c-WBV (<17.14 208 mPa-s) (p<0.001). Bone narrow fibrosis was inversely related to survival, with higher grades being associated with lower survival rates. The two-year expected survival time respectively bone narrow fibrosis 2 and 3 was determined to be 56.7% and 43.6% 41.4% and 23.3% (p<0.001). This study highlights the potential of whole blood viscosity and bone narrow fibrosis as prognostic markers in patients with newly diagnosed multıple myeloma patients. **Conclusion:** Incorporating these parameters into the existing staging systems may enhance prognostic prediction and guide treatment decisions. Further prospective studies are warranted to validate these findings and explore the mechanistic links between whole blood viscosity, bone narrow fibrosis, and MM pathophysiology.





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Adult Hematology Abstract Categories

Stem Cell Transplant

OP 11

SURVIVAL OUTCOMES OF AUTOLOGOUS STEM CELL TRANSPLANTATION IN LYMPHOMA PATIENTS

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Objective: Lymphomas, a diverse group of hematological malignancies, vary significantly in their prognosis, survival outcomes and response to treatment. High-dose chemotherapy followed by autologous stem cell transplantation (ASCT) has been frequently used to treat patients with relapsed or refractory lymphoma, offering a potential for long-term remission. However, survival outcomes after ASCT can differ substantially depending on the type of lymphoma. This study aims to compare survival outcomes across six different lymphoma subtypes—Hodgkin's lymphoma (HL), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), marginal zone lymphoma (MZL), mantle cell lymphoma (MCL), and T-cell lymphoma—in patients who have undergone autologous stem cell transplantation. While most reported data in the literature focus on a single lymphoma subtype, this study examined multiple subtypes within a single center, allowing for a direct comparison of survival outcomes. This study also aimed to compare these outcomes with survival and relapse rates reported in the literature, identifying potential areas for further investigation into the underlying causes of observed differences. **Methodology:** This retrospective study took place at Bezmialem Vakif University Hospital, İstanbul, Turkey. Medical records were reviewed of 81 patients from six

different lymphoma subtypes who underwent autologous stem cell transplantation (ASCT) between January 2012 and December 2023. We included 20 HL, 22 DLBCL, 17 FL, 6 MZL, 10 MCL, and 6 T-cell lymphoma patients. Lymphoma diagnoses were confirmed through pathology reports. Data were collected on each patient's age, sex, time of post-transplant relapse, time of death and last follow-up visit from patient records. Only patients who followed up at least 12 months after the ASCT were included for analysis. For survival analysis, research will evaluate overall survival (OS) and progression-free survival (PFS). PFS was defined as the time from transplantation to disease progression, relapse, or death from any cause, while OS was defined as the time from transplantation to death or the last follow-up. PFS and OS were calculated using the Kaplan-Meier method, and survival curves were compared using the log-rank test. Cox proportional hazards regression was used to evaluate the effect of age, sex, and lymphoma subtype on both PFS and OS. A p-value of less than 0.05 was considered statistically significant. Univariate and multivariate logistic regression were used to check how other factors might affect survival outcomes. **Results:** A total of 81 patients' characteristics are summarized in Table 1. Patients aged between 18 and 79 years, with a mean age of 45.79±16.01. A significant age difference was found between HL and other groups and between DLBCL and MCL patients ($p < 0.05$). 2-year PFS was %72.4 [Standart Error (SE)=%5.3] and OS was %77.6 (SE=%4.8) The estimated mean PFS for the six groups analyzed was 72.45±6.73(SE) months (95% CI 59.25%-85.65%) and the mean OS was 114.03±7.91 (SE) months (95% CI 98.51%-129.55%)(Table 2). When comparing the 2-year PFS for HL, DLBCL, FL, MZL, MCL, and T-cell results were 69.9% (SE=0.114), 80.9% (SE=0.086), 75.5% (SE=0.107), 80% (SE=0.179), 70% (SE=0.145), and 50% (SE=0.204) and 2-year OS were 79.3% (SE=0.092), 57.7% (SE=0.108), 100% (SE=0), 62.5% (SE=0.213), 88.9% (SE=0.105) and 53.3% (SE=0.248) respectively. When we compared PFS and OS durations among the groups, DLBCL had the best PFS with 70.2 months (SE = 9.59, 95% CI 51.4% −89%), while T-cell lymphoma had the worst PFS with 14.66 months (SE=3.92, 95% CI 6.96%−22.36%). For OS, the group with the best outcome was FL with 113 months (SE =8.48, 95% CI 96.36%−129.63%), and the worst outcome was T-cell lymphoma with 33.33 months (SE = 6.76, 95% CI 20.083% −46.583%)(Table 2). No significant differences in PFS ($p = 0.311$) or OS ($p = 0.263$) were observed between the groups based on the log-rank test, indicating no statistically meaningful variation in survival between the lymphoma subtypes. Cox regression analysis, adjusted for age and gender, revealed a significant difference in PFS between Hodgkin lymphoma and T-cell lymphoma ($p = 0.020$). However, no significant difference was found in OS (Table 3). Univariate and multivariate logistic regression analyses did not reveal any statistically significant differences between the groups. **Conclusion:** Our study revealed significant differences in survival rates among some groups. T-cell lymphoma patients had worse outcomes for both PFS and OS, while DLBCL showed the best PFS, and follicular lymphoma showed the best OS. Understanding these varying survival expectations after autologous transplantation in different lymphoma types can help identify strategies to improve success rates for those with shorter survival durations. When comparing our study to previous research, both similarities and differences were identified. For Hodgkin's lymphoma, our 5-year PFS was 69.9% and OS was 72.1%, they were higher compared to the 48% PFS and 53% OS reported by Majhail et al. The differences in subtype distribution, with 65% nodular sclerosis and 15% mixed cellular in our cohort compared to 87% and 8% in their study, may have contributed to this variance. For DLBCL, our 5-year PFS was 60.6%, which surpassed the 42.8% reported by Tun et al., possibly due to the younger average age in our cohort (45 vs. 59 years). For follicular lymphoma, the OS was observed to be much higher compared to other studies and to PFS. This may be due to the quick diagnosis and treatment processes in our clinic or the uneven distribution of the sample group. For other lymphoma subtypes, our findings were generally consistent with the literature. The primary limitation of our study is the small sample size, which likely influenced some of the observed differences. The absence of data on patients' risk factors and disease status at the time of ASCT is another

Table 1 – Patient Characteristics

	HL	DLBCL	FL	MZL	MCL	T-cell	Total
No. of patients	20	22	17	6	10	6	
Sex							
Male, *n(%)*	11 (55%)*	14 (63.6%)*	5 (29.4%)*	0*	8 (80%)*	2 (33.3%)*	40 (49.4%)*
Female, *n(%)*	9 (45%)*	8 (36.4%)*	12 (70.6%)*	6 (100%)*	2 (20%)*	4 (66.7%)*	41 (50.6%)*
Age							
Mean± Standard Deviation	33.15±15.160**	45.14±12.981**	49.59±11.587**	54.83±8.998**	55.60±14.065**	54.17±24.302**	
Median [Q1-Q3]	27[20-46]**	48[38.5-52.5]**	52[41-58.5]**	54[46.75-64.5]**	59.5[50.75-65]**	58[27.75-76]**	
Disease status after *ASCT*							
Progression, *n (%)*	5 (25%)	7 (31.8%)	8 (47.05%)	2 (33.33%)	5 (50%)	3 3 (%50)	30 (37%)
Mortalities, *n(%)*	5 (25%)	9 (40.9%)	1 1 (5.88)	2 (33.33%)	3 (30%)	2 (33.33%)	22 (27.2%)

HL Hodgkin Lymphoma, *DLBCL* Diffuse Large B-cell Lymphoma, *FL* Follicular Lymphoma, *MZL* Marginal Zone Lymphoma, *MCL* Mantle Cell Lymphoma, *ASCT* Autologous Stem Cell Transplantation, *p=0.008, **p<0.001

Table 2 – Mean for Survival

Subtypes	PFS Mean				OS Mean			
	Estimate	Std. Error	95% CI		Estimate	Std. Error	95% CI	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
HL	63.640	8.071	47.821	79.460	65.546	7.501	50.844	80.248
DLBCL	70.205	9.593	51.402	89.008	94.927	16.105	63.361	126.492
FL	60.899	13.367	34.700	87.098	113.000	8.485	96.369	129.631
MZL	36.200	9.543	17.495	54.905	69.250	19.674	30.689	107.811
MCL	61.075	15.882	29.947	92.203	84.429	15.081	54.870	113.988
T-cell	14.667	3.928	6.969	22.365	33.333	6.760	20.083	46.583
Total	72.452	6.735	59.252	85.652	114.038	7.918	98.519	129.557

HL Hodgkin Lymphoma, *DLBCL* Diffuse Large B-cell Lymphoma, *FL* Follicular Lymphoma, *MZL* Marginal Zone, Lymphoma, *MCL* Mantle Cell Lymphoma

Table 3 – Cox Regression for PFS and OS

	PFS				OS			
			95% CI				95% CI	
	p	HR	Lower	Upper	p	HR	Lower	Upper
age	.311	.986	.959	1.013	.793	1.004	.974	1.035
group	.290				.423			
HL-DLBCL	.515	1.516	.432	5.317	.365	1.733	.527	5.703
HL-FL	.251	2.059	.600	7.062	.143	.190	.021	1.754
HL-MZL	.357	2.377	.376	15.011	.805	1.263	.199	8.015
HL-MCL	.194	2.523	.624	10.199	.954	.954	.193	4.710
HL-T-cell	.020	7.663	1.385	42.389	.635	1.528	.265	8.805
sex	.743	1.146	.507	2.591	.851	1.096	.419	2.871

HL Hodgkin Lymphoma, *DLBCL* Diffuse Large B-cell Lymphoma, *FL* Follicular Lymphoma, *MZL* Marginal Zone Lymphoma, *MCL* Mantle Cell Lymphoma, *CI* Confidence Interval, *HR* Hazard Ratio

limitation. However, the strength of our study is the ability to compare six lymphoma subtypes within the same study. Further research is needed to focus on larger patient cohorts and incorporate detailed evaluations of risk factors in patients undergoing autologous transplantation.

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OP 12

RESULTS OF UNRELATED ALLOGENEIC STEM CELL TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Objective: Evaluation of data from unrelated hematopoietic stem cell transplants performed in our transplant center. **Methodology:** At the Private Emsey Hospital Adult Stem Cell Transplantation Unit were evaluated retrospectively between 2016 and 2023 to Allogeneic hematopoietic stem cell transplantations performed on 76 patients with different diagnoses from unrelated donors. **Results:** Data of patients with a mean age of 41.9 years were retrospectively analyzed. All donors were from a Turkish stem cell bank and 51% had HLA 1 allele incompatibility. 28 transplants were performed between different genders. Average follow-up was 17.3 months. Neutrophil engraftment occurred in an average of 18.1 days. Acute GVHD was detected in 26% and chronic GVHD in 41%. 1-year overall survival was 37% and disease-free survival was 32%. **Conclusion:** Non-relative stem cell transplantation is an important option especially in hematological diseases where there is no family donor and allogeneic transplantation is required. It has been observed that non-relative data performed in our clinic are similar to data from other centers.

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OP 13

MANTLE CELL LYMPHOMA PATIENT WITH SKIN GVHD AFTER AUOTOLOGOUS STEM CELL TRANSPLANT

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Objective: Graft-versus-host disease (GVHD) after ASCT is an immunologically developing process. T cells and inflammatory cytokines formed against the recipient'ss alloantigens are responsible for this. It is less common in autologous SCT than in allogeneic SCT. It has been reported in the literature that there are MM patients who developed autologous GVHD after Auotologous SCT. **Case report:** Here, we present a case

of mantle cell lymphoma who developed autologous GVHD after ASCT, not previously reported. Fifty-four-year-old male patient was diagnosed with Stage 4A Mantle cell lymphoma according to the Ann Arbor staging system based on the result of inguinallymph node excisional biopsy performed in July 2021. Three courses of R-CHOP,DHAP treatment was started for the patient who did not respond after R-CHOP treatment. Complete response was achieved after three cycles of R-DHAP therapy,and mobilization was performed with filgrastim and plerixafor protocol. Then, autologous SCT was performed with the BEAM protocol(Karmustine 300mg/m2, Etoposide 200mg/m2, Cytosine Arabinoside 2×100mg/m2, Melphalan 140mg/m2). Post-transplant neutrophil engraftment occurredon the+14th day and platelet engraftment on the +32nd day. Piperacillin Tazobactam was started due to fever and sore throat on the 3rd day of ASCT. Teicoplanin was added to the treatment after the fever persisted on the 5th day of ASCT. Piperacillin Tazobactam treatment was discontinued due to acute phase reactant increaseand fever on ASCT +7th day and Meropenem was started. Teicoplanin treatment was stopped on the +16th day after transplantation, and Meropenem was stopped on the +17th day. On the +14th day of autologous SCT, complaints of itching and rash started on the patient's body The biopsy result of the patient who underwent skin biopsy was compatible with grade 1-2 GVHD The patient was started on high-dose corticosteroid therapy. On the+21st day, the complaint of itching and on the +28th day, the skin findings disappeared. On the +28th day of ASCT, corticosteroid therapy was tapered and discontinued. The patient is still being followed without disease. **Conclusion:** Autologous GVHD is an autoimmune syndrome initiated by autoreactive T cells that recognize major histocompatibility complex (MHC) class II antigens.CD8+ T cells recognize MHC class II determinants .There are three types of autologous GVHD: 1. spontaneous autologous GVHD 2.induced autologous GVHD; using cyclosporine, tacrolimus, interferon-α, interferon-y and alemtuzumab to induce the effect of GVT; GVHD induced by transfusion of non-irradiated blood products in patients with Hodgkin lymphoma, Non-Hodgkin Lymphoma (NHL), chronic lymphocytic leukemia, and acute myeloid leukemia 3. induced by transfusion of non-irradiated blood products.In the study of Drobyski et al. in 2008, it was reported that autologous GVHD developed in 5 of 386 patients who underwent autologous SCT. Response to steroids was not good. It was the first transplant of 223muliple myeloma patients. Only 2 patients developed autologous GVHD. Autologous GVHD developed in 3 of 27 patients with a second transplant.Autologous GVHD did not develop in Hodgkin lymphoma, non-Hodgkin lymphoma and AML patients. Therefore, it will be important to consider this complication while planning the second autologous stem cell transplant in these patients .Our case presents skin GVHD developing after autologous SCT. However, since our patient has lymphoma and/or did not take a proteasome inhibitor before, it is important by distinguishing it from other cases.When the literature is examined, it is thought that the preparation regimens and post-transplant CsA application prepare the ground for autologous GVHD In addition, it is known that patients with hematological malignancies who are female, given high-dose CD34+ stem cells,bortezomib, lenalidomide, pomalidomide and alemtuzumab used in their pre-transplant treatments are at risk for autologous GVHD.

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OP 14

ACUTE GRAFT-VERSUS-HOST DISEASE (AGVHD) PRESENTING AS STEVENS-JOHNSON SYNDROME (SJS)

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Case report: This case report describes a 34-year-old male with AML, intermediate risk, initially treated with standard 7 +3 induction chemotherapy followed by high-dose cytarabine consolidation. Despite achieving medullary remission, minimal residual disease(MRD) persisted. The patient underwent allogeneic-HSCT from an HLA-matched sibling donor. At the 33rd-month post-transplant, the patient, in full donor chimerism, developed a pituitary macroadenoma and hypopituitarism, alongside CNS relapse and medullary remission was confirmed in the bone marrow. Management included cranial radiotherapy and pituitary hormone replacement. Subsequent bone marrow relapse was treated with salvage chemotherapy (high-dose cytarabine and mitoxantrone), achieving medullary remission. Persistent CNS disease necessitated intrathecal triple therapy until cerebrospinal fluid clearance. MRI response was also obtained. A second allogeneic HSCT was performed from the same donor using a myeloablative FLU-TBI conditioning regimen. GVHD prophylaxis consisted of Cyclosporine-A and Methotrexate. On post-transplant day +25, the patient presented with severe cutaneous manifestations with some bullous lesions initially suspected as aGVHD or drug eruptions. The patient was initiated on a high-dose corticosteroid (2 mg/kg prednisolone) as a primary treatment. However, due to an inadequate response, ruxolitinib(10 mg twice-daily) was added to the treatment regimen after the first week. Dermatological evaluation raised suspicion of SJS, leading to IVIG administration. The skin biopsy report indicated the possibility of grade 2 GVHD, although the possibility of a drug reaction could not be excluded. Significant clinical improvement was observed within one week of ruxolitinib initiation. Corticosteroids were tapered over six weeks to physiological replacement doses. Ruxolitinib was continued for 56 days before gradual discontinuation. Cyclosporine was maintained with target trough levels of 100-250 ng/mL and

discontinued on day +90 post-transplant. This case highlights the diagnostic challenges in differentiating aGVHD in the post-HSCT setting from SJS/TEN-like presentations. It emphasises the importance of rapid intervention and the potential efficacy of JAK inhibitors in steroid-resistant cutaneous GVHD.

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Adult Hematology Abstract Categories

Other Diseases
OP 15

RAB27A MUTATION AND EBV INFECTION ASSOCIATED HEMOPHAGOCYTIC SYNDROME: A CASE REPORT

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Objective: Hemophagocytic lymphohistiocytosis (HLH) is a nonmalignant immune regulation disorder within the histiocytosis group of diseases. It is a clinical condition in which there is fever, hepatosplenomegaly and cytopenia due to dysfunction of cytotoxic T-lymphocytes and natural killer (NK) cells, activation of macrophages and T-lymphocytes, excessive production of proinflammatory cytokines and hemophagocytosis. It can be primary (familial) and secondary. HLH may also be seen in the course of some immune deficiencies. We aimed to present a case of HLH that developed due to EBV infection and Griscelli syndrome with RAB27A mutation. **Case Report:** An 11-month-old male patient who presented with complaints of fever and swelling in the neck was hospitalized with respiratory distress and poor general condition. On physical examination hepatosplenomegaly, cervical lymphadenopathy and silver-gray hair color was detected. It was learned that the patient had a sibling who died at 3 months old with a similar phenotype. In his tests; wbc:10600/mm3, neu:5000/mm3, lympho:5100/mm3, hb:6.3 gr/dl, plt:29,000/mm3, ALT:167 IU/l, AST:410 IU/L, total bilirubin:2.7 mg/dl, direct bilirubin:2.6 mg/dl, sodium:126 mmol/L, albumin:2.3 g/L, LDH:765 U/L, fibrinogen:69 mg/dl, ferritin: 59334 ng/ml were detected. Hemophagocytosis was observed in the bone marrow. The patient was started on the HLH 2004 chemotherapy protocol, but died within the first 24 hours of treatment. The patient's tests at the time of admission showed EBV VCA IgM: 7.77 (positive), EBV PCR: 72,000 copies. A homozygous c.149delG (p. Arg50Lysfs*35) mutation was detected in the RAB27A gene. **Conclusion:** Griscelli syndrome is a rare autosomal recessive disease that can be accompanied by silver-gray hair, hypopigmentation, recurrent fever and infections, immune deficiency and neurological disorders. Primary HLH is common in our country due to the high prevalence of consanguineous marriages. The patients who cannot be diagnosed early and develop HLH can be fatal, so early diagnosis of these patients is of vital importance.

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OP 16

A CASE OF HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN A CHILD: A RARE AND CHALLENGING DIAGNOSIS

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Case report: Hemophagocytic lymphohistiocytosis (HLH) is an aggressive and life-threatening increased inflammatory syndrome characterized by over-activation of the immune system. Although it is more common in the first years of life, it can be seen in children and adults of all ages. HLH is divided into primary (familial) and secondary (sporadic). Secondary HLH may be associated with malignancy, rheumatologic diseases, chemotherapy or immunosuppressive therapies, but the most common cause is infections. Many viral, bacterial, fungal and protozoa infections can be triggers for both secondary and familial HLH. A 7-year-old male patient was admitted to our clinic with complaints of fever, malaise and anorexia. Blood tests revealed WBC:2260/mm^3, Hb:7.1 g/dL, ANS:920/mm^3, Platelets:41.000/mm^3, Fibrinogen:127 mg/dL, Triglycerides:247 mg/dL, Ferritin:687 ng/mL and splenomegaly on physical examination. Bone marrow aspiration (BMA) examination revealed hemophagocytosis. HLH was diagnosed according to HLH-2004 criteria and HLH-2004 protocol including dexamethasone and cyclosporine treatment was started. Fever, cytopenia and splenomegaly developed again during outpatient follow-up of the patient who responded adequately to the treatment. Ferritin level increased above 3000 ng/mL and another BMA was performed. This time, amastigotes were seen in addition to hemophagocytosis in the BMA evaluation. Leishmania rapid diagnostic test (RK-39) and PCR were positive. Liposomal amphotericin B treatment failed to elicit an adequate response. Meglumine Antimoniate (Glucantime) treatment was then initiated. No mutation was detected in the HLH genetic examination sent at the time of

the initial diagnosis. At the end of 4 weeks of treatment, PCR was negative and clinical improvement was seen. Visceral leishmaniasis (kala-azar) is an infectious disease caused by *Leishmania donovani* and *Leishmania infantum* and causes secondary HLH. In cases where there is no response to HLH treatment, evaluation for leishmania should be performed if it has not been done before. If diagnosed early, patients may recover with antileishmanial treatment alone. In cases of visceral leishmaniasis presenting with the hemophagocytic syndrome, if no response to amphotericin B treatment is obtained, Meglumine Antimoniate treatment should be considered for complete clinical recovery improvement.

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OP 17

CONGENITAL DYSERYTHROPOIETIC ANEMIA TYPE I: PATIENT WITH ANEMIA AND SKELETAL ANOMALY

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Objective: Congenital dyserythropoietic anemias (CDAs) are inherited anemias that affect the erythroid lineage. CDAs are classified into the 3 major types (I, II, III) according to morphological, clinical and genetic features. [(1)] Before genetic diagnostic methods, bone marrow morphological abnormalities were the key diagnostic features of CDAs, such as erythroid hyperplasia with thin internuclear chromatin bridges between erythroblasts, binuclearity or multinuclearity of erythroblasts.[(2)] Next generation sequencing (NGS) has revolutionized the field of diagnosis. CDA type I (CDAI) is characterized by severe or moderate anemia and congenital anomalies such as skeletal abnormalities, chest deformity and short stature with identification of biallelic pathogenic variants in *CDAN1* or *CDIN1*. [(3)] The standard clinical management of CDA patients is measurement of hemoglobin and iron, transferrin saturation and serum ferritin concentration to monitor iron overload every three to six months. **Case report:** 28 year old female patient presented to our clinic with normocytic anemia (hb: 6,50 g/dL), splenomegaly, short stature, limb and vertebral deformities. Clinically, the patient was evaluated for anemia. All routine blood investigations were done (Table 1). Bone marrow biopsy showed hypercellularity for age with increased rate in the erythroid series with marked dysmorphism findings. (figure 1) Next-generation sequencing was performed for diagnosis in the patient with dyserythropoiesis and morphological anomaly. Homozygous variant of CDIN1 gene was detected. Detailed NGS and karyotype analysis of the patient are shown in table 2 and 3. The patient diagnosed with congenital dyserythropoietic anemia type 1 and followed up with deferasirox and erythrocyte replacement. **Conclusion:** CDAs are characterized by clinical and genetic heterogeneities. NGS based testing allows diagnosis. The increased knowledge of the genetic features and the detailed phenotyping of these patients will allow for the earliest start of the necessary treatment for the affected patients, as well as the monitoring of hemoglobin and iron levels. References:(1) Iolascon A, Andolfo I, Russo R. Congenital dyserythropoietic anemias. Blood. 2020 Sep 10;136(11):1274-1283. doi: 10.1182/blood.2019000948. PMID: 32702750. (2) Roy NBA, Babbs C. The pathogenesis, diagnosis and management of CDA type I. Br J Haematol. 2019. doi: 10.1111/bjh.15817. (3) Heimpel H, Kellermann K, Neuschwander N, Högel J, Schwarz K. The morphological diagnosis of congenital dyserythropoietic anemia: results of a quantitative analysis of peripheral blood and bone marrow cells. Haematologica. 2010;95(6):1034-1036

Table 1 – Laboratory investigations

Laboratory Tests	Results	Normal Value
Hemoglobin	6,50 g/dl	12,1 - 16,6
Total Leukocyte Count	$4{,}09 \times 10^3/\mu l$	3,46 - 10,04
Platelets	$232 \times 10^3/\mu l$	172 - 380
Mean Corpuscular Volume	96,20 fl	81,8 - 98
Reticulocytes	$0{,}0747 \times 10^6/\mu l$	$0{,}0188 - 0{,}1086 \times 10^6/\mu l$
Total Bilirubin	1,15 mg/dl	< 1,2
LDH	126	135-214
İndirect Coombs	Negative	-
Haptoglobulin	<0,1 g/l	0,3 - 2

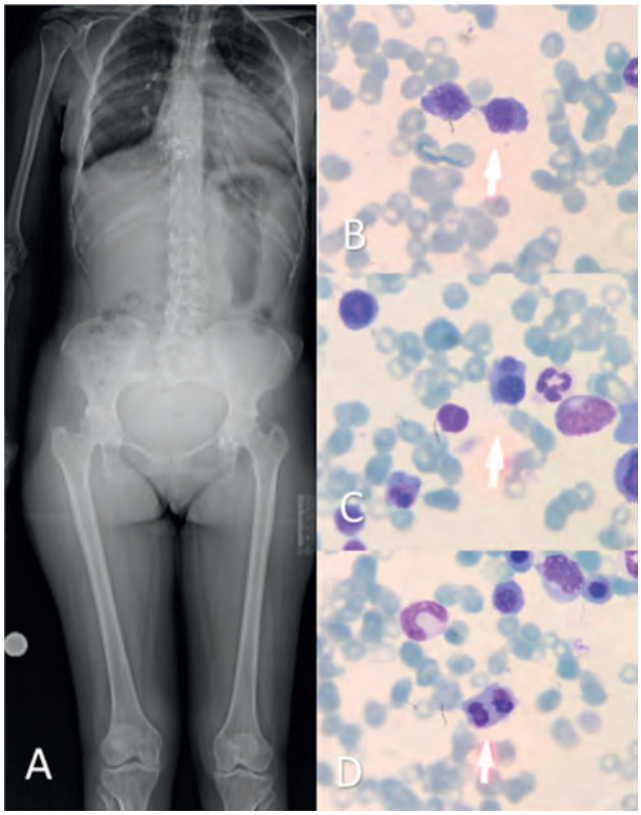

Figure 1: A) The patient's height was measured as 140 cm and scoliosis was detected in the skeletal survey. Bone marrow aspiration findings: **B)** Nuclear chromatin bridges between

erythroblasts. **C)** Binucleate erythroblasts **D)** Multinuclear eryhtroblasts.

Table 2 – Results of NGS analysis: Homozygous variant of CDIN1 gene was detected. (AR: Autosomal recessive, CDIN1: congenital dyserythropoietic anemia type 1, PRF1: perforin 1, TAF6: TATA-Box Binding Protein Associated Factor 6)

Gene transcript	Position	Inheritence	Genotype
CDIN1	Chromosome 15	AR	Homozygous
PRF1	Chromosome 10	AR	Heterosygotic
TAF6	Chromosome 7	AR	Heterosygotic

Table 3 – Cytogenetic analysis of the patient: With the cytogenetic analysis of the patient, tetraploid chromosome formation was detected in 17 of 18 of the metaphases as 92XXXX. (DEB: clastogenic effect of diepoxybutane, G6PD: Glucose-6-Phosphate Dehydrogenase)

Chromosomal analysis	92,XXXX	TP53 deletion	%85
Del20q12	%85	Del7q31.2	%83
Del5q31.2	%85	Tetrasomy7/tetrasomy8	%85
DEB	%0	G6PD	20,3 ıu/g Hb (normal)
Pyruvate kinase	397,9 (normal)	Osmotic Fragility of Erythrocytes	Normal

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OP 18

DETERMINATION OF FREQUENCY AND RISK FACTORS OF SECONDARY MALIGNANCY DEVELOPMENT IN HEMATOLOGICAL MALIGNANCIES

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Objective: Cancer remains a significant challenge within the healthcare system. According to the 2022 GLOBOCAN report, approximately 20 million people were diagnosed with cancer, and 10 million people passed away due to the disease. A significant improvement in the prevention, diagnosis, and treatment of cancer has resulted in a greater chance of overall survival for patients. Although survival rates for these patients have improved, they may be at risk for secondary malignancies. Secondary malignancy (SM) is defined as a tumor that differ from the primary tumor in terms of location, histopathology and genetics. Secondary malignancies could be classified into two categories based on the time of occurrence: synchronous tumors occur within six months of an initial primary cancer, while metachronous tumors occur after six months. Despite various genetic and environmental factors being implicated, the pathogenesis remains unclear. There are no standard protocols for screening, prevention, diagnosis, or treatment. Additionally, most studies on this topic conducted on data from the SEER (Surveillance, Epidemiology, and End Results) database. Although this database has the advantage of including many patients, it is insufficient to examine potential risk factors because it doesn't include individual medical information such as personal and family medical history, or alcohol and smoking use. In this study, we aimed to reveal the incidence of secondary malignancy in hematological cancer patients, analyze the potential risk factors and determine which factors are associated with the development of secondary malignancies. **Methodology:** This retrospective study was conducted on 2,003 patients diagnosed with Hodgkin Lymphoma (HL), Non-Hodgkin Lymphoma (NHL), Chronic Lymphocytic Leukemia (CLL), Essential Thrombocytosis (ET), Chronic Myeloid Leukemia (CML), Primary Myelofibrosis (PMF), Polycythemia Vera (PV), Myelodysplastic Syndrome (MDS) and Multiple Myeloma (MM) who applied to the Hematology Clinic of Bezmialem Vakif University Hospital between February 2012 and May 2024. Patients aged above 18 years and had adequate medical records were included in the study. Patients with a prior history of cancer or an inadequate medical history were excluded. The study group consisted of patients with secondary malignancies. Control subjects were matched to the study group based on age, gender, and diagnosis. Clinical parameters compared between the study and control groups included age, gender, presence of B symptoms, stage (early or advanced), primary involvement (nodal or extranodal), extranodal involvement, relapse, hematopoietic stem cell transplantation (HSCT), treatments received (radiotherapy and chemotherapy), modifiable risk factors (diabetes, hypertension, smoking, alcohol use), and a family history of cancer. For statistical analysis, occurrences of SM by the site of diagnosis were described by counts and frequencies. Differences between groups were evaluated by the pearson chi- square or fisher exact test. Logistic regression models were used to determine predictors of occurrence of SM in patients with hematological malignancies. Survival probabilities and relapse were estimated using the Kaplan-Meier method. Cox regression analysis was performed to evaluate the factors affecting survival times and relapse. The hazard ratio (HR) with corresponding 95% confidence interval was determined based on the Cox proportional hazards model. Statistical significance level was set as 0.05 and SPSS (version 28) package program was used in calculations. All p values < 0.05 were considered statistically significant. This study was approved

by Bezmialem Vakif University Ethical Committee (2024/50). **Results:** 1,757 of 2,003 hematological malignancies were analyzed, 51 of whom developed SM. There was no SM in patients with PV, and one patient with MDS was excluded for inadequate records. A total of 248 cases were selected as controls. The 299 patients with hematological malignancies had a median follow-up of 70 months (95% CI 46.7-93.2) and a median age of 64 years (range 24-89), and 154 (51.50%) were female. Among these 51 cases of SM, the mean time to secondary malignancy development was 103.61 months (95% CI 88.7-118.4), and 11 had synchronous (21.6%) and 40 had metachronous (78.4%) tumors (Figure-1A). A majority of SM were found in Non-Hodgkin Lymphoma (NHL) (n=26, 51%). The most common type of SM was lung cancer (n=9, 17.6%) (Figure-1B). In terms of age, gender, B symptoms, stage, primary and extranodal involvement, HSCT, chemotherapy, or modifiable risk factors, there was no statistically significant difference between patients with and without SPM. However, relapse and radiotherapy were significantly more common in the control (p=0.023 and p=0.038, respectively). Moreover, a family history of cancer was statistically significant in the study group (p= <0.001) (Table-1). In the multivariate logistic regression analyses, family history of cancer, no relapse, and no radiotherapy were associated with an increased risk of secondary cancer (Table-2). There were no significant differences in survival times between the groups (Figure-2A). Cox multivariate analysis showed advanced age and male gender to be risk factors for OS (Table-3). The mean time to relapse for hematologic malignancies was 106.6 months (range 98.8–114.4 months). SM patients had a longer time to relapse than controls (p=0.004) (Figure-2B). Cox multivariate analysis showed that patients who got autologous transplantation and those who did not develop secondary malignancy were at higher risk of relapse (Table-3). **Conclusion:** In conclusion, this study indicates that a family history, no relapse history, and no radiotherapy are associated with an increased risk of secondary malignancy development. Survival times between patients with and without secondary malignancy didn't differ significantly. It's also important to note that both synchronous and metachronous cases were included in our study. Interestingly, the study group had better clinical outcomes than the control group. The findings may be a result of a conscious and meticulous approach taken by patients with multiple malignancies and their clinicians. Therefore, early screening, follow-up, and a multidisciplinary approach should be considered in managing these patients from the moment of initial diagnosis. Further studies are needed to validate our findings and provide a more comprehensive understanding of the risk factors and outcomes associated with secondary malignancies.

	Synchronous n (%)	**Metachronous n (%)**	**Total n (%)**
HL	0 (0.0%)	7 (17.5%)	7 (13.7%)
NHL	7 (63.6%)	19 (47.5%)	26 (51.0%)
CLL	2 (18.2%)	3 (7.5%)	5 (9.8%)
ET	0 (0.0%)	5 (12.5%)	5 (9.8%)
CML	0 (0.0%)	1 (2.5%)	1 (2.0%)
PMF	0 (0.0%)	1 (2.5%)	1 (2.0%)
MM	2 (18.2%)	4 (10.0%)	6 (11.8%)
TOTAL	**11 (100.0%)**	**40 (100.0%)**	**51 (100.0%)**

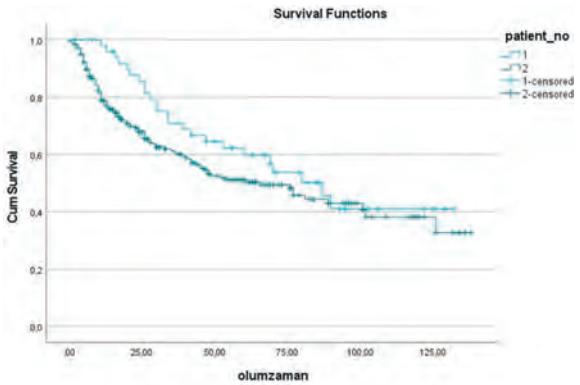
Figure-1A. The distrubution of secondary malignancies based on hematological malignancies.

	Synchronous n (%)	**Metachronous n (%)**	**TOTAL n (%)**
Lung	0 (0.0%)	9 (22.5%)	9 (17.6%)
Thyroid	3 (27.3%)	3 (7.5%)	6 (11.8%)
Breast	1 (9.1%)	3 (7.5%)	4 (7.8%)
RCC	1 (9.1%)	3 (7.5%)	4 (7.8%)
BCC	0 (0.0%)	3 (7.5%)	3 (5.9%)
Bladder	1 (9.1%)	2 (5.0%)	3 (5.9%)
Colon	0 (0.0%)	3 (7.5%)	3 (5.9%)
DLBCL	0 (0.0%)	2 (5.0%)	2 (3.9%)
Endometrium	1 (9.1%)	1 (2.5%)	2 (3.9%)
Pancreas	1 (9.1%)	1 (2.5%)	2 (3.9%)
Mesothelioma	1 (9.1%)	0 (0.0%)	1 (2.0%)
Larynx	0 (0.0%)	1 (2.5%)	1 (2.0%)
Rectal	0 (0.0%)	1 (2.5%)	1 (2.0%)
CMML	1 (9.1%)	0 (0.0%)	1 (2.0%)
Prostate	0 (0.0%)	1 (2.5%)	1 (2.0%)
GIST	0 (0.0%)	1 (2.5%)	1 (2.0%)
SCC	0 (0.0%)	1 (2.5%)	1 (2.0%)
Stomach	0 (0.0%)	1 (2.5%)	1 (2.0%)
Ovary	0 (0.0%)	1 (2.5%)	1 (2.0%)
Testicular	0 (0.0%)	1 (2.5%)	1 (2.0%)
Gallbladder	1 (9.1%)	0 (0.0%)	1 (2.0%)
Bowen	0 (0.0%)	1 (2.5%)	1 (2.0%)
Cervix	0 (0.0%)	1 (2.5%)	1 (2.0%)
TOTAL	**11 (100.0%)**	**40 (100.0%)**	**51 (100.0%)**

Figure-1B. Distribution based on the types of secondary malignancies.

Table 1 – Clinical features of patients

	With SM (N=51) Count (%)	Without SM (N=248) Count (%)	p
Age median (range)	66 (24-89)	63 (24-89)	0.423
Gender			0.934
Female	26 (51.0%)	128 (51.6%)	
Male	25 (49.0%)	120 (48.4%)	
Status			0.887
Alive	27 (52.9%)	134 (54.0%)	
Death	24 (47.1%)	114 (46.0%)	
B Symptoms			0.566
Absent	30 (58.8%)	135 (54.4%)	
Present	21 (41.2%)	113 (45.6%)	
Stage			0.083
Early	26 (51.0%)	94 (37.9%)	
Advanced	25 (49.0%)	154 (62.1%)	
Primary Involvement			0.326
Nodal	18 (35.3%)	106 (42.7%)	
Extranodal	33 (64.7%)	142 (57.3%)	
Extranodal Involvement			0.911
No	14 (27.5%)	70 (28.2%)	
Yes	37 (72.5%)	178 (71.8%)	
Relapse			**0.023**
No	48 (94.1%)	201 (81.0%)	
Yes	3 (5.9%)	47 (19.0%)	
HSCT			0.140
No	43 (84.3%)	226 (91.1%)	
Autologous	8 (15.7%)	22 (8.9%)	
Radiotherapy			**0.038**
No	36 (70.6%)	136 (54.8%)	
Yes	15 (29.4%)	112 (45.2%)	
Chemotherapy			0.335
No	6 (11.8%)	19 (7.7%)	
Yes	45 (88.2%)	229 (92.3%)	
Modifiable Risk Factors *(Diabetes, Hypertension, Smoking, Alcohol)*			0.206
No	8 (15.7%)	59 (23.8%)	
Yes	43 (84.3%)	189 (76.2%)	
Family History of Cancer			**<0.001**
No	36 (70.6%)	242 (97.6%)	
Yes	15 (29.4%)	6 (2.4%)	



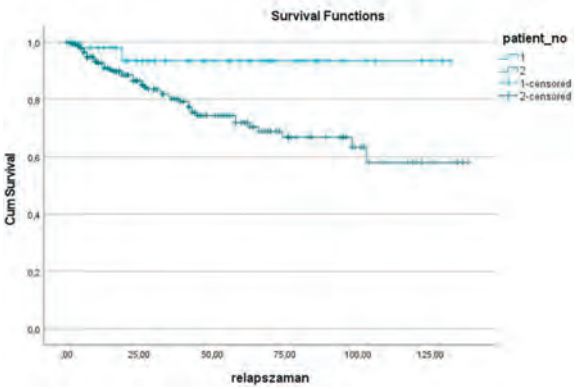


Table 2 – Multivariate analysis result to determine risk factors for SM development

	Multivariate OR (95% CI)	p
Stage		0.262
Early	1.47 (0.74-2.91)	
Advanced	1.00	
Relapse		**0.022**
No	5.18 (1.27-21.16)	
Yes	1.00	
Radiotherapy		**0.020**
No	2.44 (1.15-5.20)	
Yes	1.00	
Modifiable Risk Factors *(Diabetes, Hypertension, Smoking, Alcohol)*		0.179
No	1.00	
Yes	1.86 (0.75-4.64)	
Family History		**<0.001**
No	1.00	
Yes	21.90 (7.30-65.64)	

Table 3 – Risk factors for overall survival and relapse in patients.

	Multivariate HR (95% CI)	p
OVERALL SURVIVAL (OS)		
Age		**0.009**
Young	1.00	
Old	1.07 (1.01-1.13)	
Gender		**0.009**
Female	1.00	
Male	3.60 (1.37-9.44)	
Type of SM		0.157
Synchronous	1.00	
Metachronous	2.23 (0.73-6.78)	
Stage		0.779
Early	1.13 (0.43-2.93)	
Advanced	1.00	
Primary Involvement		0.089
Nodal	3.32 (0.83-13.26)	
Extranodal	1.00	
Extranodal Involvement		0.214
No	1.00	
Yes	2.13 (0.64-7.06)	
Relapse		0.879
No	1.34 (0.03-58.09)	
Yes	1.00	
HSCT		0.233
None	1.00	
Autologous	5.771 (0.32-102.5)	
Radiotherapy		0.622
No	1.00	
Yes	1.32 (0.42-4.07)	
RELAPSE		
Patients		**0.006**
with SM	1.00	
without SM	5.16 (1.59-16.17)	
Stage		0.429
Early	1.00	
Advanced	1.29 (0.68-2.45)	
Extranodal Involvement		0.969
No	1.00	
Yes	1.01 (0.48-2.12)	

Table 3 (*continued*)

	Multivariate HR (95% CI)	p
HSCT		**<0.001**
None	1.00	
Autologous	6.25 (3.40-11.51)	
Chemotherapy		0.203
No	1.00	
Yes	3.63 (0.49-26.44)	

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OP 19

FLT3-ITD POSITIVE ACUTE MYELOİD LEUKEMIA MIMICKING ACUTE PROMYELOCYTIC LEUKEMİA

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Objective: Acute myeloid leukemia (AML) is a heterogeneous disease due to genetic abnormalities and differences in immunophenotypes. The diagnosis of AML requires a careful evaluation of clinical morphology, immunophenotyping, cytogenetics, and molecular analyses. [1] In current practice, flow cytometry-based immunophenotyping provides a rapid and reliable method for diagnosing AML, including acute promyelocytic leukemia (APL). APL is a subtype of AML with distinct morphological, biological, and clinical characteristics. It can be effectively treated with ATRA-based therapy protocols. However, if not treated quickly, it can be fatal due to the risk of disseminated intravascular coagulation (DIC). Therefore, the diagnosis and treatment of APL represent a true medical emergency.[2] The absence of CD34, HLA-DR, and CD11b is a characteristic immunophenotypic feature that often distinguishes APL from other AML subtypes. However, AML subtypes other than APL that lack CD34 and HLA-DR expression have also been reported. APL accounts for 8% to 17% of AML patients. In AML patients without the PML-RARA fusion gene, 12% to 21% of cases have been identified as HLA-DR negative. These HLA-DR negative AML cases are distinct from APL because they do not carry the characteristic PML-RARA fusion.[3] HLA-DR and CD34 negativity is generally observed in AML-M1 and AML-M2 subtypes and is associated with nucleophosmin (NPM1) gene mutations and FMS-like tyrosine kinase-internal tandem duplication (FLT3-ITD) mutations.[4] NPM1 mutations are among the most common genetic abnormalities in AML, occurring in 27-35% of adult AML cases. Although rare, an "APL-like" immunophenotype has been reported in some de novo acute myeloid leukemia (AML) cases with NPM1 gene mutations. These cases show some immunophenotypic similarities to APL, despite being genetically different. AML cases with NPM1 mutations have unique clinical and biological characteristics.[5] In this study, we aimed to highlight the association of FLT3-ITD positivity, as opposed to NPM1, in HLA-DR negative non-APL AML cases in our clinic. **Methodology:** We examined three acute leukemia patients who were referred to our clinic within one month and were initially reported as APL based on flow cytometry analysis. Our focus on these patients stemmed from the fact that a condition with an incidence of 1-2 cases per 1 million people per year was diagnosed consecutively as APL in flow cytometry analysis within a short period. Fluorescent in situ hybridization (FISH) analysis for the 15;17 translocation and polymerase chain reaction (PCR) for FLT3-ITD and FLT3-TKD mutations were performed on the patients' peripheral blood. NPM1 mutations could not be analyzed in these patients. **Results:** Morphological examination of the patients' peripheral blood smears showed prominent nucleoli, Auer rods, and cup-like nuclei. Due to the CD34 and HLA-DR negativity in the flow cytometry analysis, these cases were initially considered APL. However, cytogenetic results revealed a negative t(15;17) translocation in all three patients, excluding APL. Additionally, all three patients tested positive for FLT3-ITD mutations. The peripheral blood white blood cell (WBC) count, blast percentage, and D-dimer levels were significantly elevated at the time of presentation in all patients. (Table 1) **Conclusion:** In cases with APL-like immunophenotypes, these similarities pose diagnostic challenges in daily practice. In this study, the APL-like AML cases exhibited CD34 and HLA-DR negativity and carried FLT3-ITD mutations. These de novo cases were characterized by high WBC counts, blast percentages, and elevated D-dimer levels. NPM1 is one of the most frequently mutated genes in AML, often seen alongside FLT3-ITD. Morphological and immunophenotypic similarities between many AML cases with NPM1 mutations and APL are well-known. In the first case, the blasts resembled the abnormal promyelocytes of APL (Figure 1.A). In the second case, a blast with a cup-like nucleus was observed (Figure 1.B). The "cup-like" nucleus morphology is specifically associated with acute myeloid leukemia (AML) with NPM1 gene mutations. The WBC count was very high in all cases a feature that is unusual for APL, especially the hypergranular variant. High WBC counts and blast cell percentages are typically described in NPM1-mutated AML.[6] Similarly, this could also be considered for FLT3-ITD, based on our findings. However, further studies with more cases are needed to confirm this. All patients demonstrated elevated D-dimer levels, which is more strongly associated with APL.[7] Unlike high D-dimer levels, fibrinogen levels were within acceptable limits. One patient had prominent gum hypertrophy, and frequent gum bleeding was observed during clinical follow-up. In conclusion, for cases with APL-like features but negative PML-RARA results by FISH and/or molecular methods, it is important to consider AML with NPM1 and/or FLT3-ITD mutations.

Table 1 – Clinical-Pathological Parameters of the Patients

	Patient 1	Patient 2	Patient 3
Age	34	35	57
Gender	Female	Female	Female
Hemoglobin(gr/dl)	6,3	9,4	8,8
Plateletes	12,000	75,000	91,000
Leukocytes(WBC)	159,000	120,000	307,000
LDH	841	405	471
Fibrinogen	246	419	341
D-dimer	7499	7853	1020

Table 1 (*continued*)

	Patient 1	Patient 2	Patient 3
Gum hypertrophy	-	+	-
Peripheral Blast %	%77,2	%89,8	90,9
CD 34	%9,8	negative	%1,4
CD 19	negative	negative	negative
CD13	%25	% 8	% 30,6
CD33	%99,8	%99,9	% 95
HLA-DR	negative	negative	negative
FLT-3 ITD	positive	positive	positive
t(15;17)PML/RARA	negative	negative	negative

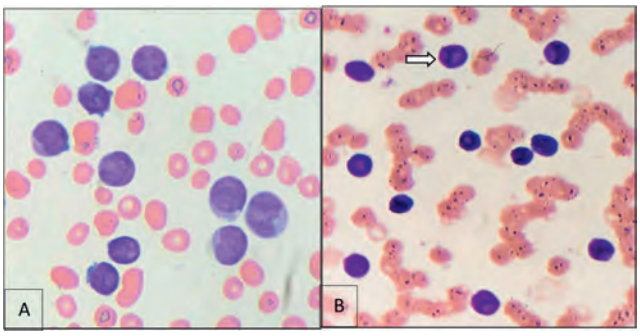

Figure 1: A) Blast Cells B) "Cup-like" Nucleus Morphology

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OP 20

A CASE OF ACUTE CORONARY SYNDROME DEVELOPING AFTER GRANULOCYTE COLONY STIMULATING FACTOR (G-CSF) ADMINISTRATION

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Objective: Common side effects after use of granulocyte colony-stimulating factor (G-CSF) include bone and muscle pain, headache, fever, and inflammation at the injection site. Less common side effects that cause serious morbidity and mortality in the early period include stroke, myocardial infarction (0.1%), and clinical conditions resulting from thrombosis, such as deep vein thrombosis . **Case Report:** A 60-year-old, Stage 3A, Multiple Myeloma (MM) patient with a very good partial response was planned stem cell mobilization with GCSF. The patient, who had no abnormalities in blood values and a normal cardiological examination approximately 1 month ago, was administered 10 micrograms/kg/day GCSF and approximately 6 hours after the first dose, the patient developed severe chest pain radiating to the left arm. The patient's ECG evaluation showed sinusoidal rhythm but tachycardia (115/beat/one minute). WBC: $29.7 \times 103/\mu$L, d dimer: 3510 μg/L and troponin: positivity. Angiography was performed on the patient because troponin values were increasing. A decrease in blood flow was detected in the LAD and right coronary artery branches. The patient's complaints improved with medical antiaggregant, anticoagulant and vasodilator treatment and he was discharged. **Discussion:** G-CSF acts as a regulator of myeloid progenitors and acts by promoting cell proliferation, differentiation, and maturation. The G-CSF receptor is found on hematopoietic stem cells, granulocytes, monocytes, and lymphocytes and also expressed on non-hematopoietic cardiovascular, neuronal, endothelial, and placental cells . there are rare reports that G-CSF and hematopoietic stem cells play a role in the development of atherosclerosis. Halter et al. reported in their study on 388 donors that 4 of the donors developed cardiac arrest within 30 days after stem cell mobilization, and 3 of these were due to myocardial infarction. This case is important in terms of emphasizing that we should follow the patient's clinical and biochemical evaluations very closely and be careful during the mobilization process.

https://doi.org/10.1016/j.htct.2024.11.021

OP 21

A HEMATOLOGICAL CHAMELEON: THE TRANSITION FROM MDS TO NON-SECRETORY MULTIPLE MYELOMA AND BACK – UNRAVELİNG DIAGNOSTIC COMPLEXITIES AND ADAPTING THERAPEUTIC PATHWAYS

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Objective: The interplay between myelodysplastic syndrome (MDS) and non-secretory multiple myeloma (MM) can confound even seasoned hematologists, particularly when these conditions shift over time. This case presents a remarkable instance of a patient transitioning from MDS to non-secretory MM and then reverting back to MDS, underscoring the need for meticulous monitoring and adaptable treatment strategies when dealing with complex hematological landscapes. **Case Presentation:** An 82-year-old patient initially sought care for severe anemia, leading to a diagnosis of MDS based on bone marrow findings. At this point, no signs of MM were present. However, later investigations—specifically urine immunofixation—suggested the emergence of non-secretory MM, which was confirmed through a second bone marrow biopsy. The patient began treatment with Velcade, Revlimid, and Dexamethasone (VRD), showing marked improvement in anemia. Yet, given the patient's age and frailty, hematopoietic stem cell transplantation (HSCT) was not considered viable. As treatment progressed, the regimen evolved to ixazomib, lenalidomide, and dexamethasone, achieving remission for several years. Despite this stability, a resurgence of anemia signaled a reversion to MDS. A fresh treatment strategy was introduced, combining azacitidine, low-dose lenalidomide, and erythropoietin, aimed at maintaining functionality and quality of life without aggressive interventions. **Discussion:**

This case encapsulates the volatile nature of hematologic disorders, illustrating how diseases like MDS and non-secretory MM can morph and evolve. It emphasizes the importance of adaptive management, especially in elderly patients, where rigid treatment paradigms may fall short. The use of lenalidomide throughout the patient's journey reflects its dual utility in both plasma cell and myeloid disorders, while also sparking questions about whether prolonged exposure could influence secondary disease development. **Conclusion:** The patient's journey through MDS, MM, and back again underscores the critical need for dynamic reassessment, vigilance, and personalized care. This case exemplifies the blurred boundaries between plasma cell dyscrasias and myeloid neoplasms, raising thought-provoking questions about disease progression and therapeutic strategies. In navigating these complexities, clinicians are reminded of the importance of flexible, patient-centered approaches in managing intricate hematological disorders.

Keywords: Myelodysplastic Syndrome, Non-Secretory Multiple Myeloma, Disease Evolution, Adaptive Treatment, Elderly Patient Care.

https://doi.org/10.1016/j.htct.2024.11.022

OP 22

BRAIN-INVOLVED MULTIPLE MYELOMA: STABILITY ACHIEVED WITH BENDAMUSTINE-POMALIDOMIDE, RADIOTHERAPY AND DARATUMUMAB-BASED THERAPY

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Objective: Multiple myeloma is a plasma cell malignancy that mainly affects the bones and skeletal system. The involvement of the brain as a site is very rare; it usually takes place via calvarial lesions with intracranial extension and is considered resistant to treatment. This report presents the case of a patient presenting with refractory MM and discusses in detail the efficiency of bendamustine-pomalidomide therapy and daratumumab-based maintenance after ASCT. **Case Report:** A 62-year-old female was diagnosed with kappa-positive MM in 2015, when plasma cell infiltration in the bone marrow was 20%. The patient underwent chemotherapy followed by ASCT in 2016. This patient attained remission after the transplant. Three years later, she presented with brain involvement, and MRI confirmed lesions of the parietal calvarium along with soft tissue expansion into the brain. The patient received radiotherapy to the affected area of the brain and initiated bendamustine-pomalidomide therapy; indeed, remarkable improvements were made in lesions of the brain and skeleton. Following that response, daratumumab, lenalidomide, and dexamethasone maintenance therapy was initiated to ensure ongoing disease control. Currently, the patient is clinically stable, with no evidence of further progression on follow-up imaging. **Discussion:** This case underlines the rarity of brain involvement in MM, as well as the role of ASCT as part of first-line treatment. The late appearance of extramedullary brain involvement three years post-transplantation truly epitomizes the whim of MM. Bendamustine-pomalidomide therapy was effective for refractory disease management, whereas daratumumab-based maintenance has helped maintain stability.

Keywords: Multiple Myeloma, Brain Involvement, Extramedullary Disease, Bendamustine, Autologous Transplantation.

https://doi.org/10.1016/j.htct.2024.11.023

OP 23

SUCCESSFUL LONG-TERM REMISSION IN AGGRESSIVE YOUNG-ONSET CHRONIC LYMPHOCYTIC LEUKEMIA WITH IBRUTINIB AND VENETOCLAX: A DECADE-LONG CASE STUDY

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Chronic Lymphocytic Leukemia (CLL) typically affects older individuals and is frequently associated with genetic mutations that help predict its progression. However, this report presents a rare case of aggressive CLL in a young woman with no unfavorable genetic markers, who achieved lasting remission following the use of dual targeted therapy, after standard treatments repeatedly failed. A 40-year-old woman was diagnosed with CLL during a routine blood examination. Despite lacking any high-risk genetic indicators, her disease advanced swiftly over the next ten years. Initial treatment with CVP (cyclophosphamide, vincristine, prednisone) provided only a brief partial remission. A subsequent course of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) also led to relapse within a few months. Ibrutinib was introduced as a single-agent treatment but failed to control the disease. The patient's condition continued to deteriorate, with recurring lymph node enlargement and rising lymphocyte counts. Three years ago, venetoclax was added to her treatment alongside ibrutinib. This combination therapy produced an extraordinary result—complete remission was achieved, blood counts normalized, lymphadenopathy disappeared, and bone marrow tests showed no trace of residual disease.

Keywords: Chronic Lymphocytic Leukemia, Early-Onset CLL, Resistant CLL, Venetoclax, Ibrutinib.

https://doi.org/10.1016/j.htct.2024.11.024

OP 24

SUCCESSFUL REDUCTION OF TRANSFUSION DEPENDENCE WITH LUSPATERCEPT IN A PATIENT WITH THALASSEMIA MAJOR: A CASE REPORT

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Objective: Thalassemia Major is a disorder of ineffective erythropoiesis with severe anemia, often requiring transfusions of RBCs throughout life. Transfusions are often required so frequently that the risk for iron overload and other complications strongly impairs the quality of life. Recently, this new erythroid maturation agent, luspatercept, has shown promise in reducing the transfusion requirements in patients with transfusion-dependent thalassemia. **Case Report:** A 40-year-old male patient with Thalassemia Major has been receiving regular erythrocyte suspensions since 2011, amounting to a total of 472 units by November 2023. The patient initially required an average of 2 units of RBCs per month to manage symptoms of fatigue and anemia. On February 17, 2023, the Luspatercept therapy was started at 75 mg every three weeks. Over the span of 22 treatments, one week after another, the need for RBC transfusions gradually diminished. The last transfusion was on November 21, 2023. The patient has since then maintained stable hemoglobin without further transfusion needs for approximately 10 months, a very impressive clinical improvement. **Discussion:** Therefore, this case offers a real-world view of the regard in which luspatercept proves effective in reducing transfusion requirements among patients suffering from Thalassemia Major. The sustained response for a period beyond 10 months really opens up possibilities for an overall better quality of life and reduction of the transfusion burden, which are important objectives in the management of transfusion-dependent patients. This report underlines early adoption of novel therapies such as luspatercept, which is considered instrumental in lessening complications resulting from chronic transfusions. This needs further studies and clinical discussions to optimize the dosing and duration of treatment in similar patients. This case adds to the growing body of evidence regarding the integration of erythroid maturation agents into standard management in patients with thalassemia.

Keywords: Thalassemia Major, Luspatercept, Transfusion Dependence, Erythrocyte Suspension, Ineffective Erythropoiesis.

https://doi.org/10.1016/j.htct.2024.11.025

OP 25

PLEURAL EFFUSION DEVELOPING AS A CONSEQUENCE OF G-CSF ADMINISTRATION IN A PATIENT UNDERGOING AML TREATMENT

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Objective: Human granulocyte colony-stimulating factor (G-CSF) plays a vital role in boosting neutrophil production from hematopoietic progenitor cells, both in lab settings and within the human body. Beyond just raising neutrophil counts, G-CSF primes these cells, enhancing their ability to defend the body, making it a key player not only for neutropenic patients but also for those who are immunocompromised but not necessarily neutropenic. G-CSF is widely used in treating acute myeloid leukemia (AML), either alongside or following chemotherapy. One of its primary benefits is to speed up neutrophil recovery after chemotherapy, reducing both the length of hospital stays and the risk of infection. Here, we share a case involving a 17-year-old male with AML who developed pleural effusion after receiving G-CSF during his cytotoxic treatment. **Case Report:** The patient, a 17-year-old male, came to our clinic with an elevated white blood cell count and was subsequently diagnosed with acute myeloid leukemia (AML) after a bone marrow aspiration. He was immediately started on the 7+3 induction chemotherapy protocol. During the post-chemotherapy phase, when his neutrophil levels dropped, filgrastim (G-CSF) was introduced to help reduce the risk of infection and shorten the neutropenic period. For the first five days, everything seemed normal, and no side effects were noted. However, after that initial period, the patient began to experience worsening shortness of breath. Imaging revealed a growing pleural effusion on the left side. A diagnostic thoracentesis was performed, and the fluid was drained to provide relief. The analysis confirmed the fluid was transudative, with no signs of infection or malignancy. When the pleural effusion returned, G-CSF was promptly stopped, and the effusion rapidly resolved. After consolidation therapy, G-CSF was reintroduced, and once again, pleural effusion reappeared on the third day of treatment, but this too resolved spontaneously once the G-CSF was discontinued. A pleural biopsy showed no pathological findings, confirming that the G-CSF was likely responsible for the effusion. **Discussion:** In neutropenic patients, pleural effusion is typically linked to infections, but in this case, no signs of infection or AML involvement were found. The recurring pleural effusion, which resolved after stopping G-CSF, suggests a rare side effect of the treatment. Research indicates that G-CSF may trigger local inflammatory responses, including elevated cytokines like IL-6 and TNF-α, potentially leading to fluid accumulation in the pleura. This case highlights the importance of monitoring for unusual side effects during G-CSF therapy in AML patients.

Keywords: G-CSF, AML, pleural effusion, neutropenia, cytokine response.

https://doi.org/10.1016/j.htct.2024.11.026

OP 26

MODERATE CLINICAL COURSE IN SEVERE ANAEMIA

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Introduction: Although iron deficiency anemia is more common in children and women, it can also occur in adult men, depending on their socioeconomic status and health conditions (1). Symptoms of anemia, such as dyspnea, tachypnea, tachycardia, pallor, heart failure, and cognitive dysfunction, can vary based on the severity of the anemia, its onset speed, the patient's age, and physiological condition. In young and generally healthy individuals, chronic anemia may go unnoticed until hemoglobin levels fall below a critical threshold or until physically demanding situations arise (2). We present a case of iron deficiency anemia with a hemoglobin level of 2.8 g/dL, yet the patient did not exhibit anemia symptoms that would disrupt hemodynamics. **Case Report:** A 43-year-old male patient with mental retardation secondary to meningitis during childhood presented to the emergency department in September 2024 with complaints of weakness, fatigue, and exertional dyspnea. On physical examination, blood pressure was 90/60 mmHg, heart rate was 94 bpm, respiratory rate was 18/min, skin and conjunctiva were pale; other findings were normal. Laboratory results showed WBC: $9.2 \times 10^3/\mu$L, hemoglobin: 2.8 g/dL, hematocrit: 9.1%, and platelet count: $365 \times 10^3/\mu$L. The patient was clinically admitted due to severe anemia. LDH and indirect bilirubin levels were normal. Peripheral smear revealed severe hypochromia and microcytic erythrocytes. No schistocytes or atypical cells were observed. For the etiology of anemia, serum Fe: 7 μg/dL TIBC: 294 μg/dL, ferritin: 3.6 ng/mL, folate: 6.68 ng/mL, and vitamin B12 was 375 pg/mL. Due to the hemoglobin level of 2.8 g/dL, the patient received 3 units of red blood cell suspension. After replacement, hemoglobin increased to 7.4 g/dL, and iron replacement was planned. Considering the patient's mental retardation and the difficulty in regular medication adherence, parenteral iron replacement was administered. The patient was discharged with a recommendation for follow-up in 2 weeks. **Results:** According to many anemia grading systems, a hemoglobin level dropping below 6.5 g/dL is considered life-threatening, and patients are theoretically expected to experience a range of symptoms (3). However, the literature reports cases where individuals sought medical assistance with hemoglobin levels below 3 g/dL and hematocrit levels below 10% (4,5). Despite our patient having a hemoglobin level of 2.8 g/dL at the time of admission, serious anemia symptoms such as tachycardia and tachypnea were not observed. As a result, as seen in our male patient, the activation of adaptive mechanisms in chronic anemia can allow for a mild clinical presentation. Even at critical hemoglobin levels, patients may present with moderate symptoms

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Acute Leukemias
PP 01

ACUTE MYELOID LEUKEMIA PRESENTING AS ACUTE PANCREATITIS WITH MULTISYSTEM LEUKEMIC INFILTRATION: A CASE REPORT OF PANCREATIC, BILIARY TRACT AND PULMONARY INVOLVEMENT

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[1] *Dicle University*

Objective: Acute myeloid leukemia (AML) classically presents with symptoms related to anemia, infections, or bleeding. However, atypical presentations involving abdominal pain, acute pancreatitis, and biliary ducts infiltration are rare but have been documented. These unusual manifestations can complicate the diagnosis and delay recognition of AML. Here, we present a case of a young female patient diagnosed with AML, who initially presented with acute pancreatitis and subsequent findings suggestive of biliary tract infiltration and possible pulmonary involvement. **Case Report:** A 22-year-old female with no notable medical history presented to a local healthcare facility with abdominal pain and diarrhea. She was diagnosed with acute pancreatitis based on clinical evaluation. Abdominal ultrasonography revealed a mass at the head of the pancreas, along with dilatation of both intrahepatic and extrahepatic bile ducts. The patient was referred to Dicle University Educational Hospital for further investigations, including endoscopic retrograde cholangiopancreatography (ERCP). Upon admission to the general internal medicine clinic, the pancreatic mass and biliary duct dilation were confirmed, and further laboratory investigations showed an elevated white blood cell count as 24.900/mm3. A peripheral blood smear demonstrated abnormal white cells, raising suspicion of a hematologic disorder. A bone marrow biopsy was subsequently performed, confirming the diagnosis of AML. Magnetic resonance cholangiopancreatography (MRCP) was conducted to further assess the pancreatic and biliary tract lesions, revealing findings consistent with extramedullary hematologic infiltration. The patient was started on the 7+3 chemotherapy regimen (cytarabine 200 mg/m2 for 7 days and an idarubicin 12 mg/m2 for 3 days). Following treatment, her abdominal pain and distension improved, and laboratory abnormalities normalized, but She died because of neutropenic sepsis during 35th day of treatment. **Conclusion:** AML can exhibit extramedullary involvement of any organ, though pancreatic, biliary tract, and hepatic enzyme abnormalities are rare and occurs in approximately 8–10% of cases. A study from one center indicated that the most common sites of extramedullary AML involvement are the skin (65%), the central nervous system (23%), and the pleura (7%) . Multiorgan involvement has been reported in around 9% of cases, but pancreatic and biliary duct infiltration is extremely rare, accounting for only 1% of cases. In our case, the patient exhibited involvement of the pancreas, biliary tracts, spleen, and lungs, a situation that is exceedingly rare, with no similar cases found in the existing literature.

Keywords: Extramedullary, Leukemia, Myelogenous, Acute pancreatitis.

https://doi.org/10.1016/j.htct.2024.11.029

PP 02

AN AML CASE PRESENTING WITH EXTRAMEDULLARY MYELOID SARCOMA

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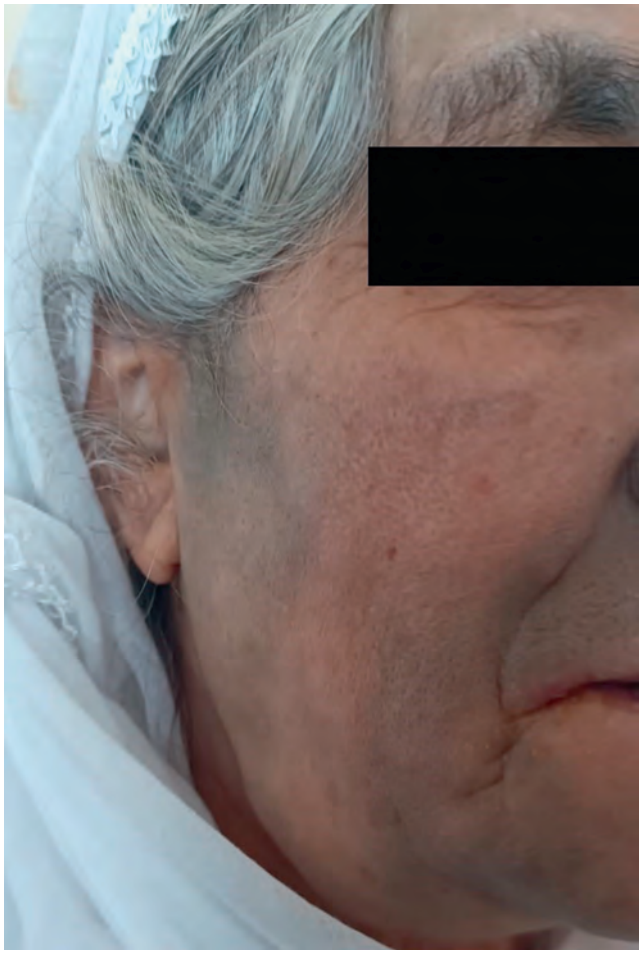
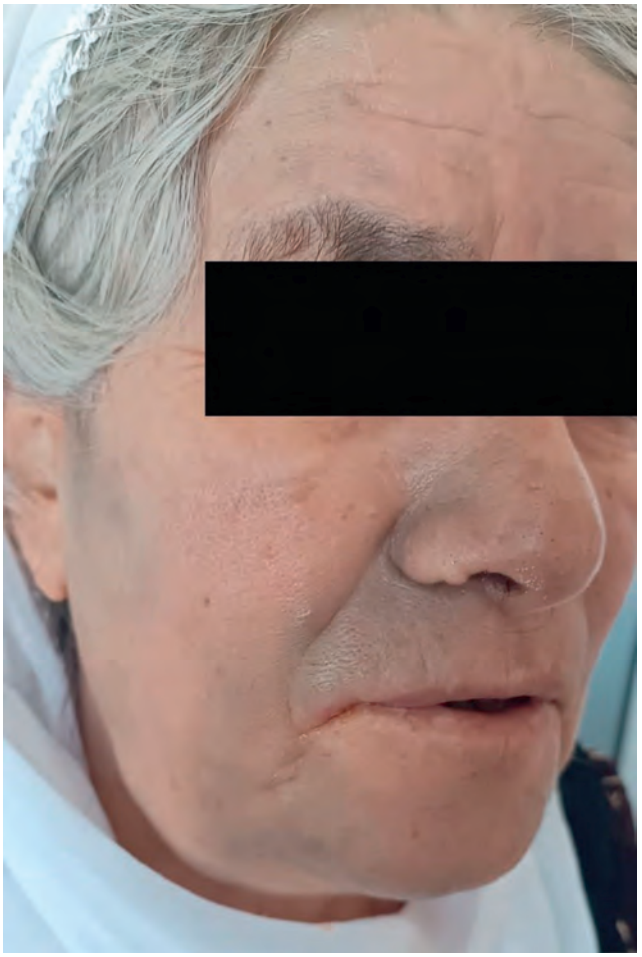
Objective: This case highlights an atypical presentation of myeloid sarcoma in a patient with acute myeloid leukemia (AML), focusing on diagnostic challenges, treatment decisions, and outcomes. The case emphasizes extramedullary involvement and therapeutic approaches for patients with

poor performance status. **Case Report:** A 68-year-old woman presented with neck swelling. Ultrasound and CT imaging revealed multiple enlarged cervical lymph nodes, with the largest measuring 30 × 25 mm in the right submandibular region. A tru-cut biopsy confirmed myeloid sarcoma infiltration. Upon admission, she was not cytopenic, but peripheral blood smear revealed blasts. Bone marrow biopsy confirmed AML, and diffuse chloroma foci were noted on her face. Due to poor performance status, the 5+1 chemotherapy regimen (5 days cytarabine, 1 day anthracycline) was initiated. After achieving remission in bone marrow, HDAC (high-dose cytarabine, 1500 mg/day) was administered as consolidation therapy. Severe cytopenias during HDAC led to a switch to azacitidine (Vidaza, 75 mg/m^2) and venetoclax. Allogeneic stem cell transplantation (AlloSCT) was recommended, but the patient declined. **Conclusion:** This case illustrates the diagnostic challenges of myeloid sarcoma in rare locations like the neck, compounded by diffuse chloroma. For patients with poor performance status, low-intensity regimens such as azacitidine and venetoclax are viable alternatives to intensive chemotherapy. AlloSCT remains the preferred treatment for high-risk AML, but in this case, azacitidine and venetoclax provided an alternative therapeutic pathway.





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PP 03

A CASE OF ACUTE LYMPHOBLASTIC LEUKEMIA PRESENTING WITH HYPEREOSINOPHILIA

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Case Report: Hypereosinophilia (HE) is eosinophil count >500/μL. The association of HE with acute lymphoblastic leukemia (ALL) is extremely rare, with an incidence of less than 1%. HE may precede the common symptoms and signs of ALL by several months or weeks. In some cases, the symptoms may be due to eosinophilic organ or system infiltration, and these findings may be different from the classical ALL symptoms, thus delaying the diagnosis. Here, we report a male patient who presented with HE and was diagnosed as PreB-ALL. A 9-year-old boy patient was admitted to Inonu University Turgut Özal Medical Center with complaints of testicular pain and swelling. The patient's hemogram showed HE, but there was no leukocytosis or cytopenia.. No atypical cell was observed

in peripheral smear. On scrotal ultrasonography (USG), the left epididymal head had a mildly heterogeneous appearance and the patient was treated for epididymitis with suspicion of epididymitis. Approximately one week later, the patient presented with fever . The patient's peripheral smear showed 36% blasts, 38% eosinophils, 2% monocytes, 6% lymphocytes, 10% segments and 8% bands. Bone marrow aspiration was performed for the diagnosis of acute leukemia and PreB-ALL was diagnosed. Control testicular USG was evaluated as testicular involvement of leukemia. During follow-up, the patient had nausea, vomiting, dizziness, decreased visual field, nuchal rigidity, and outward gaze limitation. Magnetic resonance (MR) venography revealed thrombosis in the inferior sagittal sinus and anticoagulant therapy was initiated. The patient with central nervous system symptoms was considered to have leukemic involvement and his treatment was adjusted. ALL is a condition that can cause HE. The prognosis is poor in ALL patients presenting with HE. HE may occur before the classical ALL symptoms therefore the diagnosis of ALL should also be considered in patients presenting with HE.

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PP 04

EVALUATION OF DRUG EFFECTIVENESS AND CONTROLLED RELEASE PROFILES OF CLAY MINERALS LOADED WITH ANTI-CARCINOGENIC AGENT AS A DRUG DELIVERY SYSTEM ON LEUKEMIA

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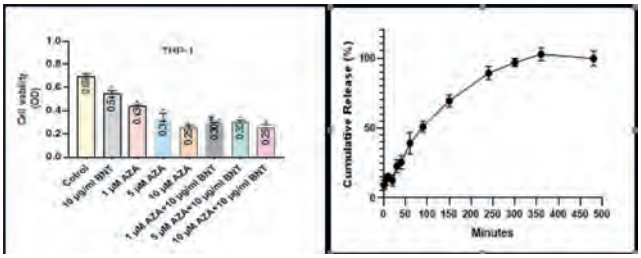
Objective: This study aimed to evaluate the slow release and internalization of azacitidine-bentonite combination in THP-1 and K562 cell cultures in acute myeloid leukemia morphology. **Methodology:** The morphology of bentonite clay was assessed using two Scanning Electron Microscopes. The bentonite-azacytidine combination was assessed in THP-1 and K562 cell cultures via in vitro cell proliferation tests, proliferation with CCK-8, and drug release tests with dialysis membranes. Additionally, apoptosis and internalization were determined using the Annexin V-FITC Kit and fluorescence methods, respectively. **Results:** Our findings showed that azacytidine achieved complete and controlled release within 8 hours. Bentonite displayed significant antiproliferative effects at concentrations of 10, 25, 50, and 100 μg/ml in both cell lines. The combination of azacytidine and bentonite exhibited a synergistic effect in inhibiting cell proliferation, with significant decreases in cell viability in the 1 μM azacytidine + 10 μg/ml bentonite, 5 μM azacytidine + 10 μg/ml bentonite, and 10 μM azacytidine + 10 μg/ml bentonite groups compared to the controls. The drug release profile of the bentonite-azacytidine combination demonstrated slow release, with 50% released in the first two hours and approximately 90% released in the fourth hour, with prolonged release exceeding eight hours, potentially reducing side effects and increasing efficacy in target cells. **Conclusion:** In conclusion, bentonite NPs exhibited significant potential as drug carriers for azacytidine in the treatment of leukemia and offered benefits such as improved solubility, bioavailability, controlled release, protection from harsh environments, and cost-effectiveness.



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PP 05

LIVER INVOLVEMENT IN ACUTE MYELOID LEUKEMIA: A CASE REPORT

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Objective: Although rare, extramedullary involvement can be observed in patients with acute myeloid leukemia (AML). These extramedullary involvements are also known as myeloid sarcoma, granulocytic sarcoma, or chloroma. The most common sites of involvement are soft tissues, bone, periosteum, and lymph nodes. Patients with extramedullary involvement may exhibit a more aggressive clinical course. In this case report, we evaluated an AML patient with liver involvement at the time of diagnosis. **Case Report:** A 66-year-old female patient presented to our hospital with complaints of fatigue, bruising on the skin, and yellowing of the eyes for about a month. Physical examination revealed icterus in the sclera, and widespread ecchymoses on the arms and abdomen. Laboratory findings showed a hemoglobin level of 7.8 g/dL, a leukocyte count of 4.4 $\times$ 10^9/L, a neutrophil count of 1.1 $\times$ 10^9/L, a platelet count of 30 $\times$ 10^9/L, CRP at 29 mg/L, and direct bilirubin at 5.8 mg/dL. Peripheral blood smear revealed notable myeloblasts and auer rods. Bone marrow aspiration smear showed over 20% myeloblasts, supporting the diagnosis of acute myeloid leukemia. Flow cytometry analysis was evaluated as consistent with AML. Abdominal ultrasonography revealed the liver was 19.5 cm and the spleen was 16 cm in size. The patient underwent 7+3 remission induction

chemotherapy. After chemotherapy, bilirubin levels returned to normal, and the patient was diagnosed with liver involvement of AML. **Conclusion:** The clinical presentation of extramedullary involvement varies depending on the affected organ and region. A definitive diagnosis is made through biopsy. In patients with AML, as in our case, a biopsy may not always be feasible due to the risk of bleeding. Therefore, in cases where hepatomegaly, abnormalities in liver function tests, and elevated bilirubin levels cannot be explained by other diseases, liver involvement should be considered.

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PP 06

IS ALL-TRANS RETINOIC ACID EFFECTIVE IN PULMONARY HAEMORRHAGE IN PATIENTS WITH ACUTE PROMYELOBLASTIC LEUKAEMIA?

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Objective: Acute myeloid leukaemia (AML) develops from myeloid precursor cells in the bone marrow. Acute promyelocytic leukaemia (APL) is an aggressive subtype (5-10%) of AML with the t(15;17) translocation. It is sensitive to all-trans retinoic acid (ATRA). The aim of this article is to emphasise the efficacy of ATRA treatment in pulmonary haemorrhage associated with APL and to contribute to the literature. **Case Report:** A 14-year-old girl presented with malaise, pallor and bruises since 1 month. On examination, she was pale and had bruises on the trunk and extremities, but no organomegaly. Investigations revealed pancytopenia and atypical mononuclear cells in peripheral blood smear. Bone marrow aspirate showed promyeloblasts (80%) and AML-M3 surface markers were positive in flow cytometry. Cytogenetic analysis revealed t(15;17) translocation. AML-BFM 2012 chemotherapy protocol was initiated. During induction chemotherapy, the patient developed dyspnoea and pulmonary haemorrhage. The child was transferred to intensive care unit and ATRA was added to the chemotherapy at a dose of 25 mg/m2/day. Coagulation tests improved 2 days after ATRA treatment and clinical findings improved 4 days later. On the 9th day of intensive care unit admission, the patient was transferred to inpatient ward and there was no bleeding during follow-up. **Discussion:** Haemorrhagic complications are frequent in APL patients and are one of the main causes of early death (5-9%) (1,2). Increased plasmin production (60-fold) due to excessive annexin-II receptor expression in promyeloblasts has been shown to cause fibrinolysis. It is thought that patients develop increased hyperfibrinolysis rather than consumption coagulopathy (2). ATRA is highly effective in bleeding control (3). **Conclusion:** Patients should be monitored with coagulation tests at regular intervals due to the high risk of bleeding. Undesirable haemorrhagic conditions may develop before and during treatment. ATRA can provide effective control in treatment.

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Adult Hematology Abstract Categories

Chronic Leukemias
PP 07

MULTI-TYROSINE KINASE INHIBITOR-ASSOCIATED APLASTIC ANEMIA AND A BRIEF LITERATURE REVIEW

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Objective: Chronic myeloid leukemia (CML) is a malignancy classified under the group of chronic myeloproliferative neoplasms. It is characterized by uncontrolled leukocytosis, bleeding, thrombosis, recurrent infections, and hepatosplenomegaly. With the introduction of imatinib in 2001, followed by the second- and third-generation tyrosine kinase inhibitors (TKIs), a new era in the treatment of CML began, as overall survival rates have since reached levels comparable to normal life expectancy. In this article, we review the first case of aplastic anemia that developed after bosutinib treatment, along with other cases of aplastic anemia reported in the literature following the use of TKIs. **Case Report:** A 57-year-old female was referred for leukocytosis identified during evaluation for fatigue, weakness, and early satiety. Initial lab results showed a WBC of 384×10^9/L, NEU of 246×10^9/L, Hb of 7.2 g/dL, and Plt of 281×10^9/L. Abdominal ultrasound revealed splenomegaly (23 cm), and peripheral blood smear suggested chronic myeloid leukemia (CML), leading to BCR-ABL transcript testing. Hydroxyurea was initiated while awaiting results. Two weeks later, the BCR-ABL transcript level was 49%, and imatinib 400 mg/day was started on December 15, 2022. The February 2023 earthquake disrupted the patient's imatinib use for three months. Upon return in May 2023, labs showed a WBC of 17×10^9/L, NEU of 14×10^9/L, Hb of 14.1 g/dL, Plt of 424×10^9/L, and BCR-ABL remained at 49%. Imatinib was resumed. In August 2023, BCR-ABL decreased to 41%. However, in October 2023, pancytopenia emerged, leading to imatinib discontinuation (WBC: 2.98×10^9/L, NEU: 0.5×10^9/L, Hb: 4.1 g/dL, Plt: 2×10^9/L). ABL mutation analysis showed no resistance mutations (Hemogram values at diagnosis and after treatment are shown in Figure 1). After two weeks without medication and no improvement in pancytopenia, bone marrow biopsy confirmed aplastic anemia (Figure 2A). Following ten weeks of recovery, normocellular marrow was observed (Figure 2B), and dasatinib 50 mg/day was started on February 1, 2024, later increased to 100 mg/day. Due to worsening cytopenias in late February, dasatinib was reduced and eventually discontinued in March. Bosutinib 500 mg/day was initiated in May, with BCR-ABL at 27.9%. As cytopenias progressed, bosutinib was reduced to 300 mg/day. Despite a BCR-ABL decrease to 8.63% in August, cytopenias persisted, and bosutinib was further

reduced 100 mg/day. The patient is currently being evaluated for allogeneic stem cell transplantation. **Methodology:** Until the 2000s, chronic myeloid leukemia (CML) was a fatal malignancy within the group of chronic myeloproliferative neoplasms. However, a significant breakthrough occurred following the approval of imatinib mesylate, the first tyrosine kinase inhibitor (TKI) for CML treatment, by the FDA in 2001 and the EMA in 2003. This was followed by the development of second-generation (dasatinib, nilotinib, bosutinib) and third-generation (ponatinib) TKIs, which greatly improved disease outcomes and significantly reduced TKI resistance. Common side effects of TKIs include pleural/pericardial effusion, pretibial edema, hyperglycemia, hyperlipidemia, liver dysfunction, diarrhea, and thrombosis, most of which can be managed by temporarily discontinuing the drug or reducing the dosage. Transient myelosuppression is also a frequently observed side effect of TKI therapy. However, prolonged aplastic anemia (AA) is a rare adverse effect secondary to TKIs. To date, cases of bone marrow aplasia associated with imatinib, dasatinib, and nilotinib have been reported in the literature, and the approaches to managing these cases are summarized in Table 1. Common management strategies include discontinuation of the drug, observation without medication, switching to another TKI, or performing allogeneic stem cell transplantation. Additional treatments such as cyclosporine, antithymocyte globulin (ATG), and filgrastim have also been employed. Unfortunately, despite various interventions, some patients have succumbed to septic mortality associated with prolonged neutropenia and intracranial hemorrhage linked to thrombocytopenia. The small number of cases makes it challenging to establish a standardized treatment approach. The mechanism of TKI-induced aplastic anemia (AA) remains unclear, but four potential pathophysiologies are considered: 1) acellularity in the hematopoietic system due to bone marrow infiltration by the CML clone [19], 2) blastic evolution during treatment [13], 3) suppression of hematopoietic stem cell proliferation through inhibition of kinases like c-kit, PDGFR, and SRY [8], and 4) toxic drug levels due to genetic polymorphisms in drug metabolism [20] **Results:** Studies have shown that higher doses of TKIs are associated with increased rates of myelosuppression [21]. Since routine monitoring of drug levels is not available in many healthcare facilities, using lower-than-standard TKI doses may be a viable alternative in cases of prolonged, severe cytopenias. In our patient, the progressive decline in BCR-ABL transcript levels suggests that the cause of AA is more likely due to nonspecific suppression of hematopoietic stem cells by TKIs rather than blastic evolution. Due to the unavailability of drug level testing at our center, we could not rule out bone marrow suppression related to drug toxicity. However, our patient tolerated bosutinib better, with the BCR-ABL transcript level dropping below 10% for the first time, distinguishing bosutinib from other TKIs. The milder cytopenic profile observed may be related to bosutinib's weaker inhibition of PDGFR and c-kit [22]. **Conclusion:** In cases of aplastic anemia following TKI therapy, various case-based treatment approaches exist, but no standardized method has been widely accepted. During the TKI era, allogeneic stem cell transplantation remains a necessary option for CML patients with AA. Asciminib, with its distinct mechanism of action, could be considered a treatment option in such cases, though no data currently exist in the literature. While the patient's BCR-ABL transcript level after bosutinib 100 mg/day is eagerly awaited, lower-dose bosutinib may present a viable alternative for this patient group.

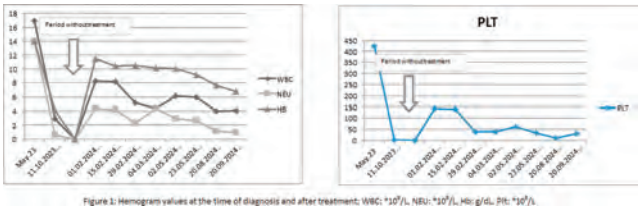

Figure 1

Figure 1: Hemogram values at the time of diagnosis and after treatment; WBC: *10⁹/L, NEU: *10⁹/L, Hb: g/dL, Plt: *10⁹/L

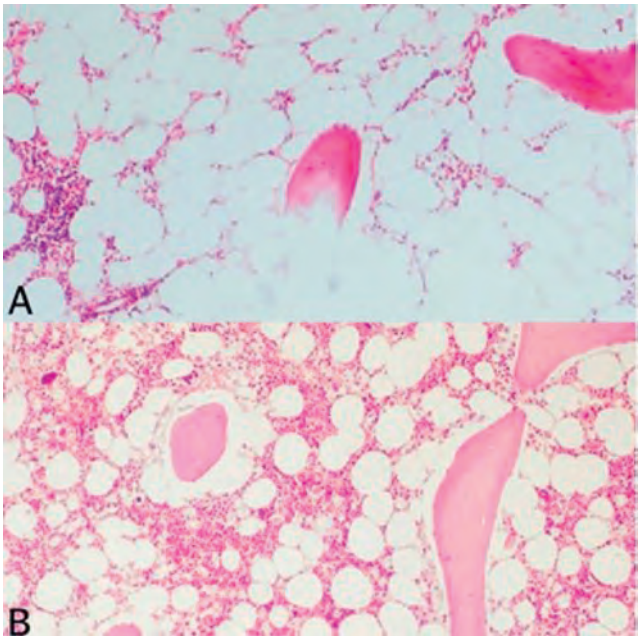

Figure 2: A) Bone marrow biopsiy demonstrating loss of cellularity following imatinib-associated pancytopenia. B) Bone marrow biopsy showing increased cellularity performed 10 weeks after discontinuation of imatinib.

Table 1: Cases of aplastic anemia secondary to tyrosine kinase inhibitors reported in the literature to date

	Age/sex	Hematological parameters at starting treatment with TKI or diasnosis	BCR-ABL FISH levels	Type of TKI	Aplaziye kadar geçen tedavi süresi	Hematological parameters at aplasia	Duration of treatment before aplasia2	Management of aplasia	Clinical situation when recovery from aplasia	References
Patient 1	46/m	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	128 days	Hb: 5-6 gr/dL, NEU 400*10^9 /L, Plt: 10-20000*10^9 /L	222 days and ongoing	cessation of drug	optimal response	Chng WJ et al. (2)
Patient 2	72/m	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	3 years	WBC: 0.2 × 109 L, Hb: N/A, Plt: N/A	1 month	cessation of drug, sisklosporin +ATG ve GCSF treatments were given	major molecular response	Hernández-Boluda JC et al (3)
Patient 3	47/f	WBC: 123*10^9/L (tanı anı)	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	3 years	WBC: 0.2 × 10^9 L, Hb: 4,6 g/dl, Plt: 34*10^9/L	1 month	IVIG and prednisolon treatments were given	recovery from aplasia, but BCR-ABL FISH: +41,4 postivei	LeMarbre G et al (4)
Patient 4	46/f	Hb: 10,2 gr/dL, WBC: 73*10^9/L Plt: 533*10^9/L (tanı anı, TKI başlangıç değeri belirtilmemiş	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	53 days	WBC: 0,2*10^9/L, Hb: 5 gr/dl, Plt: 17*10^9/L	2 weeks, then died	cessation of drug, GCSF was given	died	Lokeshwar N et al (5)
Patient 5	51/m	WBC:56*10^9/L, Hb: N/A, plt: N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	19 months	WBC: 1900*10^9/L, Hb: 7,3 gr/dl, Plt: 42*10^9/L	35 days, then died	cessation of drug, GCSF was given	died	Khan KA (6)
Patient 6	54/f	WBC:130*10^9/L, Hb: 10,6 g/dl; Plt:212*10^9/L	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	6 months	WBC: 2.2*10^9 /dl, Hb: 5,4 g/dl, Plt: 32*10^9 /L	N/A	cessation of drug	BCR-ABL FISH: Positive	Srinivas U et al (7)
Patient 7	38/f	WBC: 122*10^9/L, Hb: 7,2 g/dl, Plt: 100*10^9/L	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	6 months	WBC: 1.9*10^9 /L, Hb: 5,3 g/dl, Plt: 17*10^9	N/A	cessation of drug	BCR-ABL FISH: Positive	Srinivas U et al (7)
Patient 8	28/m	WBC: 135*10^9/L, Hb: 6,4 g/dl, Plt: 222*10^{-9}/L	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	6 months	WBC: 1.58*10^9 /L, Hb: 4,8 g/dl, Plt: 12*10^9 /L	N/A	cessation of drug	BCR-ABL FISH: Positive	Srinivas U et al (7)
Patient 9	15/m	WBC: 157*10^9 /L, Hb: 6,6 g/dl, Plt: 268*10^9 /L	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	3 months	WBC: 1.3*10^9 /L, Hb: 5,5 g/dl, Plt: 23*10^9 /L	N/A	cessation of drug	BCR-ABL FISH: Positive	Srinivas U et al (7)
Patient 10	50/m	WBC: 123*10^9 /dL, Hb: 8,6 g/dl, Plt: 168*10^9 /L PB-blasts:32%	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	3 months	WBC: 2.5*10^9 /L, Hb: 6,8 g/dl, Plt: 40*10^9 /L	N/A	cessation of drug	BCR-ABL FISH: Positive	Srinivas U et al (7)
Patient 11	61/f	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	3,5 months	N/A	N/A	patient expired due to intracranial haemorrhage	N/A	Madabhavi I (8)
Patient 12	65/f	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	4 months	N/A	10 months	cessation of drug, hydroxiurea was given	BCR-ABL FISH: Positive	Madabhavi I (8)
Patient 13	63/f	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	2 months	N/A	14 months	cessation of drug, hydroxiurea was given	BCR-ABL FISH: Positive	Madabhavi I (8)
Patient 14	70/f	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	1,5 months	N/A	9 months	cessation of drug, hydroxiurea was given	BCR-ABL FISH: Positive	Madabhavi I (8)
Patient 15	74/m	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	6 months	N/A	N/A	patient was succumbing due to septicemia	N/A	Madabhavi I (8)
Patient 16	68/f	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	6 months	N/A	5 months	cessation of drug, hydroxiurea was given	BCR-ABL FISH: Positive	Madabhavi I (8)
Patient 17	76/f	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	4 months	N/A	7 months	cessation of drug, hydroxiurea was given	BCR-ABL FISH: Positive	Madabhavi I (8)
Patient 18	34/m	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	2,5 months	N/A	15 months	cessation of drug, hydroxiurea was given	BCR-ABL FISH: Positive	Madabhavi I (8)
Patient 19	42/m	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	2 months	N/A	12 months	cessation of drug, hydroxiurea was given	BCR-ABL FISH: Positive	Madabhavi I (8)
Patient 20	55/f	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	3 months	N/A	11 months	cessation of drug, hydroxiurea was given	BCR-ABL FISH: Positive	Madabhavi I (8)
Patient 21	32/m	N/A	BCR-ABL FISH: + Transcript levels: N/A	Imatinib	2,5 months	N/A	11 months	cessation of drug, hydroxiurea was given	BCR-ABL FISH: Positive	Madabhavi I (8)
Patient 22	49/m	WBC: 130*10^9 /L, Hb: 10,4 gr/dl, Plt: 781*10^9/L	BCR-ABL FISH: + Transcript levels: N/A	Nilotinib (switched from 7 months dasatinib treatment)	19 months	WBC: 2,4*10^9 /L, Hb: 9,8 gr/dl Plt: 16*10^9 /L	2 months	cessation of drug, 2 months later started nilotinib again due to BCR-ABL FISH postivity	FISH for BCR-ABL negative during aplasia, positive after 2 months later	Prodduturi P (9)

(continued)

	Age/sex	Hematological parameters at starting treatment with TKI or diasnosis	BCR-ABL FISH levels	Type of TKI	Aplaziye kadar geçen tedavi süresi	Hematological parameters at aplasia	Duration of treatment before aplasia2	Management of aplasia	Clinical situation when recovery from aplasia	References
Patient 23	26/m	N/A	BCR-ABL FISH: + Transcript levels: N/A	dasatinib 100 mg	5 months	WBC: 2,2*10^9/L, Hb: 7,2 gr/dl, Plt: 35*10^9 /L	3 months	cessation of drug, 3 months later started dasatinib 20 mg/d >>pancytopenia>>imatinib 100 mg/d >>imatinib 600 mg/d>>pancytopenia>>nilotinib 2*400 mg>>undetectable BCR-ABL>>ASCT	BCR-ABL FISH positive, Trizomy 8+	Feld J (10)
Patient 24	53/m	WBC: 575*10^6 /L, Hb: 7,6 gr/dl, Plt: 380*10^6 /L	BCR-ABL FISH: + Transcript level: %85+	dasatinib 100 mg	5 months	N/A	4 months	cessation of drug, cyclosporine +eltrombopag +GCSF >>4 months later imatinib restarted again	BCR-ABL FISH: Positive	LEWALLE P (11)
Patient 25	59/f	WBC:22*10^9 /L, Hb:13,1 g/dl, Plt::951*10^9 /L	BCR-ABL FISH: + Transcript level: %100	imatinib	2 months	WBC: N/A, Hb: 8 gr/dl, Plt: <10*10^9 /L	2 months	maintenance with imatinib after infusion of peripheral blood stem cell collected at diagnosis	BCR-ABL FISH: Positive	LEWALLE P (11)
Patient 26	34/f	WBC:135*10^9 /L, Hb: 10,6 g/dl, Plt: 326*10^9 /L	BCR-ABL FISH: + Transcript level: %100	imatinib	3 years	WBC: 3,6*10^6/L, Hb: 8 gr/dl, Plt: 45*10^9 /L	9 monts, then died	cessation of drug, cyclosporine was given	major molecular response	KASSAR O (12)
Patient 27	64/m	WBC: 323*10^9 /L, Hb:N/A, Plt: 428*10^9 /L	BCR-ABL FISH: + Transcript level: %81	imatinib	8 months	WBC: 15*10^9 /L, Hb: 10 gr/dl, Plt: <10*10^9 /L	3 months	cessation of drug, dasatinib started>>aplasia after 15 months later>>dose reduction to 50 mg/d>>high frequency of BCR-ABL as %70+>>omacetaxine started>>4 months later ASCT has done	BCR-ABL FISH: Positive	Ramdial JL (13)
Patient 28	50/m	WBC:26*10^9 /L, Hb: N/A, Plt: 1042*10^9 /L	BCR-ABL FISH:+ Transcript level: N/A	imatinib switched to dasatinib due to suboptimal response then nilotinib due to intolerance	2 months	N/A	19 months, then died	cessation of drug, eltrombopag started	BCR-ABL FISH: Positive	Ramdial JL (13)
Patient 29	58/m	WBC: 233*10^9 /L, Hgb: N/A. Plt: N/A	BCR-ABL FISH:+ Transcript level: %97	dasatinib 150 mg	6 months	WBC: 1,2*10^9 /L, Hb: 2,5 gr/dl, Plt: 7*10^9 /L	3 months	cessation of drug, ponatinib started and aplasia occured again then ASCT has done	BCR-ABL FISH: Positive	Kamijo K (14)
Patient 30	63/f	WBC: 380*10^9 /L, Hb: 3,9 g/dl, Plt: 436*10^9 /L	BCR-ABL FISH:+ Transcript level: N/A	imatinib	4 months	WBC:0,4*10^9 /L, Hb: 3,1 gr/dl, Plt: 21*10^9 /L	6 months	cessation of drug, followed without treatment	N/A	Dogra R (15)
Patient 31	46/m	N/A	BCR-ABL FISH:+ Transcript level: N/A	imatinib	8 weeks	WBC: 1,4*10^9 /L, Hb: 6,4 gr/dl, Plt: 6*10^9 /L	9 months, then died	cessation of drug, ATG, cyclosporine, steroid and GCSF started	partial response	Mabed M (16)
Patient 32	77/m	WBC: 12,3*10^9 /L, Hb: 12,6 g/dl, Plt: 563*10^9 /L	BCR-ABL FISH:+ Transcript level: N/A	imatinib switched to nilotinib due to intolerance	2 months	WBC: 0,3*10^9 /L, Hb: 4,7 gr/dl, Plt: 3*10^9 /L	4 months	cessation of drug	major molecular response	Song M (17)
Patient 33	73/f	WBC: 8,4*10^9 /L, Hb:12 g/dl, Plt: 19*10^9 /L	BCR-ABL FISH:+ Transcript level: N/A	imatinib	17 days	N/A	N/A	N/A	N/A	Sumi M (18)
Patient 34	53/f	WBC: 56*10^9 /L, Hb:N/A, Plt: 650*10^9 /L	BCR-ABL FISH:+ Transcript level: %96	nilotinib	2,5 months	WBC: 0,9*10^9 /L, Hb: 10 gr/dl, Plt: 9*10^9 /L	5 months	cessation of drug, romiplostim started then dasatinib 50 mg/d started	Optimal response	Estephan F (19)

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PP 08

CASE PRESENTATION: TREATMENT AND FOLLOW-UP EXPERIENCE FROM MYELODYSPLASTIC SYNDROME (MDS) REAB II TO CHRONIC MYELOMONOCYTIC LEUKEMIA (CMML)

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Objective: The purpose of this case presentation is to discuss the clinical course, pathological findings, and treatment process of a patient diagnosed with MDS REAB II. It examines the transformation to CMML under the treatment of Venetoclax + Azacitidine. Challenges encountered during the follow-up process of CMML are mentioned. By addressing the continuation of MDS REAB II treatment in CMML, it is aimed that the findings obtained from this case contribute to the diagnostic and treatment processes for similar patients. **Case Report:** A 79-year-old male patient was found to have anemia, thrombocytopenia, and leukocytosis in the hemogram. Atypical cells were observed in the peripheral smear. The patient had lost 8 kg in the last 3 months and experienced night sweats. His medical history includes prostate cancer and heart diseases. Abdominal tomography revealed hepatomegaly and splenomegaly. At presentation: WBC - 16.12 × 10^3/uL; absolute monocyte count (MONO) - 3.61 × 10^3/uL; Hemoglobin (HGB) - 9.1 g/dL; Hematocrit (HTC) - 29.5%; Mean corpuscular volume (MCV) - 94.9 fL; Platelet (PLT) - 129 × 10^3/uL; Creatinine - 1.27 mg/dL; Lactate Dehydrogenase (LDH) - 340 U/L; eGFR - 67 mL/min/1.73 m^2; Albumin - 3.5 g/dL; Total Protein - 7.9 g/dL; Ferritin - 171.42 μg/L; Folate - 16.9 μg/L; B12 - 353 ng/L. Anti-HBc IgG: (+), HBsAg: (-), Anti-HCV: (-), Anti-HIV: (-). On 09/02/2024, the bone marrow pathology result showed an increase in blasts, leading to the diagnosis of MDS REAB-II. Flow cytometry revealed an 11.1% blast rate in the bone marrow. Treatment with Venetoclax and Azacitidine was initiated for MDS REAB-II. After 4 cycles, follow-up results showed: WBC - 16.38 × 10^3/uL; MONO - 3.54 × 10^3/uL; HGB - 11.6 g/dL; HTC - 35.7%; MCV - 90.4 fL; PLT - 110 × 10^3/uL; Creatinine - 1.27 mg/dL; LDH - 257 U/L. Due to ongoing bicytopenia and for treatment response evaluation, a biopsy performed on 24/07/2024 revealed findings consistent with CMML without an increase in blasts. An off-label application was made for the continuation of current treatment. The effectiveness of the combination of Venetoclax and Azacitidine in the treatment of CMML is also being investigated, with the goal of monitoring the patient with the current treatment. **Methodology:** On December 6, 2023, the patient underwent surgery after preoperative severe anemia and thrombocytopenia, requiring blood transfusions. After discharge, the patient was referred to the hematology outpatient clinic. A bone marrow biopsy was planned due to atypical cells observed in the peripheral smear related to bicytopenia, which was sent for pathology and flow cytometry studies. **Results:** Abdominal tomography revealed: liver size increased to 165 mm, with millimetric parenchymal calcifications observed in the liver dome; spleen size increased to 141 mm. On 22/01/2024, pathology results showed MDS REAB II with increased blasts. Flow cytometry indicated a blast rate of 11.1% (CD13/CD117/CD34). Such findings are typically observed in cases favoring "MDS." After 4 cycles of Venetoclax and Azacitidine treatment, a repeat biopsy on 24/07/2024 showed results indicating RAEB-II type MDS. The bone marrow was sampled regarding blast percentage. It is unclear if the patient has been treated recently. Peripheral blood reports indicate relative (30.7%) and absolute (2.97 k/uL) monocytosis, normochromic normocytic anemia, and thrombocytopenia. With absolute (2.97 k/uL) and relative (30%) monocytosis present; the hypercellular bone marrow (%60) represents slight maturation anomalies compatible with CMML-I, and no blast increase was detected. **Conclusion:** The challenges in diagnosing and treating CMML arise from the coexistence of dysplasia and myeloproliferative features. According to World Health Organization criteria, the diagnostic criteria have been met considering the patient's condition. For the first time in this case, a transition from MDS REAB II to CMML has been observed under this treatment. Azacitidine and Decitabine, approved for the treatment of MDS, have also been approved for CMML patients. Furthermore, more advanced studies are underway regarding the effectiveness of Azacitidine and Decitabine in CMML treatment. The effectiveness of the combination of Venetoclax and Azacitidine is also being investigated, with the goal of monitoring the patient with the current treatment.

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PP 09

PERITONEAL MESOTHELIOMA AS A CO-MALIGNANCY IN A PATIENT WITH CLL/SLL: CASE REPORT

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Objective: Malignant mesothelioma (MM) is an aggressive tumor typically arising from the pleura, with malignant peritoneal mesothelioma (MPM) accounting for 10-15% of cases. The occurrence of MPM alongside hematologic malignancies is rare. Here, we present a case of peritoneal mesothelioma developing synchronously with CLL/SLL. **Case Report:** A 68-year-old male was referred to our clinic in August 2023 with lymphocytosis, reporting weight loss and night sweats. His medical history included diabetes, hyperlipidemia, and hypertension, and a family history of stomach cancer. The patient had quit smoking 30 years ago and had a history of chronic alcohol use. There was no known asbestos exposure despite his occupation as a construction worker. Physical examination was normal. Routine laboratory tests and flow cytometry were conducted.

Imaging via thoracic and abdominal USG and PET/CT identified multiple lymphadenopathies and omental thickening indicative of peritoneal infiltration (Image-1). The patient was diagnosed with RAI Stage 3 CLL/SLL. In addition to hematological follow-up, the patient was referred to oncology and general surgery. He chose to continue his hematological follow-up in our clinic while receiving oncological and surgical follow-up at an external center. He is treated for CLL with ibrutinib and cisplatin-pemetrexed-altuzan for mesothelioma. **Discussion:** There is limited knowledge about the epidemiology and treatment of malignant peritoneal mesothelioma due to its rarity. In studies of mesothelioma associated with hematological malignancies, patients published predominantly have pleural mesothelioma. **Conclusion:** As a result, mesothelioma should be considered as a differential diagnosis in hematological cancer patients with abdominal masses, and further investigation needs to be conducted.

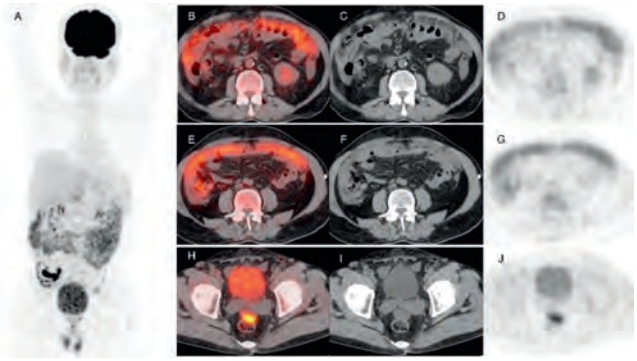

Image 1: Full Body PET scan (**A**),Axial PET/CT images showing omental thickening and peritoneal involvement (**B, E,H**), Corresponding axial CT images (**C,F,I),**PET images highlighting FDG uptake **(D,G,J)**Bone marrow and omentum biopsies were performed. The bone marrow biopsy confirmed CLL/SLL.

Table 1: Omentum biopsy revealed low-grade malignant epithelial mesothelioma

Immunohistochemistry	Case
Calretinin	Positive
BAP1	Negative
P16 (CDKN2A / 9p21)	Homozygous positive

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Adult Hematology Abstract Categories

Chronic Myeloproliferative Diseases

PP 10

HAIR REPIGMENTATION IN AN OLDER PATIENT TREATED WITH ASCIMINIB

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Objective: Asciminib may be a promising treatment option for intolerance of tyrosine kinase inhibitors (TKIs). It is a first-in-class inhibitor with a more selective mechanism of action different from the ATP-competitive inhibition that occurs with TKIs. Adverse effects (AEs) related to the inhibition of non-BCR::ABL1 kinases have been expected to be greatly diminished According to the literature, fifty-five percent of patients experienced some AEs: mostly mild (grades 1–2), with 18% being grade 3–4. The most frequent AEs were fatigue (18%), skin rash (18%) thrombocytopenia (17%), and anemia (12%). The most frequent grade 3–4 AEs were thrombopenia (3.9%) and fatigue (3%). Other AEs were pneumonitis and hypoglycemia reported post-marketingly. **Case Report:** A 61-year-old man was diagnosed with chronic myeloid leukemia (CML) and started on 80 mg asciminib. After 20 weeks of treatment, he experienced an unexpected change in hair color from gray to dark brown, without using hair dye or supplements. The same color change was also present in his mustache and beard. No other side effects were observed **Management and outcome:** It was decided to monitor the patient with no action taken as he feel pleasant with this unexpected side effect of asciminib. CMl remained in deep molecular remission. The dark brown hair color persisted over time. **Discussion/Conclusion:** Hair hyperpigmentation likely occurred through melanocyte activation via asciminib. Severe side effects may require dosage adjustments, while milder effects can be monitored closely. The newly observed hair color restoration in this case highlights potential dual (therapeutic and aesthetic) applications of this class of agents.

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PP 11

VULVAR AND VAGINAL GRAFT VERSUS HOST DISEASE IN A PATIENT WITH CHRONIC PHASE CHRONIC MYELOID LEUKEMIA AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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Objective: Graft versus Host Disease (GVHD) is one of the serious complications of allogeneic stem cell transplantation used in the treatment of many hematological malignancies. Skin, liver, and eyes are frequently affected areas. In addition to frequently affected areas, genital region involvement can also be seen. Allogeneic stem cell transplantation is one of the definitive treatments for hematological malignancies seen in the young age group. And its use for therapeutic purposes in young patients is increasing day by day. Vulvovaginal GVHD is a disease type that concerns female patients of reproductive age. In this case report, we wanted to include in the literature a case that underwent allogeneic stem cell transplantation after CML diagnosis and TKI resistance and then developed vulvovaginal GVHD. In vaginal disease involvement; in addition to many genitourinary complaints, many negativities in sexual life and deterioration in quality of

life are experienced. The chronic GVHD patient we treated is currently continuing her treatment response follow-ups. Our aim in presenting this case to the literature is to emphasize that GVHD should be included in the differential diagnosis in female patients with hematological disease and vaginal involvement. **Case Report:** 42 years old female patient was diagnosed as chronic phase chronic myeloid leukemia in 2015. She was treated with imatinib 400 mg/day. After 6 months molecular response not obtained and treatment changed to dasatinib 100 mg/day, but after 3 months of dasatinib treatment molecular and hematologic progression occurred and treatment changed to nilotinib and bone marrow transplantation planned. After 4 months the patient transplanted succesfully with HLA matched sibling stem cell donor. Tyrosine Kinase inhibitory used till 1 years after transplantation, Bcr/abl was negative after transplantation and until now. At 2 months of transplantation acute GvHD occurred and healed without any serious complication, but after 10 months symptoms and signs of chronic GvHD developed. Dry skin, itching, dark hyperpigmentation occurred in generalized of the body especially in the upper extremities and ocular GvHD was the main symptoms of the patient. She was used siklosporin and steroids for prophylaxis and treatment of GvHD, also she use ursodeoxycholic acid for liver protection. Chronic GvHD sustained more than 2 years especially ocular findings (drying, itching and scarring of conjunctiva and eyelid). After 5 years of transplantation she told to our nurse some symptoms such as vulvodinia, pain during sexual intercourse and decreased sexual function. She has problems with her husband for this reason. She applied on october 2023 for gynecological examination, there were findings consistent with vulvodynia, but there was no genital atrophy. We prescribed 2% amitriptyline + 2% baclofen cream two times a day for the treatment of vulvodynia **Methodology:** When she came for a check-up 1 month later of local treatment, she stated that she was better in terms of sexual function but could not urinate completely. Bacteriuria, pyuria and hematuria was observed in urinalysis. Since there was not much residual urine in the pelvic ultrasonography. We treat her for urinary tract infection. Since the patient's genital atrophy was not evident, we did not prescribe vaginal estrogen during both examinations. If she came for a checkup, we was planning to re-evaluate and treat her if necessary. Hematopoietic stem cell transplantation (HSCT) is a treatment method for malignant and benign hematological diseases as well as in the treatment of some non-hematological disorders such as autoimmune diseases (1). Graft-versus-host disease (GVHD) is an immunity related disease which affects 30-70% of patients after hematopoietic stem cell transplantation (alloHSCT) and is a significant contributor of morbidity and non relapse mortality (NRM) is the reason (2). Chronic GVHD is a mucosal disease of the mouth, eyes, genitals, intestines, and lungs. It includes inflammation and fibrosis of membranes. There are some evidences which indicates clinical symptoms and pathogenesis of GVHD is similar to various autoimmune disorders such as Scleroderma, Sjögren's syndrome and lichen planus. (3,4). Female genital GVHD was first described by Corson et al. By observing Sclerosing vaginitis and structure problems in 5 women in 1982 (5). Nowadays, it is an underdiagnosed condition and affects the quality of life which occurs in one quarter of long-term surviving women after allogeneic stem cell transplantation (6). The rates of genital GVHD vary widely, with rates ranging from 24.9-69% (7). **Results:** The wide variation in the incidence of genital GVHD is due to a variety of abnormalities, including the time at which incidence is calculated, the systematic and time-dependent gynecological evaluations, and the diagnostic criteria used (findings of examination with or without symptoms, etc.) (8). The main risk factor for the development of chronic genital GVHD issuing of peripheral blood as a source of progenitor cells; It represents a risk of three times higher than that obtained from bone marrow cells (9-11). The presence of GvHD in another organ is also considered one of the risk factors (12) . While one study found that 79% of patients with VVGvHD were treated for GvHD in a different organ, another study reported that almost all patients with VVGvHD had active chronic GvHD in the skin, mouth, and eyes (13-14). Our patient was receiving treatment for skin and liver involvement caused by chronic GVHD . It is supported by various studies that it develops after an average of 10.2 months after transplantation (6). In our patient, this condition was detected approximately 5 years after allogeneic transplantation. Clinic may be asymptomatic; The main signs and symptoms are vulvar tenderness to palpation of openings of the mucosa, erosion of the mucosa, cracks, leukokeratosis, labial or clitoral fusion, fibrous vaginal ring, vaginal shortening, vaginal adhesions and complete vaginal stenosis. Other symptoms include dryness, burning, itching, pain to touch, dysuria, dyspareunia and resulting sexual dysfunction takes place (5). **Conclusion:** She has vulvodynia, pain during sexual intercourse and decreased sexual function. Although symptoms are similar to primary ovarian insufficiency which occurs after allogeneic stem cell transplantation, synechia and adhesive bands are not encountered in primary ovarian failure. In addition, studies have shown that hormone replacement therapy is used for the prophylaxis of this condition does not effects development rate of vulvo vaginal GVHD (11). The National Institutes of Health (NIH) Consensus Development Project proposed guidelines for screening, diagnosing, and preventing genital GVHD in HSCT survivors. Treatment goals for Female genital GVHD include symptom relief, disease control and prevention of further damage (7). In its treatment various patient-specific treatment modalities are advocated such as topical estrogens, topical steroids, topical immunosuppressive agents (such as cyclosporine, tacrolimus), vaginal dilators and surgicallysis (9,16). Diagnosis and treathment of post-transplant genital GVHD requires a systematic approach and collaboration between bone marrow transplant pyhsicians and coordinators and gynecologists. A systematic approach is required, requiring close cooperation between gynecologists. Incidence and severity of genital GVHD in women should be included in GVHD intervention studies.

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PP 12

EFFECT OF FREQUENT GENERIC IMATINIB SWITCHING ON TREATMENT RESPONSE IN PATIENTS WITH CHRONIC MYELOID LEUKEMIA

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Objective: The aim of this study was to evaluate the effect of switching one or more generic imatinibs during treatment on outcomes in patients with chronic phase chronic myeloid leukemia.. **Case Report:** Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm associated with the Philadelphia chromosome t(9;22)(q34;q11) and the BCR::ABL1 fusion gene, which produces a constitutively active BCR::ABL1 tyrosine kinase.CML accounts for approximately 15 to %20 of adult leukemia. It has an annual incidence of 1 to 2 cases per 100,000, with a slight male predominance.The median age at presentation is approximately 50 years, and the prevalence of CML is steadily increasing in the Western world because of the dramatic effect of ABL1 kinase inhibitors on survival. Imatinib was the first commercially available TKI to approved by the U.S Food and Drug Administration (FDA) and the European Medicines Administration (EMA) for the initial treatment of CML. The high cost of new cancer drugs, including those developed for CML, is a major concern for healthcare payers, especially in countries with limited resources. Reimbursement policies around the world therefore encourage the use of generics to reduce prices.The European LeukemiaNet 2020 recommendation for the use of generic imatinib is as follows : "As long as a generic medicine meets the national standards of the country concerned in terms of quality of production, bioavailability and efficacy, it is an acceptable alternative to the branded product. *It is recommended that the patients continue to use the same generic brand whenever possible to avoid potential side effects due to changes in drug structure, bioavailability and excipients*." In the NCCN guidelines, the recommendation for generic drugs is as follows: "Innovator and generic drugs approved by regulatory authorities on the basis of pharmacokinetic equivalence can be used interchangeably" and "*In countries where more than one generic drug is available, switching from one generic drug to another is not recommended*". **Methodology:** We retrospectively analyzed data from patients diagnosed with CML-CP treated with imatinib from 2010 - 2024. Patients with chronic phase chronic myeloid leukemia who were over 18 years of age and who started treatment with original or generic imatinib and switched to generic imatinib at any time during treatment were included. Patients who were diagnosed before the age of 18, patients whose treatment was interrupted during pregnancy, patients who did not use generic imatinib or patients who used only one brand of generic imatinib permanently were excluded from the study.The characteristics of the patients and the follow-up periods were collected retrospectively from the patients' electronic files.The efficacy of treatment was evaluated via standard hematological and molecular assessments to determine the rates of complete hematological response (CHR), molecular response (MR), and treatment failure, which was defined as a bcr-abl level of 1 % or higher on two occasions with an interval of one month. **Results:** A total of 46 patients, 26 (56.5%) male and 20 (43.5%) female (male/female ratio, 1.3), were included in the study. The median age was 45 years (range, 20-77 years). Forty-one (89.1%) of the patients were under 65 years of age, and 5 (10.9%) were over 65 years of age.The starting dose of imatinib was 400 mg/d in all patients. Treatment was started with Gleevec in 11 patients and generic imatinib in 35 patients. All patients were switched to two or more generic imatinibs during treatment.During the treatment process, 12 patients 2, 13 patients 3, 12 patients 4, 7 patients 5 and 1 patient 6 used different types of generic imatinib.Loss of response occurred in 8 of 46 (17.3%) patients. The earliest loss of response occurred at month 6, and the latest loss occured at year 9. One patient lost response at month 6, 1 patient at year 1, 2 patients at year 2, 1 patient at year 3, 2 patients at year 7, and 1 patient at year 9.All patients who experienced a loss of response responded to second-generation tyrosine kinase inhibitors, and none developed an accelerated or blastic phase. No dose increases or switches back to the original product in patients with loss of response. No patients had their dose changed or discontinued due to adverse events.When evaluated according to age, sex and number of generic imatinib switches, none of these variables were found to have any effect on response loss. **Conclusion:** Following the introduction of generic imatinib, several studies have shown that there is no loss of efficacy in patients who are switched from Glivec to generic imatinib. Although the ELN and NCCN CML guidelines do not discourage the use of generic imatinib, switching between generic imatinibs is not recommended. A review of both guidelines and the literature revealed no information on the development of adverse outcomes related to treatment response in patients switching between generic imatinibs.In the abovementioned retrospective studies, data on the responses obtained from patients receiving more than one type of generic imatinib were not shared.In our study, the response loss in patients who received more than one generic imatinib was 17.3%, which is comparable to the response losses observed in other studies of patients who received the original imatinib or generic imatinib.The findings of our study indicate that switching between generic imatinibs does not have a detrimental effect on treatment response.

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PP 13

ONE CASE OF CHRONIC MYELOID LEUKEMIA IN PEDIATRIC GROUP

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Objective: Chronic myeloid leukemia (CML) is a myeloproliferative syndrome caused by monoclonal myeloid proliferation with the passage of immature granular elements into the peripheral blood. It is a rare disease in children and adolescents,

accounting for 2-3% of all leukemias in the pediatric population under the age of 15. (1) It is defined by the presence of a translocation (9;22), a cytogenetic abnormality associated with the disease. We report one of these rare cases because of its unusual frequency. **Case Report:** Fourteen year male child came to the pediatric hematology policlinic complaints of abdominal distension, bone pain and weakness. Clinical examination revealed mucocutaneous pallor and hepatosplenomegaly. The complete blood count received on the day of admission showed hyperleukocytosis at 178000/μL, normocytic normochromic anemia at 10,8 g/dl and thrombocytosis at 281000/μL. When the blood smear was examined, it was seen that there were myelocytes, metamyelocytes and promyelocytes, neutrophils and 4% myeloid-appearing blasts. Subsequent bone marrow aspiration showed hyperplasia of the neutrophilic granulocytic lineage at all stages of maturation, with promyelocyte, hyper granular myelocyte, metamyelocyte. (Figure 1) Cytogenetic analysis of the bone marrow as part of the etiological work-up confirmed the presence of the Philadelphia chromosome. Molecular testing for the BCR-ABL1 fusion transcript by RT-PCR on EDTA whole blood detected 64% (IS). The patient was admitted to the pediatric hematology service and started on hydroxyurea treatment. After the genetic diagnosis was confirmed, he was treated with Imatinib, a first-generation tyrosine kinase inhibitor (TKI). In the molecular evaluation performed at the 3-month follow-up, BCR-ABL1 fusion transcript was detected as 5% (IS) by RT-PCR. **Discussion:** Chronic myeloid leukemia (CML) is a rare hematological malignancy in the pediatric population. For treatment, our patient benefited from specific Imatinib therapy. According to the literature, Imatinib is the first-line drug.

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Adult Hematology Abstract Categories

Coagulation Diseases
PP 14

PAGET SCHROETTER SYNDROME AND HOMOZYGOUS FACTOR V LEIDEN MUTATION: A CASE PRESENTATION

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Case Report: Thrombosis in the deep veins of the upper extremity accounts for only 5% of symptomatic cases but constitutes approximately 50% of hospital-acquired thromboses. The vast majority of upper extremity thromboses, result from the presence of permanent venous catheter. Unprovoked cases are often secondary to "effort" thrombosis. Here, we present a case of Paget-Schroetter syndrome combined with a homozygous mutation of factor V Leiden. A 19-year-old female patient presented with pain and swelling in her right arm. The report of the right arm venous Doppler ultrasound indicated the presence of thrombus within the lumen at the proximal and distal segments of the basilic vein at the fossa cubiti level. The patient was found to have a homozygous mutation of factor V Leiden, and it was learned that she had been undergoing intense training and was engaged in water polo for the last two months. She had no history of medication use or chronic illnesses, nor any previous history of thrombosis. The patient was started on low molecular weight heparin for three months. A control Doppler ultrasound showed that the existing thrombus had resolved. It was recommended that the patient continue on her current anticoagulation with a new generation oral anticoagulant for one year. During this period, the patient, who ceased sports activities, did not develop any new thrombosis. The combination of young age, intense physical activity, especially in sports that utilize the upper extremities, and risk factors such as the factor V Leiden mutation strengthens the diagnosis. In the pathophysiology of this syndrome, vascular microtravma and exercise, muscle hypertrophy and thrombophilias contribute to the condition. Low molecular weight heparin and new generation oral anticoagulants are effective in preventing thrombosis formation and in inhibiting the growth of existing thrombus. Thrombolytic therapy may be considered in cases of large thromboses or severe symptoms.

https://doi.org/10.1016/j.htct.2024.11.042

PP 15

DESENSITIZATION TO RIVAROXABAN IN A PATIENT WHO EXPERIENCED ANAPHYLACTOID SHOCK AFTER ANTICOAGULANT USE: CASE REPORT

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Case Report: Over the last two decades, new anticoagulants have been developed to prevent and manage thromboembolic diseases, including direct-acting anticoagulants like rivaroxaban, which is used for venous thromboembolism prevention, stroke prevention in atrial fibrillation, and ischemic heart disease. Here, we present the experience of a case with a history of multiple thromboses and an anaphylactoid reaction to anticoagulants, who was able to continue prophylaxis without allergic reactions after rivaroxaban desensitization. A 42-year-old female patient visited the hematology outpatient clinic to obtain a prescription for a new anticoagulant due to a supply issue with her current medication, fondaparinux..

Her medical history included thrombosis in both upper and lower extremities ten years earlier, along with heterozygous mutations for factor V Leiden and MTHFR, necessitating lifelong anticoagulant therapy. She had previously experienced anaphylactic shock from enoxaparin, warfarin, tinzaparin, and rivaroxaban, which led her to use fondaparinux without issues. When faced with a supply problem prescribed apixaban, she suffered anaphylactic shock thirty minutes after administration, requiring epinephrine treatment. Following this, the allergy and immunology department recommended a desensitization protocol for rivaroxaban, crucial for her ongoing anticoagulation. After a one-day desensitization, she successfully continued treatment with 20 mg of rivaroxaban without any allergic reactions during follow-up visits. Desensitization is a technique that allows patients with drug hypersensitivity reactions to safely maintain drug therapy by creating temporary tolerance, especially for IgE-mediated reactions. It works by inhibiting mast cell activation and reducing the release of inflammatory mediators, often resulting in decreased skin sensitivity and potentially negative skin test results after the procedure. In this case, the patient had a grade 3 early-type drug allergy, and while literature on desensitization for new-generation oral anticoagulants is scarce, the successful desensitization to rivaroxaban suggests that it may be an effective option for similar patients in the future.

https://doi.org/10.1016/j.htct.2024.11.043

PP 16

INTERVENTIONAL PROCEDURE IN HEMOPHILIA A PATIENT WITH EXTENDED HALF-LIFE FACTOR THERAPY- CIRCUMCISION- CASE REPORT

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Case Report: Hemophilia A is a hereditary bleeding disorder due to factor VIII deficiency. With the advances in the treatment of hemophilia in recent years, the average life expectancy of patients has reached the healthy population. Along with prolonged life, additional diseases and intervention requirements are developing in this patient group. Due to the developments, management of patients going under interventions are more clear and easier. In this case, a patient who underwent an intervention with extended half-life factor therapy was presented. Forty-three-year-old male patient with severe hemophilia A was evaluated on request for circumcision surgery while using prophylactically extended half-life factor therapy 2×1000 Units / week. Tranexamic acid was started one day preoperatively to the patient whose basal factor level was below 1% and whose inhibitory level was negative. Body weight of the patient was 63 kg. Extended half-life factor VIII preparation (efmorogtocog alfa) loading dose of 3000 units was administered befrore half an hour of the procedure. aPtt was detected for 30 seconds and factor VIII level was 55% 30 minutes after loading dose. The patient was given appropriate sedative treatment to prevent pre-perioperative erection. The operation was carried out without any problems. 1500 Units 12 hours after the loading dose, and 24 hours after this dose was performed. The patient was discharged without complications without bleeding. Factor therapy was continued with prophylaxis dosing. Tranexamic acid was continued for 7 days. No complications were observed. Interventional procedures of hemophilia patients can be performed without complications with a multidisciplinary approach under appropriate dose and scheme factor therapy. In the case, an interventinal procedure was made by giving an extended half-life factor to a severe hemophilia patient who could not have a circumcision operation for many years due to previous hesitations of both patient and surgeons. ,

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Adult Hematology Abstract Categories

Lymphoma
PP 17

RARE CASE! SECOND PRIMARY MALIGNANCY IN LANGERHANS CELL HISTIOCYTOSIS, A JAK2+ CASE

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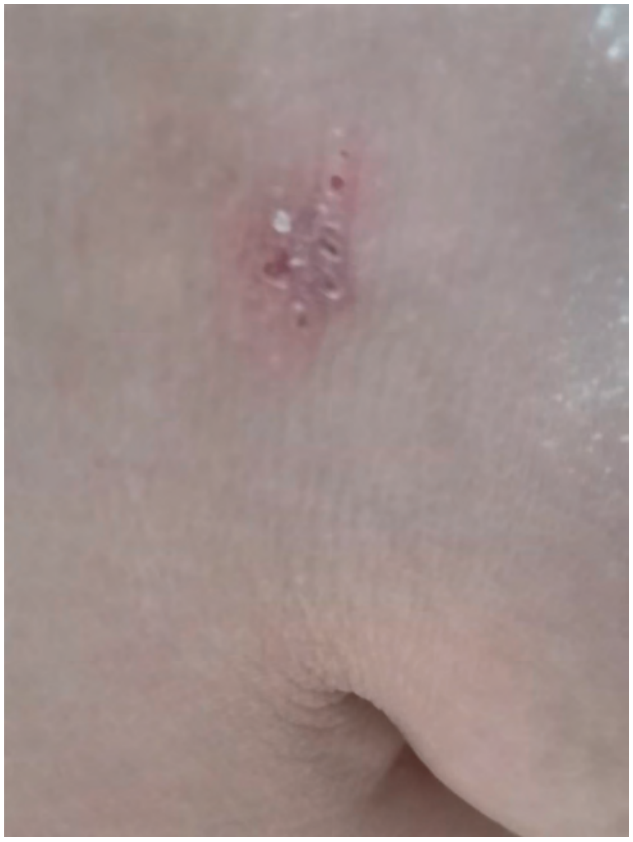
Objective: Langerhans cell histiocytosis (LCH) is a rare inflammatory myeloid neoplasm characterised by the infiltration of CD1a+CD207+ myeloid dendritic cells and immune cells, thus described as an inflammatory myeloid neoplasm that clonally expands. LCH is a histiocytic neoplasm affecting both paediatric and adult populations, with an estimated incidence of 3 to 5 cases per million children and 1 to 2 cases per million adults. LCH can involve all organ systems, with symptoms ranging from single organ disease to multi-system disease. While it can appear in any organ system, LCH has a particular affinity for bones, skin, lungs, and the pituitary gland. In 2016, LCH was reclassified from a reactive disorder to an inflammatory myeloid neoplasm following the identification of the recurrent BRAF V600E mutation in half of the cases and the observation of clonality. Recently, additional BRAF mutations that activate the MAP kinase pathway have been demonstrated, shedding more light on the pathogenesis of LCH. Several studies have suggested a high prevalence of second primary malignancies, including haematological and solid organ neoplasms, in LCH patients. **Case Report:** A 58-year-old male patient, with a known history of hypertension and hypothyroidism, presented to a medical facility in Germany in 2011 with skin lesions on the chest and neck swelling. Following lymph node and skin punch biopsies from the sternum, the patient was diagnosed with LCH, with imaging

revealing involvement in the frontal bone of the skull, neck, spleen, axillary, liver, lungs, and skin. The patient was treated with steroids. In 2014, while on holiday in Istanbul, the patient was given 6 cycles of vinblastine in addition to steroids. Steroid treatment was completed over 5 years, followed by regular follow-up. In 2021, the patient presented to Ordu State Hospital with fatigue and skin rashes resembling LCH lesions. Investigations revealed thrombocytosis, erythrocytosis, and leukocytosis. Bone marrow biopsy was reported as normal, and a punch biopsy of the skin lesions showed no evidence supporting LCH. Cytogenetic tests, however, revealed a JAK2+ mutation, which had not been detected in previous tests. The patient was started on hydroxyurea, and imaging showed a 5 cm mass in the spleen, for which splenectomy was recommended, though the patient declined and sought further consultation. Our cytogenetic studies confirmed BCRABL polymerase chain reaction (PCR), PML/RARA, and AML/MDS panel negativity, with JAK2+ positivity. Erythropoietin levels were 6 mU/ml (normal range: 3.7-31.5), LDH was 218 u/l, sedimentation rate was 60 mm/hour, platelet count was 517,000/μl, and white blood cell (WBC) count was 13,000/μl. Physical examination revealed remnants of old skin lesions (Figure 1), and there were no palpable lymph nodes or masses. Imaging showed a significant mass in the spleen and involvement in the frontal bone, liver, lungs, stomach, and neck lymph nodes, similar to previous findings. During follow-up, the patient occasionally reported pain in both legs, and Doppler studies revealed widespread thrombosis, which the patient stated had been occurring for the past 1.5 years but was disregarded. Subcutaneous anticoagulants and anti-stasis treatment (Daflon 1000) were initiated, later transitioning to oral anticoagulants. Follow-up showed improvement in symptoms under hydroxyurea and anticoagulant therapy, but recurring thrombotic events were noted during subsequent check-ups while on oral anticoagulants. Figure 1: Skin findings and biopsy scar marks on the neck, sternum, and abdominal areas of the patient. **Conclusion:** Discussion Several case reports and smaller case series have observed that malignant diseases may occur before, concurrently with, or after LCH, with a frequency higher than by chance alone. Edelbroek, J. R., and colleagues linked the emergence of second malignancies in LCH to prior treatments with chemotherapeutic agents such as etoposide or vinblastine, with the second malignancies being identified as leukaemia and myelodysplastic syndrome (MDS). Another study by Goyal, Gaurav, and colleagues followed 1,392 LCH cases, showing that Hodgkin and non-Hodgkin lymphomas developed in children during follow-up, while adults developed MDS in early follow-up and had an increased risk of developing B-cell acute lymphoblastic leukaemia (B-ALL) after about five years. In children, the leading cause of death was infections, while in adults, it was second primary malignancies. In our literature review, we did not encounter any JAK2+ cases or studies following LCH, making the JAK2+ positivity observed in our LCH patient a potentially unique case. We did find that JAK2+ positivity has been observed in the follow-up of non-Langerhans cell histiocytosis. Given that LCH is rare and second primary malignancies are even more uncommon, identifying such cases remains challenging, and further clinical studies are clearly needed.

Keywords: Langerhans Cell Histiocytosis, JAK2+.



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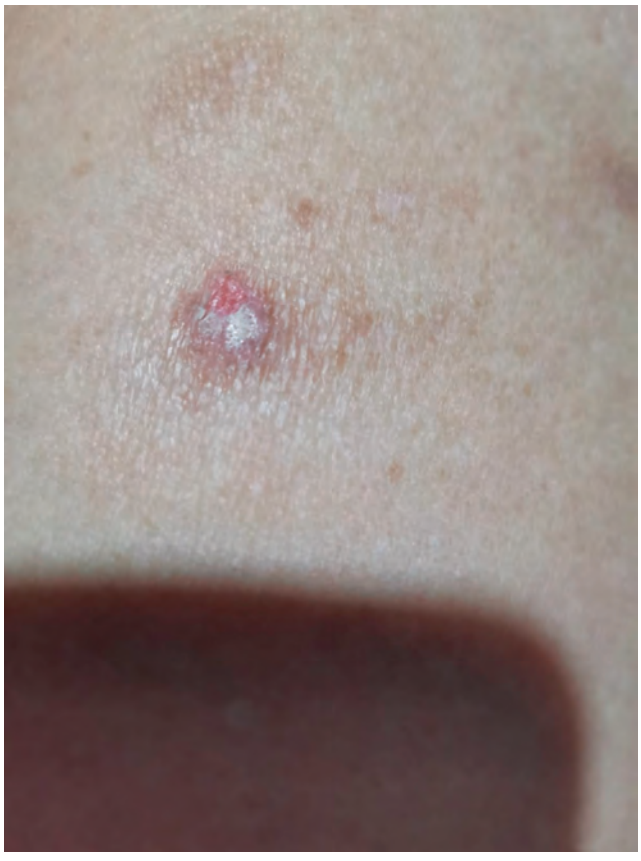

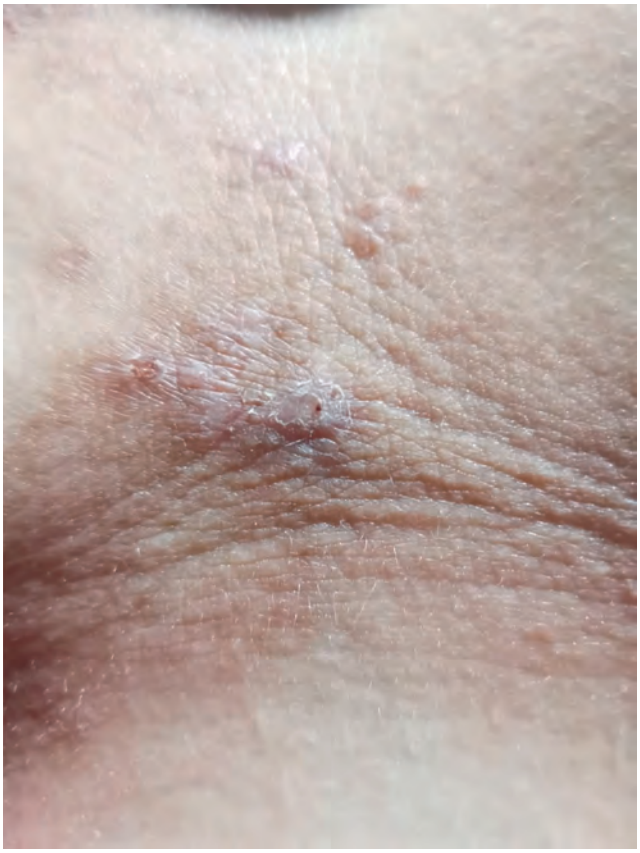

https://doi.org/10.1016/j.htct.2024.11.045

PP 18

A CASE OF DIFFUSE LARGE B CELL LYMPHOMA PRESENTING AS OSTEOSARCOMA

Mine Ezgi Payaslı [1,*], Müzeyyen Aslı Ergözoğlu [1], Berksoy Şahin [1]

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Case Report: Diffuse large B cell lymphoma (DLBCl) is the most common histologic subtype of non-Hodgkin lymphoma (NHl) accounting for approximately 25 percent of NHl cases. Additionally, Diffuse Large B Cell Lymphoma is the most common lymphoma. In the United States and England, the incidence of DLBCL is approximately 7 cases per 100,000 persons per year. In Europe as a whole, the incidence is approximately 4.92 cases per 100,000 persons per year. Like most other NHLs, there is a male predominance with approximately 55 percent of cases occurring in men. Incidence increases with age; the median age at presentation is 64 years for patients as a whole. IB, 45 years male patient. MRI scan taken in 2022 after a complaint of pain in right knee revealed a malignant tumoral lesion (osteosarcoma?) that caused intramuscular invasion in a segment of approximately 20 cm in the 1/2 distal femur and caused extensive cortical destruction in the distal. A biopsy was taken from the distal right femur. He was diagnosed with non-Hodgkin lymphoma and diffuse large B-cell lymphoma. Bcl-2, Bcl-6 and c-myc were found to be negative. After 4 cycles of R-CHOP protocol, PET-CT revealed minimal progression in the left clavicle and the IPI score was high. The patient's R-CHOP treatment was completed for 6 cycles with 2 cycles of intrathecal MTX. Afterwards, 2 cycles of maintenance rituximab were given. The patient, who subsequently went into remission, was followed up. This case shows us that NHL cases may present in a location such as primary bone tumor. The possibility of lymphoma should be considered in patients with atypical localization.

https://doi.org/10.1016/j.htct.2024.11.046

PP 19

EFFICACY OF GLOFITAMAB IN PRIMARY REFRACTORY LYMPHOMA: A CASE REPORT

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Objective: Diffuse large B-cell lymphoma (DLBCL) constitutes 30% of non-Hodgkin lymphomas and is often curable with frontline chemoimmunotherapy. However, in some patients, remission cannot be achieved, and this situation necessitates the application of second, third or even fourth-line salvage therapies. The limited treatment options for relapsed or refractory (r/r) DLBCL underscore an unmet clinical need, which urges the development of new therapies for this patients. Glofitamab is a humanized IgG1 bispecific monoclonal antibody binds to CD20 on malignant B lymphocytes and to CD3 on cytotoxic T cells with promise for treating r/r DLBCL. Here we present a primary refractory DLBCL patient to whom we applied glofitamab treatment as the 5th line. **Case Report:** A 28-year-old male patient was diagnosed with stage IV germinal center DLBCL biopsy of sacral mass. The patient received dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab (EPOCH-R) as first-line treatment. However, progression was detected by 18F-Fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) with computed tomography (CT). Then, rituximab plus ifosfamide, carboplatin, etoposide (R-ICE), ifosfamide gemcitabine vinorelbine prednisolone (IGEV), salvage radiotherapy (RT), rituximab plus bendamustine (R-B) therapies were given, respectively. Since no response was obtained to all these treatments, glofitamab was started as the 5th line therapy. After the twelve cycles of glofitamab therapy, the patient achieved complete remission (CR). Four months post-treatment, he was still alive. **Discussion:** Glofitamab is approved as a third-line treatment for r/r DLBCL, inducing a CR in nearly 40% of patients in this situation. According to literature, CR can be maintained for years after completion of glofitamab treatment. Data from a follow-up in a cohort of patients who were treated with glofitamab showed a median duration of complete response of 34 months. Our case post-treatment fourth months was still alive. This case indicates that glofitamab is quite effective primary refractory DLBCL.

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PP 20

A CASE OF MARGINAL ZONE LYMPHOMA PRESENTING WITH DIPLOPIA

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Objective: Marginal zone lymphoma (MZL) is characterized by the proliferation of B cells in post-germinal centers located in mucosa-associated lymphoid tissue (MALT), lymph nodes, and the spleen. MZL typically presents with an indolent clinical course. The average age at diagnosis is 60, with a slight female predominance, and it accounts for 5-17% of non-Hodgkin lymphomas (NHL). MZL is categorized into three subtypes based on the site of involvement: extranodal, splenic, and nodal MZL. Although these subtypes share many morphological and immunophenotypic characteristics as well as a slow clinical course, they can differ in terms of frequency, pathogenesis, clinical presentation, and treatment approach. The most common subtype is extranodal MZL, while nodal MZL is the least common. **Case Report:** A 51-year-old female patient presented to the clinic with a complaint of diplopia that had lasted for the past week. Physical examination revealed limited lateral gaze and anisocoria in the right eye, with other systemic examinations were normal. There were no B symptoms. Complete blood count, biochemical tests, serum electrolytes, and coagulation tests were within normal limits. Contrast-enhanced orbital MRI showed a lesion in the right intraorbital intraconal area, adjacent to the lateral aspect of the optic nerve and the medial aspect of the lateral rectus muscle. The lesion extended from the retroocular area to the orbital apex, obliterating intraorbital fat planes. It measured 35 × 13 mm in the axial plane, was hypointense on T2-weighted imaging and T1-weighted imaging, and showed homogeneous diffusion restriction on diffusion-weighted imaging. Post-contrast series revealed intense homogeneous enhancement of the soft tissue. The lesion measured 27 × 17 mm in the coronal plane. The findings were primarily suggestive of lymphoma involvement. PET-CT scan identified a hypermetabolic soft tissue lesion in the right intraorbital-retrobulbar area, continuous from the lateral aspect of the lateral rectus muscle to the lateral orbit, consistent with lymphoma. No extraocular nodal or visceral hypermetabolic foci were detected. Orbital biopsy results confirmed marginal zone lymphoma. Although radiotherapy could have been considered as a treatment option for localized involvement, the decision was made to administer 6 cycles of RB (Rituximab and Bendamustine) chemotherapy to the patient in order to avoid complications associated with radiotherapy due to the lesion's location in the orbital region. Follow-up PET-CT after 6 cycles of RB showed complete metabolic response with total regression of the hypermetabolic soft tissue lesion in the right retroocular area. The patient is currently in remission. This case is discussed due to the rare occurrence of ocular involvement in marginal zone lymphoma.

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Adult Hematology Abstract Categories

Myeloma
PP 21

CASE REPORT: PLASMA CELL LEUKEMIA IN A PATIENT WITH CHRONIC LYMPHOCYTIC LEUKEMIA

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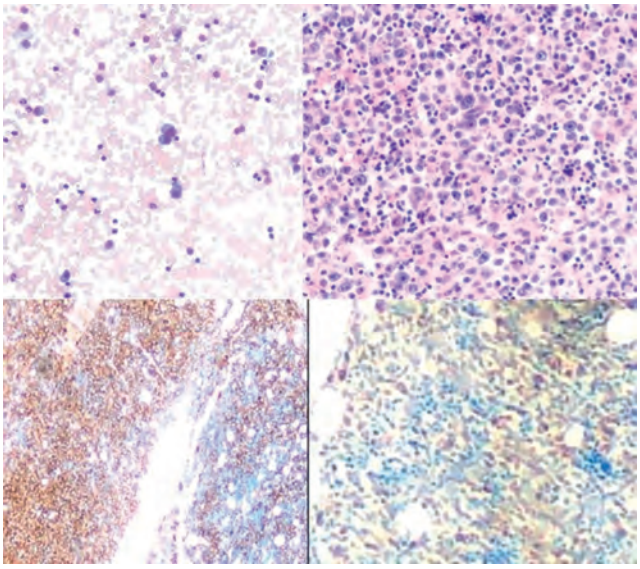
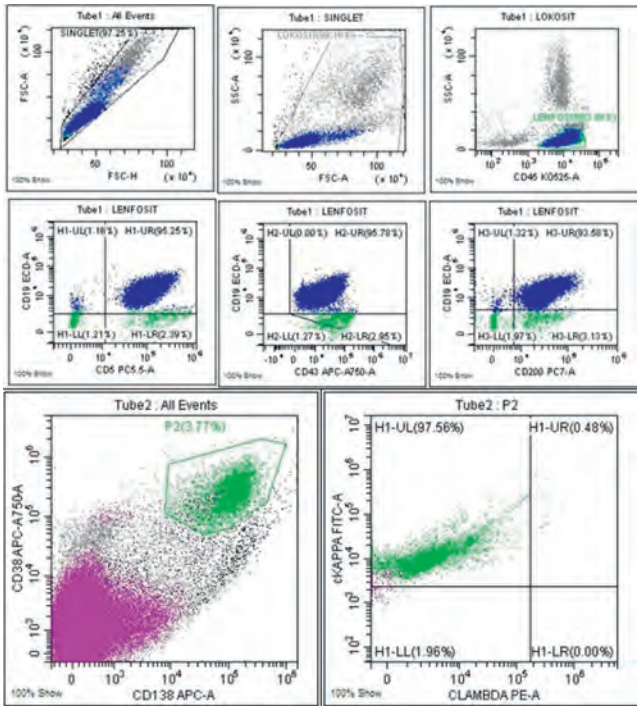
[4] *Kocaeli City Hospital, Department of Pathology*

Objective: Plasma cell leukemia (PCL) is a rare and highly aggressive plasma cell neoplasm that develops in 0.5% to 4% of patients with multiple myeloma (MM). In the diagnostic criteria updated in 2021, the circulating plasma cell rate, which is 20%, is defined as 5% or more. Plasma cell neoplasms originate from post-germinal center B cells and share many biological features with other B-cell lymphoproliferative diseases. Rarely, it can occur simultaneously with some indolent B-cell lymphomas, which may provide insight into common disease-initiating events and genetic changes. In this article, we present a case of primary plasma cell leukemia that presented with acute tumor lysis syndrome in a patient initially diagnosed with chronic lymphocytic leukemia. **Case Report:** A 74-year-old male with RAI Stage 1 Chronic Lymphocytic Leukemia (CLL), previously managed without therapy for the past 3 years, presented with fever, weakness, and elevated white blood cell counts over the past month. Initial laboratory tests revealed anemia (Hb 9.3 g/dL), elevated WBC ($52 \times 10^3/\mu L$), renal impairment (creatinine 2.5 mg/dL), elevated uric acid (12 mg/dL), and elevated LDH levels. The patient was diagnosed with tumor lysis syndrome and began treatment with intravenous hydration and allopurinole. Peripheral blood smear showed an increase in mature lymphocytes, smudge cells, and plasma cells. Serum protein electrophoresis detected 0.5 g/dL of M-protein, and immunofixation identified a monoclonal IgG kappa band. Bone marrow aspiration revealed two morphologically distinct populations of lymphocytes and plasma cells. Flow cytometry demonstrated a B cell population positive for CD5 and CD19 with kappa light chain restriction, and an increased number of clonal plasma cells (CD38+ CD138+ CD19+ CD45+) with kappa light chain dominance. Bone marrow biopsy confirmed the presence of 85% plasma cells positive for CD138, with kappa monoclonality. FISH analysis was negative for p53 deletion and t(11;14) translocation. Despite initiating anti-myeloma therapy, the patient's condition rapidly deteriorated. The patient was ultimately diagnosed with Stage 1 CLL complicated by plasma cell leukemia but succumbed to respiratory failure. **Conclusion:** Plasma cell leukemia is a disease characterized by abnormal, agressive plasma cells, while CLL involves malignant mature B-

cell lymphocytes. Although it is extremely rare for both conditions to occur simultaneously, it is important for clinicians to carefully evaluate patients, as both cell types originate from the same multipotent stem cells. Multiparametric flow cytometry of bone marrow samples can aid in the accurate and timely diagnosis of such cases. Key questions have arisen regarding whether B-cell CLL and multiple myeloma originate from a single clone or from two distinct clones appearing simultaneously. Previous studies have utilized various techniques, such as FISH or immunoglobulin gene rearrangement analysis, to explore this issue.



a-b Bone marrw aspirate and biopsy showing two morphologically distict populatıons od lymphocytes & plasma cells, many immature. c Immunohistochemical stain on bne biopsy showing plasma cell positive for CD130. D Plasma cells positive for kappa light chains



https://doi.org/10.1016/j.htct.2024.11.049

PP 22

LONG-ACTING ZOLEDRONIC ACID: ONCE-YEARLY ADMINISTRATION AND EFFICACY EVALUATION IN MYELOMA BONE DISEASE

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Objective: The objective of this study was to investigate the preventive effect of long-acting zoledronic acid on the development of new vertebral fractures in multiple myeloma patients with osteoporosis and/or vertebral fractures. **Case Report:** It is observed that osteolytic lesions in multiple myeloma patients lead to skeletal-related events (SRE), which result in a deterioration in quality of life and a shortened life span. It is estimated that up to 80% of all myeloma patients will experience a skeletal-related event.Although surgical and radiotherapy treatments may be required in specific cases, the most effective approach to avoid recurrence of SREs is to implement preventative measures. The current guidelines for the treatment of myeloma recommend the initiation of bisphosphonate therapy for all patients who meet one of the following criteria: 1. those with osteolytic bone disease, 2. those without bone disease but with symptoms, 3. those with osteoporosis. It is recommended that zoledronate be administered on a monthly basis for a minimum of 12 months. In terms of the length of treatment, it is indicated that the treatment interval can be extended to once every three months or discontinued in patients who have achieved a VGPR or above in response to myeloma treatment.Zoledronate is available in two different forms as 4 mg and 5 mg. Once-yearly administration of the 5 mg form is indicated for patients with osteoporosis and long-term steroid use. However, there is currently no data supporting the use of the 5 mg form in patients with myeloma. **Methodology:** The Zoledronate 5 mg formulation was administered parenterally, in a 250 cc isotonic solution for a period of 30 minutes, in patients who fulfilled the requisite study criteria. Patients were monitored for any fracture symptoms and side effects related to the administration of zoledronate at each visit to our clinic for myeloma treatment. In cases where a suspected fracture was identified, an MRI assessment was scheduled to be conducted on the relevant area. MRI scan of the spine and pelvis was conducted to assess the effectiveness of the zoledronate treatment at the six-month mark. **Results:** The results of the evaluation at six months were available for 16 of the 18 patients. Two patient was excluded from the study due to non-attendance at scheduled control visits and a decision to cease myeloma treatment. All 16 patients underwent a vertebral and pelvic MRI evaluation at the six-month mark. Bone fracture symptoms and biochemical values were assessed at each treatment visit. During the follow-up period, none of the patients reported any symptoms suggestive of new bone fractures. There were no instances of hypocalcaemia, renal dysfunction or albuminuria due to zoledronic acid administration. However, one patient did develop jaw osteonecrosis as a result of dental intervention in the fourth month of zoledronic acid administration.At the six-month MRI examination, none

of the patients had developed new fractures. **Conclusion:** 1. The 5 mg formulation of zoledronate has been proven to prevent the development of new vertebral fractures or the recurrence of fractures in all myeloma patients, regardless of whether they have a fracture or osteoporosis.2. In addition to its efficacy, this application eliminates the shortcomings associated with the aforementioned treatment regimen. With a single administration at the time of diagnosis, compliance is greatly enhanced.3.From a financial perspective, this has a notable impact on the cost of treatment. In Turkey, the lowest monthly price for a 4 mg dose of zoledronate is 884 TL. If the treatment is administered monthly for 12 months, the total cost is 10,608 TL. The cost of a box of denosumab is 4788 TL, with a total treatment cost of 57,456 TL if applied once a month for 12 months. The cost of a box of zoledronate 5 mg is 898 TL, reflecting the annual application frequency.In accordance with the recommendations set forth by the IMWG guideline, the treatment cost of the zoledronate 5 mg formulation is 11 times less expensive than that of the zoledronate 4 mg formulation and 63 times less expensive than that of denosumab, based on a one-year application period. 4. It is recommended that all myeloma patients, with or without osteolytic bone disease, be evaluated for osteoporosis. There is no clear recommendation in this direction in the guidelines. 5. If we add secondary osteoporosis, glucocorticoid use and previous fracture to the FRAX score, we see that all patients are at very high risk of major osteoporotic fracture and hip fracture. This shows that we need to raise awareness in this area.

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Adult Hematology Abstract Categories

Stem Cell Tranplant
PP 23

PRESENTATION OF 4 CASES OF AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION AFTER HIGH-DOSE CHEMOTHERAPY WITH REFRACTORY SOLID TUMOR DIAGNOSIS

Muhammed Murati [1,*], Yakup Ünsal [1], Güler Delibalta [1], Serdar Bedii Omay [1]

[1] *Emsey Hospital*

Case Report: Hematopoietic stem cell transplantation (HSCT) is a treatment method that can provide cure for most hematological malignant diseases. In addition to hematological malignancy, HCT is also used as a treatment method in benign hematological diseases, solid tumors, and autoimmune diseases. Autologous hematopoietic stem cell transplantation (AHCT) is the most common procedure performed in solid tumors. Transplantation is performed first as high-dose chemotherapy (HDC) and then as OHCT. In our transplant center between 2021 and 2023, were evaluated data of high-dose chemotherapy (HDC) and OHCT. Our first case is a 43-year-old female patient who received multiple treatments with the diagnosis of refractory primary peritoneal adenocarcinoma. Our second case is a 22-year-old male neuroblastoma patient who was first diagnosed with a retroperitoneal mass. Our third case is a 27-year-old male patient diagnosed with refractory Ewing Sarcoma. Our fourth patient is a 29-year-old male, who was diagnosed with refractory testicular cancer and to whom we performed a transplant.

https://doi.org/10.1016/j.htct.2024.11.051

PP 24

DOES BMI/BSA AFFECT STEM CELL MOBILISATION?: SINGLE CENTRE EXPERIENCE

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Objective: Haematopoietic stem cell transplantation is accepted as an important treatment strategy in the treatment of many haematological diseases including acute leukaemia, lymphoma, multiple myeloma as well as sickle cell anaemia and beta thalassaemia major. BMI is an important factor affecting the donor's response to mobilisation and thus haematopoietic progenitor cell yield. This effect is thought to be due to the relatively high dose of filgrastim administered to donors with higher BMI or to the presence of unknown intrinsic factors affecting mobilisation related to the amount of adipose tissue in each donor. In studies examining the relationship between obesity and CD34, negative effects of BMI on the number of progenitor cells have been shown. **Methodology:** A total of 41 patients, including 32 patients and 9 healthy donors, who underwent stem cell mobilisation for bone marrow transplantation in the therapeutic apheresis unit of Konya City Hospital between 10/2023 and 8/2024 were included in our study. The effects of disease diagnosis, age, number and content of chemotherapy, radiotherapy history, body surface area (BSA), body mass index (BMI), chronic habits such as smoking and alcohol, comorbidity and vitamin D level on stem cell mobilisation were investigated. **Results:** In our study, data of 9 healthy donors, 21 multiple myeloma and 11 lymphoma patients were analysed. Median age was 61 (18-72) years, 46.3% (19) were female and 53.7% (22) were male. There was a history of radiotherapy in 9.8% of the patients. While 46.3% of the patients were mobilised with cyclophosphamide+filgrastim, 41.5% with filgrastim, 4.9% with other chemotherapeutic agents+ filgrastim, 4.9% with filgrastim +plerixafor, 2.4% of the patients had stem cell collection by harvest procedure. On day 1 of stem cell mobilisation, there was no difference between those who collected sufficient CD34 positive stem cells and those who failed in terms of gender, height, weight, BMI, BSA, chronic habits, presence of comorbidities, vitamin D level and number of chemotherapy received. There was no statistically significant correlation between the total amount of CD34 positive stem cells and gender, height, weight, BMI, BSA, chronic habits, presence of comorbidities, vitamin D level and number of received

chemotherapy. A negative, strong and statistically significant correlation was found between the number of CD34 positive stem cells and BMI in multiple myeloma patients (rho: -0.705 p<0.001). **Conclusion:** Hematopoietic stem cell transplantation used in the treatment of many haematological disorders has become the gold standard treatment. Therefore, the factors affecting the success of transplantation have been the subject of research, and the effects of factors such as BMI, vitamin D, and gender have been investigated. In a cohort of 149 volunteers participating in a weight loss programme, the absolute number of CD34 positive progenitor cells and VEGF receptor-2, CD133 and CD117 positive cell subtypes decreased in relation with increasing BMI and waist circumference. Weight loss caused an increase in CD34 and CD117/CD34 cell counts. In our study, it was shown that high BMI in multiple myeloma patients caused lower CD34 levels in the cell collection process. We believe that it would be useful to perform this analysis with a larger patient population.

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Adult Hematology Abstract Categories

Transfusion Medicine and Apheresis
PP 25

EVALUATION OF IRON ACCUMULATION DURING CHILDHOOD CANCER TREATMENT

Şule Çalışkan Kamış [1,*], Metin Çil [1], Begül Yağcı [1], Barbaros Şahin Karagün [1]

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Objective: Iron overload is a major concern in pediatric oncology, particularly with frequent blood transfusions. Although serum ferritin levels are commonly used as a marker, cardiac and hepatic T2* MRI is the gold standard for accurate assessment. This study aimed to evaluate the relationship between serum ferritin levels and T2* MRI values in pediatric cancer patients, focusing on cases with ferritin levels exceeding 1000 mcg/L. **Methodology:** This prospective study included pediatric patients aged 10-25 diagnosed with malignancies at Adana City Training and Research Hospital from June 2023 to December 2024. Ferritin and C-reactive protein (CRP) levels were measured during non-infectious periods. Elevated ferritin was confirmed if CRP was also raised. Data on transfusions and ferritin levels were collected at 3, 6, and 12 months post-diagnosis. Patients with ferritin levels above 1000 mcg/L underwent cardiac and hepatic T2* MRI to assess the need for iron chelation therapy. **Results:** A total of 28 patients (median age: 14 years) were analyzed, with 12 females and 16 males. The median ferritin level at diagnosis was 32.5 mcg/L. Significant associations were found between transfusion frequency and ferritin levels over 1000 mcg/L within 3 months (p=0.029) and annually (p=0.001). Three patients had ferritin levels above 1000 mcg/L: two with acute lymphoblastic leukemia (ALL) and one with non-Hodgkin lymphoma (NHL). One patient died, another received a bone marrow transplant, and the third had normal cardiac but moderate hepatic iron levels. In one case, ferritin dropped below 1000 mcg/L without chelation by 12 months. Elevated ferritin in the transplant patient was likely related to the procedure. **Conclusion:** Iron overload is a significant challenge in pediatric cancer, particularly during transplants. Early monitoring and timely chelation can help manage this risk. Future research should focus on optimizing iron management strategies in this vulnerable population.

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Adult Hematology Abstract Categories

Other Diseases
PP 26

IMMUNE THROMBOCYTOPENIA WITH EPSTEIN-BARR VIRÜS-ASSOCIATED INFLAMMATORY PSEUDOTUMOR OF THE SPLEEN

Ulviyya Hasanzade [1,*], Metban Mastanzade [1], Kürşat Rahmi Serin [2], Gorkem Uzunyolcu [2], Mehmet SemihÇakır [3], Ali Yılmaz Altay [4], Gulcın Yeğen [4], Sevgi Kalayoglu Beşışık [1]

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Objective: Introduction: Inflammatory pseudotumors (IPTs) are rare and may occur in various anatomic sites. Splenic IPTs are extremely rare, often associated with Epstein–Barr virus (EBV) and have a low-malignant potential with recurrences. The tumor showed a mixed inflammatory infiltrate with spindled cells focally composed of follicular dendritic cell (FDC) proliferations. It can mimic hematopoietic diseases as mostly with solitary mass lesion, but can also be discovered incidentally. **Case Report:** A 64-year-old male patient, admitted to the general surgery department with complaints of hematochezia. He had severe thrombocytopenia (2. x10^9/L) with mild increased leukocyte count (12.270 × 10^9/L). Endoskopic evaluation of gastrointestinal did not reveal any significant abnormality. Abdominal tomography showed a splenic mass lesion sized of 40 × 37mm. On MRI the lesion was mildly hypointense on T2-weighted images, not visible on T1-weighted images, and demonstrated progressive peripheral contrast enhancement in dynamic post-contrast series. Bone marrow biopsy showed no hematopoietic disease. A diagnostic splenectomy was decided. Prednisone (1.0 mg/kg/day) was started with a possible diagnosis as immune thrombocytopenia which resulted a significant response and the patients was vaccinated according to the splenectomy vaccination guideline. With a platelet count of 450. x10^9/L he underwent splenectomy. Spleen specimen showed a nodular lesion.

Histologic evaluation revealed polytipic lymphoplasmacytic infiltration with focal spindle-shaped cells which were found to be EBER positive. EBV-associated IPT was diagnosed. The patient had no post-operative complaints, and one month after surgery, the platelet count was 386,000 × 10^9/ml with no recurrence of thrombocytopenia. Serum EBV-DNA results remained negative before and after diagnosis. **Discussion:** The IPTs of the spleen can develop either via proliferation of myofibroblasts or FDC that may be infected by EBV. They may be discovered by investigation of another disorder similar to our case as ITP, leukemoid reaction or hypercalcemia. Total resection of the tumor results in general improvement.

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PP 27

CHOROID PLEXUS CARCINOMA AND CHOROID PLEXUS PAPILLOMA; RARE CASES

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Case Report: Choroid plexus carcinoma (CPC) is a rare and aggressive intracranial neoplasm, constituting 1–4% of all brain tumors and approximately 40% of choroid plexus tumors. Classified as a WHO Grade III malignancy, CPC is characterized by a poor prognosis, with reported 5-year survival rates around 40%. In contrast, choroid plexus papilloma (CPP), classified as a WHO Grade I tumor, is a benign and slow-growing lesion originating from the epithelial cells of the choroid plexus. This report presents four cases of choroid plexus tumors: two diagnosed as choroid plexus carcinoma (WHO Grade III) and two as choroid plexus papillomas (WHO Grade I). The CPP cases were managed with observation and followed up without active treatment. Among the CPC cases, a 3-year-old patient received initial radiotherapy followed by chemotherapy based on the CPT-SIOP-2000 protocol. A 7-month-old patient with CPC was treated with chemotherapy (CPT-SIOP-2000 protocol), while radiotherapy was deferred due to her age of less than 3 years. Multidisciplinary treatment strategies for CPC include maximal surgical resection followed by chemotherapy and radiotherapy. The CPT-SIOP-2000 study has demonstrated that the Carboplatin/Etoposide/Vincristine (CarbEV) chemotherapy protocol is effective in treating CPC.

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PP 28

CLINICAL AND GENETIC FEATURES IN CONGENITAL GLYCOSATION DEFECTS PRESENTING WITH HEREDITARY HEMOLYTIC ANEMIA AND PROLONGED JAUNDICE

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Objective: Congenital glycosylation disorders (CGD) are a large group of genetic diseases that occur due to a decrease or increase in the glycosylation of glycoconjugates. Congenital glycosylation disorders; They can be grouped under 4 groups: protein N-glycosylation, protein O-glycosylation, combined N- and O-glycosylation and lipid glycosylation disorders. Congenital glycosylation disorders are divided into 2 main groups: Type I and II (CGB-1 and GB-2). In this article, we would like to present a cases of CGB with an atypical presentation, presenting clinical findings with hemolytic anemia and prolonged jaundice, and diagnosed by clinical exon panel genetic study, since it is very rare in the literature. **Case Report:** Our first patient, H1, was a 6-month-old male infant who received erythrocyte transfusion at an external center at the age of 14 days due to jaundice and anemia during the neonatal period (when HB: 5 g/dl), and then applied to the pediatric hematology clinic of our hospital with the same complaints at the age of 43 days. As a result of molecular tests, he was diagnosed with CGD type 2. Our other patient, H2, is a 10-year-old male, our third patient, H3, is a 13-year-old male, and our last patient, H4, is a 17-year-old male; These 3 patients were siblings. All three of them were hospitalized at an external center with jaundice and anemia during the neonatal period, but after diagnostic genetic tests, H4 was diagnosed after 3 years of age, but the other siblings were diagnosed after 6 months of age due to the oldest sibling's history. C.657c>A homozygous mutation was detected in the GSS gene in these siblings. **Methodology:** The diagnostic difficulties and treatment options of 4 patients (H1, H2, H3, H4), who received inpatient treatment with anemia and jaundice in the pediatric hematology clinic between 2022 and 2024 and were ultimately diagnosed with CGD, were obtained from the hospital information processing system and presented because they are very rare in the literatüre. **Results:** Our first patient, H1, was a 6-month-old male infant who received erythrocyte transfusion at an external center at the age of 14 days due to jaundice and anemia during the neonatal period (when HB: 5 g/dl), and then applied to the pediatric hematology clinic of our hospital with the same complaints at the age of 43 days. As a result of molecular tests, he was diagnosed with CGD type 2. Our other patient, H2, is a 10-year-old male, our third patient, H3, is a 13-year-old male, and our last patient, H4, is a 17-year-old male; These 3 patients were siblings. All three of them were hospitalized at an external center with jaundice and anemia during the neonatal period, but after diagnostic genetic tests, H4 was diagnosed after 3 years of age, but the other siblings were diagnosed after 6 months of age due to the oldest sibling's history. C.657c>A homozygous mutation was detected in the GSS gene in these siblings. **Conclusion:** Although prolonged jaundice and anemia are quite common, we wanted to emphasize with this very unique study that metabolic diseases may be among the differential diagnoses that are very rare in the literature. CGD has been diagnosed in only 40 cases in the last 30 years; Diagnostic evaluation with genetic consultation is very important for diagnosis. Literature data on rare diseases will be strengthened with new studies.

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PP 29

A RARE CASE OF PANCREATOBLASTOMA IN A PEDIATRIC PATIENT

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Case Report: Pancreatoblastoma (PB) is a rare malignant neoplasm. PB is frequently detected in children under 10 years of age. Symptoms are nonspecific. When diagnosed, most tumors are enlarged (> 5 cm). Abdominal pain is often the first complaint (44%). Alpha-fetoprotein (AFP) levels are high. Provides long-term survival with surgical resection. It has been reported that the prognosis is poor if metastases are detected. Here we present a seven-year-old female PB case. She applied with the complaint of abdominal pain. On physical examination, a mass was palpated in the epigastric region. The changed laboratory findings were an increased serum AFP level of 171.1 micrograms/L (normal range 0-9 micrograms/L). Abdominal computed tomography (CT) examination revealed a solitary mass of approximately 6 × 4 cm in the tail of the pancreas. Multiple mass lesions were observed in the liver. These lesions were evaluated as compatible with metastasis. She was diagnosed with PB histopathologically after Tru-cut biopsy. Pathologically increased Fluorodeoxyglucose (FDG) uptake (SUVmax: 9.99) was observed in the mass lesion around the right upper quadrant gastric corpus in F-18-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (^{18}F-FDG PET/CT). Malignant hypermetabolic metastatic multiple hypodense mass lesions (SUVmax:7.7) were seen in the liver. OPEC chemotherapy was given. In the evaluation performed after 5 cycles of chemotherapy, a decrease in FDG uptake ^{18}F-FDG PET/CT was detected. The patient was evaluated as responsive to treatment. This case report may contribute to the literature with its rarity and treatment approach.

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PP 30

RPL5 NOVEL MUTATION IN A PATIENT WITH DIAMOND BLACKFAN ANEMIA

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Case Report: Diamond-Blackfan anemia (DBA) is a rare inherited disorder characterized by macrocytic anemia, congenital malformations, and growth retardation, typically presenting in the first year of life. RPL5 encodes a component of the 60S ribosomal subunit, and mutations in this gene are associated with DBA, which is usually inherited in an autosomal dominant. Our case is presented after identifying a novel mutation that lacks the typical phenotypic features associated with the condition. A 17-month-old female patient was sent to our hospital because she was pale and had anemia. During the physical examination, the patient exhibited growth and developmental retardation (height in the 3rd to 10th percentile, weight in the 3rd percentile) and a pointed nose; however, no organomegaly or congenital malformations were detected. Laboratory results showed a hemoglobin level of 4.9 g/dL, an MCV of 90 fL, and a corrected reticulocyte count of 0.8%. HbF level in hemoglobin electrophoresis was 3.5%. Bone marrow examination revealed severe hypoplasia in the erythroid series. Genetic examination using next-generation sequencing detected a novel mutation in the RPL5 gene c. 10G>C (p. Val4Leu) (Heterozygous)). Although RPL5 mutations show more severe phenotypic features in DBA, the new mutation detected in our patient caused anemia and developmental and growth retardation without congenital malformation. This genetic change has not been previously reported in the literature as a novel mutation. However, according to the American College of Medical Genetics and Genomics (ACMG) criteria, this variant has been classified as a "variant of uncertain significance". Given that no additional mutations were identified in the whole exome sequencing (WES) analysis conducted on our patient, the hematological and bone marrow findings were consistent with a diagnosis of DBA. **Methodology:** A blood transfusion was administered to the patient, and steroid treatment was started. Our patient responded to steroid treatment during follow-up. WES analysis was also requested for our patient's mother, father, and sibling. Based on the results, donor screening for bone marrow transplantation will be initiated. Once the results are available, the phenotype-genotype relationship can be interpreted more accurately.

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PP 31

HYPEREOSINOPHILIC SYNDROME

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Case Report: A 58-year-old female patient was referred to the hematology clinic in July for examination after leukocytosis was detected in her tests. She has a known history of CKD, Type 2 DM, HT, hyperlipidemia. The patient's general condition is good, and she had a complaint of numbness in her hands. First 1.5 months ago, numbness in her right hand up to the wrist began,especially severe in the first 3 fingers The same complaints started in her left hand 1 month ago. Physical examination findings were within normal limits. On sensory examination, there was hypoesthesia in the first 3 fingers of both hands, especially on the right. In the blood tests performed at the time of admission, leukocytes were 34.440μL, neutrophils 8.840μL, eosinophils 20.540μL, absolute lymphocyte count 3.890μL, monocytes 1.080 μL, hemoglobin 12 g/dL, platelets 348.000 μL, creatinine 1.07 mg/d/L, CRP: 56.6 mg/dL, sedimentation - 10 mm/h were measured. The patient has had borderline eosinophilia (1510μL) since 2022. Flow cytometry was performed on peripheral blood. 11% lymphoid series and 89% myeloid series cells were seen. No abnormality was observed in the lymphoid series. A slight regression in maturation was seen in myeloid series cells and

an increase in eosinophilic series cells. Blast ratio was detected as negative. ECHO findings were normal. No pathology was observed in the lung. Diagnostic bone marrow biopsy was performed.EMG revealed sensorimotor demyelination with block at the wrist levelin the right median and neuropathy with secondary axonal damage. It was evaluated as CTS. After the biopsy, corticosteroid treatment was startedOn the 2nd day of treatment, the patient's eosinophil count was 350μLShe was discharged with oral steroid treatment and discharged with oral steroid.In the control eosinophils decreased to2160 μL. In the pathology report of biopsy, hypereosinophilic syndrome was considered.No diagnostic findings were detected in favor of neoplastic/clonal eosinophil expansion

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PP 32

A RARE CAUSE OF THROMBOCYTOPENIA: MALARIA

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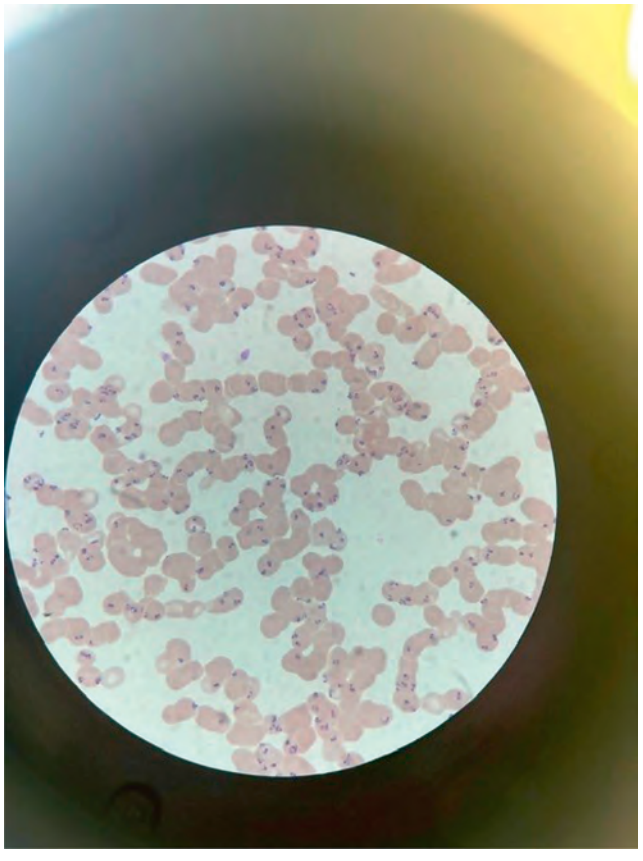
Objective: Malaria is a potentially fatal condition caused by parasites that are spread to humans through the bites of infected female Anopheles mosquitoes, according to the World Health Organization (WHO). Two parasite species, Plasmodium falciparum and Plasmodium vivax, are the most significant threats globally, both known to be infectious to humans. Hematological changes are the most frequent consequences of malaria and have a significant impact on the pathophysiology of the disease. Changes in platelet parameters are considered a hallmark of malaria infection. Often, these changes in malaria infection may be a result of higher levels of parasitemia. Thrombocytopenia is frequently observed in malaria infection. This report presents a case of malaria as a rare cause in a patient investigated for thrombocytopenia. **Case Report:** A 34-year-old male patient with no known medical history presented to the emergency department with complaints of fever, chills, and rigors. Upon admission, his lab results showed wbc: 3,2 thousand/ul, hgb:13.2 gr/dl, neutrophils: 2400, plt:12 thousand/ul, CRP: 232 mg/dl, creatinine: 0.9 mg/dl, AST: 100 u/l, total bilirubin: 2.7 mg/dl, ALT: 66 u/l. The patient was a sailor and had recently returned from the Ecuador Gine region 15 days ago. He had also stayed in Ghana for 40 days prior to that. The patient had taken prophylactic medication for malaria once. Physical examination revealed abdominal tenderness and fever. Peripheral blood smear evaluation revealed widespread ring forms (Figure 1). Following consultation with microbiology, the patient was diagnosed with malaria. The health authority was notified, artemether + lumefantrine medication was procured and the patient was referred to the tertiary care facility. It was later learned that the patient started IV treatment for malaria, but his condition deteriorated, he was intubated and subsequently expired. **Discussion:** Malaria remains a global public health concern considering the number of cases and death rate worldwide. Changes in platelet parameters are considered a hallmark of malaria infection, and often these changes in malaria infection may be a result of higher levels of parasitemia. Studies have shown that the median platelet count was significantly decreased in adult patients with malaria compared to apparently healthy individuals. Thrombocytopenia is one of the most frequent complications of malaria infection, though it is not a criterion for severe malaria, and it is commonly observed in both Plasmodium vivax and Plasmodium falciparum malaria. Previous studies have shown a correlation between parasite density and the severity of malaria infection complications. There is uncertainty regarding the degree of platelet parameter changes that occur during malaria infection and the underlying biological mechanisms associated with parasitemia levels. The speculated mechanisms leading to thrombocytopenia include coagulation disturbances, splenomegaly, bone marrow alterations, antibody-mediated platelet destruction, oxidative stress, and the role of platelets as cofactors in triggering severe malaria. There is no clear recommendation for the adequate management of these hematological complications. It is essential to consider thrombocytopenia and changes in platelet parameters in malaria patients. This report also highlights the need for further research on the subject.



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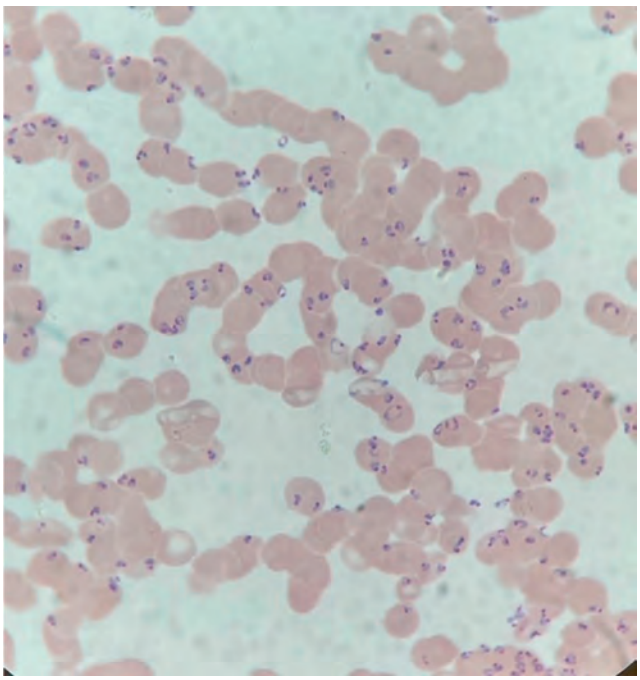

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PP 33

A CASE OF THROMBOTIC THROMBOCYTOPENIC PURPURA RELATED TO MALIGNITY AND CHEMOTHERAPY

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Objective: Thrombotic thrombocytopenic purpura (TTP) is a life-threatening multisystem disease. TTP progresses with Microangiopathic hemolytic anemia (MAHA), fever, thrombocytopenia, neurological symptoms, and renal failure. Due to microangiopathic hemolytic anemia, schistocytes are seen in the peripheral blood smear, resulting in thrombocytopenia. Damage to the brain and kidneys occurs due to microvascular thrombosis, and this is how symptoms appear. In pathogenesis, it is caused by the deficiency of ADAMTS 13 (a disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13), which breaks down the von Willebrand factor (VWF) found in the endothelium into multimers, or the development of antibodies against it. Due to ADAMTS 13 deficiency or decrease in its activity, VWF cannot be separated into small pieces and is arranged in large pieces in the endothelium, causing widespread intravascular thrombosis. Many factors can be considered as triggers for the development of TTP, such as pregnancy, malignancy, medications, and autoimmune diseases. **Case Report:** A 59-year-old female patient was admitted due to thrombocytopenia, epileptic seizure, hematemesis and decreased consciousness while being followed up due to cholangiocellular carcinoma. Due to malignancy, 6 cycles of gemcitabine and carboplatin treatment were applied. The last cure was 6 months ago. In followers, WBC 3.24 10^3/uL (3.7-10 10^3/uL), Hbg 8g/dL(12.9-14.2 g/dL), MCV 84 f/L(81-96fL), platelet 27 10^3/uL (155-356 10^3u/L), total bilirubin 13 mg/dL (0.3-1.2 mg/dL), indirect bilirubin 5.36 mg/dL (0-1.5 mg/dL), LDH 408 U/L (0-247u) /L), creatinine 1.59 mg/dL (0.51-0.95 mg/dl), protein 1+ in full criterion examination, INR 1.36, PT 15.4 sec (10-15 sec), APTT 22.2 sec (21-29 sec) fibrinogen was 1.46 g/L (1.8-3.5 g/L), 3-5 schistocytes were seen in each area in the peripheral smear. Plasmapheresis treatment was started with the preliminary diagnosis of TTP and steroid 80 mg was given. ADAMTS 13 tests were requested. ADAMTS 13 level is 3.78% (40%-130%) low and ADAMTS 13 inhibitor > 80 U/mL (<12U/mL negative, 12-15 U/mL borderline >15U/mL positive), ADAMTS 13 antigen<0.01lU/ mL (0.19-0.81 lU/mL) was seen. As the patient's thrombocytopenia continued, plasmapheresis was started to be performed twice a day after a week. With this treatment, weekly treatment of medicinal rituximab, which could not be treated with platelets, was arranged. However, the patient did not respond to treatment and died. **Conclusion:** In cancer assosiated TTP, endothelial cells are damaged due to abnormal angiogenesis and tumor cell invasion, and vWF multimers in the endothelial wall are exposed. In addition, ADAMTS 13 activity decreases due to antibodies formed against ADAMTS 13. Some chemotherapeutics such as mitomycin c, gemcitabine can cause TTP. When a diagnosis of TTP is considered, plasma exchange should be started immediately. In addition to plasma exchange, steroids are given in the treatment and if there is no response, other immunosuppressive treatments are added. Our patient with high ADAMTS 13 inhibitors is a condition that is thought to contribute to the mortality of TTP. In a study, it was observed that low ADAMTS 13 activity, as well as high ADAMTS 13 inhibitor and low ADAMTS antigen, caused an increase in mortality.

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PP 34

A RARE DISEASE ASSOCIATED WITH IG4, CHARACTERIZED BY SYSTEMIC AMYLOIDOSIS AND LYMPHOPLASMACYTIC CELL DOMINANCE: A CASE PRESENTATION

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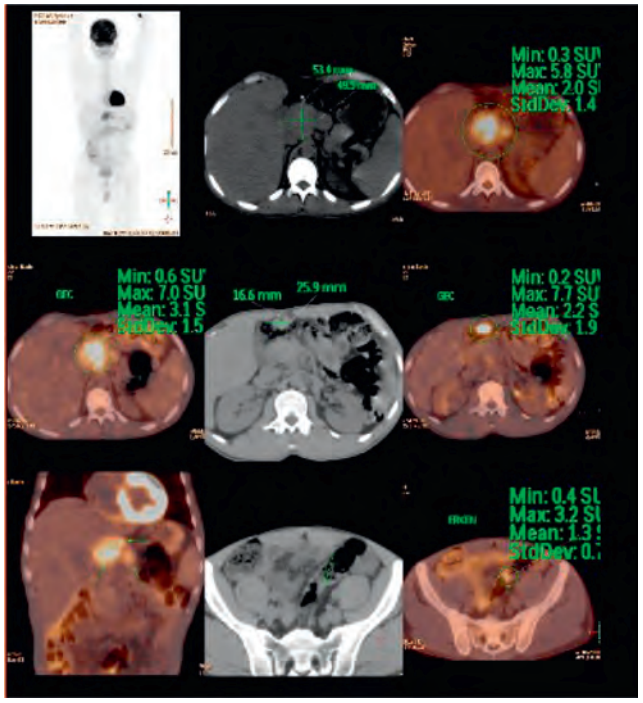
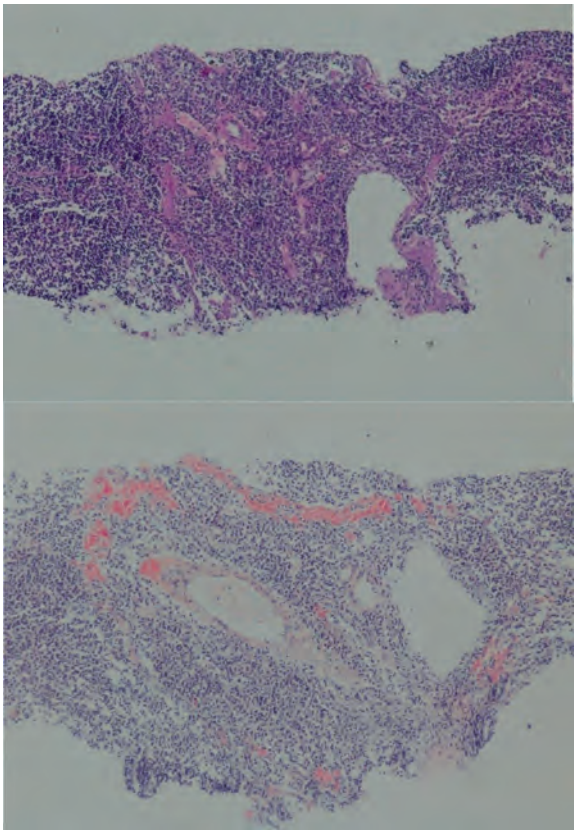
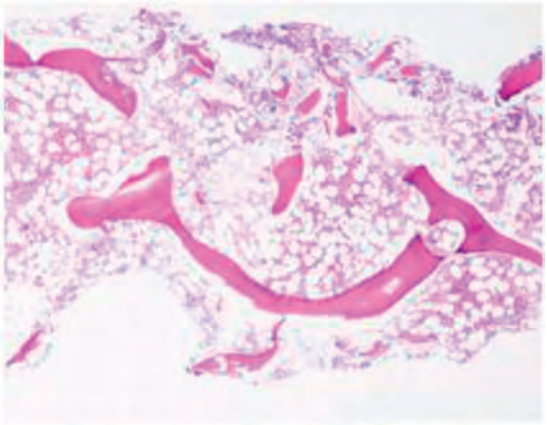
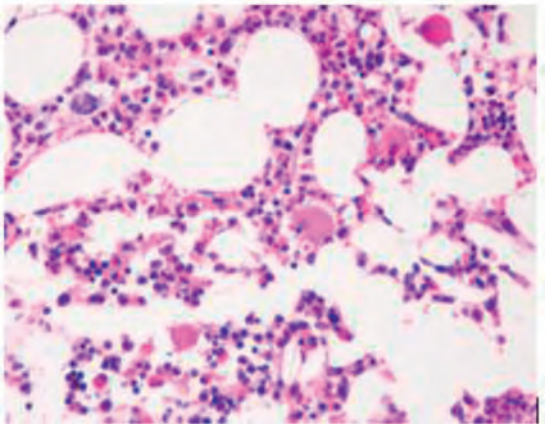
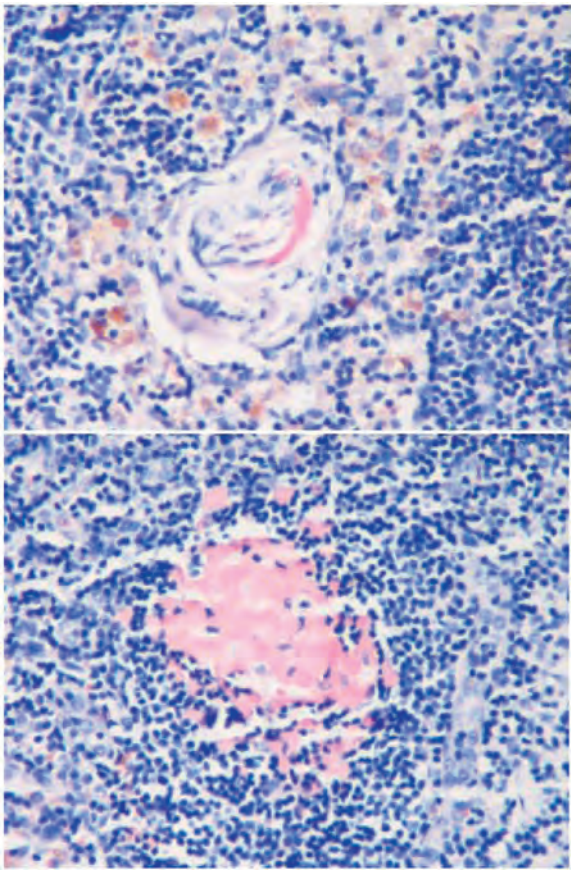
Objective: Immunoglobulin G4 (IgG4)-related disease has been identified in the last 10-15 years, though it was previously known in the literature under different names as an autoimmune disorder. The spectrum of the disease is quite broad. It can present with involvement of a single organ or multiple organs simultaneously, including autoimmune pancreatitis, Mikulicz syndrome, Küttner tumor (chronic sclerosing sialadenitis), sclerosing cholangitis, and retroperitoneal fibrosis. It most commonly occurs in males over the age of 50. In this case presentation, we will discuss a patient who presented with systemic amyloidosis and was diagnosed with IgG4-related disease. **Case Report:** A 36-year-old male patient presented to the hospital with complaints of abdominal pain and constipation. He was evaluated through detailed anamnesis and physical examination. The patient was found to have iron deficiency anemia and elevated acute phase reactants. An abdominal ultrasound revealed a mass in the epigastric region, leading to admission to the gastroenterology department. A CT scan of the abdomen showed a 62 × 55 mm lesion in the epigastric region. A trucut biopsy was performed, which was reported as amyloidosis. The biopsy revealed an increase in plasma cells. A PET-CT scan identified hypermetabolic lymph nodes in the celiac trunk region. A biopsy taken from these nodes was also reported as amyloidosis, with no evidence of monoclonality. Results showed positivity for CD138, Kappa, Lambda, Congo red, and IgG4, with negativity for HHV8. Serum IgG level was 3256 mg/dL, albumin was 3.59 g/dL, total protein was 8.59 g/dL, sedimentation rate was 65 mm/h, and elevated levels of free kappa and lambda light chains were detected. The patient developed renal failure and hyperkalemia. A renal biopsy showed positive staining for AA amyloid, and a bone marrow biopsy was subsequently performed. The PET-CT scan did not reveal plasmacytoma or osteolytic lesions. The bone marrow biopsy showed 7-8% staining with CD38 and CD138. Positive staining was noted for AA amyloid, IgG, and IgG4, particularly in plasma cells. An initial diagnosis of lymphoplasmacytic lymphoma was considered, and excisional biopsies of lymph nodes were planned. The excisional biopsy of the left axillary lymph node was reported as amyloidosis, leading to a referral to the rheumatology department to investigate secondary causes of amyloidosis. IgG subclasses were tested, revealing an IgG4 level of 700 mg/dL. The patient was started on corticosteroid therapy at a dose of 1 mg/kg. **Conclusion:** IgG4-related disease is a fibroinflammatory condition that can affect any organ simultaneously or at different times. It is a systemic disease that can involve all organs and often presents with organomegaly, mimicking malignancy. The immunopathogenesis of the disease is not yet fully understood. The most critical step in diagnosis is the histopathological evaluation of the affected organ. Histopathological features distinguishing the disease include dense lymphoplasmacytic infiltrates with predominance of IgG4-positive plasma cells, storiform fibrosis, and obliterative phlebitis. There are no specific diagnostic tests for IgG4-related disease, making differential diagnosis very important. The first comprehensive diagnostic criteria for IgG4-related disease were established in 2011, and new classification criteria were introduced in 2019. A serum IgG4 level of ≥ 135 mg/dL is significant for diagnosis. The primary treatment for IgG4-related disease is corticosteroids, which typically respond well to therapy. Most patients show a response to treatment within 4 weeks. With therapy, patients often experience a reduction in symptoms, a decrease in the size of masses in affected organs, improvement in organ function, and a general decline in serum IgG4 levels over several weeks. After the initial response, the dose should be gradually reduced by 5 mg every 2 weeks to maintain remission, ideally for a duration of 3-6 months at the lowest effective dose. However, relapses can occur, and in cases of resistant or recurrent disease, additional treatments such as rituximab and other immunosuppressive agents may be required. These include azathioprine (2 mg/kg/day), mycophenolate mofetil (1-1.5 g/day), and cyclophosphamide (50-100 mg/day). Biological agents such as infliximab, tocilizumab, calcineurin inhibitors, and bortezomib may be used for refractory cases. Studies evaluating the effectiveness of monoclonal agents like abatacept, inebilizumab, and elotuzumab in the treatment of IgG4-related disease are also available. Early diagnosis and appropriate treatment are crucial for controlling the disease and preventing complications.

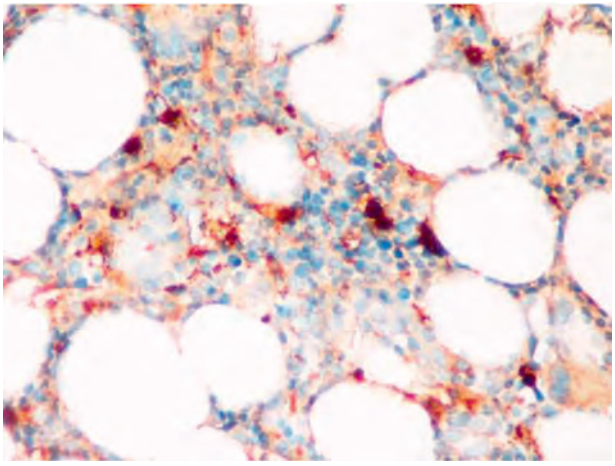


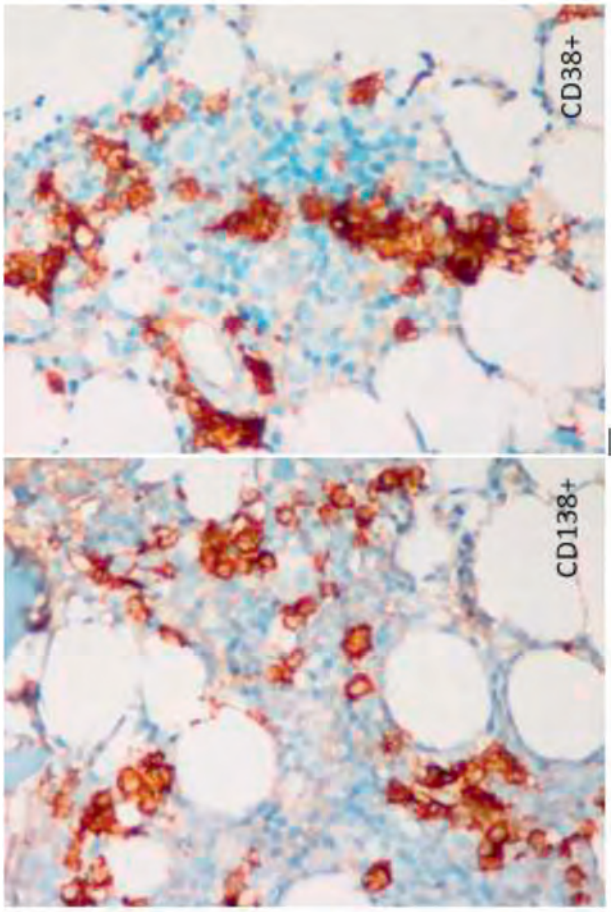












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PP-35

B-LINEAGE PROGENITORS AND CD38-POSİTİVE B CELLS ARE ASSOCIATED WITH SURVIVAL RATES IN BREAST CANCER PATIENTS

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Objective: The immune system plays an increasingly important role in the development of targeted strategies for breast cancer. According to mRNA sequencing data from The Cancer Genome Atlas (TCGA) high expression B cell signatures has beneficial effects on survival rates in many tumors. Bone marrow (BM) is poorly understood from the point of view of the prognostic role of hematopoietic cells and subpopulations of lymphocytes in patients with breast cancer (BC). **Methodology:** . Study was carried out in 107 BC patients. The immunological and morphological methods were applied. Multiparameter flow cytometry with antibodies to B-cell populations was used (CD19, CD20, CD5, CD38, CD10, CD45, HLA-DR, CD27), FACSCANTO II. Studies of BM lymphocyte subpopulations were carried out in the gate of CD45++ cells. The duration of the follow-up period after surgery was 8 years. **Results:** The total percentage of B cells in BM was significantly associated with the prognosis of BC. B-1 cells were associated with progression-free and disease-free survival. Disease progression was observed at low levels of B1 cells. In cases more than 10% B-lymphocytes in the BM of BC patients overall survival (OS) rates were more favorable ($p = 0.01$). Especially for BC with a high Ki-67. Disease progression was observed in 1/3 of BC patients with low levels of B1 cells. CD38 expression on B cells was a prognostically favorable factor: the role is realized during 5–10 years of follow-up after surgery. Level CD38+ B cells more then 10% correlated with high OS, $p = 0.02$. The presence of CD10+CD19+ B-lineage precursors was associated with a more favorable prognosis (OS, the threshold level 12%, $p = 0{,}04$). The prognostic role of the CD10 antigen was realized when patients were observed for more than 5 years. **Conclusion:** . Total relative number of (more than 10 %) of BM CD19+ cells were significantly related to OS in BC. B-cell precursors and CD38+ B cells were associated with favorable prognosis. Prognositic role of B-lineage precursors and CD38-positive cells was in the periods of 5–10 years after surgery.

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PP 36

SUCCESSFUL CHEMOTHERAPY ADMINISTRATION DESPITE HYPERSPLENISM AND PANCYTOPENIA: A CASE OF METASTATIC RECTAL ADENOCARCINOMA

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Introduction: Cytopenias in oncology patients present a significant barrier to the administration of chemotherapy. Hypersplenism is one of the leading causes of cytopenia. In this case report, we aim to present a patient diagnosed with metastatic rectal adenocarcinoma, who developed hypersplenism due to liver metastasis and was successfully treated with chemotherapy despite the cytopenias. **Case Report:** In September 2023, a 42-year-old female patient was diagnosed with rectal adenocarcinoma with liver metastasis. Genetic analysis revealed K-Ras, N-Ras, and BRAF mutant/wild type, MSI stable, and Her2 negative. The patient received 3 cycles of FOLFIRINOX chemotherapy. During follow-up, her hemogram results were as follows: hemoglobin: 8.6 g/dL, platelets: $26 \times 10^3/\mu$L, leukocytes: $0.81 \times 10^3/\mu$L, and neutrophils: $0.37 \times 10^3/\mu$L. PET-CT evaluation showed regression in the metastatic lesions and newly developed splenomegaly

(spleen size: 18 cm). The tumor board assessed the resectability of liver metastases, but surgery was not considered due to the anticipated insufficient remnant liver function, and local ablative therapy was administered. Arterial and venous portal ultrasonography performed to investigate the etiology of the splenomegaly showed normal findings, and no focal lesion was detected in the spleen. No infectious pathology was identified as a cause of the splenomegaly. The cytopenia was attributed to hypersplenism secondary to liver metastasis of rectal cancer. The patient was subsequently treated with 3 additional cycles of FOLFIRINOX and 11 cycles of FOLFOX combined with Bevacizumab. Granulocyte colony-stimulating factor was not administered during the treatment process. The patient remains under oncological follow-up, and chemotherapy treatment is ongoing. **Conclusion:** Splenomegaly and hypersplenism are important causes of pancytopenia. Our clinical experience demonstrated that chemotherapy did not exacerbate cytopenias in a patient with metastatic rectal adenocarcinoma who developed hypersplenism and pancytopenia. We have shown that with close monitoring and supportive care, chemotherapy can be safely administered in patients with pancytopenia due to hypersplenism.

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PP 37

COEXISTENCE OF BREAST CANCER AND MANTLE CELL LYMPHOMA

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İntroduction: Patients cured of any cancer have an increased risk of developing a new primary malignancy compared to the general population. However, synchronous presentation of two tumours is a very rare condition. Here we aim to review the treatment approach of a case of synchronous mantle cell lymphoma and invasive ductal carcinoma of the breast. **Case Report:** A 64-year-old woman presented with a right breast mass. Physical examination revealed a 3cm diameter mass lesion in the right breast and lymphadenopathy in the right axilla. Her past medical history was unremarkable except hypertension. In her family history, there was a history of breast cancer in her niece. Breast ultrasonography revealed 3 centimetres (cm) of malignant breast and multiple lymph nodes with thick cortex in bilateral axillae with indistinguishable fatty hilus. Tru-cut biopsy was performed for the mass in the breast and bilateral axilla lymph nodes. The breast biopsy was compatible with invasive ductal carcinoma with ER 90%, PR 10%, her2 negative and Ki67 proliferation index 10%. Bilateral axilla lymph node biopsy was reported as mantle cell lymphoma and immunohistochemically CD20: Positive, CD5: Positive, Cyclin D1: Positive, CD23: Negative, Lef1: Negative, Keratin: Negative, Ki67 proliferation index 25-30%. PET-CT revealed a mass in the right breast, lymph nodes with pathological appearance in the axillae, various lymph node stations in the abdomen and inguinal areas, and diffuse involvement suggestive of lymphoma infiltration in the right lung. Bone marrow aspiration/biopsy revealed mantle cell lymphoma involvement. The patient was discussed in the multidisciplinary tumour council and right axillary lymph node dissection was performed for staging. 5 lymph nodes showed ductal carcinoma metastasis and the rest of the lymph nodes showed mantle cell lymphoma involvement. Stage IV MHL and hormone positive IDC (T2N2) were detected and R-CHOP treatment was applied. PET-CT performed after three cycles of treatment showed complete response. The patient was discussed again in the multidisciplinary tumour council and surgical treatment for the breast was planned after completing 6 cycles of R-CHOP treatment. After treatment, the patient underwent modified radical mastectomy and the pathological stage was T3N3. After adjuvant RT, endocrine therapy was started and the patient is being followed in remission. **Conclusion:** Coexistence of breast cancer and mantle cell lymphoma is a rare condition. In the few cases reported in the literature, treatment planning was made by considering the stage and treatment priority of both diseases. We planned to prioritise the treatment of lymphoma because our patient had stage 4 mantle cell lymphoma.

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PP 38

PRİMARY CONJUNCTIVAL LYMPHOMA, 2 CASES

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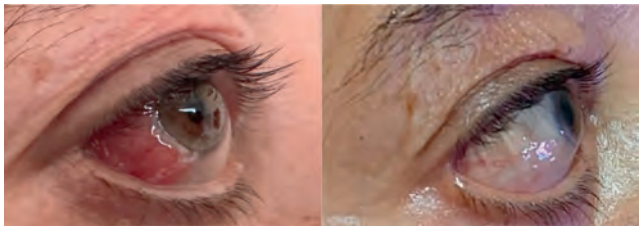
Introduction: Extranodal marginal zone lymphoma (EMZL) is the most common subtype of conjunctival lymphoma. Management of conjunctival lymphoma consists of radiotherapy, surgery, chemotherapy, antibiotics and targeted therapies (Anti-CD 20) based on case series and retrospective studies. Appropriate treatment should be chosen based on the type of lymphoma, extent of spread, and patient-specific factors. We present two patients with localized disease diagnosed with primary conjunctival EZML by biopsy, for whom we planned different treatment plans. **Case Reports: Case 1:** A 64-year-old female patient presented with a pink-red mass on the lateral conjunctiva of her right eye. (Fig. 1A) Conjunctival biopsy was reported as Non-Hodgkin lymphoma, EMZL.(CD 20(+) and Ki-67 3-4%) No extraocular involvement on PET/CT. Orbital MRI showed a 2.5 cm soft tissue lesion surrounding the right globe laterally and posteriorly. The patient started rituximab and

bendamustine treatment, and the lesion in the right orbit was not observed in the current follow-up imaging after 3 cycles of treatment. (Fig. 1B) The patient continued with rituximab and bendamustine treatment. **Case 2:** When the 52-year-old female patient first appeared two years ago, a conjunctival biopsy revealed that she had EMZL. Radiotherapy was recommended for her localized disease, but she declined it. She received eight cycles of rituximab treatment and was monitored in remission. One year later, salmon-colored lesions were found in the inner corner of both eyes. EZML was also found in the new biopsy. There was no ocular involvement. The patient received 6 cycles of rituximab bendamustine and maintenance rituximab for recurrent and bilateral lesions. We are currently monitoring the patient and the disease is in complete remission. **Discussion:** Lymphoma is one of the most frequently occurring malignant tumors of the conjunctiva. In patients with lesions that like a "salmon patch" and unexplained chronic follicular conjunctivitis, lymphoma should be suspected.



(Fig. 1A) (Fig. 1B)

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PP 39

A RARE CASE: NODAL FOLLICULAR T HELPER CELL LYMPHOMA, ANGIOIMMUNOBLASTIC TYPE

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Objective: Angioimmunoblastic T-cell lymphoma (AITL) is the second most common subtype of mature T-cell lymphoma (MTCL). It is caused by monoclonal proliferation of T-follicular helper (TFH) cells. Although advances have been made in its biological knowledge, its treatment is still an unmet medical need. We would like to present a case of Nodal-TFH; AITL that we followed in our clinic. **Case Report:** A 67-year-old male patient presented with cough. Thorax CT revealed left supraclavicular-mediastinal multiple lymphadenopathy with pleural effusion. Supraclavicular LN excision was reported as NHL; nodal follicular T helper cell lymphoma, angioimmunoblastic type. Immunohistochemical CD3, PD-1 and CXC13 were positive, CD4, CD8 and CD10 were sparse, CD21 and 23 were positive in increased dentritic cells, CD20, CD30, EBER and IDH-1 were negative. PET-CT revealed Stage 4BS (multiple LNs with FDG uptake in head-neck, thorax-mediastinum and abdominopelvic FDG uptake, increased FDG uptake in bone marrow-spleen; B symptom: positive). Subcutaneous (sc) Azacitidine + intravenous CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) was started. The 1st course of azacitidine was administered at 75 mg/m2 for 7 days 1 week before CHOP treatment and the following courses were administered at 75 mg/m2 for 14 days 2 weeks before CHOP treatment. After 4 cycles of Azacitidine+CHOP, PET-CT regressed and 2 more cycles of treatment were administered. During the follow-up, the patient's general condition deteriorated and he went into septic shock. **Discussion:** AITL-containing T-follicular helper; nodal PTCL is characterized by recurrent mutations affecting epigenetic regulators. The association of abnormal DNA methylation with lymphomagenesis provides rationale for the administration of hypomethylating agents. The epigenetic modifier azacitidine, which inhibits DNA methyltransferase, has demonstrated clinical activity alone or in combination in relapsed/refractory PTCL. In a phase-2 clinical trial of 20 patients who experienced oral azacitidine + CHOP as initial treatment for PTCL, CR was 76.5%, 1-year PFS 61.1%, 1-year OS 88.9%. In our case, we added the hypomethylating agent azacitidine to the CHOP protocol and aimed to evaluate the efficacy of this combination in the initial treatment of CD30 negative PTCL.

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PP 40

SINGLE-CENTER EXPERIENCE IN DIFFUSE LARGE B-CELL LYMPHOMA: PROGNOSTIC VALUE OF DEMOGRAPHIC AND MOLECULAR CHARACTERISTICS

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İntroduction: Diffuse large B-cell lymphoma (DLBCL) is a heterogeneous hematological malignancy, accounting for approximately 30% of all lymphomas, and is associated with diverse clinical outcomes. The onset of DLBCL typically occurs in the sixth decade of life, with a higher incidence in males. The morphological, clinical, and biological diversity of DLBCL underscores the presence of multiple subtypes, each exhibiting distinct behavior. **Objective:** The objective of this study is to assess the demographic characteristics and clinical outcomes of DLBCL patients, as well as to evaluate the prevalence and prognostic significance of MYC and BCL2 co-expression on survival. **Methodology:** A retrospective study was performed on 51 patients with a confirmed diagnosis of DLBCL. We conducted an analysis of the demographic data

and molecular characteristics of patients diagnosed with diffuse large B-cell lymphoma who underwent R-CHOP therapy and were monitored between 2016 and 2022. The MYC and BCL-2 expression levels in the patients were analyzed using immunohistochemical methods, while their genetic rearrangements were assessed by fluorescence in situ hybridization (FISH) at Çukurova University Faculty of Medicine Hospital. **Results:** The median age at diagnosis was approximately 55 years, with a predominance of female patients. The cervical region was the most frequent nodal site of the primary tumor, whereas the stomach represented the most common extranodal site. The majority of patients were diagnosed at Stage III. MYC/BCL2 protein co-expression was identified in approximately 27% of DLBCL cases and was significantly associated with poorer overall survival and progression-free survival compared to cases lacking co-expression. MYC/BCL2 double-hit cases were detected in approximately 2.5% of the total cases. **Conclusion:** MYC and BCL2 co-expression is a significant prognostic marker, correlating with worse survival. Early identification of MYC/BCL2 co-expression could guide personalized treatment strategies for high-risk patients.

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PP 41

A RARE CASE REPORT OF ADRENAL GLAND DIFFUSE LARGE B-CELL LYMPHOMA PRESENTING WITH PITUITARY INSUFFICIENCY FINDINGS

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Objective: The adrenal glands do not contain lymphoid tissue, and primary adrenal lymphoma (PAL) is extremely rare, accounting for less than 1% of all non-Hodgkin lymphomas and 3% of primary extranodal lymphomas [1, 2]. PAL is primarily bilateral. Approximately 250 cases have been described in the literature to date, with most published articles on PAL being case series with only a limited number of patients. **Case Report:** 74-year-old male patıent with known type 2 dm diagnosis, the patient was admitted to our hospital emergency department with complaints of nausea, fatigue, and drowsiness and was followed up in the endocrinology department. laboratory parameters revealed tsh: 0.02 t4: 0.58 Acth: 32.3 Cortisol 7.05 Na: 124 mmol/l K: 4.6 mmol/l. the patient was first given corticosteroids and then levothyroxine replacements in endocrine follow-ups. contrast-enhanced pituitary and brain mrıs revealed a suspected microadenoma in the left posterior adenohypophysis and suspicious inflammation findings in both optic nerve sheaths. pet ct showed a lesion measuring 41 × 31 mm (suvmax: 19.8) in the right adrenal gland and approximately 40 × 35 mm (suvmax: 21.07) in the left adrenal gland. low-level increased fdg uptake was observed in the th4 vertebra, l4 vertebra and left femur proximal diaphyseal region. the patient underwent a right adrenal gland biopsy and it was found to be non-hodgkin lymphoma, diffuse large b cell lymphoma (germinal center phenotype) cd 20 +, cd10 +, bcl 6 +, bcl 2+, cmyc: 50% +. mild lymphocytosis was observed in the bone marrow aspiration biopsy. DA-R-EPOCH treatment was applıed to the patıent, who was conscıous, orıented, co-operated, general condıtıon and good oral ıntake under cortıcosteroıd and levothyroxıne treatment ın the follow-up performance and was externed as no complıcatıons were observed. **Discussion:** PAL is extremely rare, primary adrenal DLBCL (PA-DLBCL) is of a non-germinal center B cell (nonGCB) phenotype. PAL usually has no excretory endocrine function and the symptoms are due to the pressure effect of the mass, whereas adrenal insufficiency usually exists.The most common manifestations were B symptoms, which include unexplained fever, weight loss, night sweats (68%), vague abdominal pain (42%), and fatigue (36%), some of which were present in the current patient. There is no correlation between tumor size and adrenal insufficiency. Generally, obvious clinical manifestations of adrenal insufficiency tend to appear when > 90% of the adrenal gland is damaged . It can improve with the destruction of the lymphomatous tissue at the end of the chemotherapy.

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PP 42

EXTRANODAL NON-HODGKIN'S LYMPHOMA OF THE ORAL CAVITY: A CASE REPORT

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Objective: Lymphomas are indeed complex malignancies with diverse clinical and pathological characteristics. Non-Hodgkin's lymphoma (NHL) is particularly notable for its varying presentations, with a significant number of cases manifesting as lymphadenopathy. The extranodal involvement in about one-third of NHL cases highlights the importance of recognizing atypical presentations. In this case, we present a 59-year-old male patient with non-Hodgkin lymphoma in the right buccal mucosa. **Case Report:** A 59-year-old male patient with a history of allergic asthma and gastroesophageal reflux disease presented to our clinic with swelling in the right maxillary region lasting more than one year. The patient did not have any B symptoms. A biopsy of the right buccal mucosa revealed extranodal marginal zone non-Hodgkin lymphoma. Immunohistochemistry showed: CD20 (+), CD43(+), CD38 positive in plasma cells, diffuse BCL2(+), suboptimal BCL6(+), and a proliferation index of 5% reported with Ki67. An MRI of the orbit demonstrated a mass lesion extending from the right maxillary region into the temporal fossa, with partial external protrusion from the right cheek. After intravenous contrast administration, diffuse

enhancement was observed in the right lateral wall of the sphenoid sinus, which was in close proximity to the right cavernous sinus and caused contrast retention at these levels, extending into the subcutaneous adipose tissue of the right temporal region. The right globe appeared exophthalmic. Simultaneous laboratory parameters were normal, with a beta-2 microglobulin level of 1.65 mg/L and LDH of 180 U/L. An F-18 PET-CT scan showed irregular soft tissue densities in the right maxillary region exhibiting hypermetabolism (primary disease). Several lymph nodes in the right cervical chain showed relative hypermetabolism (possible metastasis). The treatment plan was decided upon in consultation with the ear, nose, and throat and neurosurgery departments regarding potential involvement of the central nervous system. **Discussion:** Non-Hodgkin's lymphomas comprise a varied group of malignancies that primarily affect lymph nodes. Extranodal NHL represents approximately 20-30% of all reported cases. Among the extranodal sites, the head and neck region is the second most frequently involved area, after the gastrointestinal tract. Intraoral non-Hodgkin lymphoma accounts for only 0.1% to 5% of all cases. In summary, our case emphasizes the importance of considering lymphomas in the differential diagnosis of rare malignant lesions in the oral cavity. It is believed that prompt referral for histopathological and immunohistochemical examinations can facilitate early diagnosis and appropriate treatment.

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PP 43

EXTREME NORMOBLASTOSIS IN A THALASSAEMIA INTERMEDIA PATIENT POST-SPLENECTOMY: THE ROLE OF FLOW CYTOMETRY IN DIAGNOSIS AND MANAGEMENT

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Background: Thalassaemia intermedia is characterized by inefficient red blood cell production (erythropoiesis) and has a wide range of clinical symptoms. Splenectomy, often performed to manage complications, can lead to significant long-term changes in blood cell composition. This case illustrates a striking example of extreme normoblastosis in a patient two decades after a splenectomy. The case also underscores the critical role of flow cytometry in diagnosing blood disorders and differentiating abnormal findings from potential malignancies. **Case Report:** A 45-year-old woman with thalassaemia intermedia, who had her spleen removed at age 25, presented with severe anaemia, iron overload, and an unusually high normoblast count ranging from 50,000 to 100,000 cells/μL, as seen in a routine complete blood count (CBC). The CBC mistakenly identified the normoblasts as white blood cells, raising concern for possible blood cancer. Closer analysis of the CBC sub-parameters revealed an increased nucleated red blood cell (NRBC) ratio. Further investigation through bone marrow biopsy and flow cytometry was undertaken to rule out malignancy and better understand the extreme normoblastosis. **Methodology:** The diagnostic process involved multiple stages of flow cytometric analysis. First, a chronic lymphocytic leukaemia (CLL) panel was employed, followed by an acute leukaemia panel. Finally, a specialized flow cytometry panel targeting markers such as CD45, CD71, CD41, CD235a, CD19, CD10, CD13, HLA DR, CD36, CD38, and CD117 was used. The gating strategy focused on differentiating erythroid precursor cells based on their size, granularity, and marker expression. **Results:** Flow cytometry identified a significantly elevated population of normoblasts, with these cells displaying low CD45 expression and reduced side scatter. They tested weakly positive for CD71, strongly positive for CD36, and negative for CD235a, confirming their identity as erythroid precursors. Around 70% of the nucleated cells consisted of these normoblasts, representing various stages of erythroid maturation. The absence of lymphoid markers (CD19, CD10, CD5) ruled out lymphoid malignancies, while the exclusion of myeloid malignancies was confirmed through negative results for markers such as CD13, CD33, CD34, CD117, and HLA DR. **Discussion:** This case highlights the occurrence of extreme normoblastosis in a post-splenectomy patient and the challenges in managing such cases. It demonstrated that flow cytometry is essential for accurately identifying erythroid precursors, preventing a misdiagnosis of malignancy based solely on CBC results. The findings underscore the value of flow cytometry in evaluating complex haematological conditions, especially in patients with thalassaemia intermedia after splenectomy. Additionally, the strategic order of tests in the flow cytometry lab, along with collaboration between laboratory and clinical teams, was key to achieving a correct diagnosis. This case reinforces the need for a tailored flow cytometric testing algorithm for complex cases.

Keywords: Thalassaemia intermedia, Normoblastosis, Splenectomy, Flow cytometry, Haematological malignancies.

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PP 44

BLINATUMOMAB BRIDGING THERAPY FOR EFFECTIVE MANAGEMENT OF MRD IN PRO-B ALL WITH CNS INVOLVEMENT: A CASE REPORT OF POST TRANSPLANT PATIENT AT 23 MONTHS AFTER ALLOGENIC HEMATOPOIETIC CELL TRANSPLANTATION

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Objective: Pro-B ALL is an unusual and highly malignant form of ALL often presenting with CNS involvement. The involvement of the CNS makes the central objective of these treatments that is attaining and maintaining remission more challenging. This is a report of Pro-B ALL of a 52-year old female who had a CNS involvement and received blinatumomab both as bridge to allo -HSCT and post transplantation consolidation for MRD positivity. Case Report This 52 year old female is presented with Pro-B ALL. Standard chemotherapy was complicated by intracranial extension of the disease. The patient was positive for the Philadelphia chromosome with BCR-ABL (9;22) translocation hence dasatinib was added. Intrathecal therapy of blinatumomab was used as well due to infiltration of cytokines in the central nervous system. Following several sessions of treamtnet, complete remission including of central nervous system was achieved. Afterall the patient was to receive matche allo-HSCT post which clinical stabilization was ascertained. However bone marrow aspiration, biopsy and flow cytometry showed that there was persistence of MRD. However the patient had blinatumoma as targeted therapy. **Discussion:** This case illustrates the effective use of blinatumomab in managing Pro-B ALL with CNS involvement, particularly in the post-transplant setting. CNS involvement complicates treatment due to the blood-brain barrier, requiring targeted intrathecal therapy alongside systemic chemotherapy. Blinatumomab played a crucial role as a bridging therapy to allo-HSCT and in addressing MRD post-transplant, significantly reducing the risk of relapse. This case demonstrates that blinatumomab can effectively target MRD, even in patients with CNS involvement, contributing to better disease control and outcomes.

Keywords: Acute Lymphoblastic Leukemia Pro-B, Central Nervous System Involvement, Blinatumomab, Allogeneic Stem Cell Transplantation, Minimal Residual Disease.

https://doi.org/10.1016/j.htct.2024.11.072

PP 45

CARCINOID SYNDROME PRESENTING AS AN ELEVATED 5-HIAA IN A PATIENT EVALUATED FOR AN ELEVATED WBC COUNT: BEWARE OF THE POSSIBLE DIAGNOSTIC DIFFICULTY.

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Introduction: Carcinoid syndrome is an extremely rare paraneoplastic disorder associated with serotonin-secreting neuroendocrine tumors, which classically present with flushing, weight loss, hypertension, and gastrointestinal complaints. In fact, symptoms are often nonspecific, and the presentation could promote confusion with hematologic or inflammatory diseases. Early diagnosis is of great importance in allowing proper therapy to avoid delays. **Case Report:** A 45-year-old female was referred to the hematology clinic owing to high WBC count (21,000/μL), associated with fatigue, flushing, and unintentional weight loss of 10 kg over the past 3-4 months. Her history included hypothyroidism on thyroxin and asthma —both on symptomatic medications. Gastroenterology workups, including endoscopy, showed mild antral gastritis and a hiatal hernia but no evidence of malignancy. Thus, the imaging studies demonstrated a low-density nodule measuring 1 cm in size on the right adrenal gland, hence the suspicion of a neuroendocrine tumor. Excess serotonin production was confirmed by demonstrating a 24-hour urinary 5-HIAA level of 18.7 mg/day, with a reference range being 2-9 mg/day, compatible with carcinoid syndrome. Confirmatory Ga-68 DOTA-TATE PET-CT revealed moderate increased somatostatin receptor expression in the adrenal lesion. No anemia or other hematologic disorders were observed, despite the initial suspicion of one. **Discussion:** This case highlights carcinoid syndrome as a potential cause of systemic symptoms such as flushing, weight loss, and leukocytosis, even in cases referred for suspected hematologic conditions. Confirmation was based on the elevated level of 5-HIAA and advanced imaging with Ga-68 DOTA-TATE PET-CT. This report emphasizes the need for interdisciplinary collaboration between hematology, endocrinology and oncology for managing complex systemic cases. Early diagnosis of carcinoid syndrome ensures appropriate care, prevents misdiagnosis, and improves outcomes.

Keywords: Carcinoid Syndrome, Neuroendocrine Tumor, 5-HIAA, Flushing, Leukocytosis.

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PP 46

MYCOSIS FUNGOIDES PROGRESSING TO PERIPHERAL T-CELL LYMPHOMA AND THE POTENTIAL ROLE OF ROMIDEPSIN THERAPY

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Introduction: PTCL-NOS is an uncommon and highly aggressive kind of non-Hodgkin lymphoma. Transformation of MF, a cutaneous T-cell lymphoma, into systemic PTCL is infrequent and poses serious challenges both diagnostically and therapeutically. This report describes the challenges in diagnosis and therapy of a transformation case from MF to PTCL which responded to romidepsin. **Case Report:** A 58-year-old male presented to the OPD in the year 2022 with complaints

of chronic itching. Skin biopsy diagnosis was lichen planus. Further skin biopsies done in the year 2023 established mycosis fungoides with patch-stage disease. Thereafter, the disease evolved to involve lymph nodes within a year. Excisional biopsies of these lymph nodes showed dermatopathic lymphadenopathy, which later was transformed into T-cell lymphoid neoplasia indicating transformation into PTCL-NOS. Immunohistochemical analysis showed positivity for CD3+, CD4+, CD7+, GATA3+, and Ki-67 expression. CD30 was negative. In spite of first-line therapies administered, such as phototherapy, methotrexate, and PUVA, the disease further progressed, as indicated in the PET-CT scan with increased metabolic activity in multiple lymph nodes and cutaneous thickening. The patient was initiated with romidepsin—a histone deacetylase inhibitor—on salvage therapy for PTCL. The current follow-up represents clinical stability, with no development of new lesions or disease progression. **Discussion:** The case serves to underline the complex evolution as seen from mycosis fungoides to systemic PTCL and challenges in the management of refractory disease. Use of romidepsin underlines the potential of epigenetic therapies in the treatment of advanced T-cell lymphomas, especially in relapsed or refractory states. The patient's journey underlines the importance of early diagnosis, a multidisciplinary approach, and adaptive treatment strategy in the management of these aggressive lymphomas.

Keywords: Peripheral T-Cell Lymphoma, Mycosis Fungoides, Romidepsin, Epigenetic Therapy, PET-CT.

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PP 47

INNOVATIVE MANAGEMENT OF REFRACTORY CLASSICAL HODGKIN LYMPHOMA WITH ATYPICAL HEPATIC PRESENTATION: A CASE STUDY

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Introduction: Classical Hodgkin Lymphoma (cHL) typically manifests through swollen lymph nodes, yet unusual cases do arise with atypical presentations. This report focuses on the management of a challenging case of refractory cHL, where the disease initially presented in the liver. The case underscores the effectiveness of a customized, multimodal treatment strategy. **Case Report:** A 59-year-old man was diagnosed with stage 4A cHL after a liver biopsy confirmed the disease. His initial PET-CT scans showed extensive involvement, with spread to cervical lymph nodes, nasopharyngeal and oropharyngeal regions, as well as diffuse splenic activity. The patient underwent six cycles of ABVD chemotherapy, but follow-up PET-CT scans revealed disease progression, confirming primary refractory status. Subsequently, he was given salvage therapy with BV-DHAP, followed by high-dose chemotherapy and an autologous stem cell transplant (ASCT). Post-ASCT PET-CT scans demonstrated a significant metabolic response, with near-complete resolution of previous lesions, though splenomegaly persisted. Currently, the patient is undergoing maintenance therapy with brentuximab vedotin and has completed seven cycles successfully. **Discussion:** This case illustrates key challenges in the treatment of refractory cHL, particularly with atypical liver involvement, stressing the importance of considering lymphoma in cases of unexplained liver lesions. When the standard ABVD regimen failed, prompt initiation of aggressive salvage therapy was crucial in halting disease progression. The role of serial PET-CT imaging was pivotal in monitoring treatment effectiveness and guiding further clinical decisions. The tailored combination of salvage chemotherapy, ASCT, and maintenance with brentuximab vedotin showcases the evolving strategies in handling refractory cHL. Despite a significant overall response, the persistence of splenomegaly post-ASCT highlights the need for vigilant follow-up. This case emphasizes the potential for successful remission in refractory cHL through personalized, comprehensive treatment approaches, while also recognizing the need for continued exploration of emerging therapies.

Keywords: Classical Hodgkin Lymphoma,Refractory cHL, Hepatic Involvement, Autologous Stem Cell Transplant, Personalized Treatment.

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PP 48

MULTIPLE MYELOMA IN A PATIENT WITH SJOGREN'S SYNDROME: A CASE REPORT OF DIAGNOSTIC AND THERAPEUTIC CHALLENGES

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Introduction: MM is a hematologic malignancy characterized by the proliferation of a clone of plasma cells that ultimately causes organ damage and the production of abnormal proteins. Sjögren's syndrome rarely coexisted with MM, a chronic autoimmune disease affecting exocrine glands and presenting very unique diagnostic and management challenges to the physician. This case illustrates the therapeutic journey of a patient with coexisting MM and Sjögren's syndrome and points out the importance of care provided in a multidisciplinary fashion. **Case Report:** A 64-year-old female patient with a history of hypertension for 14 years and prostheses of both hips was referred to the rheumatology department with

dry eyes and joint pains. The presence of anti-SSA antibodies and diminished results of the Schirmer test supported the diagnosis of Sjögren's syndrome; thus, hydroxychloroquine and prescription of artificial tears were started. Symptomatic treatment was begun because the development of albumin and total protein inversion suggested plasma cell dyscrasia. Further work-up for immunofixation electrophoresis and bone marrow biopsy confirmed IgG lambda-positive MM. She was subsequently treated with VRD (bortezomib, lenalidomide, and dexamethasone), followed by an autologous BMT in May 2024. Post-transplant maintenance was given with lenalidomide. She also developed sensory neuropathy, which was managed with pregabalin, with no recurrence of MM on follow-up. **Discussion:** The case epitomizes the complex diagnostic interplay between MM and Sjögren's syndrome. Symptoms of fatigue and protein abnormalities can easily be attributed to an autoimmune condition, with a delayed diagnosis of MM. Multidisciplinary collaboration has been critical for management of comorbidities and assurance of timely diagnosis. The patient responded well to BMT and maintenance therapy, proving personalized care. Furthermore, long-term treatment shows the necessity of monitoring drug-induced neuropathy. This case report adds to the growing awareness of rare concomitant autoimmune disorders and hematologic malignancies, with a reminder for vigilance in complex presentations and the delivery of adaptive multidisciplinary care.

Keywords: Multiple Myeloma, Sjögren's Syndrome, Bone Marrow Transplantation, Lenalidomide, Neuropath.

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PRIMARY PALATAL ALK-NEGATIVE ANAPLASTIC LARGE CELL LYMPHOMA: RARITY TREATED SUCCESSFULLY WITH BRENTUXIMAB VEDOTIN

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Introduction: ALCL is an extremely rare T-cell non-Hodgkin lymphoma subtype made up of CD30-positive tumor cells, which are very aggressive. Though it most frequently involves lymph nodes and skin, less frequently, it affects other organs as well. Primary oral involvement, particularly of the palate, is highly uncommon. The paper reports a peculiar case of localized primary ALK-negative ALCL of the palate in a 73-year-old female patient treated successfully with brentuximab vedotin, pointing to the importance of identifying atypical presentations. **Case Report:** A 73-year-old female with a history of presenting a painless ulcer on her palate, which did not heal with local treatments for two months, presented to the otolaryngology clinic and underwent an incisional biopsy. Histopathological findings showed large atypical lymphoid cells with prominent nucleoli, consistent with ALCL. Immunohistochemical staining was positive for CD30 and negative for ALK; in addition, Epstein-Barr virus testing returned negative. PET-CT showed localized uptake of FDG in the palate, SUVmax 8.5, with no significant lymphadenopathy and no systemic involvement. Bone marrow biopsy showed normal hematopoiesis with no evidence of infiltration. The patient was diagnosed with primary breast ALK-negative ALCL and started on brentuximab vedotin. The patient went into complete remission after three cycles of therapy with no residual disease evident on follow-up imaging. **Discussion:** This case illustrates the need to consider ALCL in the differential diagnosis of atypical sites, such as the palate, when lesions fail to respond to conventional therapy. Early biopsy and a wide panel of immunohistochemical tests are crucial for accurate diagnosis. Due to the high recurrence rates as well as poor prognosis associated with ALK-negative ALCL, highly active targeted therapies include brentuximab vedotin. The complete remission attained in this patient underlines the promise of personalized therapies in dealing with rare malignancies. Awareness of such atypical presentations may help in early diagnoses and improve patient outcomes. This case further stresses that management of lymphoma with such unusual presentations may be effectively accomplished using an interdisciplinary approach.

Keywords: anaplastic large cell lymphoma, ALK-negative, CD30, brentuximab vedotin, palatal lymphoma.

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PRIMARY EXTRAMEDULLARY PLASMACYTOMA OF THE LYMPH NODES

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Introduction: Extramedullary plasmacytomas are rare malignant neoplasms that can arise in various organs; however, lymph node involvement is uncommon. The cervical lymph nodes are most frequently affected. We present the case of a 68-year-old female diagnosed with a primary extramedullary plasmacytoma involving multiple lymph nodes, primarily in the cervical region. **Case Report:** A 68-year-old female patient presented with a one-month history of progressive enlargement and painful swelling of the right subclavicular and cervical areas. Imaging revealed pathological lymphadenopathy, and excisional biopsy was performed from the right cervical level 5 lymph node. Histopathological analysis confirmed the diagnosis of a plasmacytoma. A subsequent bone marrow biopsy revealed normocellular marrow without any evidence of infiltration. Positron emission tomography-CT staging

demonstrated further lymph node involvement in the right cervical, subclavicular, supraclavicular, axillary, and mediastinal regions. **Discussion:** This case was classified as a primary extramedullary plasmacytoma of the lymph nodes, given the absence of multiple myeloma markers in the bone marrow and immunoelectrophoretic studies. Lymph node plasmacytomas are exceedingly rare, comprising approximately 2% of all extramedullary plasmacytomas. Clinically, these patients often present with localized masses and minimal systemic symptoms. While recurrence is possible, primary lymph node plasmacytomas rarely progress to multiple myeloma and are associated with a more favorable prognosis than other solitary extramedullary plasmacytomas. The distinct clinical behavior of these lesions suggests that they may represent a unique subset of plasmacytomas with a lower risk of transformation into multiple myeloma. Most patients respond well to surgical excision, with minimal risk of recurrence or progression, even in the absence of adjuvant therapy. Although some patients develop osseous plasmacytomas, none have progressed to multiple myeloma in reported series.

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MANAGEMENT OF CHEMOTHERAPY-RESISTANT GASTRIC DIFFUSE LARGE B-CELL LYMPHOMA: A CASE REPORT

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Introduction: Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma, often affecting extranodal sites like the stomach. While R-CHOP chemotherapy is the standard treatment, some patients fail to respond, requiring alternative approaches. In this report, we describe a case of gastric DLBCL in a 68-year-old man who became resistant to R-CHOP but achieved remission with R-DHAP. **Case Report:** A 68-year-old man came to the hospital with symptoms of persistent indigestion. After undergoing an endoscopic biopsy in October 2020, he was diagnosed with high-grade gastric diffuse large B-cell lymphoma. A PET-CT scan revealed a large mass in his stomach. He started R-CHOP chemotherapy, completing eight cycles. However, after five cycles, imaging showed remaining disease in the stomach, along with new lesions in the left lung. Despite ongoing treatment, a biopsy after the sixth cycle confirmed that the lymphoma was still active. The situation worsened—his disease had become resistant to R-CHOP. In response, his treatment shifted to R-DHAP chemotherapy. After just two cycles, an endoscopic biopsy revealed no active lymphoma, and only signs of chronic atrophic gastritis remained. PET-CT scans over the following months showed no recurrence of lymphoma. However, in March 2023, a PET-CT showed some hypermetabolic lymph nodes in the cervical region, but these had regressed significantly compared to previous scans. As of October 2024, the patient continues to be closely monitored and remains asymptomatic. **Discussion:** This case highlights the challenges faced when dealing with chemotherapy-resistant DLBCL. It emphasizes the need to pivot quickly to alternative therapies, like R-DHAP, when first-line treatments fail. The successful response in this patient demonstrates that adjusting treatment strategies can make a significant difference in outcomes. Additionally, it shows the importance of long-term follow-up, especially with extranodal lymphomas, where the risk of relapse is ongoing.

Keywords: Diffuse large B-cell lymphoma, R-CHOP, Chemotherapy resistance, R-DHAP, Gastric lymphoma.

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SYSTEMIC NODULAR SCLEROSING HODGKIN LYMPHOMA WITH UNUSUAL HEPATIC AND GASTRIC INVOLVEMENT: A CASE REPORT

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Introduction: Hodgkin lymphoma (HL) is typically known for presenting as enlarged lymph nodes, but occasionally, it takes an unexpected turn, spreading to less common locations. In this report, we dive into a rare case of nodular sclerosing Hodgkin lymphoma, where the disease had aggressively spread, invading the liver and stomach—locations rarely associated with HL. **Case Report:** A 40-year-old woman came to the clinic with persistent back pain, trouble walking, and noticeable weight loss. At first, these symptoms seemed to point to a spinal issue, prompting an L4 kyphoplasty. However, things quickly worsened, and her condition began to deteriorate. A PET-CT scan soon revealed troubling results—multiple areas of hypermetabolic activity across her lymph nodes and bones, which were now lighting up with disease. A biopsy of the inguinal lymph node confirmed the diagnosis: classical Hodgkin lymphoma, nodular sclerosing type. Treatment started with Brentuximab vedotin paired with the AVD regimen (Adriamycin, Vinblastine, and Dacarbazine), but complications arose. During therapy, she developed a painful perianal abscess,

which needed surgical drainage. Yet the disease kept advancing. New imaging showed a more aggressive spread: multiple hypermetabolic lesions were found in the liver, and another was detected in the gastric fundus. Despite a clear endoscopy, which didn't show any visible abnormalities in the stomach, a liver biopsy confirmed what the team feared—Hodgkin lymphoma had infiltrated her liver. Her treatment continues with careful monitoring as the medical team adapts to these complications. **Discussion:** This case paints a picture of the diagnostic and treatment challenges that arise when Hodgkin lymphoma doesn't follow the expected path. Instead of typical lymphadenopathy, the disease made itself known through musculoskeletal pain and neurological issues, creating a complex clinical puzzle. The rare involvement of the liver and stomach emphasizes just how unpredictable the systemic spread of this disease can be. While hepatic involvement in HL is unusual, it's critical to confirm this through biopsy, as it can easily be mistaken for other liver-related conditions. Gastric involvement, though rare, must be kept in mind when dealing with extensive disease spread. Advanced imaging, particularly PET-CT, played a pivotal role in uncovering these unexpected sites of involvement, guiding the treatment plan. This case is a testament to the importance of recognizing atypical presentations of Hodgkin lymphoma and the need for flexible, evolving treatment strategies. The use of Brentuximab vedotin in combination with AVD has shown promise, especially in complicated cases like this one, where the disease has spread far beyond the usual lymphatic system. Understanding HL's ability to infiltrate uncommon sites like the liver and stomach is essential for improving patient outcomes. This case reminds us of the disease's unpredictable nature and the need for vigilance in detecting and managing its spread to rare locations.

Keywords: Nodular Sclerosing Hodgkin Lymphoma, Hepatic Infiltration, Gastric Involvement, Systemic Spread, Brentuximab Vedotin Treatment.

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PP 53

SYSTEMIC AMYLOIDOSIS PRESENTING WITH LYMPHADENOPATHY: A DIAGNOSTIC OVERLAP WITH MULTIPLE MYELOMA AND POSSIBLE CARDIAC INVOLVEMENT

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Introduction: Systemic amyloidosis is a condition where amyloid proteins accumulate in organs and tissues, causing multisystem dysfunction. Its presentation often overlaps with other conditions like lymphoproliferative disorders and multiple myeloma (MM). Lymphadenopathy is rare in amyloidosis but can complicate the clinical picture, mimicking more common hematological diseases. We present a case of systemic amyloidosis in a patient initially suspected of having lymphoma, complicated by underlying multiple myeloma and probable cardiac amyloidosis. **Case Report:** A 63-year-old male with a history of heart failure and chronic kidney disease presented with frequent hospital admissions due to dyspnea. Axillary lymphadenopathy prompted referral to hematology. PET-CT revealed widespread FDG-avid lymphadenopathy, suggesting lymphoma. Biopsy showed plasma cell infiltration (10-11%) with kappa light chain monotypic plasma cells and amyloid deposits, indicating systemic amyloidosis. Concurrent imaging revealed pleural effusions, calcified lymphadenopathies, and findings consistent with granulomatous disease. Further hematological evaluation suggested underlying plasma cell dyscrasia, likely multiple myeloma. The patient's history of heart failure raised the suspicion of cardiac amyloidosis, a common complication in systemic amyloidosis, warranting cardiology evaluation and planned cardiac MRI. **Discussion:** This case underscores the diagnostic challenge posed by systemic amyloidosis, especially when lymphadenopathy is present, leading to initial misdiagnosis as lymphoma. Amyloidosis-related lymphadenopathy is uncommon but should be considered, especially when plasma cell dyscrasias like multiple myeloma are involved. The concurrent diagnosis of multiple myeloma further complicates the clinical course, necessitating a tailored therapeutic approach. Cardiac amyloidosis is a serious complication often seen in patients with systemic amyloidosis, especially AL-type, where amyloid deposits infiltrate the myocardium, leading to restrictive cardiomyopathy. In this case, the patient's long-standing heart failure and arrhythmia raised the likelihood of cardiac involvement. Early detection is crucial, as cardiac amyloidosis is associated with a poor prognosis. The integration of advanced cardiac imaging, such as MRI, is essential in confirming the diagnosis and guiding treatment. This case illustrates the importance of considering systemic amyloidosis in patients with unexplained lymphadenopathy and highlights the need for multidisciplinary management, particularly when cardiac involvement is suspected.

Keywords: Amyloidosis, Lymphadenopathy, Multiple Myeloma, Cardiac Amyloidosis, Plasma Cell Dyscrasia.

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