SOUVENIR PROGRAMME

Organised by:

Malaysian Society of Haematology

EHA

ASEAN Federation of Haematology

21st Malaysian Society of Haematology

Annual Scientific Meeting 2024

with **EHA Pre-Congress Tutorial**

MSH 2024

17th > 18th April 2024
Pre-Congress:
EHA Tutorial & Pharmacy Programme

18th > 20th April 2024
Main Congress

Shangri-La Hotel,
Kuala Lumpur

www.msh2024.com

Studying Current Trends for a More Informed Future Practice

WELCOME MESSAGE FROM THE ORGANISING CHAIR

Welcome to the 21st Malaysian Society of Haematology Annual Scientific Meeting, taking place at the Shangri-La Hotel in Kuala Lumpur from April 17th to April 20th, 2024.

This year is marked by our inaugural collaboration with two prestigious organisations: the European Hematology Association (EHA) and the ASEAN Federation of Hematology. Together, we will delve into the theme **"Studying Current Trends for a More Informed Future Practice."**

The journey begins with an exclusive EHA tutorial on April 17th and 18th, offering insights into the latest haematology trends and the treatment of Hodgkin Lymphoma. From April 18th onwards, our Annual Scientific Meeting features engaging sessions, inspiring keynotes, and scientific presentations, all designed to keep you at the forefront of our rapidly evolving field. Our focus is on fostering discussions and sharing experiences.

Beyond the scientific sessions, we have planned social events and networking opportunities to facilitate lasting connections and friendships.

Kuala Lumpur, a vibrant city, will be the backdrop for this remarkable event where innovation, science, and camaraderie converge. We eagerly anticipate your participation in shaping a more informed future practice in haematology.

With open arms, we invite you to join us in Kuala Lumpur for this profound exploration of the latest trends in haematology. Together, with the help of my capable team led by Dr Ong Tee Chuan as my Scientific Chair, we will make the 21st Annual Scientific Meeting a resounding success.

Dr Haris Abdul Rahman
Organising Chair
21st MSH ASM 2024

WELCOME MESSAGE FROM THE PRESIDENT OF THE MALAYSIAN SOCIETY OF HAEMATOLOGY

Dear Friends and Colleagues,

It is with great pleasure that I extend our warmest invitation to all of you to the 21st Annual Scientific Meeting organized by Malaysian Society of Haematology, in collaboration with European Hematology Association (EHA) and ASEAN Federation of Haematology (AFH).

I am very excited as this is the first time Malaysian Society of Haematology is collaborating with EHA to organize a pre-congress tutorial, and to have Professor Dr Graham Collins as the program advisor will certainly guarantee a great learning experience for all of us.

This meeting also marks the resumption of ASEAN Federation of Haematology after a hiatus due to the pandemic. I am glad that once again, we are able to provide a platform for the different haematology societies within ASEAN to meet, exchange ideas and learn from one another.

So many exciting scientific programs are being planned by the organizing team chaired by Dr Haris Abdul Rahman. I am certain this meeting will provide us opportunities to delve into the latest developments in the field of haematology, inspire fresh ideas, and foster connections among one another.

I very much look forward to welcoming you to this meeting. Mark your calendars now and be prepared to have an enjoyable and fruitful time in Kuala Lumpur. To our friends from overseas, don't forget to spend some time exploring the beautiful local sights and attractions and to savour our delicious local cuisines.

Prof Dr Gan Gin Gin
President
Malaysian Society of Haematology

MANAGEMENT OF ADVANCED CLASSICAL HODGKIN LYMPHOMA AND LONG TERM SURVIVAL OUTCOME

A Singapore case sharing perspective

19th April 2024 | Friday

12:30 PM – 1:30 PM

Shangri-La Hotel, Kuala Lumpur

Navigating the complexities and conundrums of Hodgkin Lymphoma management presents a formidable challenge to healthcare professionals worldwide.This multifaceted disease demands a sophisticated approach, blending the latest in medical research with the nuanced understanding of patient care.

Recognizing the critical need for advanced education and dialogue in this area, join us in the management of Hodgkin Lymphoma, led by the distinguished Dr. Daryl Tan from Singapore. Dr. Tan, a venerated figure in the oncology community, brings to the table a depth of expertise and a track record of innovation in the treatment of Hodgkin Lymphoma.

Join us for an engaging session through the intricacies of Hodgkin Lymphoma management with Dr. Daryl Tan, and take a step forward in mastering the art and science of oncology care.

SPEAKER PROFILE

Dr Daryl Tan

Specialist In Haematology
Singapore - Dr D.Y.H Poon & Associates Medical Oncology Clinic

Dr. Daryl Tan, an esteemed haematologist renowned for his work in the field of lymphoma and multiple myeloma, has significantly advanced the treatment of blood cancers through his postdoctoral training at Stanford University and as an Assistant Professor at Duke-NUS Graduate Medical School.
His extensive research, highlighted by over 100 publications in top-tier journals and pioneering contributions to immunotherapy, has been internationally recognized, influencing treatment guidelines and is a key part of the medical societies such as the International Myeloma Working Group and the advisory panel of the International Myeloma Foundation's Asia Myeloma Network.
Committed to advancing medical education and patient care, Dr. Tan serves on several advisory committees, including the Ministry of Health's Residency Advisory Committee for Haematology in Singapore, and actively participates in guiding both postgraduate education and clinical trial involvement.

CHAIRPERSON

Dr Ng Soo Chin

Consultant Haemotologist
Subang Jaya Medical Centre

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Hon. Secretary	Dr Veena Selvaratnam
Hon Treasurer	Dr Sharifah Shahnaz Syed Abd Kadir
Council Members	Dato Dr Goh Ai Sim Dr Tan Sen Mui Prof Dr Bee Ping Chong Prof Dr Azlan Husin Dr Gan Ee Leng Dr Abu Dzarr Abdullah

MEETING INFORMATION

OFFICIAL CONFERENCE VENUE
Basement Two, Shangri-La Hotel Kuala Lumpur

REGISTRATION COUNTER OPENING HOURS
- 17th April 2024 (Wednesday) - 7:30am to 5.30pm
- 18th April 2024 (Thursday) - 10.00am to 5.30pm
- 19th April 2024 (Friday) - 7:30am to 5:30pm
- 20th April 2024 (Saturday) - 8.00am to 5:00pm

COFFEE & TEA BREAK
Coffee and Tea Break will be served inside the exhibition area and foyer.

LUNCH
Bento Lunch Boxes will be served during the Lunch Symposiums inside the ballroom.

LANYARD
Only those with a lanyard and name tag will be allowed into the conference area.

CPD POINTS
20 CPD points will be awarded for all MSH ASM 2024 delegates. 12 MMA CPD points will be awarded for all attendees of EHA tutorial workshop. 6 MPS CPD points will be awarded to all attendees of Pharmacy Programme.

CERTIFICATE OF ATTENDANCE, INVOICE AND RECEIPT
Certificate of Attendance, Invoice and Receipt will be available on your delegate dashboard.

PARKING
- The flat rate is RM16.00. (Cashless Parking)
  - » Tap when entering (TNG, Credit/Debit Card).
  - » Tap on the flat rate device.
  - » Tap again on exit.

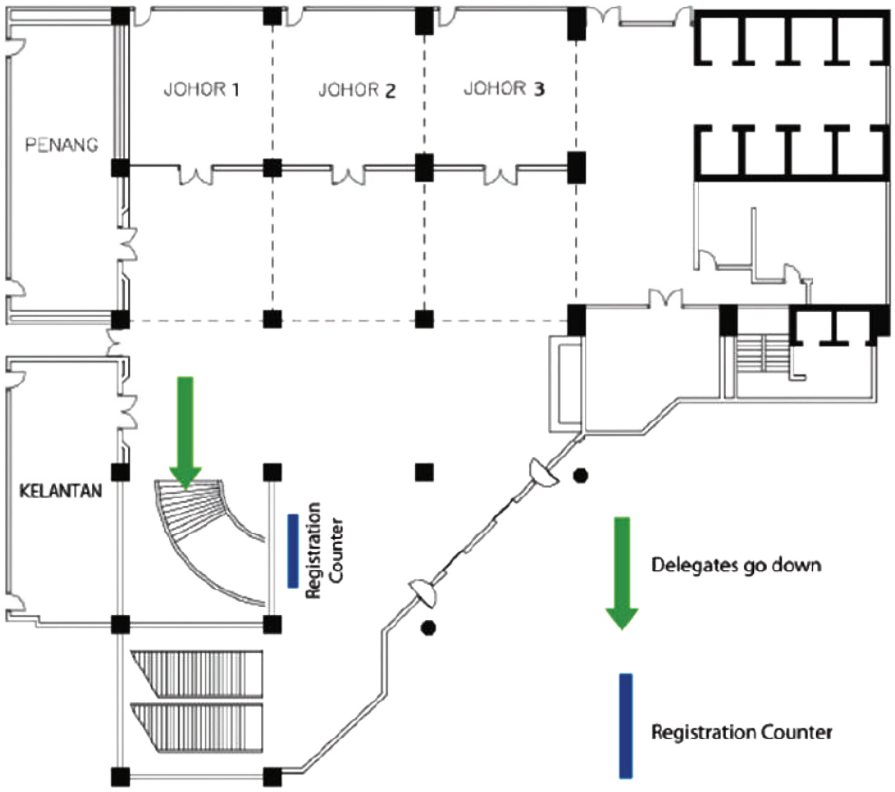
Note: The Flat Rate Machine and Device will be placed together in the function room foyer.

MOSQUE & SURAU
- Surau located at Basement Two (same as Ballroom level).
- Nearest mosque Masjid Asy-Syakirin KLCC & Bank Islam @ Jalan Perak

CONGRESS SECRETARIAT
Handphone: +6016 335 0036 (Available on WhatsApp)

Email: secretariat@msh2024.com
c/o Medical Conference Partners
9, Jalan 9/3, Section 9,
46000 Petaling Jaya, Selangor
Website: medicalconferencepartners.com

VENUE LAYOUT - BASEMENT II



VENUE LAYOUT

Platinum

P1	Takeda Malaysia Sdn Bhd

Gold

G1	Abbvie Sdn Bhd
G2	Novartis Corporation (Malaysia) Sdn Bhd
G3	Bristol-Myers Squibb (Singapore) Pte Ltd
G4	AstraZeneca Sdn Bhd
G7	Roche Malaysia Sdn Bhd

Silver

S1	Dr. Reddy's Laboratories Malaysia Sdn Bhd
S2	Astellas Pharma Malaysia Sdn Bhd
S3	KYAN Technologies Pte Ltd
S4	Celltrion Healthcare Malaysia Sdn Bhd
S7	Duopharma Marketing Sdn Bhd
S8	Auxi Therapeutics Sdn Bhd
S10	Plutonet Sdn Bhd
S11	Max Family & The Max Foundation

Exhibition Booth

B10	Kyowa Kirin Malaysia Sdn Bhd
B11	Link Healthcare Sdn Bhd
B23	MSD (Malaysia) Sdn Bhd
B24	GlaxoSmithKline Pharmaceutical Sdn Bhd
B25	Accord Healthcare Sdn Bhd
B26	Pharmaniaga Marketing Sdn Bhd
B27	Sandoz Products (M) Sdn Bhd
B28	Oncode Scientific Sdn Bhd
B29	Teraju Pharma Sdn Bhd
B30	Zuellig Pharma Sdn Bhd
B31	Smart Medicine Sdn Bhd
B32	Aspen Medical Products Malaysia Sdn Bhd
B33	Johnson & Johnson Sdn Bhd

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Prof Dr Zilfalil Alwi
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JAKAVI is indicated for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis.

RESPONSE | CONTROL | SURVIVAL

1st Line Treatment for MF[1]

Don't Wait, Start Early

- Prolongs survival[2,3]
- Reduces spleen size[4]
- Improves symptoms and QoL[5]
- All international guidelines include JAKAVI® as a treatment option for patient with intermediate -1 risk disease[6]
- JAKAVI® can be used irrespective of risk stratification[4]

MF, Myelofibrosis; **QoL,** Quality of life.

References: 1. JAKAVI® (ruxolitinib) PI: Jakavi_PI_RD_26Oct20_EU 28 Jul 21;Appr 2Mar22_(PUBLIC). **2.** Verstovsek S. *et al.* Long-term results of Ruxolitinib therapy in patients with myelofibrosis: Final analysis of the 5-year efficacy and safety data of the COMFORT-I study. Lecture S452 presented at the 21st EHA Conference, Copenhagen/Denmark. **3.** Verstovsek S. *et al.* A Pooled Overall Survival Analysis of 5-Year Data from the COMFORT-I and COMFORT-II Trials of Ruxolitinib for the Treatment of Myelofibrosis. Presentation 3110 at the 58th Annual Meeting of the ASH, San Diego/USA, December 3-6, 2016. **4.** Verstovsek S. *et al. N Engl J Med.* 2012;366:799-807. **5.** Passamonti F. *et al.* Comparing the Safety and Efficacy of Ruxolitinib in Patients With DIPSS Low/Intermediate-1-, Intermediate-2-, and High-Risk Myelofibrosis in JUMP, a Phase 3b, Expanded-Access Study, Presentation E1333 at the 22nd EHA Conference, Madrid/Spain, June 22-25, 2017. **6.** Barbui T. *et al.* (2018) Leukemia, Epub ahead of print. NCCN guidelines. Available from: https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed on: 29 April 2020.

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Clinically meaningful spleen response[1-3]

Both JAK-inhibitor–naïve patients and patients who experienced ruxolitinib failure achieved ≥35% SVR (37% and 31%, respectively)

Rapid and sustained symptom control[1-3]

Both JAK-inhibitor–naïve patients and patients who experienced ruxolitinib failure achieved ≥50% reduction in TSS (40% and 27%, respectively)

The most common ARs were GI and hematologic; GI ARs decreased over time and can be effectively managed[1,4,5]

Once-daily oral treatment that can be given at the full dose (400 mg/day), regardless of platelet level[1]

Indications

INREBIC® is indicated for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who are Janus Associated Kinase (JAK) inhibitor naïve or have been treated with ruxolitinib.[1]

IMPORTANT SAFETY INFORMATION[1]

WARNING: ENCEPHALOPATHY INCLUDING WERNICKE'S

Serious and fatal encephalopathy, including Wernicke's, has occured in patients treated with INREBIC. Wernicke's encephalopathy is a neurologic emergency. Assess thiamine levels in all patients prior to starting INREBIC, periodically during treatment, and as clinically indicated. Do not start INREBIC in patients with thiamine deficiency; replete thiamine prior to treatment initiation. If encephalopathy is suspected, immediately discontinue INREBIC and initiate parenteral thiamine. Monitor until symptoms resolve or improve and thiamine levels normalize.

WARNINGS AND PRECAUTIONS[1]

Encephalopathy, Including Wernicke's: Serious and fatal encephalopathy, including Wernicke's encephalopathy, has occured in INREBIC-treated patients. Serious cases were reported in 1.3% (8/608) of patients treated with INREBIC in clinical trials and 0.16% (1/608) of cases were fatal.

Please see local Prescribing Information for full details, including Posology and method of administration, Special warnings and precautions of use, Undesirable effects and Overdose.

ARs=adverse reactions; GI=gastrointestinal; SVR=spleen volume reduction; TSS=Total Symptom Score.

References: 1. Inrebic NPRA Approved Prescribing Information October 2023. **2.** Talpaz M, Kiladjian JJ. Fedratinib, a newly approved treatment for patients with myeloproliferative neoplasm-associated myelofibrosis. *Leukemia*. 2021;35(1):1-17. doi:10.1038/s41375-020-0954-2. **3.** Harrison CN, Schaap N, Vannucchi AM, et al. Fedratinib in patients with myelofibrosis previously treated with ruxolitinib: an updated analysis of the JAKARTA2 study using stringent criteria for ruxolitinib failure. *Am J Hematol*. 2020;95:594–603. **4.** Pardanani A, Harrison C, Cortes JE, et al. Safety and efficacy of fedratinib in patients with primary or secondary myelofibrosis: a randomized clinical trial [supplementary online content]. *JAMA Oncol*. Published online June 18, 2015. doi:10.1001/jamaoncol.2015.1590. **5.** Pardanani A, Harrison C, Cortes JE, et al. Safety and efficacy of fedratinib in patients with primary or secondary myelofibrosis: a randomized clinical trial. *JAMA Oncol*. 2015;1(5):643-651. Doi: 10.1001/jamaoncol.2015.1590.

NPRA = National Pharmaceutical Regulatory Agency.

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PROGRAMME OVERVIEW

MSH-EHA Pre-Congress Tutorial - 17 April 2024 (Wednesday)

	EHA Pre-Congress Tutorial	MSH Pre-Congress Pharmacy Programme
0800 - 0845	Registration	
0845 - 0900	Opening Briefing	
0900 - 1030	**Session 1:** **Basic Principles of Hodgkin Lymphoma** **Topic:** **Basic Principles Of Hodgkin Lymphoma- Focus On The Late Effects** ***Speaker:*** *Dr Maria Jose Kersten* ***Chairperson:*** *Dr Haris Abdul Rahman* ***Facilitator:*** *Dr Low Pei Ling*	**Session 1:** **Basic Principle of Chemotherapy** 1. Understanding Antineoplastic Drugs 2. Chemotherapy Induced Nause & Vomiting (CINV) 3. Safe Handling of Chemotherapy ***Speaker:*** *Ms Carolyn Eng Chai Hui*
1030 - 1100	Tea Break	
1100 - 1230	**Session 2:** **Histopathology and Diagnosis** **Topic:** **Hodgkin Lymphoma Histology** ***Speaker:*** *Dr Miguel Piris* ***Chairperson:*** *Dr Haris Abdul Rahman* ***Facilitator:*** *Dr Liong Chee Chiat*	**Session 2:** **Basic Principle of Compounding Chemotherapy** 1. Introduction to Aseptic Dispensing 2. Clean Room Facility, Equipment & Monitoring (ISOPP Standard) 3. Personnel Training, Validation & Education (ISOPP Standard) ***Speaker:*** *Mrs Harbans Kaur Dhillon*
1230 - 1330	Lunch	
1330 - 1500	**Session 3:** **Treatment of Newly Diagnosed Hodgkin Lymphoma** **Topic:** **Evolving Therapeutic Landscape In Newly Diagnosed Hodgkin Lymphoma: Current and Future Approaches** ***Speaker:*** *Prof Dr Anna Czyz* ***Chairperson:*** *Dr Zanapiah Zakaria* ***Facilitator:*** *Dr Ong Jiun Jyh*	**Session 3:** **Extravasation** 1. Vesicant vs Irritant 2. Management of Extravasation ***Speakers:*** *Dr John Ranjit Nesaraj & Mr Tan Wen Chieh*
1500 - 1530	Tea Break	
1530 - 1700	**Session 4:** **Managing First Relapse and Refractory Disease with Intention to Cure** **Topic:** **Classical Hodgkin Lymphoma: Not Always A Good Prognosis Disease** ***Speaker:*** *Dr Chiara Rusconi* ***Chairperson:*** *Dr Zanapiah Zakaria* ***Facilitator:*** *Dr Hany Haqimi Wan Hanafi*	**Session 4:** **Parenteral Nutrition in Bone Marrow Transplant** 1. Introduction to Parenteral Nutrition 2. Parenteral Nutrition In Bone Marrow Transplant Patients 3. Compatibility & Stability of Parenteral Nutrition with Drugs ***Speaker:*** *Ms Jasreena Kaur*
	END OF DAY 1	

PROGRAMME OVERVIEW

MSH-EHA Pre-Congress Tutorial - 18 April 2024 (Thursday)

	EHA Pre-Congress Tutorial	MSH Pre-Congress Pharmacy Programme
0900 - 1030	**Session 5:** **The Roles of Novel Agents in the Landscape of Hodgkin Lymphoma in 2024** **Topic:** **The Roles Of Novel Agents In The Landscape Of Hodgkin Lymphoma In 2024** ***Speaker:*** *Prof Dr Peter Borchmann* ***Chairperson:*** *Dr Jay Suriar* ***Facilitator:*** *Dr Andy Tang Sing Ong*	
1030 - 1100	Tea Break	
1100 - 1230	**Session 6:** **Imaging in Hodgkin Lymphoma** **Topic:** **Imaging; Cornerstone In Hodgkin Lymphoma Treatment** ***Speaker:*** *Prof Josée M Zijlstra* ***Chairperson:*** *Dr Jay Suriar* ***Facilitator:*** *Dr Chong Guan Yong*	
	END OF DAY 2	

PROGRAMME OVERVIEW

Congress Day 1 - 18 April 2024 (Thursday)

	CLINICAL 1 (Sabah Hall)	CLINICAL 2 (Kedah Room)	NURSING (Melaka Room)	PATHOLOGY (Selangor Room)
1000	Registration			
1230 - 1315	**EHA Pre-Congress Updates (in Sabah Hall)**			
1315 - 1345	Lunch			
1345 - 1500	**Education Session 1**			
	Clinical 1A Aggresive NHL	**Clinical 1B** Myeloproliferative Neoplasm	**Paramedic 1** Chemotherapy Handling	**Pathology 1** Novel Diagnostics
1500 - 1530	Tea Break			
1530 - 1545	**Official Opening Ceremony (in Sabah Hall)**			
1545 - 1630	**The John Bosco Lecture (in Sabah Hall)**			
1630 - 1715	**Satellite Symposium 1**			
	Satellite Symposium 1A Novartis	**Satellite Symposium 1B** BMS		**Satellite Symposium 1C** Roche Malaysia Sdn Bhd

PROGRAMME OVERVIEW

Congress Day 2 - 19 April 2024 (Friday)

	CLINICAL 1 (Sabah Hall)	CLINICAL 2 (Kedah Room)	NURSING (Melaka Room)	PATHOLOGY (Selangor Room)
0730	Registration			
0800 - 0915	**Education Session 2**			
	Clinical 2A Stem Cell Transplant	**Clinical 2B** Thrombocytopenia	**Paramedic 2** Basic Haematolgy Emergency 1	**Pathology 2** Diagnostic Dilemma
0915 - 1000	**Satellite Symposium 2**			
	Satellite Symposium 2A AstraZeneca	**Satellite Symposium 2B** BMS	Morphology Quiz	**Satellite Symposium 2C** Astellas
1000 - 1030	Tea Break			
1030 - 1145	**Education Session 3**			
	Clinical 3A Low Grade Lymphoproliferative Diseases	**Clinical 3B** Infection in Haematology	**Paramedic 3** Transfusion Matters	**Pathology 3** Molecular Haematology
1145 - 1230	**Plenary Session 1 (in Sabah Hall)**			
1230 - 1330	**Lunch Symposium 1 - Takeda (in Sabah Hall)**			
1400 - 1515	**Education Session 4**			
	Clinical 4A Multiple Myeloma	**Clinical 4B** Thrombosis	**Paramedic 4** Palliative Care	**Pathology 4** Bone Marrow Failure and Bleeding Disorders
1515 - 1600	**Satellite Symposium 3**			
	Satellite Symposium 3A Novartis			**Satellite Symposium 3B** Abbvie
1600 - 1630	Tea Break			
1630 - 1745				
	END OF DAY 2			

PROGRAMME OVERVIEW

Congress Day 3 - 20 April 2024 (Saturday)

	CLINICAL 1 (Sabah Hall)	CLINICAL 2 (Kedah Room)	NURSING (Melaka Room)	PATHOLOGY (Selangor Room)
0730	Registration			
0800 - 0915	**Education Session 5**			
	Clinical 5A How I Treat	**Clinical 5B** Anaemia	**Paramedic 5** Understanding Stem Cell Transplant	**Pathology 5** Transfusion Medicine
0915 - 1000	**Satellite Symposium 4**			
			Morphology Quiz Review / Results	**Satellite Symposium 4B** AstraZeneca
1000 - 1030	Tea Break			
1030 - 1145	**Education Session 6**			
	Clinical 6A Sexy Strategies	**Clinical 6B** Beyond Medicine	**Paramedic 6** Basic Haematology Emergency 2	**Pathology 6** RBCs Disorders
1145 - 1230	**Oral Poster Presentation** (Clinical)			**Oral Poster Presentation** (Laboratory)
1300 - 1400	**Lunch Symposium 2 - AMGEN (in Sabah Hall)**			
1400 - 1445	**PLENARY SESSION 2 (in Sabah Hall)**			
1515 - 1600	Tea Break			
1600 - 1645	Presidential Symposium, Prize Giving & Closing Ceremony			
	END OF CONGRESS			

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CLINICAL 1 | Sabah Hall

DETAILED PROGRAMME

Congress Day 1 - 18 April 2024 (Thursday)

1000	Registration	
1230 - 1315	**EHA Pre-Congress Updates**	
1315 - 1345	Lunch	
1345 - 1500	**Education Session 1**	
	Clinical 1A: Aggressive NHL	***Chairperson:*** *Dr Jerome Tan Tsen Chuen*
1345 - 1415	How The Concept Of Aggressive NHL Evolved Over The Years & Its Impact On Clinical Decision	***Speaker:*** *Prof Dr Bee Ping Chong*
1415 - 1445	Is There Anything Which Brings More Clinically Significant Benefit Than RCHOP-21?	***Speaker:*** *Dr Ahlam Naila Kori*
1445 - 1500	Q&A Session	
1500 - 1530	Tea Break	
1530 - 1545	**Official Opening Ceremony**	
1545 - 1630	**The John Bosco Lecture** **The Roles of Novel Agents in the Landscape of Hodgkin Lymphoma in 2024** *Prof Dr Peter Brochmann*	***Chairperson:*** *Prof Dr Gan Gin Gin*
1630 - 1715	**Satellite Symposium 1**	
	NOVARTIS **Satellite Symposium 1A** Switching To A Novel STAMP MOA, Raising The BAR In CML Management	***Speakers:*** *1. Dato' Dr Chang Kian Meng* *2. Dr Christopher Liam* *3. Prof Dr Ng Soo Chin*
1730	**MSH Annual General Meeting in Johor 2**	
	END OF DAY 1	

CLINICAL 2 | Kedah Room

DETAILED PROGRAMME
Congress Day 1 - 18 April 2024 (Thursday)

1000	Registration	
1230 - 1315	**EHA Pre-Congress Updates in Sabah Hall**	
1315 - 1345	Lunch	
1345 - 1500	**Education Session 1**	
	Clinical 1B: Myeloproliferative Neoplasm	***Chairperson:*** *Dr Gan Ee Leng*
1345 - 1415	What Is In The Name Change: Impact & Significance of Renaming MPD As MPN	***Speaker:*** *Dr Mandy Yap Yee Yee*
1415 - 1445	Chronic Myeloid Leukemia In The Era of TKI & Beyond: When Need Not To Aggressively Chasing After Deep and Deeper Molecular Remission?	***Speaker:*** *Prof Dr Kuan Jew Win*
1445 - 1500	Q&A Session	
1500 - 1530	Tea Break	
1530 - 1545	**Official Opening Ceremony in Sabah Hall**	
1545 - 1630	**The John Bosco Lecture in Sabah Hall**	
1630 - 1715	**Satellite Symposium 1**	
	Bristol Myers Squibb™ **Satellite Symposium 1B** Exploring Novel Therapies And Advancing Clinical Care In Myelofibrosis	***Chairperson:*** *Dr Jerome Tan Tsen Chuen* ***Speaker:*** *Prof Francesco Passamonti*
1730	**MSH Annual General Meeting in Johor 2**	

NURSING | Melaka Room

DETAILED PROGRAMME
Congress Day 1 - 18 April 2024 (Thursday)

1000	Registration	
1230 - 1330	**EHA Pre-Congress Updates in Sabah Hall**	
1345 - 1500	**Education Session 1**	
	Paramedic 1: Chemotherapy Handling	***Chairperson:*** *Ms Carolyn Eng Chai Hui*
1345 - 1420	Cytotoxic Drug Reconstitution (CDR): ISOPP Standards	***Speaker:*** *Mr Tan Wen Chieh*
1420 - 1455	Beyond the Blood: Clinical Pharmacist in Hematology Care	***Speaker:*** *Ms Kong Su Shan*
1455 - 1500	Q&A Session	
1500 - 1530	Tea Break	
1530 - 1545	**Official Opening Ceremony in Sabah Hall**	
1545 - 1630	**The John Bosco Lecture in Sabah Hall**	
1730	**MSH Annual General Meeting in Johor 2**	
	END OF DAY 1	

PATHOLOGY | Selangor Room

DETAILED PROGRAMME

Congress Day 1 - 18 April 2024 (Thursday)

1000	Registration	
1230 - 1315	**EHA Pre-Congress Updates in Sabah Hall**	
1315 - 1345	Lunch	
1345 - 1500	**Education Session 1**	
	Pathology 1: Novel Diagnostics	***Chairperson:*** *Prof Dr Rosline Hassan*
1345 - 1405	The Role of Circulating Cell Free Tumour DNA Analysis and Relevance To The Clinical Setting in Primary Refractory Multiple Myeloma	***Speaker:*** *Dr Sridurga Mithraprabu*
1405 - 1425	CRISPR/Cas9 Screening in T-Cell Lymphoma in Predicting Clinical Response	***Speaker:*** *Prof Jake Shortt*
1425 - 1445	Next Generation Flow Cytometry	***Speaker:*** *Dr Lee Shir Ying*
1445 - 1500	Q&A Session	
1500 - 1530	Tea Break	
1530 - 1545	**Official Opening Ceremony in Sabah Hall**	
1545 - 1630	**The John Bosco Lecture in Sabah Hall**	
1630 - 1715	**Satellite Symposium 1**	
	Roche **Satellite Symposium 1C** How I Treat DLBCL In 2024 - Managing DLBCL In The Era of T Cell-Based Immunotherapies	***Chairperson:*** *Dr Jay Suriar* ***Speaker:*** *Prof Dr Sascha Dietrich*
1730	**MSH Annual General Meeting in Johor 2**	
	END OF DAY 1	

CLINICAL 1 | Sabah Hall

DETAILED PROGRAMME

Congress Day 2 - 19 April 2024 (Friday)

0730	Registration	
0800 - 0915	**Education Session 2**	
	Clinical 2A: Stem Cell Transplant	***Chairperson:*** *Dato' Dr Vijaya Sangkar Jaganathan*
0800 - 0830	When Is the Old HSCT Still Good?	***Speaker:*** *Dato Dr Chang Kian Meng*
0830 - 0900	New Players That Might Make HSCT Looks Jurassic & Barbaric	***Speaker:*** *Dr Alan Teh Kee Hean*
0900 - 0915	Q&A Session	
0915 - 1000	**Satellite Symposium 2**	
	AstraZeneca **Satellite Symposium 2A** Beyond The Guidelines - Management Of Patient With Chronic Lymphocytic Leukemia (CLL)	***Chairperson:*** *Dr Jerome Tan Tsen Chuen* ***Speaker:*** *Dr Chandramouli Nagarajan*
1000 - 1030	Tea Break	
1030 - 1145	**Education Session 3**	
	Clinical 3A: Low Grade Lymphoproliferative Diseases	***Chairperson:*** *Prof Dr Bee Ping Chong*
1030 - 1100	The Good Old Days "Watchful Waiting": Any Patients Can Still Be Left Alone In The Era of Multiple Novel Agents?	***Speaker:*** *Dr Tan Chen Lung Daryl*
1100 - 1130	Exploring New Frontiers With New Agents: New Implications & Complications In Managing Low Grade Lymphoproliferative Diseases	***Speaker:*** *Dr Lau Ngee Siang*
1130 - 1145	Q&A Session	
1145 - 1230	**Plenary Session 1**	
	Imaging Flow Cytometry For The Assessment Of Chromosome Abnormalities In Haematological Malignancy	***Chairperson:*** *Dr Mardziah Mohamad* ***Speaker:*** *Prof Dr Wendy Erber*
1230 - 1330	**Lunch Symposium 1**	
	Takeda Management Of Advanced Classical Hodgkin Lymphoma And Long-Term Survival Outcome- A Singapore Case Sharing Perspective	***Chairperson:*** *Prof Dr Ng Soo Chin* ***Speaker:*** *Dr Tan Chen Lung Daryl*

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CLINICAL 1 | Sabah Hall

DETAILED PROGRAMME

Congress Day 2 - 19 April 2024 (Friday)

1400 - 1515	**Education Session 4**	
	Clinical 4A: Multiple Myeloma	**Chairperson:** *Dato' Dr Goh Ai Sim*
1400 - 1430	Too Many Choices But Expensive: How to Match Treatment Strategies to Available Resources	***Speaker:*** *Dr Lily Wong Lee Lee*
1430 - 1500	Myeloma In 2024: When Can Auto-SCT Be Omitted As Upfront Bundled Strategy?	***Speaker:*** *Dr Tan Sen Mui*
1500 - 1515	Q&A Session	
1515 - 1600	**Satellite Symposium 3**	
	NOVARTIS **Satellite Symposium 3A** Optimizing Myelofibrosis Management with Current Therapies	***Chairperson:*** *Dr Chew Lee Ping* ***Speaker:*** *Dr Cecily Forsyth*
1600 - 1630	Tea Break	
1630 - 1745		
	END OF DAY 2	

CLINICAL 2 | Kedah Room

DETAILED PROGRAMME
Congress Day 2 - 19 April 2024 (Friday)

0730	Registration	
0800 - 0915	**Education Session 2**	
	Clinical 2B: Thrombocytopenia	***Chairperson:*** *Dr Sharifah Shahnaz Syed Abdul Kadir*
0800 - 0830	From Idiopathic To Immune: Are We Better In Managing ITP In 2024?	***Speaker:*** *Assoc Prof Dr Azlan Husin*
0830 - 0900	TTP: How To Improve The Detection and Management In Community Hospital	***Speaker:*** *Dr Sharifah Suryani Syed Rahim Shah*
0900 - 0915	Q&A Session	
0915 - 1000	**Satellite Symposium 2B**	
	Bristol Myers Squibb™ Navigating The Landscape of LR-MDS: Current and Emerging Treatment Strategies for Optimal Outcomes	***Chairperson:*** *Dr Lily Wong Lee Lee* ***Speaker:*** *Asst Prof Chien-Chin Lin*
1000 - 1030	Tea Break	
1030 - 1145	**Education Session 3**	
	Clinical 3B: Infection in Haematology	***Chairperson:*** *Prof Madya Dr Nor Rafeah Tumian*
1030 - 1100	De-Escalation and Less Antibiotics: Is It Feasible In Hematology Malignancy?	***Speaker:*** *Dr Timothy William*
1100 - 1130	4 Years Post Pandemic: Has COVID-19 Taught Haematologists Anything ?	***Speaker:*** *Dr Liew Hong Keng*
1130 - 1145	Q&A Session	
1145 - 1230	**Plenary Session 1 in Sabah Hall**	
1230 - 1330	**Lunch Symposium 1: TAKEDA in Sabah Hall**	
1400 - 1515	**Education Session 4**	
	Clinical 4B: Thrombosis	***Chairperson:*** *Dr Jay Suriar*
1400 - 1430	Those Clots With Low Platelets	***Speaker:*** *Dr Wong Chieh Lee*
1430 - 1500	Those Clots Despite Adequate Traditonal Anticoagulation	***Speaker:*** *Dr Guan Yong Khee*
1500 - 1515	Q&A Session	
1515 - 1600	**Satellite Symposium 3 in Sabah Hall & Selangor Room**	
1600 - 1630	Tea Break	
1630 - 1745		
	END OF DAY 2	

NURSING | Melaka Room

DETAILED PROGRAMME

Congress Day 2 - 19 April 2024 (Friday)

0730	Registration	
0800 - 0915	**Education Session 2**	
	Paramedic 2: Basic Haematology Emergency 1	***Chairperson:*** *Dr Gan Ee Leng*
0800 - 0830	Haematology Emergencies - Tumour Lysis Syndrome	***Speaker:*** *Dr Sivakumar Palaniappan*
0830 - 0900	Haematology Emergencies - Febrile Neutropenia	***Speaker:*** *Dr Shasha Khairullah*
0900 - 0915	Q&A Session	
0915 - 1000	Morphology Quiz	***Facilitators:*** • Dr Mardziah Mohamad • Dr Hana Shafinaz Jamaludin
1000 - 1030	Tea Break	
1030 - 1145	**Education Session 3**	
	Paramedic 3: Transfusion Matters	***Chairperson:*** *Dr Tengku Hidayat Tengku Aziz*
1030 - 1100	Complications of Blood Transfusion	***Speaker:*** *Prof Veera Sekaran Nadarajan*
1100 - 1130	Alternatives to Blood Transfusion	***Speaker:*** *Dr Alina Md Fauzi*
1130 - 1145	Q&A Session	
1145 - 1230	**Plenary Session 1 in Sabah Hall**	
1230 - 1330	**Lunch Symposium 1: TAKEDA in Sabah Hall**	
1400 - 1515	**Education Session 4**	
	Paramedic 4: Palliative Care	***Chairperson:*** *Dr Tan Seng Beng*
1400 - 1430	Palliative Care and Wellness	***Speaker:*** *Dr Tan Seng Beng*
1430 - 1500	Palliative Care and Wellness	
1500 - 1515	Q&A Session	
1515 - 1600	Satellite Symposium 3 **in Sabah Hall & Selangor Room**	
1600 - 1630	Tea Break	
1630 - 1745		
	END OF DAY 2	

PATHOLOGY | Selangor Room

DETAILED PROGRAMME

Congress Day 2 - 19 April 2024 (Friday)

0730	Registration	
0800 - 0915	**Education Session 2**	
	Pathology 2: Diagnostic Dilemma	***Chairperson:*** *Dr Mimi Azura*
0800 - 0820	Diagnostic Challenges In MDS/MPN	***Speaker:*** *Prof Dr Wendy Erber*
0820 - 0840	Challenges In the Histopathologic Diagnosis Of Histiocytic Neoplasm	***Speaker:*** *Assoc Prof Tan Soo Yong*
0840 - 0900	Diagnosing Difficult Cases of Aggressive B and T Neoplasm	
0900 - 0915	Q&A Session	
0915 - 1000	**Satellite Symposium 2C**	
	astellas Clinical Value of XOSPATA In R/R FLT3m+ AML: Impact On Patient Outcomes	***Chaiperson:*** Dato' Dr Chang Kian Meng ***Speaker:*** Dr Ng Chin Hin
1000 - 1030	Tea Break	
1030 - 1145	**Education Session 3**	
	Pathology 3: Molecular Haematology	***Chairperson:*** *Prof Dr Hany Mohd Ariffin*
1030 - 1050	Role of RNA Sequencing in The Management of ALL	***Speaker:*** *Assoc Prof Allen Yeoh Eng Juh*
1050 - 1110	The Present and Future of Measurable Residual Disease Testing in AML	***Speaker:*** *Prof Dr Rosline Hassan*
1110 - 1130	MRD in ALL: Is <10-4 Sufficient?	***Speaker:*** *Assoc Prof Allen Yeoh Eng Juh*
1130 - 1145	Q&A Session	
1145 - 1230	**Plenary Session 1 in Sabah Hall**	
1230 - 1330	**Lunch Symposium 1: TAKEDA in Sabah Hall**	

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PATHOLOGY | Selangor Room

DETAILED PROGRAMME

Congress Day 2 - 19 April 2024 (Friday)

1400 - 1515	**Education Session 4**	
	Pathology 4: Bone Marrow Failure And Bleeding Disorders	***Chairperson:*** *Assoc Prof Dr Nurasyikin Yusof*
1400 - 1420	Current Insight Into The Diagnosis And Management of Acquired Vs Inherited Bone Marrow Failure Syndrome	***Speaker:*** *Prof Dr Hany Mohd Ariffin*
1420 - 1440	Bleeding Disorder of Unknown Cause; Diagnosis And Management	***Speaker:*** *Dr Veena Selvaratnam*
1440 - 1500	Comprehensive Update On Thrombophilia Testing In Venous Thromboembolism	***Speaker:*** *Dr Lee Shir Ying*
1500 - 1515	Q&A Session	
1515 - 1600	**Satellite Symposium 3B**	
	abbvie Advances in The DLBCL Treatment Paradigm	***Chairperson:*** *Dr Jason Chan*
1515 - 1530	The Current DLBCL Treatment Landscape	***Speaker:*** *Dr Jason Chan*
1530 - 1550	The Evolving Treatment Paradigm in R/R DLBCL	***Speaker:*** *Dr Hun Sheng Chuah*
1550 - 1600	Q&A Session	
1600 - 1630	Tea Break	
1630 - 1745		
	END OF DAY 2	

CLINICAL 1 | Sabah Hall

DETAILED PROGRAMME

Congress Day 3 - 20 April 2024 (Saturday)

0730	Registration		
0800 - 0915	**Education Session 5**		
	Clinical 5A: How I Treat		***Chairperson:*** *Dr Lau Ngee Siang*
0800 - 0830	How I Treat: Castleman Disease		***Speaker:*** *Prof Dr Goh Yeow Tee*
0830 - 0900	CML Who Wants to Conceive		***Speaker:*** *Dr Adila Anuar*
0900 - 0915	Q&A Session		
0915 - 1000	**Satellite Symposium 4B: AstraZeneca In Selangor Room**		
1000 - 1030	Tea Break		
1030 - 1145	**Education Session 6**		
	Clinical 6A: Sexy Strategies		***Chairperson:*** *Dr Muhd Zanapiah Zakaria*
1030 - 1100	Finding Druggable Targets: New Paradigm & Holy Grail of Hematology?		***Speaker:*** *Prof Dr Gan Gin Gin*
1100 - 1130	CAR-T: Can It Be a Real Game Changer in Malaysia?		***Speaker:*** *Prof Dr Ng Soo Chin*
1130 - 1145	Q&A Session		
1145 - 1300	**Oral Poster Presentation (Clinical)**		***Judges:*** *Dato' Dr Goh Ai Sim* *Prof Dr Bee Ping Chong*
1145 - 1150	Opening Remarks		
1152 - 1201	C01	Haematopoietic Stem Cell Transplantation For Children With Transfusion Dependent Thalassaemia In Malaysia: Experience From UMMC	*Chiew Xin Yee*
1203 - 1212	C02	Reducing Late Administration Of Inpatient Chemotherapy For Haematology Oncology Patients	*Andy Tang Sing Ong*
1214 - 1223	C03	Transition Of Thalassaemia Care From Paediatric To Adult Haematology Centre: A Retrospective Study	Chong Shu May
1225 - 1234	C04	Evaluation Of Venous Thromboembolism In Adult Lymphoma Using Sarawak Lymphoma Thrombosis Score (SLOTS): A Multicenter Retrospective Study In Sarawak	Leong Tze Shin

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CLINICAL 1 | Sabah Hall

DETAILED PROGRAMME

Congress Day 3 - 20 April 2024 (Saturday)

1236 - 1245	C05	Impact Of Pharmacist Led Medication Therapy Adherence Clinic (MTAC) Towards The Management Of Thalassemia Patients In A Tertiary Hospital In Malaysia: A Preliminary Result	Ranita Kirubakaran
1247 - 1256	C06	Predictors Of Survival And Successful Response To Upfront Cyto-MSC Treatment In Acute GVHD: A Randomized, Double Blinded, Placebo Controlled, Multicentre Clinical Trial	Chin Sze-Piaw
1258 - 1300	Closing Remarks		
1300 - 1400	**Lunch Symposium 2**		
	AMGEN Advances of Immunotherapies for B-cell Acute Lymphoblastic Leukemia Experience Sharing of Blinatumomab Preparation - Pharmacist Perspective		***Chairperson:*** *Prof Dr Ng Soo Chin* ***Speaker:*** *Dr Ng Chin Hin* ***Speaker:*** *Ms Eileen Ho*
1400 - 1445	**Plenary Session 2**		***Chairperson:*** *Dato' Dr Goh Ai Sim*
	Genomic Advances for Thalassaemia: Driving Change in Malaysia		***Speaker:*** *Prof Dr Zilfalil Alwi*
1515 - 1600	Tea Break		
1600 - 1645	Presidential Symposium, Prize Giving & Closing Ceremony		
	END OF CONGRESS		

CLINICAL 2 | Kedah Room

DETAILED PROGRAMME

Congress Day 3 - 20 April 2024 (Saturday)

0730	Registration	
0800 - 0915	**Education Session 5**	
	Clinical 5B: Anaemia	***Chairperson:*** *Dr Kok Keng Weng*
0800 - 0830	Hypoplastic Marrow with Myelodysplastic Changes	***Speaker:*** *Dr Lim Soo Min*
0830 - 0900	Blood Transfusion & Intravenous Iron: Do We Need Restraint?	***Speaker:*** *Dr Sharifah Shahnaz Syed Abdul Kadir*
0900 - 0915	Q&A Session	
0915 - 1000	**Satellite Symposium 4B: AstraZeneca In Selangor Room**	
1000 - 1030	Tea Break	
1030 - 1145	**Education Session 6**	
	Clinical 6B: Beyond Medicine	***Chairperson:*** *Assoc Prof Dr Azlan Husin*
1030 - 1100	Impact of New Developments in Hematology Malignancy on Patients and Healthcare Providers	***Speaker:*** *Dr Sinari Salleh*
1100 - 1130	Lives of Thalassemia & Hemophilia Patients: The Difference Today & Previous Generation	***Speaker:*** *Dr Jameela Sathar*
1130 - 1145	Q&A Session	
1145 - 1300	**Oral Poster Presentation In Sabah Hall & Selangor Room**	
1300 - 1400	**Lunch Symposium 2: AMGEN in Sabah Hall**	
1400 - 1445	**Plenary Session 2 in Sabah Hall**	
1515 - 1600	Tea Break	
1600 - 1645	Presidential Symposium, Prize Giving & Closing Ceremony **in Sabah Hall**	
	END OF CONGRESS	

NURSING | Melaka Room

DETAILED PROGRAMME

Congress Day 3 - 20 April 2024 (Saturday)

0730	Registration	
0800 - 0915	**Education Session 5**	
	Paramedic 5: Understanding Stem Cell Transplant	***Chairperson:*** *Dr Habibah Abdul Halim*
0800 - 0830	Types of Stem Cell Transplant and Donor Selection	***Speaker:*** *Dr Low Pei Ling*
0830 - 0900	Stem Cell Transplantation: The Basics of the Process	***Speaker:*** *Dr Liong Chee Chiat*
0900 - 0915	Q&A Session	
0915 - 1000	Morphology Quiz Review / Results	***Facilitators:*** Dr Mardziah Mohamad Dr Hana Shafinaz Jamaludin
1000 - 1030	Tea Break	
1030 - 1145	**Education Session 6**	
	Paramedic 6: Basic Haematology Emergency 2	***Chairperson:*** *Dr Henning Loo Cheng Kien*
1030 - 1100	DIC and Why is It Dangerous?	***Speaker:*** *Dr Hany Haqimi Wan Hanafi*
1100 - 1130	Is High WBC Really a Cause to Worry?	***Speaker:*** *Dr Chong Guan Yong*
1130 - 1145	Q&A Session	
1145 - 1300	**Oral Poster Presentation in Sabah Hall & Selangor Room**	
1300 - 1400	**Lunch Symposium 2: AMGEN in Sabah Hall**	
1400 - 1445	**Plenary Session 2 in Sabah Hall**	
1515 - 1600	Tea Break	
1600 - 1645	Presidential Symposium, Prize Giving & Closing Ceremony **in Sabah Hall**	
	END OF CONGRESS	

PATHOLOGY | Selangor Room

DETAILED PROGRAMME

Congress Day 3 - 20 April 2024 (Saturday)

0730	Registration	
0800 - 0915	**Education Session 5**	
	Pathology 5: Transfusion Medicine	***Chairperson:*** *Dr Christina Lee Lai Ling*
0800 - 0820	Application of Red Cell Genotyping in Resolving Complex Clinical Cases	***Speaker:*** *Dr Nor Hafizah Ahmad*
0820 - 0840	Platelet Transfusion and Predictors of Bleeding in Haematological Malignancy	***Speaker:*** *Prof Jake Shortt*
0840 - 0900	TRALI: Comprehensive Update on the Pathogenesis and Management	***Speaker:*** *Prof Veera Sekaran Nadarajan*
0900 - 0915	Q&A Session	
0915 - 1000	**Satellite Symposium 4B**	
	AstraZeneca FXa-Inhibitor Reversal and the Management of Life-Threatening Bleeds; Translating Data to Practice Practical Approach: Managing Direct Factor Xa-Inhibitor associated with ICH and GI Bleeding	***Chaiperson:*** Dr Jay Suriar ***Speaker:*** Dr Jerome Tan Tsen Chuen ***Speaker:*** Datuk Dr Mahatahr Abd Wahab
1000 - 1030	Tea Break	
1030 - 1145	**Education Session 6**	
	Pathology 6: RBCs Disorders	***Chairperson:*** *Dr Hafizah Hashim*
1030 - 1050	The Role of Next Generation Sequencing in Hemolytic Anaemia	***Speaker:*** *Prof Celeste Bento*
1050 - 1110	Haemoglobinopathy Variant Classification from Curation Expert Panel Perspective	
1110 - 1130	Pitfall and Caveats in The Detection of PNH Clones in Patient with MDS and Related Bone Marrow Disease	***Speaker:*** *Dr Mimi Azura*
1130 - 1145	Q&A Session	

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PATHOLOGY | Selangor Room

DETAILED PROGRAMME

Congress Day 3 - 20 April 2024 (Saturday)

1145 - 1300	**Oral Poster Presentation (Laboratory)**		***Judges:*** *Emeritus Prof Dr Cheong Soon Keng* *Prof Dr Wendy Erber*
1145 - 1150	Opening Remarks		
1152 - 1201	L01	SLC2A3 And PFKP Are Indispensable For t(8;21) Leukaemic Maintenance	Asmida Isa
1203 - 1212	L02	Deletion Of The Secreted Protein Isthmin 1 Leads To Impaired Megakaryopoiesis And Thrombopoiesis	Md Shakhawat Hosen
1214 - 1223	L03	Generation And Characterisation Of iPS Cell Lines From Donor PBMC For The Purpose Of Producing Dia+ Reagent Cells	Teo Han Yao
1225 - 1234	L04	The Use Of Leucocyte Filter To Retrieve Tumour Cells From Pleural Effusion: An Experimental Study	Sarah Abdul Halim
1236 - 1245	L05	In-Vitro Evaluation Of T-Cell Acute Lymphoblastic Leukemia Cell Line Response To A Combination Of Dual Anticancer Agents; SRJ23 And Hydroxyurea	Bahariah Khalid
1247 - 1256	L06	α2 Codon 63 (GCC>ACC) Haemoglobin Greenville - NC : Detection Rare Case Of Alpha Variant Using Direct Sequencing Method: Cases In Local Population	Nurul Hidayah Musa
1258 - 1300	Closing Remarks		
1300 - 1400	**Lunch Symposium 2: AMGEN in Sabah Hall**		
1400 - 1445	**Plenary Session 2 in Sabah Hall**		
1515 - 1600	Tea Break		
1600 - 1645	Presidential Symposium, Prize Giving & Closing Ceremony **in Sabah Hall**		
	END OF CONGRESS		

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BTKi – Bruton's Tyrosine Kinase inhibitor; CLL – chronic lymphocytic leukaemia; GClb – obinutuzumab + chlorambucil; PFS – progression free survival.

All images are for illustrative purpose only.

References:
1. CALQUENCE® Malaysia Prescribing Information V.3.0 Information DocID-004266542 March 2021.
2. Wu J, Zhang M, Liu D. Acalabrutinib (ACP-196): a selective second-generation BTK inhibitor. J Hematol Oncol. 2016;9:21.
3. Sharman JP, Egyed M, Jurczak W, et al. Acalabrutinib ± obinutuzumab vs obinutuzumab + chlorambucil in treatment-naive chronic lymphocytic leukemia: ELEVATE-TN 5-year follow-up. Poster Presented at: ASCO; June 3-7, 2022; Chicago, Illinois.
4. Bond DA, Woyach JA. Targeting BTK in CLL: beyond ibrutinib. Curr Hematol Malig Rep. 2019; 14(3):197-205.
5. Barf T, Covey T, Izumi R, et al. Acalabrutinib (ACP-196): a covalent Bruton tyrosine kinase inhibitor with a differentiated selectivity and in vivo potency profile. J Pharmacol Exp Ther. 2017;363(2):240-252.

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1. Tilly H, Morschhauser F, Sehn LH, et al. Polatuzumab vedotin in previously untreated diffuse large B-cell lymphoma. N Engl J Med. 2022;386(4):351-363. doi:10.1056/NEJMoa2115304.

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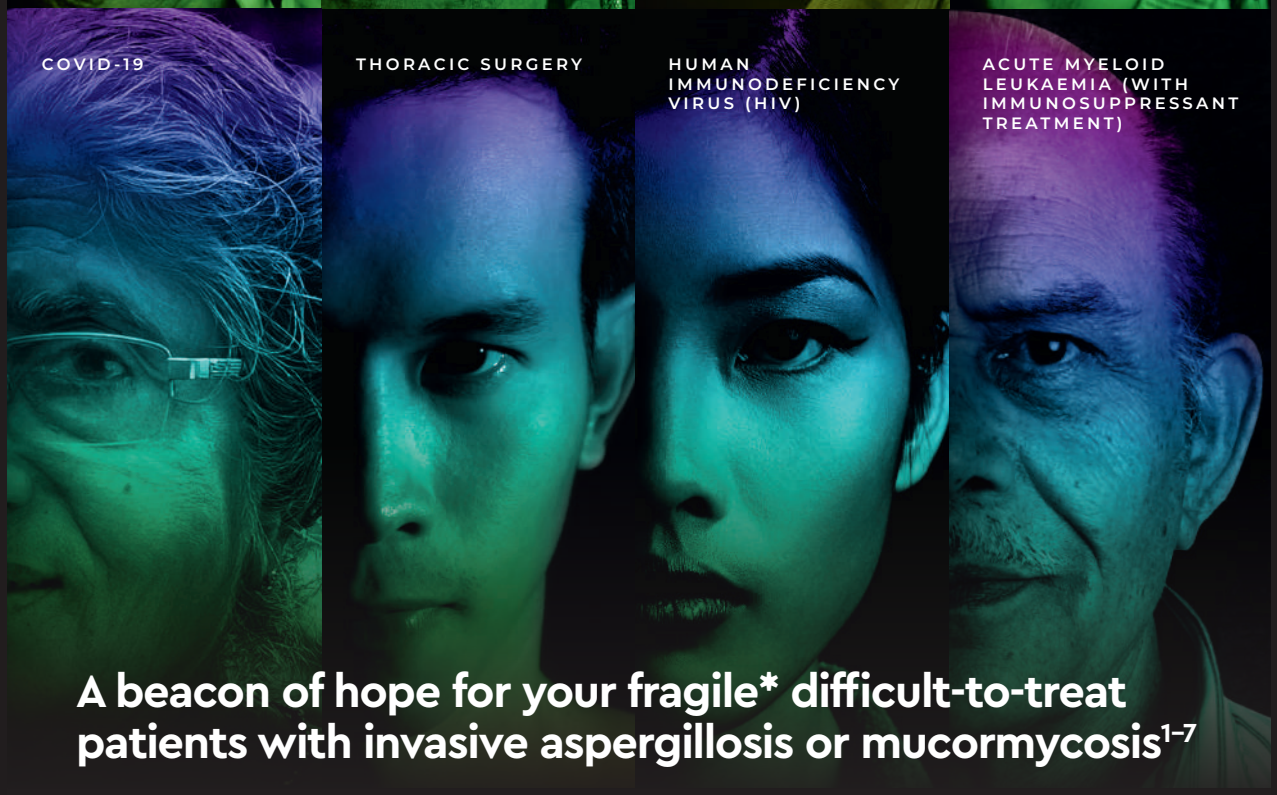

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- Mucormycosis in patients for whom amphotericin B is inappropriate

Consideration should be given to official guidance on the appropriate use of antifungal agents.[3]

References: 1. CRESEMBA Pfizer Malaysia LPD, CRESEMBA IV-1221. **2.** CRESEMBA Pfizer Malaysia LPD, CRESEMBA Capsule-1221. **3.** VFEND Pfizer Malaysia LPD, VFEND-0322. **4.** Maertens JA, *et al. Lancet.* 2016;387(10020):760-769. **5.** Marty FM, *et al. Lancet Infect Dis.* 2016;16(7):828-837. **6.** Stott KE, *et al. J Antimicrob Chemother.* 2017;72(suppl_1)i12-i18. **7.** Miceli MH, *et al. Clin Infect Dis.* 2015;61(10):1558-1565. **8.** Perfect JR, *et al. Nat Rev Drug Discov.* 2017;16(9):603-616. **9.** Perfect JR, *et al. Virulence.* 2017;8(2):143-149.

*Fragile patients refer to patients with invasive fungal infections, who may be immunocompromised, taking multiple therapeutic agents and unable to tolerate treatment with high organ toxicity[8,9]

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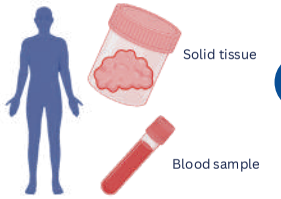

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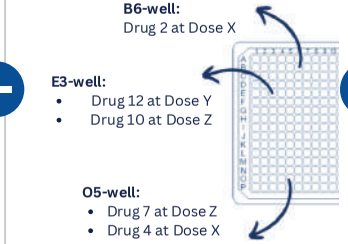

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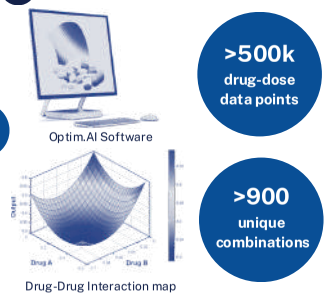

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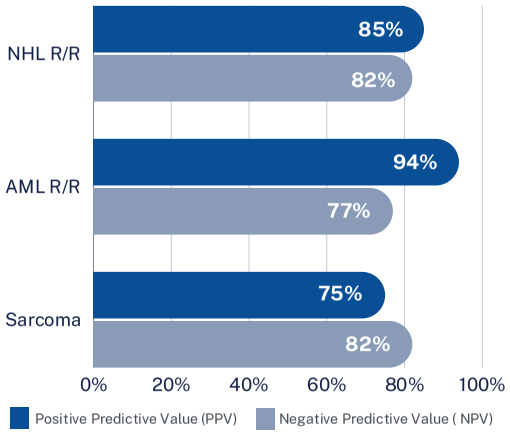

- **NHL**: Rashid et al. Analytical and clinical evaluation of a functional combinatorial precision medicine platform. As presented in AACR-EORTC 2023. Poster A128.
- **AML**: Chow et al ,Clinical Evaluation of a Functional Combinatorial Precision Medicine Platform to Predict Patient-Specific Treatment Outcomes in Acute Myeloid Leukemia. Blood (2023) 142 (Supplement 1): 2276.
- **Sarcoma**: Data on file

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Reference:

1. Sabatelli F, Patel R, Mann PA, Mendrick CA, Norris CC, Hare R, Loebenberg D, Black TA, Mc Nicholas PM. In vitro activities of posaconazole, fluconazole, itraconazole, voriconazole, and amphotericin B against a large collection of clinically important molds and yeasts. Antimicrob Agents Chemother. 2006 Jun;50(6): 2009-2015.

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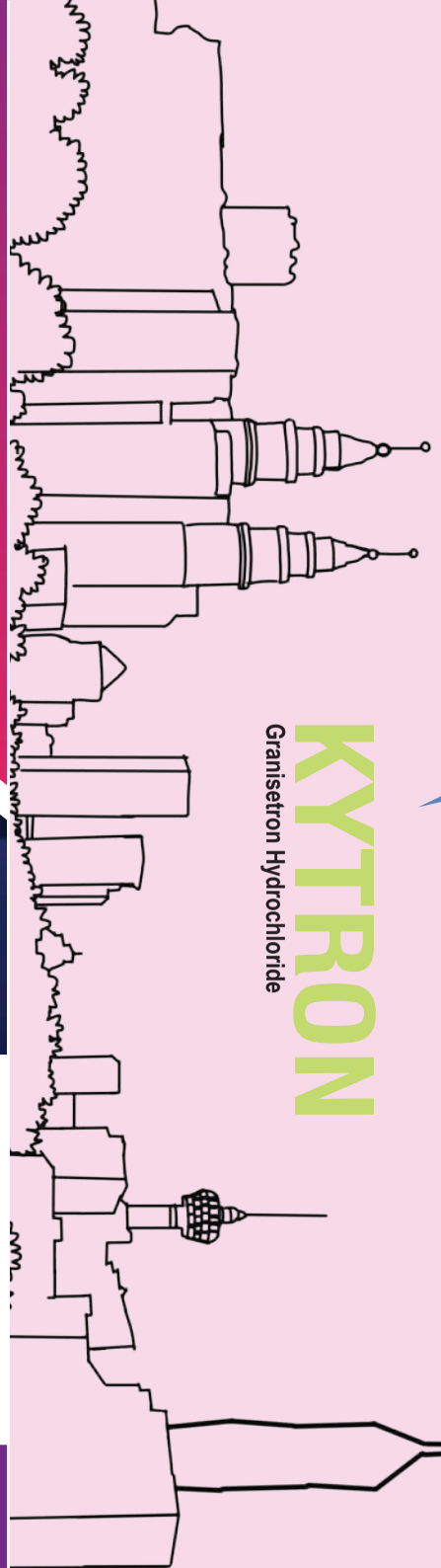

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Abstract

ORAL POSTER PRESENTATION (CLINICAL) LIST

C01	Haematopoietic Stem Cell Transplantation For Children With Transfusion Dependent Thalassaemia In Malaysia: Experience From UMMC
C02	Reducing Late Administration Of Inpatient Chemotherapy For Haematology Oncology Patients
C03	Transition Of Thalassaemia Care From Paediatric To Adult Haematology Centre: A Retrospective Study
C04	Evaluation Of Venous Thromboembolism In Adult Lymphoma Using Sarawak Lymphoma Thrombosis Score (SLOTS): A Multicenter Retrospective Study In Sarawak
C05	Impact Of Pharmacist Led Medication Therapy Adherence Clinic (MTAC) Towards The Management Of Thalassemia Patients In A Tertiary Hospital In Malaysia: A Preliminary Result
C06	Predictors Of Survival And Successful Response To Upfront Cyto-MSC Treatment In Acute GVHD: A Randomized, Double Blinded, Placebo Controlled, Multicentre Clinical Trial

ORAL (LABORATORY) LIST

L01	SLC2A3 And PFKP Are Indispensable For t(8;21) Leukaemic Maintenance
L02	Deletion Of The Secreted Protein Isthmin 1 Leads To Impaired Megakaryopoiesis And Thrombopoiesis
L03	Generation And Characterisation Of iPS Cell Lines From Donor PBMC For The Purpose Of Producing Dia+ Reagent Cells
L04	The Use Of Leucocyte Filter To Retrieve Tumour Cells From Pleural Effusion: An Experimental Study
L05	In-Vitro Evaluation Of T-Cell Acute Lymphoblastic Leukemia Cell Line Response To A Combination Of Dual Anticancer Agents; SRJ23 And Hydroxyurea
L06	α2 Codon 63 (GCC>ACC) Haemoglobin Greenville - NC: Detection Rare Case Of Alpha Variant Using Direct Sequencing Method: Cases In Local Population

ORAL POSTER PRESENTATION (CLINICAL)

CO1 HAEMATOPOIETIC STEM CELL TRANSPLANTATION FOR CHILDREN WITH TRANSFUSION- DEPENDENT THALASSAEMIA IN MALAYSIA: EXPERIENCE FROM UMMC

Main Author:
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Coauthor:
1. *Syaza Ab Rahman, Universiti Malaya medical Centre*
2. *Jen Chun Foo, Universiti Malaya medical Centre*
3. *Lee Lee Chan, Subang Jaya Medical Centre*
4. *Lin Hai Peng, Subang Jaya Medical Centre*
5. *Hany Ariffin, Universiti Malaya medical Centre*

Background: Hematopoietic stem cell transplant (HSCT) offers a chance of cure for patients with transfusion-dependent thalassemia (TDT) who would otherwise require lifelong blood transfusion and iron chelation.

Objectives: Here we report the outcome of children with TDT who underwent HSCT in Universiti Malaya Medical Centre (UMMC) between 1 July 1987 to 30 August 2023.

Materials and Methods: All children with TDT who underwent HSCT in UMMC were studied. Overall survival (OS) and thalassemia-free survival (TFS), and association with age at transplant, stem cell source and conditioning regimens were analyzed. Possible contributory factors for graft failure and graft-versus-host disease (GVHD) were identified.

Results: There were 115 subjects (53 males) with a median age of 5 years (range: 1 to 16) at time of HSCT. Median follow-up was 18 years (range: 4 months – 36 years). Donor grafts were from HLA- matched siblings (MSD) (n=97, 84%), matched unrelated donors (MUD) (n=12, 11%) and HLA- haploidentical family members (HAP) (n=6, 5%). Stem cell sources were: bone marrow (BM) (n=78, 68%), peripheral blood (PBSC) (n=8, 7%) and umbilical cord blood from either a matched sibling (MSD- UCB) (n=16, 14%), or an unrelated donor (MUD-UCB) (n=13, 11%). Disease status were: Pessaro Class 1 (n=23, 20%), Class 2 (n=57, 50%), and Class 3(n=35, 30%). Nearly all patients received busulfan-based myeloablative conditioning (MAC) with or without anti-thymocyte globulin (ATG). HAP- HSCT patients received MAC with addition of thiotepa and post-transplantation cyclophosphamide. The 35-year OS and TFS were 83.5±3.5% and 71.3±5.2% respectively. Transplant-related mortality (TRM) was 16%. Superior outcomes were seen in patients with Pesaro Class 1 (OS 91.3±5.9% ; p= 0.07 and TFS 82.6±7.4 ; p= 0.04). Those transplanted at age < 7 years had better OS (84.6±4.1%, p= 0.64) and TFS (71.8±6.7%; p= 0.17) compared to those transplanted older. In those who received Bu-Cy (n=62) conditioning, addition of ATG (n = 32) improved TFS (78.1±7.0% vs 64.5±5.1%; p =0.02) Overall graft failure rate was 26%. Graft failure was the main contributing factor for TRM. Univariate analysis for graft failure identified the omission of ATG in the conditioning regimen as a contributing factor (OR: 4.9, 95% CI 1.6-14.6; p= 0.004). The incidence of Grade II-IV GVHD was 21%. A higher risk of GVHD was found when donor grafts from MUD-UCB (OR: 19.7; 95% CI 3.0-129.8, p= 0.002) and PBSC (OR 11.9, 95%CI 1.06-34.5; p= 0.009) were used.

Discussion / Conclusion: HSCT is curative for TDT with the best outcomes observed in those undergoing HSCT when aged <7 years and using MSD grafts. Whilst gene therapy, gene and base editing are emerging as superior approaches to treat TDT, HSCT remains the best treatment option currently for children with TDT in Malaysia.

ORAL POSTER PRESENTATION (CLINICAL)

CO2 REDUCING LATE ADMINISTRATION OF INPATIENT CHEMOTHERAPY FOR HAEMATOLOGY- ONCOLOGY PATIENTS

Main Author:
Andy Tang Sing Ong, National University Hospital Singapore (NUHS)

Background: Late chemotherapy administration can impact patient safety and delay discharges. Chemotherapy preparation is a complex process involving physician prescribing, pharmacy review and compounding, portering and nursing administration. In our institution, approximately 300 inpatient chemotherapy administrations are carried out per month. Baseline data revealed that over 90% of inpatients started chemotherapy after 2pm.

Objectives: We conducted a quality improvement (QI) project with the aims of identifying the factors resulting in late chemotherapy administration, and implementing interventions to reduce chemotherapy wait time.

Materials and Methods: A multidisciplinary team comprising doctors, nursing, operations and pharmacy staff gathered to create a process flow map which was used to develop a cause-and-effect (fishbone) diagram to identify interventions to improve chemotherapy start time. Top root causes for delay were voted and the barriers were identified on a Pareto chart. Interventions were implemented stepwise from December 2022 to April 2023. Wards 8A and 8C were chosen to be the pilot wards for implementation. Interventions deemed most feasible were selected and underwent Plan-Do-Study-Act (PDSA) cycles in a stepwise approach, including (1) physicians ordering pre-planned chemotherapy at least a day prior to chemotherapy date, (2) increasing the number of pre-makeable chemotherapy drugs, (3) creation of a Nursing Chemotherapy Assessment documentation note and (4) new workflows between Pharmacy and Nursing to improve communications.

Results: After the first PDSA cycle, it emerged that the chemotherapy plan creation by physician one day before treatment, which was maintained at 92% pre- and post-implementation, was not the key factor of delayed chemotherapy. A list of pre-makeable inpatient chemotherapy drugs was created and a workflow to pre-make the drugs the day before chemotherapy was implemented. A standardized workflow for nurse-led triage was created. All doctors, nurses and pharmacists involved were briefed about this workflow and were encouraged to have efficient communication via the use of the secure messaging application (TigerConnect). Infrequent trips by porters was also identified as the cause of chemotherapy delay. A mutual agreement was made with the aims of streamlining the workflow for drug delivery to the oncology wards and minimizing batching that may result in further delay. The frequency of portering had increased to hourly trips to inpatient wards. The chemotherapy administered before 2pm had improved from 30.1% (pre-implementation) to 73.1% (post-implementation).

Discussion / Conclusion: As part of our QI plan, these initiatives will be extended to other oncology wards in our institution, bringing benefits to all parties. Given the success of our project, we hope to further refine and sustain our intervention, through the dissemination of our improvement data to all stakeholders. Results and suggestions to adopt at all inpatient oncology wards within our healthcare system will be presented to leadership for support and endorsement. In conclusion, this study allowed our institution to evaluate our current practice and reformulate the chemotherapy administration process. With additional PDSA cycle implementations, chemotherapy delays can be mitigated by adopting QI methodology involving a multidisciplinary team approach and

ORAL POSTER PRESENTATION (CLINICAL)

CO3 TRANSITION OF THALASSAEMIA CARE FROM PAEDIATRIC TO ADULT HAEMATOLOGY CENTRE: A RETROSPECTIVE STUDY

Main Author:
Chong Shu May, Hospital Seberang Jaya

Coauthor:
1. *Goh Ai Sim, Hospital Pulau Pinang*
2. *Tan Sui Keat, Hospital Pulau Pinang*

Background: Thalassemia is the most common hemoglobinopathy in Malaysia. For patients with transfusion-dependent thalassemia (TDT), the mainstay of treatment is regular blood transfusion and iron chelation therapy, as most patients do not have option for stem cell transplantation or gene therapy. With proper treatment, the survival of the patients has improved and majority of cases are entering into adulthood. Therefore optimal transition of care for TDT patients from paediatric to adult care is vital to achieve the desired outcome of the patients' health status.

Objectives: We aim to evaluate the outcome of transition of care of TDT patients from paediatric to adult haematology at Hospital Seberang Jaya.

Materials and Methods: We included a three-year cohort of referrals for transfer of care of TDT from 1st January 2020 to 31st December 2022. The data was analyzed using Microsoft Excel. The variables assessed include demographics, age of transfer of care, comparison between the pre-transfusion haemoglobin, ferritin level, hepatic and cardiac iron overload status based on MRI T2*, and any change in iron chelation therapy before and after transfer to adult care.

Results: A total of 20 patients (9 males, 11 females) were evaluated. The median age at transfer of care was 18 years old. There were 18 Malays (90 %) and 2 Indians (10 %). 55% of the TDT subtype were beta thalassaemia major, followed by HbE/beta thalassaemia (35%), HbH/CS disease (10%). Upon transfer of care, 95% of the patients had completed secondary education and 40% of them proceeded with tertiary education, and 40% had started working. None of them were married. 45% had pre-transfusion haemoglobin of less than 8.0 g/dL, 35% was within 8.0-8.9 g/dL and 20% was >9.0 g/dL. After transfer to adult care, 65% had pre-transfusion haemoglobin of less than 8.0 g/dL, 25% was 8.0-8.9 g/dL and 10% was >9.0 g/dL. Patients with severe iron overload based on serum ferritin level >5,000 ng/ml was 45% at transition compared to 40% post-transition. However, more patients had severe liver iron loading (55% vs 60%) and and myocardial iron overload (10% vs 25%) post transition. 25% of patients required change in iron chelation therapy due to suboptimal chelation target.

Discussion / Conclusion: There was worsening of pre-transfusion Hb, myocardial and liver iron overload after transition of care to adult team. Hence there was a need of change in the iron chelation therapy regimes. The frequency and volume of transfusion as well as quality of blood needs to be reviewed. Other factors contributing to this deterioration, in particular compliance need to be studied further so as to ensure that TDT patients can attain the best quality of health and achieve treatment targets

ORAL POSTER PRESENTATION (CLINICAL)

CO4 EVALUATION OF VENOUS THROMBOEMBOLISM IN ADULT LYMPHOMA USING SARAWAK LYMPHOMA THROMBOSIS SCORE (SLOTS): A MULTICENTER RETROSPECTIVE STUDY IN SARAWAK

Main Author:
Leong Tze Shin, Sarawak General Hospital

Background: Lymphoma is a haematological neoplasm associated with a higher risk of venous thromboembolism (VTE). The risk of VTE in lymphoma ranges from less than 1% to almost 20% in the first year of diagnosis, varying by lymphoma type. There is a lack of data on VTE events and outcome among lymphoma patients within Southeast Asia region. Existing risk stratify model such as Khorana and Thombosis Lymphoma (ThroLy) score might not be applicable in our setting. We developed a retrospective study to address the above issues.

Objectives: i) To determine the incidence rate and risk factors of VTE in lymphoma in adult patients in Sarawak ii) To identify an alternative risk stratify model that accurately predict VTE events in adult patients diagnosed with lymphoma in Sarawak.

Materials and Methods: Data were retrospectively collected and analyzed from all adults diagnosed with lymphoma and VTE in Sarawak General Hospital, Sibu Hospital and Miri Hospital from the year 2020 until 2023. Patients were followed at least 6 months from date of diagnosis and treatment of lymphoma and VTE. Multivariable analyses were performed to identify significant risk factors in predicting VTE events. Each variable was assigned points based on hazard ratios. The information was used to develop a 4-point scoring system called Sarawak Lymphoma Thrombosis Score (SLOTS). Patients were then categorized into low (0 to1 point), intermediate (2 points) or high-risk group (3 to 4 points) to develop VTE.

Results: 558 patients were diagnosed with lymphoma, with 57 patients (10.2%) developing VTE. Majority of them presented with thrombosis in the upper limb (n=24, 42.1%) followed by lower limb (29.8%), intraabdominal area (19.3%) and pulmonary embolism (7%). Most were detected incidentally during staging (n=40, 70.2%). VTE patients were treated with enoxaparin (n=45, 78.9%), fondaparinux (7%) and warfarin (5.2%). Median treatment duration was 3 months. Three patients (5.3%) had recurrent VTE while five patients (9.6%) had bleeding during treatment. There were no clear association between death and thrombosis (p =0.221). The independent risk factors for VTE were platelet ≥ 400k/uL (p=0.001), LDH ≥1x ULN (p=0.003) bulky mediastinal mass (p<0.001) and BMI >25 (p=0.012). When stratified according to SLOTS, the VTE event rates for low risk, intermediate risk and high-risk group were 1.29%, 4.51% and 6.23% respectively. This scoring system statistically accurate in predicting VTE events in our cohort of patients (p <0.001).

Discussion / Conclusion: In our study, the incidence rate of VTE in lymphoma was 10.2%, which is comparable to worldwide data. We have modified and adapted existing risk stratify models such as Khorana and ThroLy score into our own SLOTS model to accurately predict VTE events in our local population. Notable differences include lower cut off BMI of 25, higher cut off platelet level of 400k/uL and the use of LDH as a risk factor. A prospective VTE in lymphoma registry should be established in Malaysia. It will provide valuable information in shaping targeted thromboprophylaxis initiatives in lymphoma patients with relevant risk factors.

ORAL POSTER PRESENTATION (CLINICAL)

CO5 IMPACT OF PHARMACIST-LED MEDICATION THERAPY ADHERENCE CLINIC (MTAC) TOWARDS THE MANAGEMENT OF THALASSEMIA IN A TERTIARY HOSPITAL IN MALAYSIA: A PRELIMINARY RESULT

Main Author:
Ranita Kirubakaran, Seberang Jaya Hospital

Background: Empowering adherence to the long-term use of iron chelation therapies is imperative in preventing complications of systemic iron overload among thalassemia patients. A pharmacist-led medication therapy adherence clinic (MTAC) was implemented to deliver pharmaceutical care to thalassemia patients. Patients with serum ferritin concentrations > 2500 µg/L and/or abnormal magnetic resonance imaging T2-star (MRI T2*) measurements of cardiac and hepatic iron were recruited in the MTAC program.

Objectives: To evaluate the impact of pharmacist-led MTAC towards the management of thalassemia patients in terms of (i) knowledge of thalassemia and iron chelation therapies, (ii) serum ferritin concentrations, and (iii) MRI T2* measurements of cardiac and hepatic iron.

Materials and Methods: Data from all thalassemia patients recruited in the MTAC program were collected (n=36; adult, n=34; paediatrics) up to 22 March 2024. Knowledge assessment on thalassemia and iron chelation therapies was performed at baseline and fourth MTAC visit (3 — 9 months from MTAC recruitment). Instead, the caregiver's knowledge was assessed for patients ≤ 10 years old. The questionnaire for assessment was adopted from thalassemia MTAC protocol published by Pharmaceutical Services Programme Ministry of Health Malaysia. One MRI T2* measurement (cardiac and hepatic iron) and the mean of three serum ferritin concentrations were compared before and after MTAC recruitment. Data was analysed using IBM SPSS Statistics v28.0.

Results: The majority of patients were Malay (88%) and female (60%). The median age was 19 (range: 3 — 55) years. Most thalassemia patients (96%) were transfusion dependent. Patients were treated with either mono or dual iron chelation therapies: deferoxamine (56%), deferiprone (51%) and deferasirox (30%). The mean serum ferritin concentrations reduced by 10% ($p = 0.04$, $n = 60$); ranging from 1429 — 16269 µg/L at baseline to 829 — 13615 µg/L after 9 months of MTAC follow-up. Patient's (or caregiver's) knowledge of thalassemia and iron chelation therapies improved by 15% ($p < 0.001$, n=58) at the fourth MTAC visit. No changes in MRI T2* measurements for cardiac and hepatic iron were observed ($p > 0.05$, $n = 45$) following MTAC program.

Discussion / Conclusion: Effective involvement of pharmacists as integral members of the healthcare team in thalassemia management can positively impact patient outcomes. Longer follow-up may be required to explore changes in MRI T2* measurements of cardiac and hepatic iron.

ORAL POSTER PRESENTATION (CLINICAL)

CO6 PREDICTORS OF SURVIVAL AND SUCCESSFUL RESPONSE TO UPFRONT CYTO-MSC TREATMENT IN ACUTE GVHD: A RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED, MULTICENTRE CLINICAL TRIAL

Main Author:
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2. *S. Fadilah S. Abdul Wahid, Universiti Kebangsaan Malaysia, Cheras, Selangor, Malaysia*
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9. *Cheong Soon Keng, M. Kandiah Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman- Kampus Sungai Long, Kajang, Selangor, Malaysia*

Background: In spite of advancements in the acute graft-versus-host disease (aGVHD) management, the prognosis remains unfavorable, highlighting an ongoing unmet need for satisfactory treatment. Previously, we outlined preliminary results of administering allogenic Cytopeutics® umbilical cord-derived mesenchymal stem cells (Cyto-MSC) infusion alongside corticosteroids in aGVHD patients. Cyto-MSC demonstrated a quicker and sustained complete response, and a superior 3-month survival rate when compared to the placebo group.

Objectives: Here, we provide an in-depth analysis with a prolonged follow-up and subgroup assessment based on immune cell subsets findings.

Materials and Methods: In this phase I/II trial, patients with grade II-IV aGVHD were randomized to receive up to three upfront infusions of Cyto-MSC (5x 10^6 cells/kg bw) or placebo (ClinicalTrials.gov: NCT03847844). The measurements were taken at 14 and 28 days for the overall response (OR), and 3 and 12 months for the overall survival (OS). Based on the initial levels of circulating CD4+ terminally differentiated effector memory T (TEMRA) and CD8+TEMRA in the patients, subgroup analyses were conducted.

Results: A total of 22 patients participated in the study, with 14 receiving Cyto-MSC and 8 receiving placebo. No adverse events related to the treatment were reported. Those who received Cyto-MSC exhibited improved OR rates at Day 14 (78.6% vs 75%) and Day 28 (87.5% vs 62.5%), as well as higher OS rates at 3 months (85.1% vs 62.5%) and 12 months (56.7% vs 37.5%) compared to the placebo group. Subgroup analysis based on baseline CD4+TEMRA >35% or CD8+TEMRA >70% demonstrated elevated OS at 3 months (100% vs 80%; 100% vs 80%) and 12 months (83.3% vs 60%; 71.4% vs 60%) for Cyto-MSC recipients versus the placebo. Correlation analysis revealed that OS at 12 months was positively related to OR at Day 28 ($r=0.67, p<0.001$), baseline CD4+TEMRA ($r=0.54$, $p=0.009$), and CD8+TEMRA ($r=0.45$, $p=0.036$). In the severe grade III-IV group, individuals with >35% baseline CD4+TEMRA and received Cyto-MSC had a higher likelihood of surviving up to 12 months compared to those in the placebo group (83% vs 50%). Conversely, those with <35% CD4+TEMRA in the placebo group had 0% survival regardless of aGVHD grade ($p=0.01$). Notably, all patients with grade III-IV aGVHD who had baseline CD8+TEMRA >70% and received Cyto-MSC were alive at 12 months, while none of the patients with CD8+TEMRA <70% in the placebo group survived ($p=0.01$).

Discussion / Conclusion: OR at day 28 predicts survival at 3 months and 12 months. Our findings demonstrate that the administration of upfront Cyto-MSC led to enhanced OR at day 28 and increased survival rates at both 3- and 12-month in aGVHD patients, specifically those in grade III-IV with baseline CD4+TEMRA exceeding 35% or CD8+TEMRA surpassing 70%, as opposed to the placebo group. CD4+TEMRA or CD8+TEMRA are potential predictive markers that could be used to identify subsets of patients who experience significant benefits from upfront application of Cyto-MSC, promising precision of patient selection and a cost-effective strategy.

ORAL (LABORATORY)

LO1 SLC2A3 AND PFKP ARE INDISPENSABLE FOR t(8;21) LEUKAEMIC MAINTENANCE

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Background: Translocation (8;21) is the most common chromosomal rearrangement in acute myeloid leukaemia (AML). This translocation produces oncogenic fusion protein, RUNX1::ETO that is required for maintaining leukaemic phenotype. It acts as a master regulator and cooperates with partner genes to drive leukaemic transformation. Recent findings highlight the reliance of cancer cells on aerobic glycolysis to promote their proliferation and survival, with increased glycolysis correlated with elevated expression of glycolytic genes.

Objectives: In this study, two key genes in glycolysis, SLC2A3, a glucose transporter and PFKP, a glycolysis rate-limiting enzyme, have been identified as potential transcriptional targets for RUNX1::ETO maintenance and survival.

Materials and Methods: A cross-sectional analysis on RNAseq and Chipseq data of RUNX1::ETO knockdown samples was done to determine a list of potential RUNX1::ETO partner genes. Following this, a subsequent shRNA screen encompassing both in vitro and in vivo arms was carried out on these targets to identify the genes crucial for leukaemia maintenance and survival. Subsequently, gene knockdown experiments were executed on the identified targets to evaluate leukemic fitness under glucose- and oxygen-deprived conditions, employing a competitive experimental setup in both RUNX1::ETO-expressing cell lines and patient-derived xenograft (PDX) cells.

Results: This study has identified SLC2A3 and PFKP as potential partner genes for RUNX1::ETO leukaemic maintenance and survival. Competitive experiments showed SLC2A3 significantly maintained the survival of leukaemic cells under limited glucose and oxygen conditions in the Kasumi-1 cells. Notably, SLC2A3 knockdown impaired the competitive fitness of PDX cells in high glucose and oxygen culture condition. Moreover, PFKP knockdown results in loss of populations in vitro, whereas double knockdown of SLC2A3 and PFKP caused G1 cell cycle arrest and had a greater effect in impairing leukaemic cell propagation and fitness when compared to the single knockdowns.

Discussion / Conclusion: Cancer cells require a rapid energy turnover to support their proliferation and growth. Unlike normal cells, cancer cells rewire their metabolic program towards glycolysis even in the presence of oxygen, and often associated with elevated expressions of glycolysis-related genes such as glucose transporters and glycolytic enzymes. Notably, both SLC2A3 and PFKP exhibit elevated expression levels and are associated with poor prognosis in various cancers. In this study, we found SLC2A3 and PFKP as potential partner genes required by RUNX1::ETO to drive leukaemic maintenance and survival. Targeting these two genes may provide novel treatment strategies with potentially reduced toxicity in t(8;21) leukemia.

ORAL (LABORATORY)

LO2 DELETION OF THE SECRETED PROTEIN ISTHMIN-1 LEADS TO IMPAIRED MEGAKARYOPOIESIS AND THROMBOPOIESIS

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Background: Thrombopoiesis denotes the formation of platelets required for blood clotting in response to vascular injury and multiple physiological processes. These platelets originate from megakaryocytes which arise from Megakaryocyte erythroid progenitors (MEPs) and common myeloid progenitors (CMPs) from Hematopoietic stem cells (HSCs) in the bone marrow. Thus, impaired platelet production is likely due to the differentiation defects of progenitors including MEPs and CMPs as well as abnormal differentiation and maturation of megakaryocytes. Noteworthy, impaired interaction of megakaryocytes with secreted and extracellular matrix proteins in bone marrow niche is one of the major mechanisms behind this. Isthmin-1 (ISM1) is a secreted protein present in the sinusoid niche of bone marrow. Even though ISM1 has multifaceted functions, including organ morphogenesis, glucose metabolism, angiogenesis, and immunity, but we are still short of understanding the role of ISM1 in murine hematopoiesis.

Objectives: Initially, we observed that targeted deletion of the gene encoding secreted protein ISM1 caused defective megakaryopoiesis and thus we aimed to test the further role of ISM1 in platelets production as well as mechanistic reasons behind this.

Materials and Methods: Circulating blood was analyzed by complete blood count (CBC) test while a histology study was conducted for both the bone marrow and spleen tissues as well as immunofluorescence staining in Ism1(-/-) mice and control mice. Furthermore, flow cytometry analysis was conducted for multiple bone marrow progenitors and lineage cells along with splenocytes. Moreover, single-cell transcriptomic analysis of total bone marrow cells and mass spectrometry analysis of bone marrow niche were conducted in Ism1(-/-) mice and control mice. Additionally, Micro-computed tomography was conducted to assess the femur bone phenotype in Ism1(-/-) mice and control mice.

Results: We initially observed increased MEPs (Lin- c-Kit+ Sca-1- CD16/32- CD34+) and CMPs (Lin- c-Kit+ Sca-1- CD16/32- CD34-) in bone marrow of Ism1(-/-) mice as compared to control mice. Following that, increased megakaryocytes were reported in the bone marrow and spleen according to the flow cytometry analysis in Ism1(-/-) mice as compared to control mice. This phenotype was also further supported by the presence of increased megakaryocytes through H&E staining of both bone marrow and spleen in Ism1(-/-) mice as compared to control mice. More interestingly, intracellular expression of ISM1 was observed in megakaryocytes through immunofluorescence imaging of bone marrow. In contrast, a reduction in platelets was also observed in bone marrow and in line with that, reduced circulating platelets in the CBC test of Ism1(-/-) mice as compared to control mice. Additionally, the CBC test also demonstrated increased circulating red blood cells in Ism1(-/-) mice as compared to control mice. Moreover, our single-cell transcriptomic analysis also further demonstrated increased erythroblasts in Ism1(-/-) mice as compared to control mice. At present, We are working on our single- cell transcriptomic data analysis, and proteomic analysis simultaneously for molecular insights.

Discussion / Conclusion: To conclude at this point, it could be seen that deletion of secreted protein ISM1 leads to impaired megakaryopoiesis followed by reduced platelets along with increased erythropoiesis while these findings further warrant molecular mechanism behind this.

ORAL (LABORATORY)

LO3 GENERATION AND CHARACTERISATION OF iPS CELL LINES FROM DONOR PBMC FOR THE PURPOSE OF PRODUCING DIA+ REAGENT CELLS

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Background: As red blood cells (RBC) express various antigens on their surfaces, incompatible blood transfusion or feto-maternal transfer of RBCs, may result in immunisation against the antigens leading to haemolytic transfusion reactions and hemolytic disease of foetus and newborn. Antibody screening (ABS) is performed to identify antibodies towards these antigens as part of pretransfusion testing and antenatal screening, to prevent these complications. ABS involves the use of reagent red cells with specific red cell antigen combinations that are procured from donors. This panel of reagent cells are designed so that it can detect most clinically significant antibodies in the tested population. The pattern of red cell antibody prevalence in Asia differs from Western populations. In South-east and East Asia, anti-Mia and anti-Dia are common antibodies which are rarely found among Western populations. Although the Mia and Dia antigens are found in 2 – 5 % of the East Asian population, suitable donors with the correct combination of antigens are difficult to recruit and retain, thus limiting the available pool of donors and severely limiting sustainability. Therefore, the use of induced pluripotent stem cells (iPSC) to generate RBCs is proposed as an alternative to establish a consistent source of RBC in view of its pluripotency and limitless expansion characteristics.

Objectives: To generate and characterize iPS cell lines from donor erythroid progenitor cells and further differentiation to produce Dia+ reagent cells.

Materials and Methods: Blood was collected from a blood donor expressing Dia and the peripheral blood mononuclear cells (PBMC) were isolated using density gradient centrifugation. The isolated cells were expanded in culture with erythroid expansion medium and reprogramming was performed using Epi5 Episomal Reprogramming Kit to generate iPSCs. Characterization for pluripotency included immunofluorescence staining on pluripotency markers (Oct4, Sox2, Nanog and Tra1-81). Quantitative RT-PCR (qRT-PCR) was performed on the iPSC colonies to detect pluripotency markers. Embryoid body (EB) formation was conducted to assess the trilineage differentiation potential. The H9 human embryonic stem cell line was used as positive control for the assays. The persistence of episome was determined using PCR targeting the episomal markers used for reprogramming (oriP, EBNA-1). PCR was also performed for genotyping of the Diego blood group alleles, DI1 and DI2, which encode for the Dia and Dib antigens respectively, using allele specific primers.

Results: iPSC colonies were observed on day 20 post-transfection. The colonies were positive for all the pluripotency markers studied on immunofluorescence staining. The generated iPSCs showed expression of the selected pluripotent genes on qRT-PCR, with 0.30-fold for Oct4; 0.12-fold for Sox2; 0.16-fold for Nanog, as compared to the embryonic stem cell line, H9. EBs were successfully formed on differentiation day 1. The colonies were also confirmed to not express the episomal markers at passage-5. Genotyping by PCR confirmed the presence of DI1 and DI2 alleles in the iPSC colonies.

Discussion / Conclusion: We have successfully generated an iPS cell line from erythroid precursors derived from PBMC of a Dia antigen-expressing blood donor. This iPSC line holds promise as a reliable and consistent source of Dia+ reagent cells, with applications in ABS panels.

ORAL (LABORATORY)

LO4 THE USE OF LEUCOCYTE FILTER TO RETRIEVE TUMOUR CELLS FROM PLEURAL EFFUSION: AN EXPERIMENTAL STUDY

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Background: Leucodepletion through specific filters to remove leukocytes from packed red blood cell has been applied as a preventive measures to reduce transfusion complications. In Malaysia, the requirements of filtered red cells include residual leucocyte content of < 1x106 per unit. A 2017 study has shown that CD4+ T cells, CD8+ T cells, and CD14+monocytes were able to be purified from reverse filtration of leucocyte filters after packed red cell filtration. These cells were shown to be viable, and able to proliferate in cell culture. The retrieval of tumour cells from leucocyte filter however, has not been studied.

Objectives: This is an experimental study looking at the possibility of retrieving tumour cells from leucocyte filter.

Materials and Methods: This is an experimental study looking at the possibility of retrieving tumour cells from the leucocyte filter. At the time of study, only one subject was recruited, to gauge the feasibility of the experiment. Written consent was sought from a patient with lung cancer who was previously treated with targeted therapy, who undergone therapeutic pleurocentesis. The aspirated fluid was subjected to filtration by connecting the bag to a standard leucocyte filter. The filtrated fluid were discarded. Using a 50ml syringe, variable volume of Hanks Buffered Saline Solution were injected counter current to the leucocyte filter. The expressed fluid was collected into several 50ml Falcon tube. This process was repeated multiple times. The collected fluid was centrifuged at 3500 rpm for 5 minutes. The supernatant was discarded and the cell pellet was made into cell blocks by adding 5 drops of plasma and thrombin (in 1:1) into the pellets until clots are formed. The clot was then transferred to Bijour bottle and 10% neutral buffered formalin solution added to fix the cell block. The cell block is then placed in a labelled cassette and processed as a routine histology sample into paraffin embedded blocks. The block is then sectioned and the glass slide is stained with haematoxyline and eosin for cellularity and morphological evaluation. The slides were reported by a histopathologist who was blinded from the results of the patient's diagnosis.

Results: The slides from the cell block revealed occasional (1-2 malignant cells/ high power field). The sample with the most yield is the first flush. Subsequent flushes showed no malignant cells, only red cells were seen. Due to the small numbers of malignant cells retrieved, any significant morphological analysis was hampered.

Discussion / Conclusion: Our experimental study showed that it is possible to extract filtered tumour cells from leucocyte filter. Several limitations to our study which include poor yield which may be due to the patient already received targeted therapy. In treatment naïve patients, the yield is expected to be more as targeted therapy works well in patient with lung cancer with pleural effusion. Another limitation is poor quality of extracted cells, and contamination with red blood cells. These limitations may be overcome by careful patient selection, improvement of flushing techniques and changing the type of filter used. In conclusion, the retrieval of tumour cells from leucocyte filters after filtration of body fluid is possible, to aid in diagnosis.

ORAL (LABORATORY)

LO5 IN-VITRO EVALUATION OF T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA CELL LINE RESPONSE TO A COMBINATION OF DUAL ANTICANCER AGENTS ; SRJ23 AND HYDROXYUREA

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Background: T-cell acute lymphoblastic leukemia (T-ALL) is a hostile haematologic neoplasm caused by a malignant transformation of immature progenitors of T-cells. Due to the variable response to conventional chemotherapy regimens available to-date, a holistic chemotherapy combination drugs with greater precision to obtain the desired results are worth studying. We aim to evaluate the inhibitory effect of a hydroxycarbamide compound with SRJ23 in combination on Jurkat cell line to determine the efficacy in vitro.

Objectives: General Objectives: To determine the potential of SRJ23 drug and Hydroxyurea drug individually and in combination against T-cell lymphoblastic leukemia cell line. Specific Objectives: I. To determine whether SRJ23 and HU compounds are cytotoxic to JURKAT cell line. II. To determine the extent of effectiveness and the synergistic effects of the new combination of SRJ23 inhibitors along with HU chemotherapy drug against JURKAT cell line. III. To assess the potentiality of the combination compound in inducing apoptosis.

Materials and Methods: T-cell acute lymphoblastic leukemia (Jurkat cells) were seeded and treated with different concentrations (0.1, 1, 10, 100 µM) of SRJ23 and (7.8, 15.6, 31.25, 62.5, 125, 250, 500, and 1000 µM) of HU. After 96 hr incubation, MTT assay was used to assess the in vitro growth inhibition of the combination drug (HU and SRJ23) against Jurkat cells. In addition, apoptosis assay was conducted by using (FITC)/propidium iodide (PI) and flow cytometry were done to confirm apoptosis induced by the combination drug.

Results: According to the dose-response curve a reduction in cell viability associated with a favourable or potent synergistic effect was revealed at doses of 10 µM SRJ23 combined with 125 µM HU (combination index 0.53) or 250 µM HU (combination index 0.40). The ability of these two synergistic combinations to reduce cell viability of Jurkat cell line was superior to that of the other compound doses tested. This was determined by comparing the combination index of each of the combinations of 10 µM SRJ23 with 125 µM HU or 250 µM HU to that of the other combinations of concentrations the Jurkat cells are treated with. The apoptosis assay shows the combination of 10 µM SRJ23 with 125 µM HU or 250 µM HU showed 71.5% vs 71.5% early apoptosis, 6.6% vs 6% late apoptosis, and 1.2% vs 1.3% necrosis, respectively. When compared to single agent SRJ23 10 µM alone showed 60.4% early apoptosis, 9.6% late apoptosis, and 2.5% necrosis. Hydroxyurea alone 250 µM showed 7.4% early apoptosis, 8.9% late apoptosis, and 3.6% necrosis.

Discussion / Conclusion: The combination between HU and SRJ23 revealed a synergistic effect against T-ALL Jurkat cells, have a significant inhibitory effect in vitro, in addition to inducing apoptosis. Therefore, this exhibit an in-vitro potential novel chemotherapy for T-ALL. In order to learn the full, precise, and detailed impact of this novel synergistic combination and to evaluate how well it works as a potential novel targeted therapy, this study suggests conducting further in vitro testing such as cell cycle analysis, western blotting, transgene technique, gene knockdown testing, furthermore in vivo testing.

ORAL (LABORATORY)

LO6 α2 CODON 63 (GCC>ACC) HAEMOGLOBIN GREENVILLE - NC: DETECTION RARE CASE OF ALPHA VARIANT USING DIRECT SEQUENCING METHOD: CASES IN LOCAL POPULATION

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Background: Haemoglobin (Hb) Greenville- NC is a rare alpha variant involved alpha-2 gene. This variant i s the result o f the point mutation at alpha 2 codon 63, Alanine to Threonine (GCC>ACC). However, previous literature was reported on HBA1 gene based on ITHANET and HbVar. For the past eight years we reported only six cases of this variant. It required molecular testing to characterize based on indices of the Full Blood Count (FBC) of the patient.

Objectives: This study aims to describe the haematological parameters, phenotype and genotype characterisation of Hb Greenville - NC in our local population along with proposed classification of the variant based on American Collage of Molecular Genetics and Genom ics (ACMG) guideline.Analysis involved six confirmed cases o f Hb Greenville- NC retrieved from our databases for the past eight years.

Materials and Methods: Cases referred to Institute for Medical Research (IMR) from 2016 to 2023. The clinical information and haematological parameters provided by the hospitals were evaluated. The cases were subjected to direct sequencing of HBA gene for variant detection.

Results: All recorded cases involved Malay patients which come from Kedah (n=3, 50.00 %), Pahang (n=2, 33.33%) and Terengganu (n=1, 16.67%). There was (n=1, 16.67%) male and (n=5, 83.33%) females. The median age of the cases was 16.5 years old with age ranges between 3 to 31 years old. Most of individuals were asymptomatic during the screening, except for one antenatal case presented with mild anaemia in pregnancy. All of them had haematological features of thalassemia trait with the mean for Hb, MCV and MCH were 12.63 g/dl, 77.58 fL and 24.70 pg respectively. While Haemoglobin Analysis using Capillary Electrophoresis (CE) revealed no abnormal variant or peak accept for the pregnant lady which has slightly low Hb A 2 level (1.9%). Three genotypes were identified; Heterozygous Hb Greenville-NC (n= 4 , 66.67%), heterozygous Hb Greenville-NC with variant of uncertain significant (n=1, 16.67%), and compound heterozygous state of Hb Greenville-NC with uncharacterized two gene deletion (n=1, 16.67%).

Discussion / Conclusion: Hb Greenville-NC is a rare alpha-2 variant previously reported in African-American pregnant lady who presented with mild anaemia but was found associated with other pathogenic haemoglobin variant/ thalassemia. From our database, one antenatal case presented with mild hypochromic microcytic anaemia and slightly low in Hb A 2 levels might be contributed with concomitant iron deficiency in pregnancy. In heterozygosity, it is a phenotypically silent haemoglobin variant. Nevertheless, compound heterozygous of this mutation or underlying other medical illness may cause significant disease. Based on our data, we propose to classify this variant as a benign or likely benign variant (B/LB). Further support the classification is based on the case of compound heterozygous state of Hb Greenville-NC with uncharacterized two gene deletion which the haematological parameters of this case shows in keeping with alpha thalassemia trait. The implication for this variant classification is important for precise genetic counselling and prenatal diagnosis.

RESEARCH (CLINICAL) LIST

NO.	TITLE
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C2	A Three Year Follow Up: Real World Study Of Ending Tyrosine Kinase Inhibitor In Chronic Myeloid Leukaemia (Entic) In Malaysia
C3	Prevalence And Molecular Spectrum Of G6 Pd Deficiency In Malaysian Proto Malay Orang Asli: A Comprehensive Analysis
C4	Real World Experience Of Venetoclax And Hypomethylating Agents In Elderly Or Unfit Patients With Acute Myeloid Leukaemia: A Single Centre Experience
C5	A Pilot Study Of Sarawak All Protocol (Swkall): A Modified Paediatric Inspired Regime Suitable In Resource Constraint Setting
C6	Epidemiology And Risk Factors Of Cancer Associated Thrombosis Among Asian Population A Single Centre Experience
C7	Prevalence And Risk Of Invasive Fungal Infection Among Patients With Hematological Malignancies Undergoing Intensive Chemotherapy And Hemapoietic Stem Cell Transplantation
C8	Ponatinib Efficacy And Safety: Experience In Patients With Chronic Myeloid Leukaemia, Hospital Pulau Pinang
C9	Exploring Clinical Heterogeneicty And Outcome In Primary Extranodal Lymphoma: A 2 Year Retrospective Study
C10	Real World Single Centre Study On Daratumumab Outcomes In Relapsed/Refractory Multiple Myeloma
C11	Clinical Characteristic And Survival Outcome Of Patients With Classical Hodgkin Lymphoma At A Tertiary Hospital In Malaysia. A Retrospective Study
C12	Clinical Characteristics And Treatment Pattern Of Venous Thromboembolism In Malaysian Patients With Active Cancer A Single Centre Experience
C13	Demographics And Clinical Outcomes Of Patients Eligible For Ferric Carboxymaltose: A Single Centre Retrospective Study
C14	Treatment Outcomes Of Aggressive B Cell Lymphoma: A Single Centre Review At Sarawak General Hospital, Kuching
C15	Ovarian Reserve Assessment Using Anti Mullerian Hormone In Women With Newly Diagnosed Lymphoma
C16	Primary Gastrointestinal Lymphoma: A Two Centers Experiences In The Northwestern Region Of Sarawak, Malaysia
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C18	Outcome Of Primary Mediastinal B Cell Lymphoma Treated With Immunochemotherapy With Or Without Consolidative Radiotherapy A Single Centre Experience
C19	Retrospective Analysis On Efficacy Of Addition Eltrombopag With Immunosuppressive Therapy For Acquired Aplastic Anaemia Single Centre Experience
C20	Genomic Landscape In Newly Diagnosed Adult Acute Myeloid Leukemia: Review From A Single Local Institution

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RESEARCH (CLINICAL) LIST

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C21	Evaluation Of Ruxolitinib For Steroid Resistant Gvhd After Hematopoeitic Stem Cell Transplantation Single Center Experience
C22	Temporal Dynamics Of Flt3 Itd/Tkd And Npm1 Mutations In Aml: A Three Year Study By Oncode Laboratory
C23	Eltrombopag In Chronic Immune Thrombocytopenia: A Single Centre Experience
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C27	Thrombosis In Multiple Myeloma: A Real World Experience Over 15 Years In Sarawak
C28	A Multicenter Real-World Study Of Outcomes In Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma Treated with A Polatuzumab Vedotin-Based Regimen In A Compassionate Use Program In Malaysia

E-POSTER RESEARCH (CLINICAL)

C1 THE EFFECTS OF INTRAVENOUS IRON THERAPY IN HEART FAILURE PATIENTS WITH IRON DEFICIENCY IN HOSPITAL UNIVERSITY SAINS MALAYSIA

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Background: Anaemia and iron deficiency are factors associated with increased disease severity in HFrEF, leading to worse outcomes. European guidelines recommended IV ferric Carboxymaltose to improve symptoms and quality of life in symptomatic heart failure patients with iron deficiency. This study aims to investigate the effects of intravenous iron sucrose on functional capacity of chronic heart failure patients with iron deficiency.

Objectives: To determine the effects of IV Iron sucrose on functional status of heart failure patients with iron deficiency attending Heart failure clinic HUSM based on various assessment on functional capability.

Materials and Methods: A total of twenty-six (26) stable ambulatory heart failure patients with LVEF less than 50% were recruited. Inclusion criteria consisted of patients with iron deficiency aged above 18 years old, left ventricular ejection fraction (LVEF) ≤ 50%, and stable ambulatory heart failure patients with New York Heart Association (NYHA) class II or III. Exclusion criteria included patients with clinical evidence of active infection, diagnosed or receiving treatment for malignancy, haemoglobin ≥15 g/dL and those allergic to iron products. Additionally, patients with spine problems, osteoarthritis, or arthritis were excluded from the Short Physical Performance Battery (SPPB) test.

Results: Repeated measures analysis of variance (ANOVA) revealed significant difference in mean Kansas City Cardiomyopathy Questionnaire (KCCQ) scores from baseline to week 4 (-12.61), week 8 (- 18.66), and week 12 (-20.22) with a P value < 0.001 for all comparisons. Patient Global Assessment (PGA) scores also showed statistically significant improvement from baseline to week 4 (0.52, P<0.001), week 8 (0.60, P<0.001) and week 12 (0.68, P<0.001). Additionally, NYHA scores were significantly enhanced at Week 4 (0.52, P<0.001), Week 8 (0.60, P<0.001), and Week 12 (0.68, P<0.001) from baseline. However, the Short Physical Performance Battery (SPPB) scores exhibited a significant difference only between Week 0 and Week 8, with a mean difference of (-1.75, P=0.008).

Discussion / Conclusion: This study demonstrates that intravenous iron sucrose improved symptoms, exercise capacity and quality of life in heart failure patients with iron deficiency. Future trial with larger sample size and longer duration are warranted to further

E-POSTER RESEARCH (CLINICAL)

C2 A THREE-YEAR FOLLOW UP : REAL-WORLD STUDY OF ENDING TYROSINE KINASE INHIBITOR IN CHRONIC MYELOID LEUKAEMIA (ENTIC) IN MALAYSIA

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Background: The practice of indefinite tyrosine kinase inhibitor (TKI) provision for Chronic Myeloid Leukaemia (CML) has remained unchallenged. Furthermore, the ability of TKIs to eradicate the CML clone is still largely unknown. A multicentred observational study involving major hospitals in Malaysia to observe the clinical practise to End TKI in CML (EnTIC) was performed.

Objectives: The goal of this study is to determine the molecular response to TKI cessation in CML patients by close monitoring of BCR-ABL1.

Materials and Methods: A multi-centre observational study in Adult CML patients in chronic phase patients who received first line TKI (Imatinib, Nilotinib or Dasatinib) for at least four years and achieved sustained MR4 (IS: 0.01%) for at least 2 years were recruited. Close clinical review, and monthly BCR- ABL1 quantification analysis of molecular monitoring were done. To date, the study has observed 132 patients from January 1st , 2021 to December 31st, 2023.

Results: This interim analysis reported the outcome of 132 patients with a follow-up period of 36 months. Fifty-seven patients (43.2%) experienced a molecular relapse defined as the loss of a major molecular response (MMR). Seventy-five (56.8%) patients have since been in molecular remission with the longest remission duration achieved is 36 months. During the treatment-free phase, no progression towards advanced phases of CML occurred, and all relapsed patients regained MMR after restarting therapy.

Discussion / Conclusion: In conclusion, the preliminary findings of this EnTIC study demonstrate that a clinically significant percentage of 66.7% with sustained Deep Molecular Response at 6 months and 61.2% in 12 months. We observed the likelihood of loss of MMR during TFR trial is most often within the first 6 months of stopping TKI. However, a longer duration of follow-up and analyses of TFR data in EnTIC study and also compared other TFR studies will be needed to further evaluate the patients, and clinically significant characteristics before stopping treatment.

E-POSTER RESEARCH (CLINICAL)

C3 PREVALENCE AND MOLECULAR SPECTRUM OF G6PD DEFICIENCY IN MALAYSIAN PROTO- MALAY ORANG ASLI: A COMPREHENSIVE ANALYSIS

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Background: G6PD deficiency (G6PDd) is an X-linked hereditary condition resulting in decreased enzyme activity. The prevalence of G6PDd in Malaysia is 3.4%, and the Orang Asli demonstrated the highest prevalence of G6PDd compared to other ethnicities. G6PD-deficient individuals are usually asymptomatic until they are exposed to oxidative substances such as anti-malarial medications, that can cause acute hemolytic anemia and other related complications. G6PDd screening is critical for high- risk populations, particularly in malaria-endemic areas including the Orang Asli. Currently, the widely used G6PDd screening approach is the fluorescent spot test (FST). However, FST failed to detect numerous intermediate deficient cases where most were female heterozygotes, and FST requires laboratory equipment.

Objectives: To determine the prevalence and mutational spectrum of G6PDd in the Malaysian Proto Malay Orang Asli and evaluate a new screening method using a point-of-care test (POCT), the CareStart G6PD S1 Biosensor (S1).
Materials and Methods: A total of 258 subjects (91 males and 167 females) were screened for G6PDd using the S1 and a spectrophotometric OSMMR2000-D assay. Full blood count (FBC) analyses were performed on all blood samples. DNA extractions and mutational spectrum analyses using a reverse dot-blot flow-through hybridization assay (the Hybribio GenoArray Diagnostic kit) and Next- Generation Sequencing were performed on a subset of the blood samples.

Results: The prevalence of G6PDd among the Malaysian Proto Malay Orang Asli was 15.6%. The adjusted male median (AMM) was 9.6 U/gHb (95% CI, 8.9 – 10.3) and the spectrophotometric cut-off values were 2.9 U/gHb (30% AMM) and 7.7 U/gHb (80% AMM). Five G6PD mutations were found; G6PD Viangchan (871G>A)(36.3%), G6PD Coimbra (592C>T)(31.8%), G6PD Union (454A>C)(25.1%), G6PD Kaiping (1388G>A) (4.5%), and rs782038151 (2.3%). The S1 showed 39 – 49% sensitivity, 95 – 97% specificity, 53 – 59% positive predictive values, and 87 – 91% negative predictive values. The hemoglobin measurement between the S1 and FBC showed a good correlation (R2 = 0.63).

Discussion / Conclusion: G6PDd is highly prevalent among Proto Malay Orang Asli with significant molecular heterogeneity. Targeted population screening using a POCT method is a reliable and promising approach, with the S1 demonstrating a moderate to high clinical performance.

E-POSTER RESEARCH (CLINICAL)

C4 REAL-WORLD EXPERIENCE OF VENETOCLAX AND HYPOMETHYLATING AGENTS IN ELDERLY OR UNFIT PATIENTS WITH ACUTE MYELOID LEUKAEMIA: A SINGLE CENTRE EXPERIENCE

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Background: The combination of hypomethylating agent and venetoclax (HMA/venetoclax) has emerged as a treatment option for patients with acute myeloid leukemia (AML) who are unfit to receive intensive chemotherapy. In the phase 3 VIALE-A trial, patients who received azacitidine and venetoclax had significantly longer median overall survival and a higher rate of complete remission compared to patients receiving azacitidine alone.

Objectives: We aim to explore treatment outcomes of AML patients who are not candidates for intensive chemotherapy given HMA/venetoclax treatment in daily clinical practice in our centre.

Materials and Methods: We conducted a retrospective descriptive analysis of AML patients treated with the combination of HMA with venetoclax at Hospital Pulau Pinang from 1st January 2022 until 31st December 2023. Patients received at least one cycle of treatment: 7-28 days of oral venetoclax daily in combination with HMA (either IV decitabine for 5 days or SC azacitidine for 7 days). Cytogenetic risk was assessed according to 2022 European Leukaemia Net (ELN) recommendations for genetic risk stratification. Demographic, clinical data and outcomes were obtained. Key parameters captured and analysed were: age, ECOG performance status, ELN 2022 risk, number of cycles of HMA/venetoclax administered, response rates and overall survival.

Results: A total of 21 patients (11 male and 10 female) were included in this study with median age of 69 years (range 26-78), the majority (71.4%) were older than 65 years. Fourteen (66.7%) of them were diagnosed with de novo AML and 62% presented with bone marrow blast count >50%. Based on ELN 2022 criteria, seven (33.3%) patients were classified as adverse risk. Two thirds (66.7%) of the patients received decitabine with median of 4 cycles (range 1-15) of HMA/venetoclax. Our patients were on anti-fungal prophylaxis with suspension itraconazole and dosage of venetoclax was reduced to 100mg daily with median duration of 14 days (range 11-21 days). With a median follow up of 222 days (range 27-650) for the whole cohort, ten (47.6%) were alive at the end of follow up. The complete response rate (CR) was 52.4%. All responders achieved CR by 2 cycles of HMA/venetoclax and five responders were able to maintain response over 4-8 cycles and still on therapy at the end of follow up. However, one responder had relapsed disease after 8 cycles of HMA/venetoclax. Among the eleven responders, 2 presented with adverse cytogenetic risk. One patient completed 15 cycles of HMA/venetoclax and remained in CR after stopping treatment for 3 months. There was no tumour lysis syndrome reported in cases with high leukemic burden (blast > 50%). Five deaths occurred from infection and other six patients died from disease progression.

Discussion / Conclusion: Our real-world data shows that treatment with combination of HMA/venetoclax is a therapeutic option for AML patients who are not candidate for intensive chemotherapy with an acceptable safety profile and response rate. It is particularly beneficial in patients with de novo AML and HMA treatment naive. Further studies with larger sample size and longer follow up is needed to determine the durability of response and survival of patients receiving this combination treatment.

E-POSTER RESEARCH (CLINICAL)

C5 A PILOT STUDY OF SARAWAK ALL PROTOCOL (SWKALL): A MODIFIED PAEDIATRIC INSPIRED REGIME SUITABLE IN RESOURCE CONSTRAINT SETTING

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Background: Acute lymphoblastic leukaemia (ALL) accounts for approximately 40% of adult leukaemia in Malaysia, facing an inferior outcome (3-year OS < 30%). Despite the global shift embracing paediatric-inspired regimens like CALGB10403, GMALL, and MASPORE, Sarawak, as a state in Malaysia had not embrace a standardized approach.

Objectives: In response to our diverse patient's demographics and resource constraints, we hope to improve our patient's outcome by modifying the current regime and develop our own SARAWAK ALL Protocol (SWKALL).

Materials and Methods: This prospective pilot study, conducted at Sarawak General Hospital, enrolled all eligible patients aged 15 to 60 diagnosed with ALL in 2023 who were fit for chemotherapy. Measurable residual disease (MRD) was done if available. High risk patients would undergo allogeneic stem cell transplant if they were eligible. To ensure chemotherapy instituted in a timely manner with reduce toxicity, modifications were made to existing paediatric-inspired regimens with the following: During induction (i) Prednisolone replaced with short courses of dexamethasone, and anthracycline is given on two consecutive days weekly for 2 weeks (ii) Cytarabine reduced from 4 blocks to 1 block, with 3 weeks of 6-mercaptopurine, at a reduced dose of 25mg/m2. In consolidation, high-dose IV methotrexate was administered. A total of 22, instead of 12, triple intrathecal chemotherapies were given in this treatment regime. L-asparaginase was replaced by pegylated asparaginase. Maintenance therapy lasts 2 years for females and 3 years for males. Dosage modification will allow the protocol's use until the age of 60. Patient demographics, complete response (CR) rate, progression-free survival (PFS), overall survival (OS), factors associated with inferior OS/PFS, and adverse events were collected. Data was analyzed via IBM SPSS Statistics v29.0.

Results: Seven patients included Ph-neg B-ALL (n=4), Ph+ B-ALL (n=1), Ph-like B-ALL (n=1), and T- ALL (n=1) were initiated on SWKALL protocol. The median age was 41 years old (range 20 to 59). Four of them (57.1%) were of high-risk group. One Ph+ ALL patient proceeded to allogeneic stem cell transplant post-delayed intensification I with undetected BCR-ABL level. Six patients (86%) achieved CR after induction; one with residual disease, achieved CR post-consolidation. Induction mortality was 0%. OS and PFS analysis are ongoing, as the median follow-up is too short, at 4 months (range 1 to 9 months). At the time of writing, all patients are still alive. Grade 3 or grade 4 adverse events included febrile neutropenia (n=7, 100%), transaminitis (n=3, 42.8%), and infection (n=2, 28.6%).

Discussion / Conclusion: Despite efforts to make the protocol patient-friendly with less hospital admissions after induction, there were challenges in adhering to the strict protocol schedule. This has led to delays (median=7 days, range 7 to 21 days) between cycles due to COVID infections (n=3, 42.8%), bed availability (n=4, 57.1%) and social logistic reasons (n=4, 57.1%). The SWKALL protocol exhibited promising results and an acceptable safety profile. Limitation of the study, such as a small sample size, necessitate ongoing patient recruitment. SWKALL is suitable to be adopted in middle-income countries like Malaysia, considering our limited resources, higher infection rates, and limited next gene sequencing (NGS) and MRD monitoring.

E-POSTER RESEARCH (CLINICAL)

C6 EPIDEMIOLOGY AND RISK FACTORS OF CANCER - ASSOCIATED THROMBOSIS AMONG ASIAN POPULATION - A SINGLE CENTRE EXPERIENCE

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Background: Cancer-associated thrombosis (CAT) is a leading cause of mortality among the cancer patients. Incidences of CAT varied widely between studies due to the differences in disease biology, patient-related risk factors and cancer-directed therapy.

Objectives: To determine the incidence, clinical and cancer-related risk factors of CAT in Northern Sarawak, Malaysia.

Materials and Methods: All oncological and hematological patients aged 15 years old and above diagnosed between 2021 and 2023 in Hospital Miri, Sarawak were included. Demographic data, clinical and laboratory data were tabulated to the designated case report form. All statistical analyses were performed using Stata, version 15.0; StataCorp and SPSS, version 23; IBM Corp software packages. Conditional logistics regression was performed to assess the CAT risk factors.

Results: A total of 472 patients diagnosed with oncological cancer (n=321,68%) and hematological cancer (n=151, 32%) were included. The mean age was 55 (range 15-85 years old). The male to female ratio was 1:1. Majority were Native (n=220, 46.6%) followed by Chinese (n=132, 28.6%) and Malay (n=107, 22.7%). Breast (n=94, 19.9%) and colorectal cancer (n=92, 19.5%) were the predominant cancer followed by non-Hodgkin lymphoma (n=81, 17.7%) and lung cancer (n=38, 8%). 33 of them (7%) with median age of 59 and body mass index (BMI) of 21.4kg/m2 have CAT. Majority have deep vein thrombosis (n=15, 45.4%) and pulmonary embolism (n=11, 33.3%). Median hemoglobin, white blood cells (WBC) and platelets were 10.5g/dL, 7.81X10^9/L and 271x10^9/L respectively. 22 have passed away with median overall survival of 11 months (range 0-35). We demonstrated gender, race, BMI, presenting hemoglobin, WBC and platelet were not statistically associated with thrombosis among cancer patients.

Discussion / Conclusion: The incidence of CAT here was 7% which was comparable with that in Western population. However, we could not demonstrate any statistically significant risk factors of CAT likely due to small sample size. In view of the lacking data of CAT among Asian population, more studies were crucial in enhancing our understanding and knowledges of CAT in Asian countries.

E-POSTER RESEARCH (CLINICAL)

C7 PREVALENCE AND RISK OF INVASIVE FUNGAL INFECTION AMONG PATIENTS WITH HEMATOLOGICAL MALIGNANCIES UNDERGOING INTENSIVE CHEMOTHERAPY AND HEMAPOIETIC STEM CELL TRANSPLANTATION

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Background: Invasive fungal infection (IFI) is a cause of morbidity and mortality among patients with haematological malignancies (HM) undergoing intensive chemotherapy or hematopoietic stem cell transplantation (HSCT).

Objectives: This study aims to describe the prevalence and risk of IFI among Malaysian patients undergoing these treatments and their outcomes.

Materials and Methods: A cross sectional study involving adult patients with HM admitted for intensive chemotherapy and HSCT from 1 March 2020 to 30 June 2022 was conducted in a teaching hospital. Clinical information and outcomes of these patients were collected. Patients were classified into possible, probable, and proven IFI based on The European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium (EORTC/MSGERC) guidelines.

Results: Eighty-three patients with mean age 48.8+1.5 years accounting for 132 admissions were recruited. More than half were males, majority being Chinese (47.0%). Acute myeloid leukemia (45.8%) was the most common diagnosis, followed by multiple myeloma (16.9%) and acute lymphoblastic leukemia (15.7%). Forty-six patients were hospitalised for HSCT, majority were autologous (60.9%), followed by allogeneic (28.2%) and haploidentical HSCT (10.9%). 84.8% of patients had peripherally inserted central catheter (PICC) as the mean of venous access. Antifungal prophylaxes were prescribed in 94.7% of patients, predominantly fluconazole (88.6%). 40.9% of the admissions were complicated by bacteraemia. There were 7 possible, 1 probable and 9 proven IFI. Candida tropicalis (50.0%) and Candida krusei (30.0%) contributed to most of the proven IFI. Four patients (23.5%) died due to severe infection. Multivariate analysis showed that patients who received fluconazole has reduced risk of IFI (Odds ratio [OR] 0.229, 95% confidence interval [95% CI] 0.070 – 0.902, p=0.034), whereas patients with concomitant bacteraemia have increased risk of IFI (OR 3.950, 95% CI 1.276 – 12.233, p=0.017).

Discussion / Conclusion: IFI remains an important cause of mortality among HM patients receiving intensive chemotherapy and HSCT. Treating physicians should have low index of suspicion for IFI among patients with documented bacteraemia, with low threshold to initiate empirical antifungal treatment if clinically indicated.

E-POSTER RESEARCH (CLINICAL)

C8 PONATINIB EFFICACY AND SAFETY: EXPERIENCE IN PATIENTS WITH CHRONIC MYELOID LEUKAEMIA, HOSPITAL PULAU PINANG

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Background: Ponatinib is a third generation tyrosine kinase inhibitor (TKI) designed to overcome the gatekeeper T315I mutation in patients with chronic myeloid leukaemia (CML). It is also effective against heavily pretreated patients with native and other mutated BCR-ABL. Therefore, ponatinib is currently indicated for the treatment of all phases in CML, resistant or intolerant to previous TKI or Philadelphia chromosome-positive acute lymphoblastic leukaemia (ALL).

Objectives: We aim to explore the efficacy and safety of ponatinib in our local patients with CML.

Materials and Methods: A retrospective study was conducted on patients with CML in Hospital Pulau Pinang who received ponatinib from January 2017 till December 2023. Response to ponatinib was assessed according to the international scale (IS) as the ratio of BCR-ABL1 transcripts to ABL1 transcripts. Adverse events were graded according to The National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

Results: A total of 27 patients (male : female, 1.25:1) with a median age of 31 years old (IQR 25-48) were studied. Majority of them were Malay (59.3%) followed by Chinese (33.3%) and Indian (7.4%). 96.3% were still alive at last follow-up. Three of them underwent allogenic stem cell transplantation. 81.5% were in chronic phase, 7.4% in accelerated phase and 11.3% in blast crisis during CML diagnosis. 48.1% had high risk Sokal score, 25.9% had intermediate risk and 14.8% with low risk. 2 patients had T315I mutation. Other ABL kinase mutation detected were Y253H (n=2), E255V (n=2), F359V (n=2), M244 (n=1) and E355G (n=1). Median duration from CML diagnosis to ponatinib initiation was 58 months (IQR 22-65). Indications for starting ponatinib were resistant disease (n=18, 66.7%), intolerance and resistance (n=5, 18.5%), T315I mutation (n=2, 7.4%), suboptimal response (n=1, 3.7%), rising BCR-ABL transcript (n=1, 3.7%). Majority of them had 2 prior TKIs before ponatinib initiation (n=19, 70.4%), 18.5% (n=5) had 3 prior TKIs and 11.1% (n=3) had 1 prior TKI. Median duration on ponatinib was 43 months (IQR 22-64). Best response achieved were MR4.5 (n=11, 40.7%), MR4.0 (n=1, 3.7%), MMR (n=7, 25.9%), CCyR (n=1, 3.7%), less than CCyR (n=7, 25.9%). Their latest response on ponatinib were MR4.5 (n=8, 29.6%), MR4.0 (n=2, 7.4%), MMR (n=8, 29.6%), CCyR (n=1, 3.7%), less than CCyR (n=8, 29.6%). Median time to achieve at least CCyR was 4.5 months (IQR 2.8- 7). Most of the adverse events were grade I-II rash, transaminitis, chest pain, giddiness, headache, musculoskeletal pain, neutropenia, thrombocytopenia, constipation, diarrhea, dyspepsia and vomiting. Two patients developed serious cardiovascular complications, one had acute coronary syndrome grade III and the other had acute heart failure grade IV requiring discontinuation of ponatinib. Two patients developed thrombocytopenia grade IV.

Discussion / Conclusion: Ponatinib is well tolerated and exhibit durable response in patients with CML. Majority of the patients achieved at least a CCyR (n=19, 70.4%). Regular cardiovascular monitoring is important especially for those with risk factors.

E-POSTER RESEARCH (CLINICAL)

C9 EXPLORING CLINICAL HETEROGENEICTY AND OUTCOME IN PRIMARY EXTRANODAL LYMPHOMA: A 2-YEAR RETROSPECTIVE STUDY

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Background: Primary extra nodal lymphoma (PEL) is a non-Hodgkin lymphoma (NHL) which originates from tissue other than lymph node, it is accounted for at least one third of NHL. The incidence of PEL is rising throughout the world for the past 2 decades, however up to this date, in Malaysia there is still lacking study or published article with regards this matter.

Objectives: This is a retrospective study to ascertain the prevalence, clinical features, histological subtypes and clinical outcome of PEL in Kelantan.

Materials and Methods: This was a retrospective study of patients diagnosed with histologically proven PEL over 2 years period, 2022 to 2023. Relevant clinical and laboratory data was collected included clinical characteristics, biochemical parameters, histological subtype and treatment outcome was obtained from medical report. The data were tabulated in google sheet and descriptive analysis was done.

Results: A total of 49 patients were diagnosed with PEL over 2-year period which constituted 38.3% (49/130) of all NHL with a slight female predominance (53.1%), and the average age at diagnosis was 55. The skin emerged as the predominant extra nodal location (18.4%), followed by the tonsil (12.2%) and nasopharynx (10.2%). Diffuse large B-cell lymphoma (DLBCL) represented the prevailing histological subtype (63.3%). Most patients were diagnosed at stage 4 of the disease. Lactate dehydrogenase (LDH) level at diagnosis were remarkably high (mean; 804mmol/L). Outcomes varied, with approximately 28.6% achieving complete metabolic response with 18.4% were refractory to first line treatment. 75% of the patients were alive at the end of treatment.

Discussion / Conclusion: PEL constituted about one-third of patients diagnosed to have NHL at our centre with skin being the most common site of presentation and DLBCL being the most common histological subtype. Despite the majority of patients receiving a later-stage diagnosis, their overall survival is commendable, boasting a cure rate of approximately 28.6% with appropriate treatment.

E-POSTER RESEARCH (CLINICAL)

C10 REAL WORLD SINGLE CENTRE STUDY ON DARATUMUMAB OUTCOMES IN RELAPSED/REFRACTORY MULTIPLE MYELOMA

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Background: Daratumumab is a human IgG1κ monoclonal antibody that binds to CD38 resulting in myeloma cell death via direct antitumour activity and modulation of immunosuppressive microenvironment. In our centre, Daratumumab is predominantly used in the relapsed/refractory setting.

Objectives: The objective of this study is to evaluate the efficacy and outcomes of Daratumumab in patients with relapsed/refractory Multiple Myeloma.

Materials and Methods: A 5 year retrospective analysis was performed for all patients with Multiple Myeloma treated with Daratumumab in our centre from 2018 till 2023. Data cut off was 30th June 2023.Statistical analysis was conducted using SPSS.

Results: We studied a total of 19 patients. The median follow up time was 12 months (6-55). 63.15% were males. Our patients were younger than reported with median age of diagnosis at 53 years old (30- 71). The median age of Daratumumab initiation was 61 years old (40-79). 47.36% were ISS stage II while 52.6% were ISS stage III. 20% had high risk cytogenetics which was defined as presence of t(14;16), t(4;14), del17p and gain of 1q chromosome. 31.57% had renal impairment defined by creatinine clearance of <60ml/min at diagnosis with 3 patients on regular haemodialysis. Overall, our patients were heavily pre treated with the majority receiving a median of 5 prior lines of therapy (3-5). 84.2% were double refractory to both a proteasome inhibitor(PI) and an immunomodulatory drug (IMID). 84.2% were treated with Daratumumab-Dexamethasone while 10.52% and 5.26% were treated with Daratumumab-IMiD and Daratumumab-PI regimes respectively. The median time of Daratumumab initiation was 69 months from diagnosis (31-111) and the average number of dose received was 16. Infusion related reaction rate occurred in 21.05%. The median time to achieve ≥ PR after Daratumumab initiation was 2 months (1-10). 42.1% received a prior autologous stem cell transplant. The overall response rate (ORR) was 78.92% (15.78% CR, 15.78%VGPR, 47.36% PR) and progressive disease 21.05%. The median progression free survival was 13.5 months (2-26) with 5-year and 10-year overall survival rates of 78.3% and 50.7% respectively. Delayed initiation of Daratumumab (hazard ratio (HR) 0.94, 95% CI 0.90, 0.98, p value= 0.004) and older age of Daratumumab initiation are associated with inferior overall survival (HR 0.92, 95% CI, 0.85,0.99, p value=0.035). There was no Grade 3/4 side effects and none had discontinuation due to adverse event.

Discussion / Conclusion: Daratumumab was well tolerated with the primary reason for discontinuation was due to progressive disease. Daratumumab based therapy led to a deep quality of response in 31% of our cohort of heavily pretreated patients. Our overall response rate and survival data are comparable to those previously reported. Earlier and younger age of Daratumumab initiation significantly prolonged overall survival in the relapsed/refractory setting. Hence, early consideration and increased access to Daratumumab should be made a priority.

E-POSTER RESEARCH (CLINICAL)

C11 CLINICAL CHARACTERISTIC AND SURVIVAL OUTCOME OF PATIENTS WITH CLASSICAL HODGKIN LYMPHOMA AT A TERTIARY HOSPITAL IN MALAYSIA. A RETROSPECTIVE STUDY

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Background: Classical Hodgkin Lymphoma(cHL) is a type of B-cell neoplasm that arises from the germinal centre B cell. It is characterised by the presence of Reed-Sternberg and embedded in a microenvironment rich in immune cells. There were well-established studies worldwide that describe the clinical features, therapeutic options and outcomes of cHL However, there was still a lack of data in resource-limited countries.

Objectives: This study aims to describe the clinical characteristics and survival outcomes of patients diagnosed with cHL in our centre.

Materials and Methods: This retrospective study was conducted at a haematology clinic or daycare at Hospital Tengku Ampuan Rahimah, Klang, Malaysia. We retrieved clinical records from patients with classical Hodgkin Lymphoma who had completed treatment between the years of 2018 to 2023.

Results: A total of 57 patients with classical Hodgkin lymphoma were recruited. Of these, 30 were males(52.6%) and 27 were females(47.4%) with median age of 27 years old(range 13-76). The majority of them were Malay(n=45, 79%), followed by Indian(n=8,14%) and Chinese(n=4, 7%). In our cohort, nodular sclerosis(n=38, 66.7%) was the most common histology subtype, which was followed by mixed- cellularity(n=10,17.5%), lymphocyte-rich (n=5, 8.8%) and unclassified histology(n=4, 7%). 53 patients(93%) presented with palpable lymph node or mass, 24(42.1%) had the extranodal presentation and 33 had B symptoms(57.9%). Only 5 of them(8.8%) had thrombosis at presentation. 32(56.1%) had advanced disease. Among 25 who had early-stage disease, 18 (31.6%) had a favourable disease and 7(12.3%) had an unfavourable one. 43(75.4%) received ABVD as the first line therapy and 10(17.5%) received escalated BEACOPP. 10(17.5%) received radiotherapy as consolidation. 28 patients(49.1%) achieved complete response and 23 patients(40.4%) achieved partial response. The overall response rate was 89.5%. Among 18 of them who required salvage chemotherapy, 9 patients underwent autologous stem cell transplantation. 3 patients received brentuximab vedotin and 1 patient received nivolumab. 4 of them succumbed due to disease progression. With a median follow-up of 39 months, 3 years of progressive free survival and overall survival were 85% and 95% respectively.

Discussion / Conclusion: Our study demonstrated that most patients had advanced disease and presented with B symptoms. ABVD chemotherapy remains the standard of care in our centre. The treatment of choice might be due to its efficacy and favourable toxicity profile. Escalated BEACOPP had a better survival profile compared to ABVD regime in advanced disease but had more treatment-related toxicities. The access of novel agents like brentuximab vedotin, pembrolizumab and nivolumab remains limited due to budget constraints. Despite this, the survival outcome was comparable to other centres worldwide. In conclusion, longer follow-ups with more patients are required to evaluate the long-term survival of patients with cHL.

E-POSTER RESEARCH (CLINICAL)

C12 CLINICAL CHARACTERISTICS AND TREATMENT PATTERN OF VENOUS THROMBOEMBOLISM IN MALAYSIAN PATIENTS WITH ACTIVE CANCER-A SINGLE CENTRE EXPERIENCE

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Background: Cancer is the most important acquired risk factor for venous thromboembolism(VTE) in Asians whereby 15-40% of VTE are found in patients with active cancer. Management of VTE in these patients are not straightforward and is further complicated when adverse events such as bleeding episodes and recurrent VTE occurs. Most epidemiology studies and guidelines are derived from data from the Western countries. Epidemiology studies in Asian patients are limited. There is a paucity of data regarding cancer-associated thrombosis in Malaysia.

Objectives: We aim to look at the clinical profile and treatment pattern of VTE in Malaysian patients with active cancer.

Materials and Methods: A retrospective analysis of cancer patients with VTE from January 2016 to December 2020 at University of Malaya Medical Centre, Kuala Lumpur was performed. Patients were included if they had VTE diagnosed that was confirmed objectively by imaging. Baseline demographics and clinical characteristics related to VTE were also obtained. Patients were followed up from their initial diagnosis of VTE until they experience an outcome of interest (recurrent VTE, bleeding, stopping anticoagulant, death).

Results: We identified 262 cases of VTE(31.2% out of total of 839 cases of VTE)in patients with active cancer(male patients 61.8%, median age 63 years). The most common primary tumour sites were gynaecological in 59 patients (22.5%), gastrointestinal in 58 patients (22.1%) and lung in 33 patients (12.6%). Hospital admissions for VTE were identified in 238 patients during or after the diagnosis of VTE. VTE was concomitantly diagnosed with cancer in 52% of patients. Majority of patients had pulmonary embolism(PE) (50.4%) followed by deep vein thrombosis(DVT) (39.7%), concurrent PE and DVT (7.3%) and intra-abdominal thrombosis (n=5, 1.9%). Anticoagulant therapy was initiated in 216 patients whereby 56% were started on direct oral anticoagulants, followed by 39.3% on low molecular weight heparin and 4.6% on warfarin. Despite treatment for VTE, 16 patients (7.4%) had recurrent VTE and 34 patients (15.7%) had major bleeding. At 5 years, the cumulative survival rate was significantly better for patients who had anticoagulant therapy compared to those that did not (58.8% vs 45.7% p=0.029).

Discussion / Conclusion: The proportion of cancer patients with VTE in our hospital-based study is similar to that reported in other Asian and Western epidemiological studies. This shows that the diagnosis of VTE carry a significant additional clinical burden for cancer patients. A bigger population- based study is required to truly look at the incidence and risk factor for VTE in Malaysian cancer patients.

E-POSTER RESEARCH (CLINICAL)

C13 DEMOGRAPHICS AND CLINICAL OUTCOMES OF PATIENTS ELIGIBLE FOR FERRIC CARBOXYMALTOSE: A SINGLE CENTRE RETROSPECTIVE STUDY

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Background: Iron deficiency is a frequent problem in clinical practice. Oral iron supplementation may in some cases not be well tolerated or not be efficient. Intravenous (IV) ferric carboxymaltose (FCM) may be an alternative for iron supplementation.

Objectives: This retrospective study aimed to investigate the efficacy and safety of IV FCM infusion in a single centre in Malaysia.

Materials and Methods: All patients who received at least one dose of 500mg IV FCM infusion from 1 Jan to 31 Dec 2023 in Bukit Tinggi Medical Centre (BTMC) were identified from the electronic medical record database. Inclusion criteria were patients ≥14 years old, with baseline haemoglobin (Hb) level measured within 60 days before IV FCM infusion and at least one follow-up Hb level measured post- treatment. The primary outcome was the mean increase in Hb level. Secondary outcomes included reasons for IV FCM infusion, median dose of IV FCM infusion, and adverse drug reactions related to IV FCM infusion. Demographics and outcomes were collected through a retrospective medical record review. The efficacy outcome was analysed using complete data analysis while the safety outcome used intention-to-treat analysis. Paired t-test was used to compare the difference between the two Hb measurements.

Results: A total of 144 patients (mean age = 40 years old, predominantly Indian (46.5%), female (90.3%)) received IV FCM infusion during the 1-year study period in BTMC for the treatment of iron deficiency anaemia associated with menorrhagia (79.2%), poor nutrition (6.3%), gastrointestinal-related malabsorption (5.6%), autoimmune haemolytic anaemia (4.9%), blood malignancies (3.5%) and idiopathic thrombocytopaenia purpura (0.7%). The median dose of IV FCM infusion was 1000mg. 123 patients (84.8%) had a follow-up Hb level post-treatment. At a median follow-up time of 29 days, the mean Hb level increased significantly from 9.5 g/L to 12.2 g/L ($p < 0.05$), an increase of 2.77 g/L (95% CI: 2.39 - 3.14 g/L). No adverse drug reactions were reported.

Discussion / Conclusion: Within the limits of this retrospective study, IV FCM infusion therapy was well tolerated and effective in increasing the mean Hb level among patients with iron deficiency anaemia.

E-POSTER RESEARCH (CLINICAL)

C14 TREATMENT OUTCOMES OF AGGRESSIVE B CELL LYMPHOMA: A SINGLE CENTRE REVIEW AT SARAWAK GENERAL HOSPITAL, KUCHING

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Background: Aggressive B cell lymphoma accounts for majority of non-Hodgkin lymphoma encountered in Malaysia and worldwide. The treatment response varies among treatment centres.

Objectives: The study was carried out to determine the treatment outcomes of patients diagnosed of aggressive B cell lymphoma between years 2019 and 2021 and investigate factors associated with survival at two years of lymphoma diagnosis.

Materials and Methods: This retrospective study was performed to assess the treatment outcomes for patients diagnosed with aggressive B cell lymphoma at the Sarawak General Hospital, Malaysia between January 2019 and December 2021. Major inclusion criterion was adult patients (18 years old and above) with the diagnosis of Burkitt lymphoma (BL), diffuse large B cell lymphoma (DLBCL), high grade B cell lymphoma (HGBCL) or primary mediastinal B cell lymphoma (PMBCL) who received intensive chemotherapy within the study period. Patients who refused chemotherapy or elected for palliation were excluded. Primary outcomes were progression-free survival (PFS) and overall survival (OS) at two years of lymphoma diagnosis.

Results: There were 112 patients included in the study. Majority of the study cohort was male patients (59.8%), with a mean age of 57.3 years. DLBCL was the most frequently recorded lymphoma (86.6%). Majority of them presented in advanced stage of disease (67.9%). The median time between diagnosis and treatment was 15 days. All patients received R-CHOP or R-CHOP-like immunochemotherapy as front-line treatment. The 2-year PFS and OS were 65.2% and 67.0%, respectively. Performance status, pre-treatment haemoglobin level (< 12 g/dL), serum albumin level (> 35 g/L) and international prognostic index (IPI) score were the significant prognostic factors for both PFS and OS in the univariate analysis. Multivariate analysis showed that performance status was the sole significant predictor for the treatment outcomes (p = 0.015 for PFS, p = 0.029 for OS, respectively).

Discussion / Conclusion: In addition to the IPI score, our study showed that pre-treatment haemoglobin level could potentially be utilised as an additional prognostic marker for patients diagnosed with aggressive B cell lymphoma.

E-POSTER RESEARCH (CLINICAL)

C15 OVARIAN RESERVE ASSESSMENT USING ANTI-MULLERIAN HORMONE IN WOMEN WITH NEWLY DIAGNOSED LYMPHOMA

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Background: Impaired fertility is among the long-term side effects of chemotherapy among female patients with lymphoma. However, it is also essential to know the ovarian reserve before chemotherapy.

Objectives: This study aimed to assess the ovarian reserve in newly diagnosed lymphoma patients before treatment and its association with lymphoma characteristics.

Materials and Methods: This cross-sectional study was conducted among women with newly diagnosed lymphoma in Hospital Canselor Tuanku Muhriz and Hospital Ampang from June 2021 to September 2023. Blood samples for anti-Mullerian hormone (AMH) were collected before chemotherapy. The serum concentration of AMH was measured using the Elecsys AMH PLUS immunoassay on a Cobas E 411 analyser (Roche Diagnostics). Data on patients' demographics, lymphoma characteristics and obstetric and gynaecological history were obtained. The Institutional Review Board of the Research Ethics Committee of Universiti Kebangsaan Malaysia (FF 2021-330) approved the study protocol and was registered in the National Medical Research Register (NMRR ID-23-00111-6AIN). Written consent was obtained from the patients.

Results: A total of 25 patients were recruited. The median age of the patients in our study was 35 (19- 45) years. Nine (36%) patients were diagnosed with diffuse large B-cell lymphoma, followed by eight (32%) Hodgkin lymphomas. Twenty-one were married, and four were single. Of those who were married, four were nulliparous, and five were multiparous. Twelve of the patients had one to two children. The AMH level before chemotherapy (baseline) was low, with a median value of 0.34 (0.01- 5.03) ng/mL. Eighteen patients had AMH levels less than 1.2 ng/mL, defined as poor ovarian reserve according to POSEIDON criteria. AMH levels at baseline tended to be higher at age < 35 years than at age > 35 years [0.43 (0.04-5.03) ng/ mL vs 0.33 (0.01-2.32) ng/mL, p=0.21]. Patients with bulky disease, raised lactate dehydrogenase (LDH) and stage III-IV disease tended to have lower baseline AMH levels than non-bulky disease, normal LDH and stage I-II diseases, 0.33 (0.04-1.64) vs 0.43 (0.01- 5.03) ng/mL, 0.31 (0.04-5.03) vs 0.34 (0.01-2.32) ng/mL and 0.33 (0.01-2.32) vs 0.43 (0.04-5.03) ng/mL, respectively.

Discussion / Conclusion: In this study, low AMH levels at baseline indicate reduced ovarian reserve in women with lymphoma, even before cytotoxic chemotherapy is started. Patients with less favourable lymphoma characteristics (bulky disease, raised LDH and stage III-IV disease) tended to have lower AMH levels. However, a larger sample and a more extended follow-up period are needed to validate these results further. This information is clinically relevant for the hematologists treating patients and will be helpful when advising patients before chemotherapy. To maximize the benefits of treatment, patients should be advised to undergo fertility preservation counselling.

E-POSTER RESEARCH (CLINICAL)

C16 PRIMARY GASTROINTESTINAL LYMPHOMA: A TWO CENTERS EXPERIENCES IN THE NORTHWESTERN REGION OF SARAWAK, MALAYSIA

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Background: Primary gastrointestinal lymphoma (PGIT) is rare, accounting for only 1-4% of malignancies arising from gastrointestinal tract. It has a wide range of disease spectrum ranging from indolent low grade lymphoma to aggressive high grade lymphoma with different clinical characteristics and treatment outcomes.

Objectives: In view of the lacking data in our region. We aimed to study the clinical characteristics, treatment modalities and prognostic factors in PGIT.

Materials and Methods: This is a double center retrospective study conducted in Hospital Bintulu and Hospital Miri from January 2022 until January 2024. All patients above 18 years old diagnosed with PGIT were included. The demographic characteristics, clinical and laboratory parameters were tabulated in the predesigned case report and analyzed with SPSS (Statistical Package for the Social Sciences) version 29.

Results: A total of 21 patients were diagnosed with PGIT with median duration of follow-up of 51 weeks (ranging 0 to 105 weeks). Majority (n=16 (76%) has diffuse large B cell lymphomaa, followed by follicular lymphoma (n= 2, (9.5%)), enteropathy associated T cell lymphoma (n=1, 4.8%), mucosal associated lymphoid tissue lymphoma (n=1, 4.8%) and marginal cell lymphoma (n=1, 4.8%). The median age at diagnosis was 48 years old (range 17-80) with male predominance (n= 14, 67%). Majority were of Iban (n=11, 52%) followed by Malay ethnicity (n=5, 24%). It was notable that gastric involvement was the commonest site (n=9, 42.9%) followed by small intestine (n=7, 33%) and large intestine (n=5, 24%). The commonest abdominal symptoms on presentation was abdominal pain (n=17, 77.3%) and almost all of the patients (n=20, 95.5%) have B-symptoms. The median presenting hemoglobin, white cell count and platelet were 10g/dL, $8.2x10^9$/L and $214x\ 10^9$/L respectively. 19 patients (90.5%) underwent received chemotherapy, but only 9 patients (40.9%) were able to achieve complete remission whereas 4 patients (18.2%) achieved partial remission. 6 of them (28%) have surgical intervention before chemotherapy. Patients who received chemotherapy was associated with statistically significant better survival (p=0.019). Female gender (p=0.284), large intestine involvement (p=0.353), surgical resection (p=0.592), hemoglobin ≤10g/L (0.159), raised LDH (p=0.284) and albumin level ≤ 30g/L (p=0.163) were associated with worse survival though they were not statistically significant.

Discussion / Conclusion: We demonstrated that patients with chemotherapy was the only important statistically significant prognostic factors in predicting the survival in PGIT. We also showed that Iban ethnicity have a higher rate of PGIT as compared to others which could be explained by the fact that the formal was the predominant ethnicity in this region and could also be related to their sociocultural background. However, our study was limited by the small sample sizes

E-POSTER RESEARCH (CLINICAL)

C17 MYELOPROFLIERATIVE NEOPLASMS AND THROMBOSIS: A SINGLE CENTRE EXPERIENCE

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Background: Polycythaemia vera (PV), essential thrombocythaemia (ET) and myelofibrosis (MF) are Philadelphia-negative myeloproliferative neoplasms (MPN) that have been commonly associated with increased incidences of thrombosis. Thrombosis among MPN patients was one of the leading causes of morbidity and mortality. Our study described the characteristics of thrombosis among patients with myeloproliferative neoplasms.

Objectives: To determine the prevalence and patient-related and disease-related risk factors of thrombosis.

Materials and Methods: We performed a retrospective review of myeloproliferative neoplasm patients under Bintulu hospital follow-up from year 2019 to 2023. All patients above 18 years old diagnosed with myeloproliferative neoplasms were included in this study. Demography, clinical and laboratory data were tabulated in a predesigned case report form and analyzed by using SPSS software version 29.

Results: A total of 41 MPN patients were included in our study of which 19 (46.3%), 17 (41.5%), and 5(12.2%) patients have PV, ET, and MF respectively. The median age was 62 3 years old with an equal male to female ratio. 13 patients (31.7%) had thrombosis (n=6 (14.6%) PRV, n=6(14.6%) ET and n=1 (2.4%) MF) which were mainly arterial thrombosis (n=12). There were 5 patients (38%) who had thrombosis before the diagnosis of MPN and 8 patients (62%) were diagnosed together with MPN. The presenting mean hemoglobin (Hb) was 15g/dL and the median white cell counts (WCC) and platelets (PLT) were $13.50x10^9$/Land $800x10^9$/L respectively. All of them were high risk groups with platelet count above $450x10^9$/L. Hypertensive patients on antihypertensive agents were statistically associated with thrombosis (p=0.007), however, there was no demonstrable statistical significance between gender, race, preexisting diabetes, ischaemic heart disease, dyslipidemia, JAK2 V617F, presenting Hb, WCC, PLTS and risk classification with thrombosis.

Discussion / Conclusion: The incidence of thrombosis among MPN in our center was 31% in which most of the thrombosis occurred prior to or during the diagnosis of MPN. Most studies worldwide demonstrated several patient-related and disease-related risk factors that were postulated to have higher incidences of thrombosis. However, we demonstrated only hypertension was statistically associated with an increased risk of thrombosis. Our study was limited by the small sample sizes.

E-POSTER RESEARCH (CLINICAL)

C18 OUTCOME OF PRIMARY MEDIASTINAL B-CELL LYMPHOMA TREATED WITH IMMUNOCHEMOTHERAPY WITH OR WITHOUT CONSOLIDATIVE RADIOTHERAPY - A SINGLE CENTRE EXPERIENCE

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Background: Primary mediastinal B-cell lymphoma (PMBL) is a rare subtype of non-Hodgkin lymphoma that occurs more commonly in adolescent and young adult, with female predominance. Treatment with Rituximab-and-anthracycline containing regimen followed by mediastinal radiotherapy is used in many centres. Dose adjusted EPOCH-Rituximab (DA-EPOCH-R) is a commonly used regime, with some centres omitting radiotherapy. Due to the concern of inadequacy of immunochemotherapy in achieving tumour control as well as the poor outcome of relapsed or refractory cases, many clinicians still practise consolidative radiotherapy.

Objectives: This study aimed to look into outcome of all patients with PMBL with or without radiotherapy.

Materials and Methods: This is a retrospective study of all the patients diagnosed with PMBL who received treatment in Hospital Pulau Pinang from year 2017-2022. Patients were identified from admission census and institution registry. The patients' case notes were traced from medical record unit for data collection. All patients have PET-CT assessment after completion of treatment and remission status was based on FDG-PET-CT finding.

Results: A total of 26 patients with the diagnosis of PMBL were identified. 17 were females and 9 were males. The median age was 32.5 (range 16-69). The median follow-up was 41 months (range 23-77 months). 21 patients (81%) received DA-EPOCH-R and 5 patients (19%) received 6 cycles of R-CHOP or R-CEOP. Among the R-CHOP arm, 3 patients (60%) achieved end of treatment PET negativity in which 2 of them received consolidation radiotherapy and all of them remained disease free. 2 patients (40%) on this arm had residual disease, in which 1 of them underwent radiotherapy alone and another underwent radiotherapy and autologous stem cell transplant. In the DA-EPOCH-R arm, 7 patients (33%) achieved end of treatment PET negativity where 3 of them underwent consolidation radiotherapy whereas the other 4 didn't and all of them remained in remission. 14 patients (67%) of this arm had residual disease or disease progression. Of these 14 patients, 9 received radiotherapy, 1 patient underwent autologous stem cell transplant after salvage chemotherapy and 4 patients had combined modality treatment with radiotherapy and salvage chemotherapy followed by autologous stem cell transplant. Overall, 20 patients (77%) achieved complete remission, 5 patients (19%) achieved stable disease, and there was one mortality (4%) due to refractory disease. 10 patients (38%) achieved PET negativity upon completion of initial immunochemotherapy. There were 5 patients (19%) who were treated successfully with immunochemotherapy without radiotherapy. 5 year overall survival was 94%

Discussion / Conclusion: Our study showed that primary mediastinal B cell lymphoma has good prognosis with treatment, which is consistent with the finding from many other centres. Inadequacy of immunochemotherapy alone remains a major challenge in the management of PMBL despite the use of dose adjusted EPOCH-Rituximab. Radiotherapy still plays a major role in majority of the cases. However, a negative PET-CT upon completion of chemotherapy might be a guide to obviate the need of radiotherapy, giving the risk of long term side effects of radiotherapy.

E-POSTER RESEARCH (CLINICAL)

C19 RETROSPECTIVE ANALYSIS ON EFFICACY OF ADDITION ELTROMBOPAG WITH IMMUNOSUPPRESSIVE THERAPY FOR ACQUIRED APLASTIC ANAEMIA - SINGLE CENTRE EXPERIENCE

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Background: Eltrombopag (EPAG), an oral thrombopoietin receptor agonist (TPO-RA), has been proven to improve the hematologic response without increasing toxic effect.

Objectives: To study response of eltrombopag in acquired aplastic anaemia

Materials and Methods: We conducted a retrospective analysis on patients aged more than 18 diagnosed with acquired aplastic anemia. We compared the efficacy of immunosuppressant with eltrombopag. We aimed to look at response post treatment at 3 months, 6 months and overall response.

Results: From year 2005 to 2023, 36 patients diagnosed with acquired aplastic anaemia at a median age of 50(17-90)years were treated with eltrombopag. Concomitant immunosuppressant given were anti-thymocyte globulin (horse), and ciclosporin. For severity, 38.9% (n=14) categorized to be SAA, 36.1% (n=13) were VSAA, 25%(n=9) were NSAA. Median follow up will be 32 months(2-96 months). For overall response, 38.9%(n=14) achieved complete response, 30.6% (n=11) achieved partial response, 30.6%(n=11) have showed no response. At 3 months response, 13.9% (n=5) showed complete response, 50%(n=18) has partial response, 33.3(n= 12) Has no response, 1 patient passed away at 2 months from diagnosis. At 6 months, 32.4% (n=11) has completed response, 41.2%(n=14) has partial response, 5.9%(n=7) has no response. Eltrombopag dose usage was ranging 75mg daily to 150mg daily as tolerated and being used for at least one year. Eltrombopag will be withheld if there is no response. Common adverse effect will be reversible transaminitis which will resolve completely by reducing dose.

Discussion / Conclusion: Eltrombopag use in Aplastic anaemia showed sustainable long response and tolerable side effect profile.

E-POSTER RESEARCH (CLINICAL)

C20 GENOMIC LANDSCAPE IN NEWLY DIAGNOSED ADULT ACUTE MYELOID LEUKEMIA: REVIEW FROM A SINGLE LOCAL INSTITUTION

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Background: Genomic mutation profiling has been actively studied in recent years in patients with acute myeloid leukemia (AML). The occurrence of certain mutations has its impact on disease risk stratification, such as those that have been included in the updated 2022 European LeukemiaNet (ELN) classification. Some of the mutations have therapeutic implications with the advent of novel agents such as FLT3 and IDH1/IDH2 inhibitors.

Objectives: Here we present the genomic landscape of adult AML patients whose samples were collected and analyzed in a single institution in Malaysia over a 5-year period.

Materials and Methods: Next generation sequencing (NGS) testing was performed on samples collected in the institution from January 2019 to January 2024 using the Ion Torrent NGS technology. The AML panel consists of 40 DNA targets, 29 fusion genes and 10 expression control genes. A total of 79 newly diagnosed de novo AML patients were studied. We exclude treatment-related AML, AML with myelodysplasia-related changes, transformed AML and relapsed AML. Patients' demographic data was extracted from the electronic database, and analysis was performed using SPSS version21. We grouped the observed recurrent mutations into seven functional groups: DNA methylation, spliceosome mutation, chromatin modifier, transcription factors, tumor suppressors, signaling and kinase pathway, and cohesion complex.

Results: We analyzed a cohort of 79 adult AML patients, comprising the three main ethnic groups in Malaysia: Malay (23%), Chinese (63%), Indian (6%) and others (8%). The studied cohort showed a male predominance, (male 47; female 32) with a median age of 53 years old (range 16 - 96 years old). Samples were mainly from bone marrow (81.0%). A total of 33 gene mutations were identified in 73 patients among the 79 cases, with a frequency of 92.4%. The incidence of mutations according to their functional categories was recorded: activated signaling genes (32.1%), transcription factor genes (24.6%), DNA methylation (12.8%), chromatin modifier (11.2%), tumor suppressors (10.2%), spliceosome mutation (7.0%) and cohesion complex (2.1%). The three most common gene mutations discovered from the cohort were FLT3-ITD (26.6%), followed by RUNX1 (21.5%) and NRAS (20.3%). Patients with three or more domain mutations were older, aged >60 years.

Discussion / Conclusion: Our data showed that activated signaling gene mutation is the most common mutational subset in our AML cohort, consistent with the findings in most studies. We observed that 68.4% (54/79) of patients have more than one mutation occur concurrently; indicating a role of concerted interaction of mutations in AML pathogenesis. Our data demonstrated that there was a frequent co-occurrence of FLT3-ITD with NPM1 mutation (33.3%), which should be validated in future study with bigger sample size. Following our observation, subset of gene mutation and its frequency in elderly AML should also be further studied to improve our understanding of prognostic impact and treatment outcome among them.

E-POSTER RESEARCH (CLINICAL)

C21 EVALUATION OF RUXOLITINIB FOR STEROID RESISTANT GVHD AFTER HEMATOPOEITIC STEM CELL TRANSPLANTATION - SINGLE CENTER EXPERIENCE

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Background: Steroid resistant graft-versus-host disease (SR-GVHD) occurs in about 30% of allogeneic hematopoietic stem cell transplantation (HSCT) and one of leading cause of morbidity and mortality in transplant recipients. To date, the challenge in managing SRGVHD usually involved intensify immunosuppressant with balancing complications such as infections and cytopenia. Oversuppression of immune system may jeopardize donor stem cell viability which may impair graft versus leukaemia (GVL) effect. Insight on pathophysiology of GVHD helps to enlighten on immunosuppressant option. Ruxolitinib is a selective JAK 1/2 inhibitor by blocking signaling pathway induced by interferon-y and IL-6 receptor. While preventing GVHD, this inhibition will not interfere T cell alloreactivity, thus GVL can be preserved. This study aims to report on our experience in term of response and safety profile of ruxolitinib among our allogeneic HSCT recipients with SR-GVHD.

Objectives: To report on our experience on ruxolitinib in regards to response to GVHD and safety profile among our allogeneic HSCT recipients with SR-GVHD.

Materials and Methods: This is a retrospective case series including all allogeneic HSCT with steroid resistant GVHD treated with ruxolitinib. Patients' clinical characteristics, response to ruxolitinib and complications such as cytopenia and infection were reviewed.

Results: There were 11 patients included, 8 (72.7%) were male recipients with median age of 37 years old (20-60 years old). Majority of recipients undergone haploidentical HSCT (72.7%). 4 patients had male to male HSCT, 4 patients female to male, 2 male to female and 1 female to female. 90.9% had myeloablative conditioning regimen. Median time of GVHD after transplant was 19 days (9-41 days) with 54.6% (6 patients) had grave 3-4 GVHD. All patients GVHD involved skin , while 72.7% had gut involvement, 45.5 % had lung and 54.5% had liver involvement. Median time of initiation for SR- GVHD patients received ruxolitinib was 237 days after HSCT (40-539 days). All patient received steroids and 54.6 patients received MMF and calcineurin inhibitor as second line for GVHD prior to ruxolitinib initiation. Median time for ruxolitinib initial response was 121 days after initiation (28-763 days) with 36.4% (4 patients) achieved complete response of GVHD and 54.5% (6 patients) achieved partial response. 1 patient did not respond to ruxolitinib. Median duration of ruxolitinib was 259 days (12 – 1403 days). 45.5% patients can wean off steroid and second line immunosuppressant at time patient had initial response to ruxolitinib. 2 patients (18.2%) had CMV reactivation after initiation of ruxolitinib. 63.6% had infection, varies from herpes zoster to bacterial infection, mainly in the form of pneumonia. Almost all patient recovered well after antibiotic, 1 succumbed due to sepsis. Another patient succumbed due to relapsed disease approximately 1 year later after ruxolitinib has been stopped. In term of thrombocytopenia, 1 patient (9.1%) developed grade 4, 4 patient (36.4%) had grade 3. 1 patient had grade 3 leucopenia and 1 patient with grade 2, while the rest had grade 0 – 1.

Discussion / Conclusion: Ruxolitinib demonstrated a significant response in heavily pretreated SR- GVHD with acceptable, well tolerated safety profile.

E-POSTER RESEARCH (CLINICAL)

C22 TEMPORAL DYNAMICS OF FLT3-ITD/TKD AND NPM1 MUTATIONS IN AML: A THREE-YEAR STUDY BY ONCODE LABORATORY

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Background: Leukemia and myelodysplastic syndromes (MDS), encompassing acute myeloid leukemia (AML) and chronic myeloid leukemia (CML), represent a complex group of hematologic malignancies characterized by abnormal leukocyte production and significant genetic heterogeneity[1]. These conditions vary widely in their clinical presentation, prognostic implications, and therapeutic strategies, particularly in cases that are relapsed or refractory. Key genetic biomarkers in AML, such as Fms-like tyrosine kinase 3 (FLT3) and Nucleophosmin member 1 (NPM1) mutations, play a pivotal role in disease progression and treatment decisions. FLT3 mutations are subdivided into internal tandem duplication (ITD) and tyrosine kinase domain (TKD) types[2]. Other notable genetic alterations include mutations in CCAAT/enhancer binding protein alpha (CEBPA), Runt-related transcription factor 1 (RUNX1), additional sex combs-like 1 (ASXL1), and tumor protein p53 (TP53)[4]. Oncode Laboratory has spearheaded the use of advanced diagnostic techniques such as Polymerase Chain Reaction (PCR), Capillary Electrophoresis (CE), and Next-Generation Sequencing (NGS) to identify and characterize these mutations.

Objectives: This study intended to analyze the trend of FLT3-ITD/TKD and NPM1 mutations identified in AML patients at the Oncode Laboratory from 2021 to 2023, highlighting the evolution of diagnostic techniques from PCR to NGS and the emergence of additional biomarkers.

Materials and Methods: This retrospective study analyzed laboratory data from 548 patients diagnosed with AML cases who underwent FLT3-ITD/TKD and NPM1 mutation testing at Oncode Laboratory between 2021 and 2023, utilizing either PCR or NGS methodologies. The study employed a comprehensive approach using uniplex and multiplex PCR targeting hotspot genes, complemented by CE for assessing FLT3-ITD allelic ratios[3]. NGS was utilized for its enhanced ability to detect a broader spectrum of genetic markers, providing an in-depth molecular profiling.

Results: Of the 548 samples, 23.36% underwent traditional PCR testing, while a substantial 76.64% were tested by NGS. Notably, NGS usage increased nearly 50% year-over-year (2021: 95, 2022: 134, 2023: 191), reflecting increasing reliance in NGS. FLT3-ITD was the most frequent mutation (9.29%), followed by concurrent FLT3-ITD and NPM1 mutations (6.19%), and NPM1 mutations alone (4.52%). Furthermore, NGS testing revealed 36.90% of samples harboring variants beyond FLT3-ITD/TKD and NPM1 such as ASXL1, CEBPA, DNA (cytosine-5) methyltransferase 3A (DNMT3A) and TP53, demonstrating the value of extended gene coverage.

Discussion / Conclusion: The integration of Next-Generation Sequencing (NGS) at Oncode Laboratory has revolutionized mutation detection in AML. The increased NGS usage over the years has uncovered a rich genetic landscape, confirming FLT3-ITD/TKD and NPM1 mutations while unveiling additional critical biomarkers. These findings enhance our understanding of disease mechanisms, aid in prognostication, and guide therapeutic decisions. This study emphasizes the significance of comprehensive molecular profiling for personalized treatment strategies across hematologic diseases. As Oncode Laboratory refines diagnostic methodologies, it contributes to precise genetic profiling, shaping global management strategies for AML. Ongoing research aims to enhance diagnostic precision, integrating insights into clinical practice, ultimately improving outcomes for diverse hematologic conditions.

E-POSTER RESEARCH (CLINICAL)

C23 ELTROMBOPAG IN CHRONIC IMMUNE THROMBOCYTOPENIA: A SINGLE CENTRE EXPERIENCE

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Background: About 40-50% of adults with newly diagnosed immune thrombocytopenia (ITP) will develop chronic disease. The discovery of TPO-RA has changed the treatment landscape of ITP. There is limited data on ITP patients on eltrombopag and its treatment response in resource-limited countries.

Objectives: The objectives of this study were to determine the clinical characteristics of chronic ITP patients on eltrombopag and its treatment pattern and responses.
Materials and Methods: The clinical data of five adult chronic ITP patients who received eltrombopag in Hospital Canselor Tuanku Muhriz (HCTM) UKM from January 2018 to December 2023 were retrospectively analyzed.

Results: All five patients were female with a median age of 36 (20-36) years at initial diagnosis. The median platelet count at diagnosis of ITP was 21 (4 – 57) x 10^9/L. Apart from steroids and intravenous immunoglobulin, the other agents that were given before eltrombopag were azathioprine (five patients), rituximab (five patients), mycophenolate mofetil (two patients) and cyclosporine (two patients). One patient had a splenectomy. The median platelet count before starting eltrombopag was 25 (11 - 57) x 10^9/L. The eltrombopag starting dose for all patients was 25 mg. The median platelet count at week 4 was 136 (55 - 177) x 10^9/L. The maximum dose was 50mg in three patients and 75mg in one patient. However, all patients had a relapse of ITP when eltrombopag had to be discontinued due to cost issues and required rescue medications. The platelet counts increased back to > 50 x 10^9/L whenever eltrombopag was resumed. The median platelet count during the last follow-up was 113 (49 – 329) x 10^9/L. During eltrombopag treatment, 3 patients showed derangement of hepatobiliary laboratory parameters.

Discussion / Conclusion: In our case series, eltrombopag was mainly started after patients had failed two or more agents to maintain platelet counts > 50x 10^9/L. Patients still responded well after eltrombopag recommencement despite interrupted doses. Durable responses could be achieved if patients have sustained supply, and subsequent treatment-free remission may be possible in some ITP patients.

E-POSTER RESEARCH (CLINICAL)

C24 PREVALENCE OF FACTOR XI DEFICIENCY IN BRUNEI DARUSSALAM

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Background: Factor XI (FXI) deficiency is a rare inherited bleeding disorder with a global prevalence of 1 in 1,000,000 people for the autosomal recessive form and 1 in 30,000 for the autosomal dominant. The incidence of FXI deficiency is higher in individual of Ashkenazi Jewish descent where it is estimated to affect 8% of population. A low frequency has been found in many other populations around the world. In FXI deficiency, the severity of the disorder does not always correlate with the residual activity of FXI.

Objectives: The aim of this study is to evaluate prevalence and characteristics of FXI deficiency cases in Brunei Darussalam

Materials and Methods: A retrospective cross-sectional observational study was conducted. Data collection on all patients diagnosed with FXI deficiency from our national electronic medical record between 2013 – 2023 was performed.

Results: Total of 48 patients with Factor XI deficiency were identified. The mean age was 43 years with age range from 16 to 82 years. Among 48 cases, 20 were male and 28 were female and the sex ratio male to female was 0.71. The circumstances of discovery were incidental in 18 patients (37.5%), through family screening in 3 patients (6.3%) and preoperatively in 17 patients (35.4%). Only 10 patients (20.8%) were identified due to bleeding. Out of the 48 patients, 38 patients (79%) had non- bleeding phenotype, 10 patients (21%) had mild bleeding and no patient (0%) had severe bleeding. Factor levels were available in 47 out of 48 patients and out of which 28 patients (59.6%) had factor level <20% and 19 patients (40.4%) had factor level > 20%. From the reported race or ethnic groups, 37 patients (77%) were Malay, 6 patients (12.5%) were Chinese and 5 patients (10.5%) were Dusun. The population of Brunei Darussalam in 2021 is approximately 450 000.

Discussion / Conclusion: Our analysis identified high prevalence of FXI deficiency in Brunei Darussalam at the estimation of 10 per 100 000. The number of cases is likely an underestimation due to under reporting as family screening is not widely done and patients may not be identified unless they require treatment. This high prevalence may be contributed by consanguineous marriages. Genetic testing could characterise and provide better understanding of FXI deficiency cases in Brunei.

E-POSTER RESEARCH (CLINICAL)

C25 THE INCIDENCE OF HAEMATOLOGICAL MALIGNANCIES IN UNIVERSITY MALAYA MEDICAL CENTRE

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Background: Haematological malignancies (HM) are among the top ten most prevalent cancers and accounts for 11% of all cancers diagnosed in Malaysia. However, the epidemiologic distribution of HMs, its types, subtypes and variations in the histopathologic (HP) pattern are scarcely documented in Malaysia for the last two decades. Thus, it is important for these studies to be conducted to accurately revise and highlight the diversity of HM types and clinical outcomes.

Objectives: This study aims to report the institutional data at University Malaya Medical Centre (UMMC) in regards to the epidemiology and survival outcome of patients with HM.

Materials and Methods: A total of 2588 cases diagnosed as HM during the period of 1992 to 2023 were retrieved through the electronic medical records and validated with confirmatory histopathological reports. Patients with HMs were categorized into Myeloid and Lymphoid Malignancies, followed by their diagnosed disease (Leukaemia, Lymphoma, Plasma cell myeloma, Myelodysplastic syndrome (MDS) or Myeloproliferative neoplasm (MPN)), subtypes (B cell or T cell), and variations (Acute or Chronic). Demographic data of age, gender, ethnicity, HP pattern, and survival outcome were recorded and studied. Data was analysed with Student's t-test, Chi-Square test and survival status was assessed using Kaplan Meier analysis.

Results: The median age of the patients was 59 years (range: 4-92 years). The male-to-female ratio was 1.2:1. Majority were Chinese (49.6%) followed by Malay (36.4%), Indian (12.4%), Others (1.3%), and Aborigine (0.3%). 65.5% of malignancy were lymphoid malignancy and 34.5% were myeloid. Among the lymphoid malignancies, 76.6% were lymphomas, 15.6% were plasma cell myeloma, and 7.8% leukaemia. Non-Hodgkin lymphoma (NHL) was the most common lymphoma (84.2%) compared to Hodgkin's lymphoma (17%), where diffuse large B cell lymphoma (54.8%) was the most common NHL subtype. The most common lymphoid leukaemia variation was acute lymphoblastic leukaemia (56.4%) with a B to T cell ratio of 1.3:1. Among the myeloid malignancies, 46.1% were MPN, 40.6% were leukaemia, and 13.3% were MDS. The most common MPN was essential thrombocythemia (47.3%), followed by polycythaemia vera (37.7%), and primary myelofibrosis (15%). The acute to chronic ratio of the myeloid malignancies was 2.4:1. With a median follow-up duration of 49 months and a median survival of 11 months, the overall survival (OS) of myeloid malignancies was significantly better than that of patients with lymphoid malignancies (78.6% vs 66.2%, p =.000) and patient age below 65 had better OS than older age group (73.5% vs 62.3%, p =.000). The main cause of death was infection (41.4%) followed by underlying malignancy (34.8%).

Discussion / Conclusion: The incidence of HM reported in this study is similar to the epidemiology of haematological cancers in reported by Sarawak cancer registry. In comparison, the incidence of lymphoma in Malaysia was higher than other Asian countries. The high mortality from infections warrants further studies exploring infections in HM in order to reduce the mortality rate caused by infectious agents.

E-POSTER RESEARCH (CLINICAL)

C26 CHANGES IN GUT MICROBIOTA PROFILE AFTER STEM CELL TRANSPLANTATION AND ITS IMPACT ON CULTURE NEGATIVE FEBRILE NEUTROPENIA

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Background: In febrile neutropenia (FN), only about 50% of patients had identifiable infectious etiology (ie: culture negative) , with even lower rates in stem cell transplantation (SCT) due to routine antibiotic use. Therefore, FN without an identifiable infection remains challenging to manage due to unknown targets for treatment.

Objectives: We aim to study the microbiota changes in the gut and its impact on FN patients without an identifiable infection.

Materials and Methods: Clinical assessments were conducted daily, whilst faecal samples were collected prior to conditioning regimen, Day 0, Day+7 and 6-month post-transplant in SCT patients (≥18 years). Alpha diversity was computed as richness of species, Shannon, Simpson's, and Faith's phylogenetic diversity indices. The degree of beta diversity index was computed by Permutational Multivariate Analysis of Variance (PERMANOVA) using adonis2 function. Differences in bacterial distribution was determined by Mann-Whitney U. False discovery rates of the resulting p values were corrected using Benjamini-Hochberg algorithm.

Results: In 95 patients, 52 (54.7%) experienced FN where almost half (46.2%) did not yield any positive cultures. The onset of FN was at a median Day+6 (IQR Day+4–Day+7), which resolved after a median of 2.5 (IQR 1–5) days. FN was associated with a higher antibiotic exposure ($p=0.011$), GCSF use ($p<0.001$) and longer hospital stay ($p<0.001$). In FN, although alpha diversity was found to be generally not significant at all timepoints between patients with and without positive cultures, beta diversity indicated significantly difference ($p=0.020$). Patients without an identifiable infection (ie: cultures negative) were found to exhibit a higher relative abundance of gut Rothia at Day+7 ($p=0.003$), corresponding to the onset of FN.

Discussion / Conclusion: We demonstrated evidence of gut microbiota dysbiosis comparing FN patients with and without an identifiable infection. This potentially suggests other aetiologies of FN, such as mucosal barrier injury that may occur due to microbiota dysbiosis, and which could be potential targets for intervention.

E-POSTER RESEARCH (CLINICAL)

C27 THROMBOSIS IN MULTIPLE MYELOMA: A REAL-WORLD EXPERIENCE OVER 15 YEARS IN SARAWAK

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Background: Multiple myeloma (MM) patients are at increased risk of both arterial and venous thrombosis with an incidence rate of 3-12%, which is attributable to patient-, disease- and treatment- related factors.

Objectives: This multi-centred retrospective study was performed to describe the incidence of thrombosis among MM patients in Sarawak, identify risk factors associated with thrombosis and assess their outcome.

Materials and Methods: Patients diagnosed with MM based on International Myeloma Working Group (IMWG) diagnostic criteria from year 2008 to 2022 were identified from hospital registry of four tertiary hospitals in Sarawak. Their case notes were reviewed and those who developed arterial or venous thrombotic events after the diagnosis of MM were identified. Relevant information was tabulated in a case report form and the data was analyzed using SPSS version 22. Descriptive data and significant results of univariate analysis were reported.

Results: A total of 158 patients were diagnosed with MM from year 2008 to 2022, with a male-to-female ratio of 0.95:1. The mean age at diagnosis was 60.9 years (+/-11.6 years), while the mean age of death was 64.2 years (+/-10.7 years). 12 patients developed thrombosis (2 arterial and 10 venous) after the diagnosis of MM, with a cumulative incidence of thrombosis 7.6 per 100 over 15 years. 8 of them (66.7%) developed a thrombotic event within 6 months from MM diagnosis. Majority of them (90.5%) were not on any thromboprophylaxis, including all the 12 patients who developed thrombosis. The median overall survival (OS) was 21 months (range: 0.5-157), and there was no significant OS difference between patients with and without thrombosis. The mean BMI for patients with thrombosis was observed to be significantly higher at 27.34+/-8.17 (n=9) compared to those without thrombosis (23.01+/-4.70, n=91) (p=0.016). Those who received alkylating agents as part of the chemotherapy regimen were also found to be at higher risk of thrombosis (p=0.018). There was no significant increased risk of thrombosis in gender, ethnicity and comorbidities groups.

Discussion / Conclusion: The cumulative incidence of thrombosis in our population of MM patients is lower compared to the Western cohorts despite the majority not being on thromboprophylaxis. Nevertheless, thromboprophylaxis should still be considered in high-risk MM patients, including those who are within 6 months from diagnosis and those who have obese BMI >25 according to the Asia-Pacific obesity classification. Future prospective study should be conducted on a larger scale to gain more insight on thrombosis among our MM patients and to establish thrombosis risk assessment model applicable to our local population.

E-POSTER RESEARCH (CLINICAL)

C28 A MULTICENTER REAL-WORLD STUDY OF OUTCOMES IN PATIENTS WITH RELAPSED/ REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA TREATED WITH A POLATUZUMAB VEDOTIN-BASED REGIMEN IN A COMPASSIONATE USE PROGRAM IN MALAYSIA

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Background: A regimen consisting of polatuzumab vedotin plus bendamustine and rituximab (Pola-BR) was recently approved in Malaysia for relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL). To assess the effectiveness of this regimen in a real-world setting, a multicentric retrospective study was conducted among patients with R/R DLBCL in Malaysia who were granted early access to the Pola-BR regimen under a compassionate use program (CUP).

Case Presentation: Methods: Safety and efficacy data of 23 adult patients with R/R DLBCL who were treated with Pola-BR at nine different centers in Malaysia between September 2019 and February 2021 were analyzed retrospectively. Of the 23 patients, 13 patients received 6 cycles of Pola-BR. The median follow-up was 10 months (1-37). The primary endpoint was complete response (CR) rate and secondary endpoints were overall survival (OS), progression-free survival (PFS) and adverse events (AEs).

Results: The overall response (OR) rate was 56.5%; of these 8 (34.8%) patients achieved a complete response (CR). The 1- and 2-year OS rates of R/R DLBCL following Pola-BR therapy were 51.1%, while the 3-year OS rate was 43.2%. The median OS was 27 months. The 1- and 2- year PFS rates were 48.2% and 41.3%, respectively, with a median PFS of 10 months. Cox proportional hazard regression analysis showed that bulky disease was a significant hazard for development of disease progression. There were no significant hazards identified for OS. A total of 42 treatment related AEs were documented, of which 66.7% (n=28) were of grades ≥3. Haematological and non-haematological AEs were 90.5% (n=38; grade ≤2=13; grade ≥3=25) and 9.5% (n=4; grade ≤2=1; grade ≥3=3) of the total AEs, respectively. One patient died of neutropenic sepsis.

Discussion / Conclusion: Conclusions: Pola-BR can be considered as a potentially efficacious treatment option with a favorable safety profile among the local populations with R/R DLBCL. Further study with a larger sample size and longer follow-up is warranted to confirm the clinical benefits and to identify the predictors of non-responders of this costly treatment regimen.

RESEARCH (LABORATORY) LIST

NO.	TITLE
L1	G6PD Deficiency In Sabahan Neonates: Analysis Of Prevalence And Molecular Spectrum
L2	The Association Of TMPRSS6 Gene Polymorphisms And Haematological Parameters In Overweight And Obese Adults With Iron Deficiency
L3	Digital PCR Chips For BCR::ABL1 Quantification In CML: An Evaluation Study
L4	High Sensitivity Measurable Residual Disease Assay For B Cell Precursor Acute Lymphoblastic Leukaemia: A Validation Exercise
L5	The Role Of MHe Index In Discriminating Thalassaemia Trait From Iron Deficiencyanaemia
L6	Evaluation Fusion Genes Screening Assay (Q30) Kit On Real Time Qualitative PCR QuantStudioTM5 Analyzer For Acute Leukemia
L7	The Impact Of Automated Verification On The Workflow Of Routine Complete Blood Count (CBC)-Single Centre Retrospective Study
L8	Molecular Analysis On Beta Thalassemia Mutations Among Patients In University Malaya Medical Centre
L9	Inhibition Of Stat Signaling Could Suppress Hepcidin Expression Causing Iron Overload In HbE/β-thalassemia Patients
L10	Ikaros Gene (IKZF1) Alterations In Children With B Cell Precursor Acute Lymphoblastic Leukemia (BCP-ALL): Experience From Universiti Malaya Medical Centre
L11	A Look Into The Management Of Critical Results In The Hematology Unit, Hospital Canselor Tuanku Muhriz, Ukm
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L13	KMT2A Gene Rearrangement: 13 Years Of Experiences At The Institute For Medical Research Malaysia
L14	Unravelling The Complexity Of The Definitive Diagnosis Of Compound Heterozygous Of Haemoglobin (Hb) Constant Spring And Hb Pakse; A Study From Institute For Medical Research, Malaysia

E-POSTER RESEARCH (LABORATORY)

L1 G6PD DEFICIENCY IN SABAHAN NEONATES: ANALYSIS OF PREVALENCE AND MOLECULAR SPECTRUM

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Background: Glucose-6-phosphate dehydrogenase deficiency (G6PDd) is a highly prevalent genetic disorder caused by mutations in the G6PD gene. G6PD-deficient individuals are more vulnerable to oxidative stress, leading to acute hemolytic anemia and severe neonatal jaundice. To address the potential risks associated with the condition, Malaysia has implemented a national newborn screening program since the mid-1980s to prevent kernicterus,a bilirubin-induced neurological damage. Sabah, Malaysia's third most populous state, has a high crude birth rate and diverse ethnicities. It is home to an estimated 42 ethnic groups and over 200 distinct sub-ethnic groupings. Despite the importance of identifying G6PD deficiency, there is a dearth of studies on its prevalence and molecular spectrum within the unique Sabahan population.

Objectives: To determine the prevalence of G6PDd in the Sabahan neonate population using a new point- of-care test, the CareStart G6PD S1 Biosensor (S1), and to characterize its molecular spectrum.

Materials and Methods: A total of 4805 neonates delivered at the Sabah Women and Child Hospital, Likas, from September to December 2023 were screened for G6PDd using Fluorescent Spot Test and 544 samples were selected for G6PD assay analysis using the S1. DNA was extracted on all deficient samples by SI and G6PD mutations were analyzed on randomly selected 20 blood samples using a reverse dot-blot flow-through hybridization (RDB-FTH) assay technique via the Hybribio GenoArray Diagnostic kit.

Results: Based on the S1, G6PD-normal samples were used to calculate the adjusted male median (AMM), 30% cut-off, and 80% cut-off threshold values, which showed 8.2 U/gHb, 2.5 U/gHb, and 6.6 U/gHb, respectively. At an 80% cut-off threshold, the prevalence of G6PDd among the Sabahan neonates was 2.8% (135 out of 4805). Five G6PD mutations were found among the selected 20 samples; G6PD Viangchan (871G>A)(70%; n=14), G6PD Coimbra (592C>T) (10%; n=2), G6PD Kaiping (1388G>A)(10%; n=2), G6PD Canton (1376G>T)(5%; n=1), and G6PD Gaeho (95A>G)(5%; n=1).

Discussion / Conclusion: The S1 showed values for the AMM, 30%, and 80% cut-off thresholds that were closely identical to those reported in previous studies. A high prevalence of G6PDd was found among the Sabahan neonates. The population demonstrated a significant molecular heterogeneity for G6PDd.

E-POSTER RESEARCH (LABORATORY)

L2 THE ASSOCIATION OF TMPRSS6 GENE POLYMORPHISMS AND HAEMATOLOGICAL PARAMETERS IN OVERWEIGHT AND OBESE ADULTS WITH IRON DEFICIENCY

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Background: Obesity is increasingly recognized as a socioeconomic challenge in Malaysia, and recent evidence suggests that it amplifies the likelihood of developing iron deficiency. Research on the association of TMPRSS6 gene polymorphisms and iron deficiency (ID) and iron deficiency anaemia (IDA) in overweight and obese adults suggests a potential link between genetic variations and iron metabolism. TMPRSS6 encodes a protein involved in regulating iron homeostasis by inhibiting hepcidin, a key regulator of iron absorption and recycling. Several studies have explored the relationship between TMPRSS6 gene polymorphisms and iron status, particularly in populations with conditions like obesity, where iron deficiency may be more prevalent due to various factors such as chronic inflammation and adiposity-related alterations in iron metabolism. This study aims to investigate the relationship between TMPRSS6 gene polymorphisms and haematological parameters in overweight or obese individuals with iron deficiency.

Objectives: This study aims to investigate the relationship between TMPRSS6 gene polymorphisms and haematological parameters in overweight or obese individuals with iron deficiency.

Materials and Methods: A total of 62 overweight and obese subjects who fulfilled the inclusion criteria were recruited from the Primary Care Medicine clinic at Pusat Pakar Perubatan UiTM (PPPUiTM), Sungai Buloh. All subjects were subjected to anthropometric measurements (weight, height, BMI, waist, and hip circumference), full blood count and iron profiles. The genomic DNA was collected and analysed via the rhAmp SNP genotyping assay (qRT-PCR) to detect SNPs on the TMPRSS6 gene. Association between identified SNPs, haematological parameters and iron profiles were analysed via Pearson correlation analysis, and one-way ANOVA analyses.

Results: Approximately, 51.6% of overweight/obese subjects were iron deficient (ID/IDA) and 48.4% were non-iron deficient (non-ID/IDA). When compared to the non-ID/IDA group, the ID/IDA group had significantly lower levels of haemoglobin, Hct, MCV, MCH, serum iron, serum ferritin and had significantly higher levels of serum transferrin receptors (sTfR) and total iron binding capacity (TIBC) which indicate true ID. Genotyping analysis showed that rs855791 exhibits a significant association with the ID/IDA group. Allele A of the rs855791 variant was identified as the risk allele with higher odds of developing ID and significantly associated with low levels of haemoglobin, Hct, MCHC, and serum iron levels.

Discussion/ Conclusion: This study presents a recent report on the association of TMPRSS6 SNP specifically the rs855791 variant with the risk of ID in overweight and obese adults. A significant association of homozygous A/A of rs855791 with ID/IDA group was observed in which the A allele was identified as the risk allele. Carriers of homozygous A/A were also observed to be significantly associated with a decrease in haemoglobin, MCV, MCHC and serum iron levels.

E-POSTER RESEARCH (LABORATORY)

L3 DIGITAL PCR CHIPS FOR BCR::ABL1 QUANTIFICATION IN CML: AN EVALUATION STUDY

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Background: Monitoring treatment response for chronic myeloid leukemia (CML) poses great challenges due to the need for accurate and sensitive quantification of BCR::ABL1 at specific treatment milestones. Despite efforts to standardize qRT-PCR for BCR::ABL1 monitoring, variations persist due to inherent technology variability. A more quick, precise and sensitive method is required to detect measurable residual disease (MRD) in clinical settings and to aid a successful treatment-free remission (TFR). Digital quantitative PCR is a promising approach to detect MRD, as it has demonstrated improved sensitivity and precision for quantifying BCR::ABL1. Digital PCR (dPCR) is less affected by variations in amplification efficiency and allows for precise gene detection.

Objectives: To compare and verify BCR::ABL1 quantitative results of Optalane's Dr. PCR™ and conventional quantitative RT-PCR (qRT-PCR) for routine monitoring.

Materials and Methods: We investigated 27 specimens, comprising 21 clinical samples from CML patients and six EQA samples with varying BCR::ABL1 levels ranging from below 0.0032 IS% to over 0.0032 IS%, utilizing both our routine qRT-PCR kit and Optalane's Dr. PCR BCR::ABL1 Major IS Detection kit. Approximately 600-1000µg of extracted RNA, in a reaction mixture of 30uL, was directly applied to the Dr. PCR cartridge and tested on the LOAA system. The resulting data were then used to calculate international scale (IS%) and molecular response (MR) levels. Correlation analyses were conducted on the 27 samples using both methods. The reproducibility of the dPCR assay was evaluated using six clinical samples and two EQA samples. Each sample underwent testing with two replicates per run by an independent operator at different time points. Reproducibility was assessed for each sample based on the provided MR (observed raw values) as the outcome variable for the analysis.

Results: Correlation analysis for 27 samples showed that measured values from both qPCR and Dr. PCR were closely correlated with the R2 of 0.989. These findings indicate that Optolane's Dr. PCR is comparable to qRT-PCR in quantifying BCR::ABL1 transcript levels. The average %CV for MR 4.0 and above is 7.91% while below MR 4.0 is 26.9%.

Discussion / Conclusion: Optolane's Dr. PCR technology is a real-time dPCR reaction in a single cartridge. This assay is independent of a standard curve and can be completed in an average analysis time of just 1.5 hours. In this study performance between operators showed low variability in dPCR. Monitoring of BCR::ABL1 MRD by Dr. PCR™ kit appears to be a safe and feasible method for clinically assessing treatment effectiveness and TFR application. This approach enables the quantification of BCR::ABL1 transcripts without requiring a conversion factor, as it utilizes absolute measurements. In summary, our evaluation of Optolane's LOAA system Dr. PCR technology, indicates satisfactory analytical performance. This assay holds promise as a reliable tool for monitoring minimal residual disease in CML patients.

E-POSTER RESEARCH (LABORATORY)

L4 HIGH SENSITIVITY MEASURABLE RESIDUAL DISEASE ASSAY FOR B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKAEMIA: A VALIDATION EXERCISE

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Background: Measurable residual disease (MRD) is a strong and independent predictor for risk of relapse and long-term survival in childhood acute lymphoblastic leukaemia (ALL). EuroFlow group is the world leader in FCM-based MRD detection and its approach is standardised, widely adapted and referred to. We formulated an FCM-based two tube, eight-colour individual monoclonal antibody assay for BCP-ALL MRD detection by adapting EuroFlow approach combined with own centre prior experience. This study was aimed for in-house validation of the assay.

Objectives: To perform in-house validation for BCP-ALL FCM-based MRD assay.

Materials and Methods: Bone marrow (BM) samples from six non-leukaemic adult patients and three newly diagnosed paediatric BCP-ALL patients were utilised. The first pull of ≤3mL of BM aspirate was used to avoid haemodilution and processing was carried out within 24 to 48 hours to optimise sample yield. Erythrocyte bulk-lysis protocol was used in sample preparation to achieve FCM acquisition of five millions nucleated cells. Two tube, eight-colour individual monoclonal antibody panels for BCP-ALL MRD consisted of backbone markers CD20 V450/CD45 V500/CD34 PERCPCY5.5/ CD19 PECY7/CD10 APC/CD38 APC-H7 in both tubes with CD58 FITC/CD66c+CD123 PE and CD81 FITC/CD73+CD304 PE in Tube 1 and 2 respectively. Antibody titration was performed for CD66c+123 combo markers to achieve optimum mean fluorescence intensity. Limit of blank (LOB) analysis was performed on the three non-leukaemia BM samples. Areas of commonly encountered MRD events were scrutinised with the highest number selected as LOB for each sample. Limit of detection (LOD) was derived from LOB using mathematical calculation. Lower limit of quantitation (LLOQ) was determined by performing consecutive fixed ratios, serial dilution of three BCP-ALL in non-leukaemic adult bone marrow samples to achieve target MRD events. Each dilution was performed in triplicate to obtain coefficient of variations (CV). Sample analysis was performed on FACSLyrics (Becton Dickinson, San Jose, CA) and raw data was assessed on FACSDiva software. A world renowned MRD expert was invited to review the validation results.

Results: We obtained the limit of blank (LOB) and limit of detection (LOD) as 9 and 12 events respectively. The lower limit of quantification (LLOQ) was selected at 48 events as it gave the desired CV of 9.6%, yielding an assay sensitivity of 1 x 10-5 (0.0001%). To date, seven of 27 (7/27, 25.9%) BM samples sent for end of induction MRD assessment using the new assay, were found to be MRD positive. CD73+CD304 overexpressions were the most commonly encountered leukaemia-associated immunophenotypes, while CD38 under expression was most useful for Different from Normal (DfN) marker.

Discussion / Conclusion: The LOB, LOD and LLOQ obtained were similar to other prior studies which were generally taken at 10, 20 and 50 respectively. This assay was able to achieve the desired high sensitivity of 1 in 10-5 (0.001%) events. The combo markers, for example CD73+CD304 improved sensitivity of the assay as they were relatively stable during treatment. In conclusion, an assay validation is crucial for an in-house standardised FCM-based MRD assay to ensure reproducible and reliable laboratory procedures and results to match the desired assay sensitivity level used in treatment protocols.

E-POSTER RESEARCH (LABORATORY)

L5 THE ROLE OF MHe INDEX IN DISCRIMINATING THALASSAEMIA TRAIT FROM IRON DEFICIENCYANAEMIA

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Background: Thalassemia Trait (TT) and Iron Deficiency Anaemia (IDA) are both associated with the microcytic anaemia. RBC indices had been proposed as preliminary screening tools to differentiate between TT and IDA before proceeding to hemoglobin (Hb) analysis or serum iron testing, but no algorithms provided accurate and acceptable discrimination. Application of extended parameters from Retic Channel such as %Micro-R and %Hypo-He are available on the Sysmex XN 1000 haematology analyzer. A MHe index is a derived parameter from %Micro-R and %Hypo-He.

Objectives: The objective of this study was to evaluate the efficacy of MHe index in differentiating TT from IDA.

Materials and Methods: A total of 155 adult samples in EDTA tubes were analyzed in eight months duration. 61 patients were reported to have TT which consisted of α-thalassemia, β-thalassemia, Hb E and Hb C traits while another 61 had IDA. Additionally, 33 samples from healthy subjects were included as controls. Red cell parameters (RBC, Hb, HCT, MCV, MCH, MCHC, RDW) and extended parameters (%Micro R, and %Hypo He) were acquired from the Sysmex XN1000 Haematology Analyzer (Sysmex, Japan), while the MHe index (%Micro-R - %Hypo-He), was calculated manually. Mann-Whitney test was used to compare the MHe index of TT and IDA. Using MedCalc statistical software to determine the MHe-index cut off to advocate TT using Receiver Operator Characteristic (ROC) analysis.

Results: There was a statistically significant difference in MHe index between TT and IDA ($p<0.05$). The ROC Curve analysis identified MHe index >12.5 as the optimal cut-off for TT, demonstrating an area under the curve (AUC) of 0.707, a sensitivity of 68.85%, and a specificity of 73.77%.

Discussion / Conclusion: This study managed to obtain an AUC of 0.707 which conform to the range of AUC of 0.7-0.9 for MHe index to be considered as moderately acceptable as a screening tool. The MHe index could be highly beneficial and could play a decisive role in guiding the selection of confirmatory laboratory tests, leading to a more accurate diagnosis and treatment.

E-POSTER RESEARCH (LABORATORY)

L6 EVALUATION FUSION GENES SCREENING ASSAY (Q30) KIT ON REAL-TIME QUALITATIVE PCR QUANTSTUDIOTM5 ANALYZER FOR ACUTE LEUKEMIA

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Background: Acute leukemia is a life-threatening hematological malignancy necessitating prompt administration of treatments hence timely and accurate diagnosis is imperative.

Objectives: The study aims to evaluate the reliability of a commercial fusion genes screening assay kit based on real-time PCR (RT-PCR) principle using QuantStudioTM5 analyzer to detect fusion gene rearrangements of newly diagnosed acute leukemia cases.

Materials and Methods: A total of 36 samples of consented patients newly diagnosed with acute leukemia were collected from peripheral blood and bone marrow specimens. RNA was extracted using QIAamp RNA Blood Mini Kit and the concentration was determined by Nanodrop spectrophotometric with absorbance ratio (A260/A280) between 1.8-2.2 and was standardized at 100 ng/ul for cDNA synthesis by PCR thermal cycler machine (Eppendorf, Germany). Subsequently, the amplified cDNA was added into 96-well plate and mixed well with Q30 reagents which comprises of specific fluorescence-labelled primers and probes for PCR amplification. The Q30 kit (QuanDx, USA) also contained reagents for cDNA synthesis, negative, positive and GUSB gene internal controls. Detection of fusion gene transcript was performed on RT-PCR QuantStudioTM5 analyzer (AppliedBiosystems, USA). The analyzer used 6-decoupled filters that supported FAM, VIC/HEX, ROX and Cy5 fluorescent dyes used in Q30 kit that are excitable between 455-672nm and emits between 505-723nm wavelengths. The amplification plot was analyzed using QuantStudio™5 Design and Analysis Desktop Software. The software measured the amplification targets and generated a standard curve using standard dilution series in test samples, which was used to interpolate the absolute quantity of targets in test samples. A positive reaction was determined as the basement level for the determination of Cq values between 5.0 and 30.0 with a sigmoid-shaped amplification signal.

Results: Twenty-two of 36 samples tested were positive for fusion gene transcripts and the commonest was t(9;22)(q34;q11) BCR-ABL1 (6/22), followed by t(15;17)(q24;q11) PML-RARA (3/22), t(12;21)(p13;q22) ETV6-RUNX1 (3/22), t(8;21)(q22;q22) RUNX1-RUNX1T1 (3/22), t(10;11)(p12;q23.3) KMT2A-MLLT10 (2/22), t(1;19)(q23;p13) TCF3-PBX1 (2/22), del(1)(p32) SIL-TAL1 (1/22), t(9;11) (p21.3;q23.3) MLL-AF9 (1/22) and t(3,21)(q26;q22) RUNX1-MECOM (1/22). The Cq values for fusion gene transcripts detected were between 9.0 to 28.0. All 22 positive had successful amplification of the positive control gene transcript detected by FAM, VIC/HEX and ROX channel. Three positive samples were also repeated three times for precision analysis and the results were reproducible. Fourteen test samples were found to be negative for any fusion gene transcripts. All the results were compared with cytogenetics and conventional reverse transcriptase multiplex-ARMS for BCRABL1 with concordance rates of 99.9% and 100.0% respectively.

Discussion / Conclusion: Q30 kit PCR reactions analyzed on QuantStudioTM5 reproducibly gave accurate and reliable results for the qualitative detection 30 fusions gene transcripts of patient samples in each single run. The internal control GUSB gene detection served as integrity and performance checker of both cDNA and PCR reaction mix. The sample preparation was straightforward, but adequate care must be practiced to prevent sample cross-contamination. The QuantStudioTM5 analyzer was user friendly and provided a reliable RT-PCR system with simple visualization and analysis of the results.

E-POSTER RESEARCH (LABORATORY)

L7 THE IMPACT OF AUTOMATED VERIFICATION ON THE WORKFLOW OF ROUTINE COMPLETE BLOOD COUNT (CBC) – SINGLE CENTRE RETROSPECTIVE STUDY

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Background: Complete blood count (CBC) analysis is one of the most common routine tests performed on patients in hospitals. However, the manual validation on CBC analysis is laborious and time-consuming. The aim of this study was to evaluate the impact of introducing automated verification steps in routine CBC analysis by assessing the turnaround time (TAT) and overall workload.

Objectives: The aim of this study was to evaluate the impact of introducing automated verification steps in routine CBC analysis by assessing the turnaround time (TAT) and overall workload.

Materials and Methods: The data used were CBC samples collected retrospectively from October 2023 to December 2023 in the routine hematology unit of laboratory medicine department, University Malaya Medical Centre. Inclusion criteria were based on customized rules created for fully automated test validation for routine samples using Sysmex® XN9000 series middleware (Sysmex Corp., Kobe, Japan) as well as the laboratory information system (LIS). In these customized rules, analytical measurement ranges (AMR), delta check, critical values and all analytical flags from the analyser were used as part of the algorithm in designing the auto-verification step. The duration of the complete blood count (CBC) analysis ranges from acceptance by the laboratory to verification of the results. A t-test for hypothesis testing was applied to determine the changes in manual and automated validation to determine their significance. The change in the data is considered significant if the P value <0.05 at a 95% confidence interval.

Results: A total of 49,819 CBC profiles were analyzed. The hospital quality system targets a CBC TAT of less than 90 minutes. The study indicates a significant difference in turnaround time between auto verification (mean = 6.17 minutes) and manual validation (mean = 38.26 minutes) for CBC profiles, with a large effect size (d = 2.38), suggesting a substantial impact on efficiency. The p-value (<.001) suggests strong evidence against the null hypothesis, supporting the statistical significance of this difference.

Discussion / Conclusion: The delivery time for routine CBC test was considerably shortened by the automatic verification method. This enabled more effective detection of hematologic abnormalities during slide review by laboratory technicians or specialists on CBC results that failed the customized auto-verification rules. The reduction of the number of samples needed for manual slide review, provides the laboratory technicians or specialists, ample time to assess for any haematological abnormalities. In turn, this ensures the achievement of good-quality reports. The auto-verification rule has also improved the overall workload on routine haematology and provides a timely assessment that improves overall patient management.

E-POSTER RESEARCH (LABORATORY)

L8 MOLECULAR ANALYSIS ON BETA THALASSEMIA MUTATIONS AMONG PATIENTS IN UNIVERSITY MALAYA MEDICAL CENTRE

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Background: Beta-thalassemia is one of the common inherited disorders characterized by reduced or absent synthesis of beta-globin chains of hemoglobin. The prevalence of beta-thalassemia mutation in Malaysia is influenced by the diverse ethnic composition of the population, consisting primarily of Malays, Chinese, Indians, and other ethnic groups. This genetic disorder poses a considerable burden on affected individuals and their families, as well as on the healthcare system.

Objectives: This study aim to characterize the spectrum of beta thalassemia mutations in terms of prevalence, types and racial distribution among the thalassemia patients at University Malaya Medical Centre (UMMC).

Materials and Methods: Fifty one cases of suspected Beta thalassemia mutations sent to the Molecular and Genetic Analysis Laboratory (MGAL) of University Malaya Medical Centre from 2018 to 2023 are analyzed retrospectively. The clinical information and hematological parameters are evaluated. All cases are subjected to HBB gene sequencing analysis. We conducted a combined gap polymerase chain reaction (PCR) followed by Sanger multiplex minisequencing analysis. Two sets of sequencing primers are used which are PCR I forward and reverse primers (5'- ACGGCTGTCATCACTTAGAC-3' and 5'-CTCCCCTTCCTATGACATGA-3' respectively) and PCR II forward and reverse primers (5'-GTGTACACATATTGACCAAATC-3' and 5'-AATGCACTGACCTCCCACAT-3' respectively). The reverse sequencing product from PCR I is 696 bp which spans exon 1, intervening sequence (IVS) I, and exon 2. PCR II's reverse sequencing product is 719 bp long and covers a portion of IVS II and all of exon 3. Combined together, the forward and reverse sequencing data from PCR I and PCR II encompass virtually all known point mutations and small deletions of Beta thalassemia.

Results: Out of fifty one samples analyzed, Malay constitutes 53% of cases followed by Malaysian Chinese (29%), Indian (6%) and other racial groups (12%). A total of 18 different beta thalassemia mutations are identified. The most common mutations are Hb E [CD 26 (CAG- >AAG)] (41%), followed b y IVS-II-654 (C->T) (10%) and -28 (A->G), IVS I-5(G>C), CAP+1(A->C) Silent mutation, 6% respectively. CAP+1 [A>C] (HBB:c.-50A>C) is a rare silent Beta thalassemia mutation which shows borderline hemoglobin (Hb), mean corpuscular volume (MCV) and Hb A2 levels in a carrier patient. Hb E [CD 26 (CAG->AAG)], IVS I-5(G>C) and IVS I-1(G>T) constitute for about 85 % of Beta thalassemia mutation in Malay followed by Hb Malay [CD 19 (A > G)] around 11% and polyadenylation signal (poly A) (AATAAA->AATAGA) 7%. Hb E, IVS I-5(G>C), polyadenylation signal (poly A) (AATAAA->AATAGA) and Hb Malay have Beta+ phenotype while IVS I-1 (G>T) have Beta0 phenotype. Beta globin mutations seen in Malaysian Chinese are CD 41/42 (-TTCT), CD 17 (A->T), -28 (A->G) and IVS-II-654 (C->T) which constitute around 87 % of Beta thalassemia mutation. All have Beta0 phenotype except for -28 (A->G) and IVS-II-654 (C->T) which exhibits Beta+ phenotype. In the other racial groups, the most common mutation found is Hb E [CD 26 (CAG->AAG)] and HB S which are 33% respectively.

Discussion / Conclusion: Our study focused on genetic mutations within the beta-globin gene among various ethnic groups in Peninsular Malaysia. Notably, we identified a common set of 4 to 5 mutations within each ethnic group, constituting more than 95% of observed mutations. Our findings align with those reported in local studies, particularly in the context of the Malay and Chinese populations. This convergence in mutation patterns suggests a shared genetic heritage and emphasizes the potential significance of these mutations in the

E-POSTER RESEARCH (LABORATORY)

L9 INHIBITION OF STAT SIGNALING COULD SUPPRESS HEPCIDIN EXPRESSION CAUSING IRON- OVERLOAD IN HBE/β-THALASSEMIA PATIENTS

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Background: Beta thalassemia (β-thalassemia) is a genetic disorder due to mutation of the beta- globin gene. Down-regulation of hepcidin (HEPC) results in iron overload. Signaling pathway such as Janus kinase/signal transducers and activators of transcription (JAK/STAT) regulate many cell activities. Inhibition of JAK/STAT signaling pathways was associated with the downregulation of HEPC expression in mouse hepatocellular carcinoma. However, the inhibitory effect mechanism of HEPC on HbE/β-thalassemia patients has not been investigated.

Objectives: This study aimed to investigate the effect of STAT pathways on the HEPC expression and other target genes in HbE/β-thalassemia patients in Hospital Sultanah Nur Zahirah, Terengganu, Malaysia.

Materials and Methods: Serum HEPC level in 65 HbE/β-thalassemia patients (pretransfusion) and 65 parents compared to 130 students from Universiti Sultan Zainal Abidin, Terengganu, as healthy controls, was investigated using Human HEPC ELISA Kit (cat. no. E-EL-H0077; Elabscience Biotechnology Co., Ltd.) according to the manufacturer's protocol. Moreover, six samples from each group (HbE/β-thalassemia patients, parents, and healthy controls) were selected for molecular analysis. The expression of HEPC and other target genes was evaluated using RT-qPCR. The phosphorylation status and the levels of STAT5 was investigated using Jess Western analysis.

Results: The serum HEPC level was decreased significantly ($p<0.001$) in HbE/β-thalassemia patients and their parents compared to the healthy controls (published data). There was also a sharp decrease of HEPC expression in HbE/β-thalassemia patients and their parents (published data). The protein analysis revealed a significant inhibition ($p<0.001$) of STAT5 phosphorylation in HbE/β-thalassemia patients and their parents.

Discussion / Conclusion: For the first time, the findings of this study revealed a significant decrease in the protein level and phosphorylation of STAT5 in HbE/β-thalassemia patients and their parents, which was associated with dramatically downregulated HEPC, resulting in iron overload in HbE/β- thalassemia patients. Therefore, the activation of STAT5 signaling could be a potential therapeutic target for managing iron overload and ineffective erythropoietic (IE) in HbE/β-thalassemia patients.

Keywords: HbE/β-thalassemia; STAT signaling;

E-POSTER RESEARCH (LABORATORY)

L10 IKAROS GENE (IKZF1) ALTERATIONS IN CHILDREN WITH B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA (BCP-ALL): EXPERIENCE FROM UNIVERSITI MALAYA MEDICAL CENTRE

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Background: IKAROS, a zinc finger DNA-binding protein, is a key transcription factor in the development of mature lymphocytes. Alterations in IKZF1 can lead to a loss of normal IKAROS function to precursor B cells. IKZF1 deletion (IKZF1del) and additionally, IKZF1del-plus (IKZF1del with at least one additional deletion in PAX5, CDKN2A, CDKN2B, or BTG1) in BCP-ALL are associated with treatment resistance and inferior outcomes. The presence of IKZF1 alterations has been incorporated in therapeutic strategies of many childhood ALL regimens where treatment is intensified for this poor prognostic feature. Here we report our experience in detecting IKZF1 copy number variations (CNV) in children newly diagnosed with BCP-ALL in our laboratory.

Objectives: Here we report our experience in detecting IKZF1 copy number variations (CNV) in children newly diagnosed with BCP-ALL in our laboratory.

Materials and Methods: Genomic DNA was extracted from the bone marrow mononuclear cells at diagnosis. Multiplex Ligation-dependent Probe Amplification (MLPA) was then performed using the SALSA MLPA Probemix P335 ALL-IKZF1 according to manufacturer's instructions (MRC Holland, The Netherlands). Quantitative and qualitative evaluation of the tested genes were determined by capillary electrophoresis and analyzed using Coffalyser.Net software. The ratios obtained were normalized against reference samples from bone marrow mononuclear cells of male patients in complete remission (measurable residual disease < 1 x 10-4). Ratios of ≤ 0.7, 0.7 < to ≤ 1.0, and > 1.3 were considered to indicate deletion, normal, and duplication, respectively.

Results: Over a 24-month period from 1st Jan 2022 to 31st Dec 2023, 75 children (aged <18 years) with newly diagnosed B-cell precursor ALL (BCP-ALL) were screened for IKZF1 CNV using MLPA. Nine (12%) children exhibited IKZF1 gene deletion, comprising 5 children (56%) with IKZF1del-plus status and 4 (44%) children with IKZF1del alone. Among the IKZF1del-plus patients, deletions (individually or collectively) were also observed in PAX5 (n=3, 60%), CDKN2A (n=3, 60%), CDKN2B (n=2, 40%), and BTG1 (n=2, 40%). Of the 9 patients with IKZF1 gene deletion (IKZF1del or IKZF1del-plus), 3 (33%) were also positive for BCR::ABL1 fusion transcript, while 2 (22%) exhibited BCR-ABL1-like transcriptomics in separate analyses. The main challenges faced in obtaining accurate results in this assay arise from the low blast percentage in diagnostic marrow (< 50%), which might give rise to indeterminate results or false negatives. In our study, 8 (11%) samples had blast percentage < 50%, resulting in normal or indeterminate findings in 5 (63%) of the samples. In cases with low diagnostic blast percentages, clinicians were strongly advised to interpret the findings with caution according to the clinical contexts of the patients.

Discussion / Conclusion: Whilst IKZF1 aberrations can also be detected using polymerase chain reaction (PCR), fluorescence in situ hybridization (FISH), and sequencing platforms, we only relied on MLPA assay as it is currently the gold standard for screening IKZF1 deletions. We have successfully implemented MLPA-based screening for IKZF1 CNV in children with BCP-ALL into our local diagnostic laboratory tests. Detection of these important prognostic risk factors will guide clinicians on improving treatment precision and outcomes

E-POSTER RESEARCH (LABORATORY)

L11 A LOOK INTO THE MANAGEMENT OF CRITICAL RESULTS IN THE HEMATOLOGY UNIT, HOSPITAL CANSELOR TUANKU MUHRIZ, UKM

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Background: Hospital accreditors are placing increasing emphasis on the timeline for reporting critical laboratory results to caregivers, as it is of crucial importance in safeguarding patient safety. The critical result report is defined by MS ISO 15189 as the reporting of examination results that fall within established critical decision limits. The critical decision limit is a result that indicates a higher risk of adverse clinical outcomes or is diagnostic for the presence of a specific disease. The aim of this study was to analyze the critical value (CV) data in the Hematology Unit, HCTM UKM, and to describe the critical values for different parameters as well as the notification process.

Objectives: The aim of this study was to analyze the critical value data in Hematology Unit, HCTM UKM and to describe the critical values for different parameters as well as the notification process.

Materials and Methods: We reported and analyzed data on the notification of critical values from August to December 2023 to fulfill the MSQH accreditation. The parameters chosen for CV notification were white blood cells, platelets, hemoglobin, and the International Normalized Ratio (INR). A test result that was significantly outside the normal range and that required immediate communication was considered a "critical value". The standard in MSQH was to notify any CV within 30 minutes after result validation to the requesting health providers. The mode of communication was via verbal calls. All information about the receivers and time was recorded in a notification form. Notifications that failed to be communicated were also recorded.

Results: A total of 128 critical values were reported from August to December 2023, 95 samples (74%) of which were from the Emergency Department, and another 33 (26%) were from inpatient wards or outpatient clinics. The parameters most commonly notified were low hemoglobin < 6.0 g/dl (54/128, 42.2%) and low platelet counts <20 x 109/L (24/128, 18.8%). A total of 77/128 (60.2%) cases that had critical values were subjected to an immediate peripheral blood film morphologic assessment. While 96% of the results were successfully notified within the time, 4% of test reports failed to reach the requesters, mainly due to the inability of laboratory staff to reach the wards or clinics by phone and also incomplete request forms lacking contact person details.

Discussion / Conclusion: Notification of critical results is one of the key performance indicators (KPI) in MSQH Standard 15: Pathology Services, and our laboratory monitors the KPI monthly with a target of 100% achieved. As the analyzed data shows that 5/128 (4%) of results were unable to inform the requester, our hospital needs to improve awareness of the need for CV notification to all laboratory staff and health caregivers. We also need to develop guidelines in order to implement the notification process involving both sides. The parameters most commonly notified for critical values were low hemoglobin and low platelets, and usually they reflected a full blood film test, showing the importance of efficient notification. According to MOH guidelines, the process of notification requires a read-back from the requester, which we can implement as a required function with the LIS upgrade. The chain of notification CV procedure requires effective communication. The weakness of this process may lead to

E-POSTER RESEARCH (LABORATORY)

L12 MINDRAY'S BC-6200 AND BC-760 HAEMATOLOGY ANALYSERS: A COMPREHENSIVE EVALUATION STUDY IN A NEW AND UPCOMING UNIVERSITY TEACHING HOSPITAL

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Background: Mindray's BC-6200 and BC-760, as state-of-the-art haematology analysers, deliver precise quantification of blood parameters and a comprehensive six-population leukocyte differential (6- diff). Both of the analysers use the same method which are impedance, flow cytometry, and fluorescence technique. The only major difference is that the BC-6200 has a reticulocyte channel, while the BC-760 does not. This study aims to evaluate and compare these two newly-installed analysers and study the performance in terms of accuracy, reliability, and usability for routine clinical use in Hospital Pengajar Universiti Sultan Zainal Abidin's new medical laboratory setting.

Objectives: This study aims to evaluate these two analysers, study the performance in terms of accuracy, reliability, and usability for routine clinical use in Hospital Pengajar Universiti Sultan Zainal Abidin's new medical laboratory setting.
Materials and Methods: This study evaluated the two automated haematology analysers using blood samples collected in EDTA tubes, taken from random healthy individuals (n = 42). The primary assessment parameters include precision, carry-over, and correlation, providing an overview of each analyser's capabilities.

Results: For precision, all the parameters for both analysers performed well within allowable limits of performance in the parameters such as white blood cells (WBC), red blood cells (RBC), haemoglobin (HGB), mean cell volume (MCV), platelet (PLT). CV% for precision for analyser BC-6200 and BC-760 are as follows; WBC 1.35% & 1.36% (acceptable limit <2.5%), RBC 0.89% & 1.49% (acceptable limit <1.5%), HGB 0.56% & 0.68% (acceptable limit <1.0%), MCV 0.37% & 0.23% (acceptable limit < 1.0%), PLT 2.25% & 1.13% (acceptable limit < 4.0%). In terms of carry-over performance, both analysers demonstrated exceptional results, with less than 0.1% carry-over, indicating negligible to no carry-over. Both analysers also demonstrated a strong correlation when compared with each analyser in most tested parameters ($r \geq .97$). Exceptions to this high correlation were noted in Mono% ($r = 0.9328$) and platelet count (PLT) ($r = 0.9475$).

Discussion / Conclusion: The study highlights that both Mindray BC-6200 and BC-760 are reliable for routine hematologic assessments. The minor differences in performance metrics could be clinically insignificant for most standard parameters but may be relevant in specific clinical scenarios. The study performed on both the BC-6200 and BC-760 instruments demonstrates strong performance with good precision and a high level of correlation, aligning well with our standards of operation of a brand-new university hospital.

E-POSTER RESEARCH (LABORATORY)

L13 KMT2A GENE REARRANGEMENT: 13 YEARS OF EXPERIENCES AT THE INSTITUTE FOR MEDICAL RESEARCH MALAYSIA

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Background: Leukemia with rearrangements of the KMT2A gene, previously referred to as mixed lineage leukemia (MLL), is characterized by 11q23 fusions and is renowned for its high aggressiveness. KMT2A gene can be considered a highly 'promiscuous' oncogene, as it has been found to partner with over 90 different chromosomal translocation regions on 11q23. This KMT2A gene rearrangement has been associated with poor prognosis outcome. The main objective of the study is to determine the frequency of KMT2A gene rearrangement and its associated clinical characteristics at the Institute for Medical Research.

Objectives: The main objective of the study is to determine the prevalence of KMT2A gene rearrangement at the Institute for Medical Research.

Materials and Methods: We retrospectively analysed our data from 2010 until 2023. All the cases that showed the positive result for KMT2A gene rearrangement were included in the study. The demographic and clinical profiles of all individuals with positive KMT2A fusion gene findings were gathered. The RNA was isolated utilizing the QIAamp RNA Blood Mini Kit. The KMT2A fusion gene was detected using either reverse transcriptase polymerase chain reaction (PCR) with Hemavision 28N or real-time PCR with Quandx Q30

Results: In this study, we identified a total of 242 cases positive for KMT2A gene rearrangement. The gender distribution showed a ratio of 1 male to 1.1 females, with 48% males and 52% females. Among ethnicities, individuals of Malay descent exhibited the highest frequency of positive KMT2A gene rearrangement at 52%, followed by Chinese at 23%, others at 21%, and Indian at 4%. Furthermore, our findings indicate that KMT2A gene rearrangement was most commonly observed in individuals under 18 years of age, accounting for approximately 55% of cases. Conversely, individuals over 60 years of age exhibited the lowest frequency at 3%.The predominant fusion gene partner seen in this study was KMT2A::MLLT3 comprising of 26% follow by KMT2A::AFF1 at 22% and KMT2A::AFDN at 17%.

Discussion / Conclusion: Our study demonstrates that the frequency distribution of age groups and fusion partner genes involved in KMT2A gene rearrangement aligns closely with several previous studies. Notably, KMT2A gene rearrangement is predominantly observed in pediatric age groups rather than adults. The most frequently reported fusion partners include MLLT3, AFDN, AFFI, MLLT1, and MLLT10. Our data analysis further supports these findings. Understanding the specific fusion partner involved can provide crucial information regarding the aggressiveness of the leukemia, response to treatment, and overall prognosis. Additionally, it may guide clinicians in tailoring personalized therapeutic approaches and implementing more effective surveillance protocols to manage the disease progression effectively. Therefore, while not obligatory, the identification of the fusion partner is highly desirable as it holds the potential to significantly impact patient care and outcomes.

E-POSTER RESEARCH (LABORATORY)

L14 UNRAVELLING THE COMPLEXITY OF THE DEFINITIVE DIAGNOSIS OF COMPOUND HETEROZYGOUS OF HAEMOGLOBIN (HB) CONSTANT SPRING AND HB PAKSE; A STUDY FROM INSTITUTE FOR MEDICAL RESEARCH, MALAYSIA

Main Author:
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Background: Haemoglobin (Hb) Paksé (codon 142, TAA>TAT) was first reported in Thailand individuals. The incidence of Hb Paksé was never reported in Malaysia. The true incidence of Hb Paksé might be under reported due to misidentifying some cases as Hb Constant Spring (Hb CS, codon 142, TAA>CAA) since both abnormal haemoglobins had similar chromatographic pattern. Various interactions have been reported including HbH-Paksé, compound Hb Paksé with Hb Constant Spring, Hb H-Paksé with Hb E disease. Both mutations occur in the termination codon, cd142 of HBA2 gene (TAA>TAT) in Hb Paksé and (TAA> CAA) in Hb CS resulting in an abnormal Hb characterized by elongated α-globin chains as the results in additional of 31 amino acid residues after the substitution.

Objectives: The purpose of this study was to search for the possibility of other differential diagnosis of homozygous Hb CS.

Materials and Methods: This is a retrospective cross-sectional study on 53 samples with a presumptive diagnosis of homozygous Hb CS based on Hb analysis recorded from January 2018 to December 2023. All the cases were subjected to first line investigation with alpha multiplex Amplification Refractory Mutation System polymerase chain reaction (ARMS-PCR) and Gap-PCR to exclude common mutational and deletional alpha thalassaemia. Further confirmation of zygosity required using Allele Specific PCR using wild type and mutant Cd 142 primers in cases with Hb CS mutation based on ARMS-PCR. Cases with homozygous Hb CS based on Allele Specific PCR and clinical suspicion of a compound heterozygous with other mutations were further subjected for second line investigation with α-Multiplex-Ligation Dependent Probe amplification (MLPA) and sanger sequencing.

Results: Majority of the cases were Malay (n=50, 96 %), with one case of Orang Asli and one case of Siamese (1.92%). Out of 52 samples, 47 samples were subjected for second line investigation with α-MLPA and sanger sequencing. Five samples were genotype as compound heterozygous -α3.7/αCSα (n=1, 1.9%), --SEA/ αCSα (n=2, 3.8%) and αCSα/ααAdana (n=2, 3.8%) based on 1st line investigation. Three genotypes were identified based on further analysis with second line investigation: α-AAα / αCSα (n=3, 6.38%), αCSα / αPakseα (n=3, 5.7%) and αCSα/ αCSα (n=41, 77.4%). Noteworthy, the diagnosis of compound heterozygous of Hb αCSα / αPakseα might be missed out without clinical suspicion that led to further investigation.

Discussion / Conclusion: These results suggested that Hb Paksé and its various combinations can be misidentified as Hb CS even though the DNA study is the definitive method for diagnosis. Although the clinical symptoms of Hb Paksé and Hb CS are similar, precise diagnosis is important especially for prenatal diagnosis and genetic counselling. Current thalassaemia genotyping methods required skilful personnel for precise interpretation and diagnosis. Advanced method like second or third generation sequencing could be useful tools in complex gene or mutation interaction in near future.

Keywords: Hb Paksé, Hb Constant Spring, non-

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CASE SERIES/CASE REPORT (CLINICAL)

CC1 DEMOGRAPHIC AND CLINICAL INSIGHTS FROM A 15-YEAR CASE SERIES OF WOMEN AND GIRLS WITH RARE BLEEDING DISORDERS AT A TERTIARY REFERRAL CENTRE, HIGHLIGHTING SIGNIFICANT GYNECOLOGICAL MORBIDITY

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Background: In recent years, heightened awareness of gender-specific bleeding manifestations in individuals with rare bleeding disorders (RBDs) has led to an increased number of women and girls (WG) seeking specialized care. This surge is attributed to enhanced recognition of bleeding symptoms specific to this demographic. RBDs encompass hereditary deficiencies of fibrinogen, prothrombin (factor II[FII]), FV, FVII, FVIII, FX, FXI, and FXIII as well as disorders of fibrinolysis, presenting with a prevalence ranging from 1:500,000 to 1:2,000,000. This prevalence is notably higher in populations with a high rate of consanguinity, given the autosomal recessive inheritance pattern of RBDs. Clinical presentations of RBDs range from asymptomatic to severe spontaneous bleeding, with considerable heterogeneity among individual disorders. While affecting both genders, females experience heightened morbidity, particularly in the context of gynecological bleeding. This case series endeavors to elucidate the demographics and clinical characteristics, as well as treatment outcomes, of WG with RBDs over a 15-year period at Hospital Ampang.

Case Presentation: Thirteen WG with RBDs were monitored at the Bleeding Clinic from January 2008 to December 2023. Factor VII deficiency was the most prevalent (n = 6, 46.2%) followed by Factor XIII deficiency in a mother and daughter pair (n=2, 15.4%). There was 1 patient each for deficiencies of Factor V, Factor XI, Factor XII, Congenital hypofibrinogenemia and Factor VIII with lyonisation. Their age of diagnosis ranged from 3 to 51 years old. Diagnoses were predominantly obtained through conventional laboratory testing, with only two patients benefiting from genetic diagnosis. Heavy menstrual bleeding was the predominant clinical presentation (70%), persisting in five patients despite adjunctive measures. Median hemoglobin at presentation was 11.5g/dL, with four patients diagnosed with Iron Deficiency Anemia. Notably, five of 13 pregnancies resulted in eventful deliveries, requiring postpartum hemorrhage management or blood product transfusion. Two patients underwent surgeries for hemorrhagic ovarian cysts, with 1 patient requiring multiple surgeries.

Discussion / Conclusion: Our case series reflects the frequency observed in larger international registries. The reported correlation between the factor activity level and degree of bleeding varies from strong and predictable to no correlation and this was reflected in our small case series. Despite the absence of life-threatening bleeding episodes in our cohort, these disorders may be underdiagnosed and underreported due to limited awareness, low clinical suspicion, and inadequate diagnostic facilities. Increased awareness and education are imperative to ensure accurate identification and management of these cases. In conclusion, this case series provides valuable insights into the underexplored landscape of gynecological morbidities in WG with RBDs. A comprehensive understanding of these disorders is crucial for timely diagnosis, appropriate management, and improved outcomes for affected individuals. The findings underscore the need for increased awareness among healthcare professionals, as well as the necessity for specialized diagnostic facilities, to ensure the accurate identification and optimal management of individuals with RBDs.

CASE SERIES/CASE REPORT (CLINICAL)

CC2 EXPERIENCE OF VENETOCLAX (VEN) IN MYELODYSPLASTIC SYNDOMRE (MDS)

Main Author:
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Background: Elderly MDS patients have limited treatment options. Curative treatment of allogenic stem cell transplant is often not feasible. Many of the patients are not open to frequent visits to the hospitals for injection therapies such as parental hypomethylating agents(HMA). Palliative combination oral treatments are probably the best options besides supportive transfusions and other treatments. MDS patients from 2019 to 2023 who were given VEN as part of their treatment were included. Disease progression or death dates were collected. Survival was calculated as of 1/1/2024.

Case Presentation: A total of 5 patients were given VEN. Median Age was 73.4 years, Mean Age was 75.9 years. There were 4 male and 1 female. 2 patients had Refractory Cytopaenias with Multilineage Dysplasia with Excess Blasts, 1 patient had Chronic Myelomonocytic Leukaemia and 2 patients had transformed MDS/Myeloproliferative Disorder(MPD). All patients had combination treatment with other agents including oral thalidomide or lenalidomide. There were 2 partial response and 3 no response. Survival of the 3 patients with no response were 21, 85, 18 days. Survival of the patients who responded was 899 days(still ongoing treatment) and 461 days(progressed after 384 days, no longer on treatment).

Discussion / Conclusion: VEN is possibly an convenient but expensive palliative care option for elderly MDS that reduces the need for frequent hospital visits for parenteral treatment. Responses are not as good as combination HMA+VEN but this is expected. Hopefully more trials involving palliative treatment that includes venetoclax would be available to confirm the benefits seen.

CC3 COMBINATION OF DECITABINE(DEC) AND VENETOCLAX(VEN) IN MYELODYSPLASTIC SYNDROME (MDS) / ACUTE MYELOID LEUKAEMIA (AML)

Main Author:
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Background: MDS/AML patients, especially elderly patients are often not offered intensive chemotherapy due to the risks and patients' comorbidities. Hypomethylating agents combined with Venetoclax is a viable and effective alternative with lesser risks and side effects. Patients treated in my hospital with DEC+VEN for MDS/AML from 2019 till 2023 are included. Relevant patient and disease data are collected. The Kaplan-Meier Curve for progression free survival and overall survival are calculated.

Case Presentation: Total of 12 patients are included. Mean and Median age was 68.1 and 68. 9 respectively. There are 9 males and 3 females. 9 patients(75%) responded with 8 CR/CRu and 1 PR being the best response achieved. 3 patients(25%) had no response. Out of 9 responders, 6 patients eventually relapsed with 3 of them still in remission. Median duration of follow-up was 436.5 days. Median Overall Survival was 710 days.

Discussion / Conclusion: DEC-VEN combination is an effective and feasible option for elderly AML/MDS with good response rates. However, most of the patients relapses eventually. If the aim is for long term remission or cure, an reduced intensity allogenic stem cell transplant should be considered once patients achieve remission.

CASE SERIES/CASE REPORT (CLINICAL)

CC4 FLUDARABINE-CYTARABINE-VENETOCLAX (FLAG-VEN) AS SALVAGE CHEMOTHERAPY FOR REFRACTORY ACUTE MYELOID LEUKAEMIA (AML)

Main Author:
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Background: Patients who are refractory to AML induction chemotherapy has limited options for salvage chemotherapy. Fludarabine-Cytarabine combination(FLAG) is often used but combination with Idarubicin is extremely toxic especially at full doses. FLAG-VEN combination chemotherapy provides an alternative treatment that do not include anthracyclines that the patient has likely been refractory to during the induction. Patients who has AML who were given FLAG-VEN as salvage chemotherapy from 2019 to 2023 were included. Relevant clinical data were collected and Kaplan-Meier Survival Curve for Overall Survival was calculated based on survival on 1/1/2024.

Case Presentation: A total of 7 patients were include, 5 males, 2 females. Median and Mean age was 52.7 years and 46.9 years respectively. Median follow up duration was 306 days. 5 patients(71.4%) achieved complete remission and 2 patients(28.6%) had no response. All 5 responded patients subsequently underwent allogenic stem cell transplant. 2 out of the 5 transplanted patients died later due to transplant complications. The remaining 3 surviving transplanted patients remained in remission. Median Overall Survival was 442 days.

Discussion / Conclusion: FLAG-VEN is a feasible and effective salvage chemotherapy for refractory AML. Usage of Venetoclax instead of Idarubicin seemed to be effective in anthracycline refractory patients. Early salvage therapy is more likely to be effective compared to using it later. More trials should probably be done to using venetoclax earlier or as part of combination therapy for induction.

CASE SERIES/CASE REPORT (CLINICAL)

CC5 AN UNUSUAL CASE OF HYDROXYUREA INDUCED REFRACTORY FOOT ULCER IN A PATIENT WITH JAK2 MUTATED POLYCYTHEMIA RUBRA VERA

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Background: Polycythemia Rubra Vera (PRV) is a myeloproliferative neoplasm with clonal proliferation involving erythroid, myeloid and megakaryocytic lineage and is classically positive for JAK V617F mutation in over 98% of cases. Intolerance/resistance to hydroxyurea occurs in up to 25% of patients, with hydroxyurea induced foot ulcers estimated at 9%.

Case Presentation: The patient is a 62 year old gentleman with underlying hypertension, chronic kidney disease, dyslipidemia and fatty liver. PRV was diagnosed since 2016 at the age of 54 years. He presented with haemorrhagic stroke but had no residual neurological deficit. His presenting full blood count was WBC 21.4, Hb 19.2g/dL, haematocrit 54%, platelet 536. He was started on Hydroxyurea in December 2016 in view of high risk JAK 2 mutated PRV. He required regular venesections (2x in 2018, 4x per year in 2020 and 2021) and hydroxyurea dose was increased to aim for haematocrit of <45%. He developed non healing left foot ulcers in Jan 2023 associated with sharp pain upon ambulation which was progressively worsening. He denied having prior insect bites or trauma and he is a non diabetic. Physical examination revealed a large non infected irregular ulcer which measured 15x3cm at the left dorsolateral aspect of the foot. He was referred to the vascular team in October 2023 and was treated as sapheno-popliteal junction reflux/chronic venous ulcer. His arterial pulses were well felt. His Hydroxyurea dose was reduced gradually without significant improvement. In view of his non healing left foot ulcer, Hydroxyurea was stopped and was switched to Ruxolitinib since 17/11/23. He required admission in January 2024 for left foot cellulitis. Notably, one month after discontinuation of Hydroxyurea, he had marked improvement of his left foot ulcer.

Discussion / Conclusion: Discussion Hydroxyurea is given in high risk JAK2 mutated PRV. Hydroxyurea disrupts S phase of cell cycle which prevents production of collagen as basal keratinocytes are damaged. Inflammatory mediators from platelets and as a result of myeloproliferative disorders has been reported to be involved in the pathogenesis of foot ulcers. It is prudent to have high index of suspicion and to consider hydroxyurea as the possible cause of refractory foot ulcers as it can also mimic other causes of foot ulcers. This may present a diagnostic challenge. This condition is associated with significant morbidities which include infections, impaired quality of life as a result of debilitating pain and functional impairment. In cases of Hydroxyurea intolerance, treatment involves termination of hydroxyurea and to commence patient on alternative medication such as in this case, Ruxolitinib. Conclusion Our case highlights an unusual side effect of hydroxyurea induced refractory foot ulcer. It is imperative to have a high index of suspicion especially in cases where there are other plausible alternative causes so that patients can be managed in a timely manner.

CASE SERIES/CASE REPORT (CLINICAL)

CC6 SUBCUTANEOUS PANNICULITIS-LIKE T-CELL LYMPHOMA PRESENTED WITH HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: AN UNCOMMON PRESENTATION FOR A RARE LYMPHOMA

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Background: Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare subtype of non- Hodgkin lymphoma characterized by infiltration of cytotoxic T-cell lymphoma into the subcutaneous tissue. While SPTCL commonly manifests with skin lesions and systemic symptoms, the occurrence of its association with hemophagocytic lymphohistiocytosis (HLH) is exceptionally rare. HLH is a life- threatening hyperinflammatory syndrome resulting from immune system dysregulation. The co-occurrence of SPTCL and HLH presents a unique clinical challenge, requiring a comprehensive understanding of both conditions for effective diagnosis and management. This case represents the uncommon convergence of SPTCL and HLH, emphasizing the significance of acknowledging and managing this intricate clinical condition.

Case Presentation: We reported a case of a 25-year-old man with no prior medical history, who presented with fever, multiple truncal and extremities skin lesions, generalized body edema, and significant weight loss for 4 months duration. He had no significant travel history and family history of malignancy. Clinically, there were extensive erythematous skin nodules and plaques over the truncal and extremities with some of these lesions showing ulceration and necrotic patch. Initial investigations revealed pancytopenia with no abnormal lymphoid cell or blast cell. Autoimmune workup including anti-nuclear antibody was negative and complement C3, C4 were normal. Infective screening for Epstein Barr virus, Hepatitis viruses, and retroviral were negative. Bone marrow and trephine biopsy were carried out but failed to conclude the underlying pathology. His condition was subsequently complicated with the development of HLH [persistent fever, mild organomegaly, raised ferritin (25166mcg/L), and triglyceride (6mmol/L)], but he declined a repeat bone marrow assessment. He was started on HLH 94 treatment protocol. His skin biopsy returned as subcutaneous panniculitis-like T-cell lymphoma, positive for CD3, CD5, CD8, and TIA. As his condition improved, he was treated with 6 cycles of CHOP and end of treatment PET-CT assessment showed partial response. Peripheral blood stem cell collection were attempted but failed. Persistent residual disease both clinically and from PET-CT assessment led to the initiation of cyclosporin and resulted in a favourable clinical response, and resolving skin lesions.

Discussion / Conclusion: The coexistence of SPTCL and HLH in this case underscores the complexity of rare lymphoproliferative disorders. The recurrence of symptoms post-treatment and the challenges in determining residual disease pose clinical dilemmas, prompting a closer examination of therapeutic strategies. Furthermore, the subsequent positive response to cyclosporin introduces a noteworthy aspect, suggesting potential avenues for immunosuppressive interventions even in patients who failed intensive treatment initially. The unique clinical trajectory of this patient contributes valuable insights to the broader understanding of SPTCL and its intricate management landscape. While diagnostic and therapeutic challenges exist, a comprehensive approach involving a multidisciplinary team is essential for optimal patient care.

CASE SERIES/CASE REPORT (CLINICAL)

CC7 CO-EXISTENCE OF MEDIASTINAL GERM CELL TUMOUR WITH CHRONIC MYELOID LEUKAEMIA: A RARE ENCOUNTER

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Background: Association of hematological malignancies with extra-gonadal germ cell tumour (GCT) has been described, as an extremely rare phenomenon. Most reported cases involve mediastinal GCT associated with a haematological neoplasm affecting the megakaryocytic lineage. Here is a case of co existence of a non-seminomatous mediastinal GCT and chronic myeloid leukaemia (CML) in a previously fit young man.

Case Presentation: A 19-year-old male presented with worsening left upper quadrant pain for two weeks associated with fever for three days. He has no significant history of medical illness, nor of drug or alcohol consumption. On examination, he has moderate hepatosplenomegaly with no peripheral lymphadenopathy. Presenting counts were Hb 6.6g/dL, Platelet 74 x 10^9/L and WCC 33.6 x 10^9/L. Renal and liver function were normal except for an albumin of 25g/L. A peripheral blood film showed predominantly mature neutrophils, mild basophilia, occasional myelocytes and nucleated red blood cells, and reduced platelets. Chest radiograph unexpectedly revealed a mediastinal mass, confirmed by thoracic magnetic resonance imaging, measuring 9.1 x 5.1 x 8.2cm. Alpha-fetoprotein and Beta-HCG were elevated: 1091ng/ml (<7) and 14.53mIU/ml (<2), respectively. Marrow aspiration, immunophenotyping, and biopsy found hypercellularity with increased granulopoiesis, mainly myelocytes and neutrophils, with no increase in blast or basophils, and no GCT metastasis. Karyotyping, fluorescent in-situ hybridisation (FISH), polymerase chain reaction (PCR), and next generation sequencing (NGS) detected Philadelphia chromosome and BCR:ABL1. Percutaneous mediastinal biopsy diagnosed a malignant teratoma: oval and rounded tumour cells arranged in solid nests in a vascularised stroma, staining positive for SALL4, OCT3/4, CD117 and negative for CD30 and PLAP. Positron emission tomography showed FDG-avid lesions in both lungs as well as chest and abdominal nodes. He was started on imatinib 400mg daily. He has mild hepatitis before starting imatinib, with AST and ALT 59U/L and 55U/L, respectively and total bilirubin (TB) 59umol/L. INR was 1.94. Clinically, the spleen size shrank with imatinib, but counts never improved. His liver function improved for two days, then worsened rapidly, and imatinib had to be ceased after six doses.

Unfortunately, four days after stopping imatinib, TB rose to 155umo/L, AST to 131U/L and ALT to 234U/L, and INR was 4.14. Viral hepatitis and HIV serology were negative. The patient developed hepatic encephalopathy, and succumbed from cerebral oedema and extensive bleeding the next day.

Discussion / Conclusion: Case reports have documented concurrent hematological malignancies in patients with mediastinal GCT, mainly with non-seminomatous histology. Mediastinal GCT has been described with acute megakaryoblastic leukaemia, other acute myeloid leukaemias, myelodysplasia with abnormal megakaryocytes, acute lymphocytic leukaemia, and, in rare cases, malignant histiocytosis or systemic mastocytosis. A third of these patients presented with both disorders simultaneously. Hematological malignancies with concomitant GCT behave aggressively: patients die before treatment, do not respond to treatment, or achieve only short remission. To date, there have been three reported cases of CML following GCT therapy, but co-existence of both entities appears to be a novel finding.

CASE SERIES/CASE REPORT (CLINICAL)

CC8 RECURRENT HEART FAILURE: MULTIPLE MYELOMA WITH CARDIAC AMYLOIDOSIS

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Coauthor:
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Background: Multiple myeloma (MM) is part of plasma cell neoplasm with presence of monoclonal gammopathy and amyloidosis is a rare disorder characterized by extracellular deposition of light chain protein, called amyloid. Approximately 10-15% of MM patients will develop AL amyloidosis. It is uncommon for MM to present initially with heart failure. The present of heart failure should raise suspicion of concomitant cardiac amyloidosis by means of restrictive cardiomyopathy. Once heart failure occurs, the median survival is less than six months in untreated patients.

Case Presentation: A 56-year-old lady presented with recurrent episodes of decompensated heart failure despite optimal medical therapy. She had absence of cardiovascular risk factors. Laboratory tests showed anemia, elevated total protein, and renal impairment. Cardiac parameters revealed elevated troponin I of 67.9 ng/L and pro brain natriuretic peptide (pro BNP) of 4505 pg/mL. Echocardiography showed evidence of left ventricular ejection fraction 50-60% with grade 3 diastolic dysfunction, and additional finding of 'granular sparkling' appearance on myocardium. Further investigations with the suspicion of cardiac amyloidosis and MM were done. There was presence of moderate rouleux formation in peripheral blood film. Bone marrow aspiration and trephine biopsy analysis showed 44% mature plasma cell infiltration, serum electrophoresis showed presence of IgG lambda paraprotein with 53.3g/L. Thus, diagnosis of MM with cardiac amyloidosis was made. Bortezomib, thalidomide and dexamethasone (VTD) regime commenced together with standard optimal therapy of heart failure but patient demised despite all the resuscitative effort.

Discussion / Conclusion: Given the atypical presentation of progressive heart failure despite adequate optimal therapy, other probable diagnosis need to be considered. A high index of suspicion is required to diagnose cardiac amyloidosis. The progressive heart failure with elevated pro BNP and troponin levels, presence of grade 3 diastolic dysfunction and 'granular sparkling' appearance on myocardium from echocardiogram makes the constellation of signs and symptoms highly suggestive of cardiac amyloidosis. Diagnosis of MM is made by the evidence of myeloma-defining events and further supported by presence of 44% plasma cell in bone marrow and presence of monoclonal paraprotein of IgG lambda. Prognosis for MM associated with amyloidosis is grim in comparison to MM or amyloidosis alone. Studies show that, presence of cardiac amyloidosis related to shorter overall survival, with poor prognostic factors of granular sparkling appearance, diastolic relaxation abnormalities on echocardiogram, high pro BNP and troponin levels. In this case, despite initiation of MM-related therapy and optimization of heart failure therapy, patient still succumbed to illness.As MM and AL amyloidosis tends to co-exist, high index of suspicion is necessary, especially when cardiac involvement is seen in myeloma patients at any point throughout the course of illness. Due to its poorer prognosis, delay in diagnosis will delay treatment and subsequently affects survival.

CASE SERIES/CASE REPORT (CLINICAL)

CC9 CASE REPORT: SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS – AN UNUSUAL FROM ENTEROCOCCUS INFECTION

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a syndrome resulting from excessive and life-threatening activation of the immune system. This dysregulation of the immune system increases the activation of macrophages and the hyperproliferation of T lymphocyte cells. HLH can be classified as primary (genetic) or secondary that related to infection, rheumatologic, and malignancy diseases. Diagnosing HLH is challenging for clinicians because the symptoms are similar to those of many other diseases and it involves many non-specific laboratory tests. Immunosuppressive drugs and treatment of the underlying disease are the main therapies for HLH to reduce mortality.

Case Presentation: A 41-year-old woman was referred from primary healthcare to Dr. Saiful Anwar Hospital with suspicion of dengue fever. The patient complained of acute fever, lower abdominal pain, hypermenorrhea, and bruising on all four limbs. Examination revealed hypotension, leucopenia, thrombocytopenia, elevated liver enzymes, elevated d-dimer, hypertriglyceridemia, hypofibrinogenemia, elevated CRP, and significant hyperferritinemia. An abdominal ultrasound examination showed hepatomegaly. The dengue serology examination was negative. The urine culture showed an Enterococcus faecalis infection. The patient met 5 of 8 HLH diagnostic criteria based on the HLH-2004 consensus. Patients are given high-dose steroid therapy to suppress the hyperinflammation and eliminate the activated immune cells. Intravenous antibiotics and platelet transfusions are also added to treat infections and raise platelet levels. Clinical and laboratory conditions improved after 5 days of treatment.

Discussion / Conclusion: Enterococcus faecalis infection, in this case, triggers an excessive immune response and develops into HLH. This condition is often misdiagnosed as other diseases, such as dengue fever or sepsis. It is important to check inflammatory markers such as ferritin to differentiate HLH from other diseases. A significant increase in ferritin indicates the condition of HLH with a high degree of sensitivity and specificity. Early diagnosis and prompt immunomodulation therapy can reduce patient mortality.

CASE SERIES/CASE REPORT (CLINICAL)

CC10 AGGRESSIVE NATURAL KILLER CELL LEUKEMIA PRESENTING WITH FEATURES SUGGESTING ACUTE PROMYELOCYTIC LEUKEMIA

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Background: Aggressive natural killer cell leukemia (ANKL) is an extremely rare disease with dismal prognosis, with a median survival of 2 months. Active research in recent years has been able to define its immuno-phenotype, association with EBV, cytogenetics and molecular signature, but clear treatment guidelines remain elusive.

Case Presentation: A 65 year male with a background of diabetes mellitus, hypertension and dyslipidaemia was admitted with fever and lethargy. 2 weeks prior, he had been admitted to a private hospital with infected groin ulcers presumably due to DRESS (drug reaction with eosinophilia and systemic symptoms). The suspected offending drug was traditional medications that the patient took to seek relief from chills and rigors which occurred after his second dose of the Covid vaccine. Clinically he was alert but lethargic looking, with blood pressure supported by low dose noradrenaline, temperature of 38.2^oCand with no palpable lymph nodes or hepatosplenomegaly. In addition, the groin ulcers had completely healed. He had a haemoglobin of 98g/L, white cell count 32.1x10^9/L, platelet 101x10^9/L, urea 17.1mmol/L, creatinine 219µmol/L, procalcitonin 0.46ng/mL, pH 6.97, pCO2 46mmHg, pO2 50mmHg, lactate 14.1mmol/L, HCO3 10.6mEq/L, prothrombin time 24.4 seconds, activated partial thromboplastin time 47.9 seconds, fibrinogen 3.28g/L. Full blood picture showed 74% blasts which were small to moderate in size, with scanty to ample basophillic cytoplasm, irregular nuclear outline, open chromatin pattern with inconspicuous nucleoli, with some blasts having bilobed nuclei and minimal granules. No auer rods, faggot cells or abnormal promyelocytes were seen, but the hypogranular variant of acute promyelocytic leukemia (APML) remained a concern so all-trans retinoic acid was given via naso-gastric tube plus intravenous dexamethasone. He was intubated and admitted to the intensive care unit. Flow cytometry of peripheral blood was highly suggestive of ANKL, revealing 64.9% abnormal cells which were CD45 dim to neg, low SSC, CD34 neg, HLA-DR+ve, nTdT neg, CD99 +ve, Cd1a neg, cyCD3 neg, sCD3 hetero, CD2 +ve, CD4 neg, CD8 hetero, CD5 neg, CD56 +ve, CD16 +ve, CD26 neg, CD28 neg, TCR-αβ neg, TCR-γδ neg, CD117 neg, CD33 neg, CD13 neg, cytoMPO neg, CD10 neg, CD35 neg, CD64 neg, CD14 neg, CD300e neg, CD19 neg, cytoCD79a neg, CD20 neg. Bone marrow trephine was hypercellular with multiple areas infiltrated by neoplastic cells, occasionally showing bilobed nuclei. These neoplastic cells were CD2+ve CD56+ve while most were negative for Tdt, CD5, CD7 and CD20. He received idarubicin 12mg/m2 on day 3 of admission based on the initial diagnosis of APML. He had a stormy course and was supported with antibiotics and dialysis. On day 9 he was extubated and transferred to general ward. He received vincristine 2mg and daunorubicin 30mg/m2 on day 10. Unfortunately his fever recurred on day 13, after which he deteriorated and passed away on d16 despite reintubation and broad spectrum antibiotics.

Discussion / Conclusion: This case study adds to the growing but small number of ANKL cases identified worldwide. Unfortunately, patients with NK cell leukemia are prone to infection which is the likely cause of this patient's demise, despite initial improvement in clinical condition.

CASE SERIES/CASE REPORT (CLINICAL)

CC11 A LATE PRESENTATION OF TYPE 3 VON WILLEBRAND DISEASE: IS IT INHERITED OR ACQUIRED?

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Background: Type 3 von Willebrand Disease (vWD) and Acquired von Willebrand Syndrome (AVWS) are both rare clinical entities. Type 3 vWD patients inherit homozygous mutation of the vWF gene from both parents leading to absent or very low levels of vWF, hence will present with significant bleeding episodes from young. In contrast, AVWS results from increased clearance and proteolysis of vWF which is associated with other medical conditions. Genetic study is required to distinguish both inherited VWD and AVWS as both entities share similar clinical presentation and laboratory abnormalities.

Case Presentation: This patient is a 53 years old lady with underlying hypertension, presented with huge left buccal hematoma with persistent gum bleeding after dental scaling. She had 2 months history of intermittent unprovoked gum bleeding and bruising over limbs. At presentation, she was found to have an isolated prolonged activated partial thromboplastin time (aPTT) of 91.4 seconds. Mixing test was corrected. Further tests showed low FVIII level of 2.7 IU/dL, vWF Ag of <2.2% and vWF Ricof of 19%. She denied personal and family history of bleeding disorder. She had 3 spontaneous vaginal deliveries and incisional drainage procedure for perianal abscess uneventfully. There was no clinical or laboratory evidence of an associated malignancy or autoimmune condition. She was treated as Type 3 vWD with vWF containing FVIII concentrate and anti-fibrinolytics for one week. She achieved dramatic clinical response and satisfactory factor increment post infusion. She was discharged with anti- fibrinolytics alone. Interestingly, her FVIII, vWF Ag, vWF Ricof levels were normalized with no recurrent bleeding episodes during the follow up.

Discussion / Conclusion: Both inherited and acquired VWD have different treatment approaches. Therefore, obtaining an accurate diagnosis is crucial in deciding management plans. This patient has severe mucocutaneous bleeding with laboratory abnormalities classical of Type 3 VWD, however her late presentation with absence of personal and family history of bleeding is not in favour of inherited VWD. Furthermore, her normal FVIII and VWF Ag levels without factor replacement during follow up further supports an acquired cause for her condition.

CASE SERIES/CASE REPORT (CLINICAL)

CC12 COMBINATION OF ASCIMINIB AND PONATINIB PLUS BLINATUMOMAB IN REFRACTORY PHILADELPHIA CHROMOSOME POSITIVE ACUTE LYMPHOBALSTIC LEUKEMIA: A CASE REPORT

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Background: Relapsed/refractory (r/r) Philadelphia positive ALL are commonly associated with TKI resistance generally due to acquired mutations in BCR-ABL1 kinase domain. Asciminib, an allosteric inhibitor targeting the myristoyl-binding pocket of BCR-ABL1, is active against most single mutants but ineffective against all tested compound mutants. Combination Asciminib and Ponatinib can restore ATP- site TKI activity against untreatable compound mutant. The enhanced efficacy of the combination of asciminib and ponatinib included the three reported clinical compound mutants most resistant to ponatinib: T315M (a single amino acid change that requires two nucleotide changes [ACC to ATG]), Y253H/T315I, and E255V/T315I.

Case Presentation: A 19 years old Male, presented with intermittent fever and loss of weight. Presenting count was Total white cell: 394 k/uL Hemoglobin:11g/dL Platelet :320 k/uL, no splenomegaly. MRI pelvis showed sacral spinal canal lesion. Diagnostic IP showed B-ALL with aberrant Myeloid markers with presence of a 38% cluster of blasts. Molecular test positive for major transcript BCR-ABL1. He was started with HIDAC and Daunorubicin induction chemotherapy with Imatinib, treated as MPAL. Post induction chemotherapy showed refractory disease with BCR-ABL level exceed highest standard level. He was consolidated with MIDAC chemotherapy with Nilotinib. Post MIDAC, BMA showed morphological remission with MRD. He was given FLAG-IDA with Ponatinib 45mg OD. BMAT post FLAG-IDA was refractory disease with blast 76%, detected E255V mutation. He was then bridged with Venetoclax 100mg OD and Asciminib 80mg BD and ponatinib 45mg OD for 2 weeks followed by Blinatumomab plus ponatinib and Asciminib. Post 1st cycle Blinatumomab and Ponatinib and Asciminib, BMAT showed morphological remission with MRD with BCR-ABL level reducing to 0.0361%. He was continued with second cycle of blinatumomab plus ponatinib 30mg OD and Asciminib 200mg AM/160mg PM. BMAT assessment showed morphological remission with BCR-ABL 0.062%. Subsequently, he moved in to haploSCT. Both Ponatinib and asciminib were withheld 2 weeks before haploSCT. He underwent HaploSCT uneventfully and engrafted at Day 11. Currently, he was Day +55 post HaploSCT, complicated with grade I steroid responsive skin aGVHD . He was started back Asciminib 40mg OD on day +30.

Discussion / Conclusion: Combination of Asciminib and Ponatinib showed efficacy on Relapsed/Refractory ALL with tolerable safety profile.

CASE SERIES/CASE REPORT (CLINICAL)

CC13 CASE OF SYSTEMIC AMYLOIDOSIS PRESENTED WITH RECURRENT PLEURAL EFFUSION

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Background: Amyloidosis is a rare and underdiagnosed disease. Clinical and radiologic manifestations of pleural amyloidosis are non-specific and it can be easily missed or misdiagnosed. Hereby, we report a case of systemic amyloidosis presented with recurrent pleural effusion.

Case Presentation: A 62-year-old female who suffered with recurrent pleural effusion for more than 1 year was admitted for another episode of shortness of breath and reduced effort tolerance. She had underlying hypertension, dyslipidemia and depression. Her first presentation in April 2022 with left pleural effusion which treated as lung empyema and completed 6 weeks of antibiotic. Serial pleural fluids investigations for tuberculosis and malignancy were negative. She had second presentation in January 2023 with right pleural effusion required drainage. PET-CT imaging was unremarkable. She represented in March 2023 with SOB, vasculitis rash, loss of appetite and weight. CXR noted right pleural effusion and proteinuria with urine PCI 2.2g/day. Pleuroscopy showed focal discrete brown nodule at costoparietal pleural. She was treated as SLE with serositis, lupus nephritis, neuropsychiatry and skin involvement with methylprednisolone. Lab results showed ANA 1:100 speckled, dsDNA negative and normal C3/C4. However, pleural biopsy reported 1 week later consistent with amyloidosis. Further investigations shown SUEP 4.8g/L IgG Lambda, Beta-2 microglubin of 12.8 mg/L, serum FLC ratio 0.19. Marrow plasma cell 3%. No evidence of amyloidosis in trephine biopsy. Echo EF 34% with global hypokinesia, 'cherry on top' appearance seen. Pro BNP >9000pg/ml. Skin biopsy confirmed cutaneous amyloidosis. She proceeded systemic amyloidosis treatment with VCD regime. Unfortunately, she succumbed due to sudden cardiac arrest 1 week after treatment.

Discussion / Conclusion: Amyloidosis is a rare disorder which insoluble amyloid proteins deposited in body organs leading to organ dysfunction and death. Primary systemic amyloidosis mainly affects the heart, kidneys, gastrointestinal tract, nerves, skin, and vessels. Pleural amyloidosis is rarely reported and usually associated with AL amyloidosis. The mechanism of amyloidosis causing pleural effusion is not clear. Systemic factors like congestive heart failure, nephrotic syndrome, and hypoproteinemia if transudative effusion. If exudate, it may due to diffuse pleural inflammation by amyloid deposition. In our case, the results from thoracentesis procedures were suggestive of exudative effusions. The diagnosis of pleural amyloidosis relies on pleural tissue biopsy and Congo red stain. Typical findings of pleuroscopy consist hyperaemia of pleural surface, inflammation with nodular lesions or brown nodules of the parietal pleura as seen in our patient. Persistent pleural effusions occur in 1 to 2% of patients with systemic amyloidosis, usually associated with poor prognosis and often refractory to treatment. In our case, multiple organ systems are affected. The main manifestations are pleural effusion and restrictive cardiomyopathy. In the event of heart failure on cardiac amyloidosis patients, the average survival time for untreated patients was 6 months. In summary, we present a case of systemic amyloidosis with recurrent pleural effusion. This case deserves the attention as recurrent pleural effusions, especially when combined with systemic multiorgan dysfunction, clinicians should take other rare diseases such as amyloidosis into consideration. The disease prognosis is poor; thus, prompt diagnosis and treatment are vital.

CASE SERIES/CASE REPORT (CLINICAL)

CC14 AN ATYPICAL PRESENTATION OF EXTRANODAL NK/T-CELL LYMPHOMA

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Background: Extranodal Natural Killer T-Cell lymphoma (ENKTCL) is an aggressive form of lymphoma. In the past, it was named 'ENKTCL, nasal type' in view of its frequent involvement of nasal and upper aerodigestive tract. Under the latest 2022 WHO classification, the phrase 'nasal type' had been dropped recognising that the disease can present at various extranodal site. The neoplastic cells in ENKTCL are commonly infected with Epstein-Barr virus. Positive EBV-encoded RNA (EBER) is a diagnostic marker to differentiate NKTCL from other peripheral T cell lymphoma and can be detected by in-situ hybridization.

Case Presentation: A 66-year-old woman was admitted with a chief complaint of left eye swelling, nasal congestion, anosmia and headache. She was admitted under Opthalmology and ENT team for left eye dacrocystitis and pansinusitis. Clinically there was a left periorbital oedema with overlying purpura. CT scan confirmed the findings of left periorbital cellulitis with reactive dacrocystitis and pansinusitis with no other extension. Repeated FNAC showed chronic inflammation. Initial laboratory tests yielded serum sodium, 128mmol/L, potassium 3.7mmol/L, creatinine 45, urea 2.75, white blood cell 4.7×10^9/L, neutrophil count 2.2×10^9/L, haemoglobin 12g/dL, platelet 203×10^9/L , C-reactive protein, < 5mg/L. Full blood picture commented leucopenia with mild neutropenia, few reactive lymphocytes, no obvious blast or abnormal lymphoid cells. The surgeons referred to medical team for hyponatraemia which confirmed SIADH based on biochemical parameters. Looking hard for malignancy we found a swollen, hard, fixed, and tender cutaneous lesion on the lateral part of midshin measuring 2×1cm and it was biopsied. She completed a battery of antibiotics for the dacrocytitis and pansinusitis despite negative cultures and was discharged home whilst awaiting skin biopsy result. She was readmitted a couple of weeks later critically ill and septic. At this point she developed haemophagocytic lymphohistiocytosis as evidenced by presence of hepatosplenomegaly, pancytopenia and high grade fever. She did not survive and died a couple of days later. The biopsied cutaneous lesion detected atypical lymphoid cells positive for CD3, CD56, Granzyme and negative for CD4, CD5, CD7, CD8, CD20. Ki67 was 80%. Her full HPE report concluded NK T Cell Lymphoma with EBER positivity.

Discussion / Conclusion: Dacrocystitis is the inflammation of the lacrimal duct due to blockage of the nasolacrimal duct commonly caused by Streptococcus infection. Other lacrimal sac tumours are squamous or basal cell carcinoma. There has been reported cases of lymphoproliferative tumour of the lacrimal sac but is usually secondary to systemic spread in a patient with lymphoma or leukaemia. In this case patient did not respond to a battery of antibiotics and multiple FNAC attempts were negative. It is important to be cognizant that FNAC was not a sensitive method to capture the lymphoma cells and often it cause delay in getting the correct diagnosis and treatment. A proper biopsy should be pursued if one attempt of FNAC failed to detect the malignant cells on a suspicious lesion. This patient likely has disease involved lacrimal tract, sinuses and skin. A proper biopsy of the skin lesion over the leg later aided in the final diagnosis of ENKTCL.

CASE SERIES/CASE REPORT (CLINICAL)

CC15 CYTARABINE-INDUCED VASCULITIS: IS IT RARE? A CASE SERIES

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Background: Cytarabine-induced vasculitis has long been regarded as a rare clinical condition. Some patient developed this lesion in association with cytarabine syndrome which is characterized typically with fever, rigors diaphoresis, conjunctivitis and myalgia. Cutaneous adverse effect of cytarabine varies either, vasculitis, acral erythema, neutrophilic eccrine hidradenitis, morbilliform rashes, stomatitis. inflammation of keratoses, alopecia, and cutaneous ulcers. In Malaysia, there is still no published case yet on this condition. However, we managed to encounter three interesting cases of patients with acute myeloid leukaemia who developed this dermatologic side effect of cytarabine.

Case Presentation: Herein we describe three patients with Acute Myeloid Leukaemia admitted to Hospital Raja Perempuan Zainab II, Kelantan in 2023. They were scheduled to receive DA 3+7 chemotherapy (day 1 to 3 of daunorubicin and day 1 to seven of cytarabine), followed by HiDAC chemotherapy (high dose of cytarabine), and subsequently MidAC (combination of mitoxantrone and cytarabine). One patient developed vasculitis with non-blanchable purpura at the bilateral upper limb, upper chest, posterior ears, legs, and ankles on day 5 of HiDAC. It was treated with topical steroids and antihistamine and the lesion resolved after day 13. Second case, developed generalized erythematous on day 7 of DA 3+7 chemotherapy which was associated with high grade fever and itchiness. It was completely resolved after intravenous hydrocortisone and chlorphenamine. Another case developed purpuric skin lesion over his both inner thigh on day 4 MidAC which remained for a week before resolving on its own without any treatment.

Discussion / Conclusion: All patients presented with the symptoms much later than other reported cases with varies in dose of cytarabine. Physicians must be aware and able to recognize this possible adverse event to limit misdiagnosis and avoid potentially fatal complications. While there is no standard therapy for cytarabine syndrome, we recommend a premedication protocol of corticosteroids before subsequent chemotherapy in our facility to prevent the condition by suppressing the inflammatory response.

CASE SERIES/CASE REPORT (CLINICAL)

CC16 RIGHT VENTRICULAR MASS IN LANGERHANS CELL HISTIOCYTOSIS: CHALLENGE IN DIAGNOSIS AND TREATMENT

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Background: Langerhans cell histiocytosis (LCH) is a rare histiocytic disorder. Formerly known as histiocytosis X, it encompasses a broad spectrum of clinical manifestations in children and adults, ranging from self-limiting lesions to life-threatening disseminated disease. LCH most commonly affects bones and skin, and to a much lesser extent affects lymph nodes, liver, and spleen. Cardiac involvement is rare in LCH but not uncommon in Erdheim-Chester disease (ECD), which is another type of histiocytic disorder. Our case demonstrates the challenge in establishing the histopathologic diagnosis and in salvage treatment.

Case Presentation: A 33-year-old male presented with left preauricular swelling associated with B symptoms. The lymph node biopsy was CD68+, S100+, CD1a-, CD3-, CD20-, with low Ki67 of 7-10%, in favour of histiocytic neoplasm. He was diagnosed with LCH with bone marrow involvement. Treatment with first-line chemotherapy cladribine was initiated, however, there was a discordance response i.e. complete disappearance of the primary lesion but with the emergence of new lesions at the upper back muscle and the more distracting intracardiac mass in the right ventricle. Repeated biopsy from the upper back muscle reported the same tissue diagnosis, meanwhile, the endomyocardial tissue obtained via the femoral access was suboptimal for interpretation. The initial tissue biopsy was also re-evaluated for BRAF-V600E mutation, which was negative. The intracardiac lesion was presumed to be part of the disseminated LCH, as further option for open biopsy was very risky. He subsequently received second-line treatment with vinblastine, prednisolone, and 6-mercaptopurine, but with no satisfactory response. He eventually succumbed to progressive heart failure.

Discussion / Conclusion: Distinguishing LCH and ECD remains a histopathologic challenge, particularly with limited resources for special staining. Mixed histiocytosis overlap syndrome perhaps could best describe this atypical presentation. Nevertheless, the therapeutic landscape in histiocytic neoplasms is still defying due to the lack of robustly tested salvage therapy.

CASE SERIES/CASE REPORT (CLINICAL)

CC17 THROMBOTIC THROMBOCYTOPENIC PURPURA WITH CONCURRENT EVANS SYNDROME

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Background: Background Thrombotic Thrombocytopenic Purpura (TTP) is a hematological emergency which requires urgent treatment to prevent life threatening complications. TTP is caused by severely reduced activity of the vWF-cleaving protease ADAMTS13. TTP is classified as immune mediated TTP (iTTP) if the patient is positive for anti-ADAMTS13 autoantibodies, and as congenital TTP (cTTP) if ADAMTS13 gene abnormalities are detected. The laboratory finding of microangiopathic hemolysis with negative Coombs test is consistent with TTP. In rare cases where the Coombs test was positive, this would suggest the simultaneous occurrence of TTP with Evans syndrome. Here, we described a case of relapse iTTP with concurrent Evans syndrome.

Case Presentation: Case Presentation A 17-year-old lady initially presented with dizziness and was found to have thrombocytopenia (platelet $8x10^9$/L), hemolytic anemia (Hemoglobin 5g/dL), and 5% schistocytes in the peripheral smear, in keeping with Microangiopathic Haemolytic Anaemia (MAHA). There was no renal impairment nor coagulopathy. She was diagnosed with TTP and immediately started on plasmapheresis and high-dose steroids. ADAMTS13 level was 2% with inhibitor level of 48U/ml.

However, Coombs test was positive (anti-IgG 1+ with panagglutination). Her disease responded well after 6 courses of plasmapheresis and discharged with tapering dose of steroid. Her disease relapsed after 5 months, presented with headache, chest pain and jaundiced for 3 days after her maintenance prednisolone was off for one week. Investigation showed hemolytic anemia (Hemoglobin 9g/dL), thrombocytopenia (platelet $11x10^9$/L), 2% schistocytes in the peripheral smear. She was treated as relapsed TTP and urgent plasmapheresis and high dose steroid were started. Her counts achieved response after 5 cycles of plasmapheresis. Again, her Coombs test came back positive (anti-IgG 1+ with panagglutination). ADAMTS13 level was absent. In view of early relapse and concurrent Evans syndrome in this case, she was added on Azathioprine as immunosuppressant.

Discussion / Conclusion: The main goal of monitoring TTP patients in remission is the prevention of clinical TTP relapses, through regular measurement of ADAMTS13 activity, and the timely use of immunosuppressive therapy in those having an ADAMTS13 relapse or where ADAMTS13 activity remains low following the acute episode. In this case she was initially on maintenance prednisolone for TTP which was tapered off, and presented with relapse within one week after stopping prednisolone. The concurrent Evans syndrome could be the reason for her to relapse in a short period of time. In addition, patients with TTP and Evans syndrome should be monitored closely during follow up with ADAMTS13 level to monitor treatment efficacy and assessing the risk of relapse. Ideally, this patient will require monitoring ADAMTS13 activity every 3–6 months in future to assess risk of relapse. If ADAMTS13 activity decreases to < 10% during remission in a patient with iTTP, rituximab may be considered for preventing clinical relapse. Concurrent TTP and Evans syndrome may need long term immunosuppressant to prevent clinical relapse.

CASE SERIES/CASE REPORT (CLINICAL)

CC18 MRD MONITORING BY NPM1 MUTATION IN PREDICTING RELAPSE IN A PATIENT WITH NPM1 AND FLT3-ITD MUTATED AML

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Background: Nucleophosmin (NPM1) gene mutations are the commonest genetic abnormality encountered in acute myeloid leukaemia (AML), accounting for about one-third of adult AML patients, followed by FMS-like tyrosine kinase-3 internal tandem duplication (FLT3-ITD) mutation. Measurable residual disease (MRD) monitoring of NPM1-mutated AML can be achieved by various molecular methods including quantitative polymerase chain reaction (qPCR) targeting on NPM1 mutation. Hereby we report a case of NPM1 and FLT3-ITD mutated AML in which the clinical relapse was preceded by molecular relapse evident from qPCR of NPM1 mutations.

Case Presentation: Madam LCW, a 63-year-old Chinese lady, presented with bilateral lower limbs swelling for 2 weeks in August 2022, associated with lethargy and loss of appetite. Full blood counts (FBC) showed leucocytosis, anaemia and thrombocytopaenia (white blood cells 62 $x10^9$/L, Hb 7.1g/dL, platelets 25 $x10^9$/L), for which a full blood picture (FBP) found 90% blasts. Bone marrow aspiration and trephine biopsy (BMAT) reported AML with 81% blasts, while molecular studies came back later as FLT3-ITD (allelic ratio 0.6) and NPM1 mutation type A detected. She received induction chemotherapy with daunorubicin and cytarabine (3+7 regime) and achieved morphology remission after first cycle. She subsequently proceeded with mitoxantrone and cytarabine (MidAC) for 1 cycle, followed by high dose cytarabine (HiDAC) for 2 cycles. Interim BMAT showed no increase in blasts. MRD monitoring was done by sending bone marrow aspirate for NPM1 mutation qPCR to Singapore General Hospital (SGH). Patient achieved complete molecular remission in January 2023 after HiDAC cycle 2, with undetectable NPM1 mutation by qPCR. 3 months post molecular remission, a repeated NPM1 qPCR showed molecular relapse (NPM1 mutation detected at 26.17%), while morphologically BMAT found no evidence of relapse. With that, patient was closely monitored for disease relapse. BMAT repeated one month later showed that patient remained clear of morphological relapse. Unfortunately, patient was confirmed to have AML relapse from BMAT repeated another month later, in May 2023, reporting 83% blasts. She underwent 2 cycles of fludarabine, cytarabine and filgrastim (FLAG) regime, after which she re- achieved molecular remission. Patient remained well and subsequently underwent allogenoeic stem cell transplant in November 2023, and currently is under transplant daycare follow-up.

Discussion / Conclusion: This case depicted the importance of early detection of AML disease relapse by MRD monitoring via qPCR of NPM1 mutant transcripts, which preceded clinical relapse in our patient by over 2 months. NPM1 mutations are an ideal target for MRD monitoring as they are common, specific for AML, and are neither expressed in normal tissues nor present in preleukaemic state. MRD monitoring by PCR quantification correlates well with treatment response, and reliably predicts clinical relapse by weeks to months. In addition, MRD evaluation by NPM1 mutation postinduction and prior to transplant confers important prognosis, which serves as a guide to post remission therapy. Therefore, clinicians should consider outsourcing NPM1 mutation in the management of AML to improvepatients' outcomes.

CASE SERIES/CASE REPORT (CLINICAL)

CC19 MULTIPLE MYELOMA PRESENTING AS PROGRESSIVE THROMBOCYTOPENIA IN END-STAGE RENAL DISEASE

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Background: Multiple myeloma is characterised by clonal expansion of malignant plasma cells within the bone marrow. It is associated with end-organ damage, including anaemia, renal insufficiency, bone lesions or hypercalcemia. We present a rare case of multiple myeloma who presented with immune thrombocytopenia in end-stage renal disease.

Case Presentation: A 56-year-old lady with a background history of hypertension and end-stage renal disease for two years presented with progressive thrombocytopenia from a baseline platelet of 250x10^9/L. She was found to have thrombocytopenia after one year on dialysis with platelets ranging between 100-110 x10^9/L. The platelet level progressively reduced to 5-10 x10^9/L in the last five months. Initial investigations showed Hb 8.5 x g/dL, WBC 5 x 10^9/L, PLT 110 x 10^9/L, calcium 2.2 mmol/L, albumin 38 g/L and globulin 34 g/L. Full blood picture showed true thrombocytopenia secondary to peripheral consumption. Platelet factor 4 (PF4) level was not suggestive of heparin induced thrombocytopenia. Anti-nuclear antibodies, HIV, hepatitis B and C virus were not detected. Her platelet level also did not respond to a trial of prednisolone which was started when her platelet count had dropped to below 20 x10^9/L. Bone marrow aspiration and trephine biopsy unexpectedly revealed 37% clonal plasma cells with kappa restriction. The serum free light chain showed kappa 298.1 mg/L and lambda 63 mg/L with a kappa/lambda ratio of 4.73. Megakaryocyte was adequate and the thrombocytopenia was secondary to peripheral consumption. She was treated with antimyeloma therapy with cyclophosphamide, bortezomib, and dexamethasone (CyBorD). After the first cycle of CyBorD, her platelet count improved to 143 x109/L.

Discussion / Conclusion: We describe a case of progressive thrombocytopenia in end-stage renal disease which turned out to be multiple myeloma with concurrent immune thrombocytopenia. Thrombocytopenia was refractory to steroids. Adequate megakaryocytes in the bone marrow suggest peripheral destruction. This case aligns with immune thrombocytopenia whereby the number of megakaryocytes is normal or increased due to immunologic degradation of platelets. Immune thrombocytopenia has rarely been encountered as an association with multiple myeloma. In most cases, thrombocytopenia results from chemotherapy during multiple myeloma treatment or marrow infiltration by the plasma cells. Renal disease in multiple myeloma is commonly due to light chain deposition disease. A timely diagnosis is essential to initiate early treatment regimens to rapidly reduce free light chain concentrations in patients with myeloma kidney. In this case, there were no features of multiple myeloma like high globulin with reverse AG ratio, hypercalcemia and bony lesions except for renal disease only. Chronic kidney disease without a known aetiology, such as diabetes mellitus or obstructive uropathy, should trigger a search for primary causes, at least a high index of suspicion for multiple myeloma especially light chain myeloma by conducting non-invasive screening tests such as serum free light chain or bone marrow aspiration and trephine biopsy if indicated.

CASE SERIES/CASE REPORT (CLINICAL)

CC20 HYDROXYCHLOROQUINE IN COMBINATION WITH LOW DOSE GLUCOCORTICOID AS ADJUNCTS IN REFRACTORY OBSTETRIC ANTIPHOSPHOLIPID SYNDROME: A CASE REPORT

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Background: Antiphospholipid syndrome (APLS) is an autoimmune disease characterized by vascular thrombosis and carries significant morbidity and mortality both to the general population and especially to pregnant women. With regards to pregnancy particularly, it confers risks of recurrent early miscarriages before 10th week gestational age and one or more deaths of morphologically normal fetuses over 10 weeks or premature birth before 34 weeks due to preeclampsia, eclampsia or placental insufficiency. Apart from the widely known prothrombotic state caused by antiphospholipid antibodies itself, complement activations play a crucial role in the genesis of late trimester thrombotic events. Standard practice in managing obstetric APLS mostly revolves around low weight molecular heparin (LMWH) as well as low dose aspirin. This has contributed to successful deliveries in around 70% of cases. Nevertheless, in a minority of patients which constitute the refractory obstetrical APLS, additional therapies can be considered on top of the conventional ones. These therapies include low dose glucocorticoids, hydroxychloroquine (HCQ), intravenous immunoglobulin and recently the TNF-alpha inhibitors. Among these, HCQ has been shown to improve pregnancy outcome in this group of patients, most likely owing to its role in attenuating the complement cascade activation. Despite that, the lack of prospective studies has hampered it to be frequently used among clinicians. This case report illustrates a successful pregnancy outcome with HCQ as well as low dose glucocorticoid and its potential use in tackling the issue of refractory obstetrical APLS.

Case Presentation: A 37 years old lady was diagnosed to have APLS at the age of 25 years old after having episodes of recurrent right lower limb deep venous thrombosis (DVT) as well as right renal vein thrombosis in her younger days. She was worked up for thrombophilia disorders and turned out to be positive for anti ß-2 glycoprotein 1IgM and anticardiolipin IgM with negative Lupus Anticoagulant and she was put on a lifelong anticoagulant since then. Her obstetric history has been rather eventful with 2 recurrent early miscarriages; The 1st one at 7 weeks of period of gestation and the 2nd one at 11 weeks of period of gestation. In both cases, treatment dose LMWH (S/c Tinzaparin) and low dose aspirin were commenced prior to conception. Prior to her 3rd pregnancy, we decided to commence her on HCQ at 200mg BD prenatally and low dose glucocorticoid prednisolone 10mg daily was added once pregnancy was confirmed on top of the regular conventional therapy (therapeutic dose LMWH as well as low dose of aspirin). Prednisolone was tapered down slowly from 12th week and off at around 20th week of pregnancy. She successfully delivered at 31st week via emergency cesarean section due to fetal distress. She was discharged well 3 days after and currently her baby is now 1-year-old and healthy.

Discussion / Conclusion: High dose HCQ and low dose glucocorticoids might be considered, on top of standard therapies to be utilized in dealing with patients with refractory obstetric APLS. Their efficacy should be confirmed with prospective, well designed clinical trials.

CASE SERIES/CASE REPORT (CLINICAL)

CC21 REPEATED LOW DOSE SPLENIC IRRADIATION IN A PATIENT WITH PRIMARY MYELOFIBROSIS AND MASSIVE SPLENOMEGALY: A CASE REPORT

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Background: Primary Myelofibrosis (PMF) is a type of Myeloproliferative Neoplasm characterized by anemia, marrow fibrosis and hepatosplenomegaly. With time, progressive enlarging spleen secondary to extramedullary hematopoiesis may ensue and lead to massive symptomatic splenomegaly. JAK 2 inhibitor is the mainstay of treatment for symptomatic splenomegaly. However, the high cost of this therapy prohibited its use in many patients. Hereby, I describe a case of PMF with massive splenomegaly treated with lose dose splenic irradiation (LDSI) twice.

Case Presentation: Madam O is a 67 years old lady who was diagnosed to have PMF since 2009. At presentation, she was noted to have big spleen reaching umbilicus and FBC showed WBC of 26.6 X 10^9/L, Hb 11.7g/dL and platelet 497 X 10^9/L. Trephine biopsy showed presence of grade 3 fibrosis and JAK2 V617F mutation was detected. She was started on Hydroxyurea since 2009. She was offered allogeneic stem cell transplant but declined. In 2018, she started to lose response to Hydroxyurea with enlarging spleen. At this point, a 3 months' supply of Ruxolitinib was procured and she was put on Ruxolitinib 20mg bd from September 2018 till December 2018. She showed marginal response to Ruxolitinib with mild reduction of spleen size. She was restarted on Hydroxyurea after finished the 3- month Ruxolitinib therapy. In April 2020, she started having severe anemia secondary to hypersplenism. Despite on 2-weekly packed cells transfusion, her Hb level can only be maintained at 5- 6 g/dL. FBP ruled out blast transformation. She was treated with LDSI in July 2020 (total 3.6 Gy in 6 fractions). Her spleen size shrank from 24cm down to 17cm below the left costal margin. Post splenic irradiation, she developed pancytopenia with nadir readings of: WBC 2.3 x 10^9/L, ANC 1.94 x 10^9/L, Hb 5 g/dL, Platelet 98 x 10^9/L. The cytopenia resolved after a month and she was transfusion-free. She was restarted on low dose Hydroxyurea and also added Deferiprone for iron overload. In February 2023, she started having severe anemia again and required frequent blood transfusion. Spleen again became massive and reached pelvic region. She was treated again with LDSI (total 3.6 Gy in 6 fractions) in May 2023. Post splenic irradiation, spleen size reduced from 24cm down to 18cm below the left costal margin. Similar like first episode, she developed cytopenia after LDSI and required some red cells transfusion. After one month, she was transfusion free, she remains well till now with Hb always hanging around 8.6 to 9.3 g/dL.

Discussion / Conclusion: This case highlights that LDSI is a feasible and effective alternative therapy for symptomatic splenomegaly. While Montemaggi et al reported that his patients had median response duration of 5.5 months to splenic irradiation, my patient seems to have a longer response duration. There is no universal standardized irradiation dose, range of 1-10 Gy of total irradiation dose have been reported. One of main concern of this therapy is it will cause a short duration of cytopenia post treatment and clinicians may need to support their patients with blood transfusion and G-CSF therapy during this period.

CASE SERIES/CASE REPORT (CLINICAL)

CC22 IROSIX AMONG PAEDIATRIC TRANSFUSION DEPENDENT THALASSAEMIA PATIENTS - EARLY CLINICAL EXPERIENCE IN PAEDIATRIC HAEMATOLOGY ONCOLOGY CENTRES IN MALAYSIA

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Background: Introduction In Malaysia, a transfusion-dependent thalassaemia (TDT) patient is expected to incur a total lifetime cost of USD561,208, with iron chelation therapy (ICT) being the main driver of cost. Generic medication typically costs 20-90% less than the innovator molecules, providing an attractive option to reduce expenditure. However, there are concerns about the true comparative effectiveness and safety of the generic drug versus the originators. Aim of study To share the early clinical experience of using generic deferasirox (Irosix) in TDT patients and describe the efficacy and safety among these patients.

Case Presentation: Methodology In this multi-centre, observational, case series report, four paediatric haematology oncology centres in Malaysia were involved, whereby access to Irosix was obtained through a patient access programme. Consent was taken from the parents using 'borang keizinnan untuk menjalani rawatan dengan ubat sampel'. All patients are TDT patients, 5 of whom were on single chelation therapy, 2 on combination therapy, and 1 previously untreated patient. The patients' originator deferasirox was switched to deferasirox generic Irosix using the same dose and was given for 3 months duration. Serum Ferritin pre- and post-Irosix were measured for efficacy data; liver function and renal function were evaluated for safety profiles. Patient acceptance to formulation were evaluated using palatability and ease of swallowing. Results Total 9 patients received Irosix. One patient needed to be excluded from analysis as the patient was started on Irosix concurrently with deferiprone. Eight patients were included into analysis, aged 7-17 years; 5 females and 3 males. The dose for original deferasirox and Irosix dose ranged from 10mg-25mg/kg/day. All patients were compliant to ICT pre- and post-Irosix study. Six patients (75%) showed good response in ferritin level reduction while on Irosix; two patients did not, which may be due to insufficient time for maximum efficacy via optimised dose. Maximum reduction was 56%, with a mean of 38% compared to pre-Irosix ferritin level. None of the patients showed any liver or renal derangement during Irosix treatment. There were no concerns on palatability and swallowing of the formulation among these patients.

Discussion / Conclusion: Irosix showed good efficacy to reduce serum ferritin level with good safety profiles. Limitation of this study is that the duration was too short, hence a more accurate evaluation of iron load with MRI T2* could not be evaluated. The study suggests that quality-assured generic medication can play an important role in Thalassaemia care by improving affordability and reducing economic burden. Cost-effective analysis study is warranted to convince policy makers.

CASE SERIES/CASE REPORT (CLINICAL)

CC23 MULTI-SYSTEM LANGERHANS CELL HISTIOCYTOSIS (LCH) – A CASE REPORT OF A GIRL WITH POOR GROWTH AND UNQUENCHABLE THIRST

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Background: Langerhans cell histiocytosis (LCH) is characterized by clonal expansion of myeloid precursors that differentiate into CD1a+/CD207+ cells and is commonly associated with BRAFV600E or MAP2K1 mutations. It can be broadly divided into single-system LCH (SS-LCH) or multisystem LCH (MS-LCH) depending on the number of risk organs involved and the varying degrees of organ dysfunction. LCH is rare, more commonly encountered in children and adolescents than in adults with a reported incidence of 2.6 to 8.9 cases per million children per year. We share a case of a young lady with LCH presenting with multiple bony lesions and endocrinopathies.

Case Presentation: A 14-year-old girl presented with left ear discharge for two weeks, with associated sensorineural hearing loss. A computed tomography (CT) and magnetic resonance imaging (MRI) scan showed a soft tissue mass measuring 5.87 x 2.49 x 3.62 cm in the left temporal region, causing extensive bony destruction in the left temporal bone, greater wing of the sphenoid, anterior aspect of the mastoid bone, and orbital wall. Another lesion was seen on the left side of the inner vertex with focal full-thickness skull vault involvement. No brain parenchymal infiltration was observed. She underwent a craniectomy with tumor excision and the histopathological examination (HPE) of the bone and tumor lesion demonstrated the presence of histiocytic cells which were positive for S100, CD1a, and CD68. A bone marrow examination was normal with negative for BRAFV600E mutation. A positron emission tomography (PET)-CT scan was normal. Further clinical history and examination revealed multiple endocrinopathies involving the hypothalamic-pituitary axis. She had polyuria, polydipsia, and cold intolerance for the past 2 years. She was deemed to have primary amenorrhea and clinical examination showed that she was short in stature with a lack of secondary sexual characteristics. Her blood endocrine profile confirmed the presence of a low free T4 (7.78nmol/L) and thyroid stimulating hormone (TSH) (0.096mIU/L). Follicle-stimulating hormone (FSH) (0.18IU/L) and luteinizing hormone (LH) (< 0.12IU/L) were also found to be below the reference ranges. She was subjected to a water deprivation test with a desmopressin challenge was suggestive of cranial diabetes insipidus. She was treated with an LCH initiation protocol which consists of intravenous vinblastine 6 mg/m2 weekly for 6 weeks and oral prednisone 40 mg/m2 daily along with hormone replacement therapy. MRI assessment after 6 weeks of treatment showed a complete resolution of bony lesions.

Discussion / Conclusion: LCH is a challenging diagnosis due to the variable spectrum of clinical manifestations. This case report highlights the importance of clinical, radiological, histopathological, and immunohistochemical characteristics for early recognition and timely treatment. MS-LCH can be debilitating especially in cases with neurological or endocrinopathy features. Early systemic treatment is warranted to limit long-term sequelae in these patients.

CASE SERIES/CASE REPORT (CLINICAL)

CC24 BONE MARROW FAILURE SYNDROME WITH DELETION 13q- AN ENTITY WITH GOOD RESPONSE TO IMMUNOSUPPRESIVE THERAPY

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Background: Bone marrow failure syndrome include conditions such as aplastic anaemia (AA), myelodysplastic syndrome (MDS) and paroxysmal nocturnal haemoglobinuria (PNH). Detection of chromosomal abnormalities through conventional karyotyping study contributes to the prognosis and plays a crucial role in disease course and management. Several reports have shown that bone marrow failure patients with del 13q responded to immunosuppressive therapy (IST) and had a favourable prognosis.

Case Presentation: A 52-year-old Indian lady presented with persistent pancytopenia over a year with haemoglobin (Hb) 7.3 g/dL, white cell count (WCC) of 3.11 x10^9/L and platelets (Plt) count 5 x10^9/L on presentation. General examination was unremarkable and there was no hepatosplenomegaly Further investigation for connective tissue screening, infective viral screening, serum B12 and folate come back as negative and normal respectively. She proceeded with bone marrow aspiration which showed hypercellular marrow and mild dysplasia while trephine biopsy sample was suboptimal. She was treated as MDS with danazol and monthly transfusion. Subsequent cytogenetic result showed 46, XX, del (13q). She was then given immunosuppressive therapy with antithymocyte globulin (ATG) and cyclosporin in August 2021. She responded well to the treatment where she became transfusion free 4 months after ATG with haemoglobin 11.5 g/dL, white cell counts 4.3 x10^9/L and platelet of 71 x10^9/L. Upon latest review in December 2023 her blood counts reveal near normal with haemoglobin of 13.5 g/dL, white cell counts 6.3 x10^9/L and platelets of 135 x10^9/L.

Discussion / Conclusion: Cytogenetic is one of the components in Revised International Prognostic Scoring System (IPSS-R) for prognosis of MDS. Most frequent chromosomal abnormalities in MDS are del(5q), del(7q), trisomy 8, loss of Y and complex karyotypes. According to IPSS-R, del (13q) is classified as cytogenetic intermediate risk group and this may lead to inappropriate treatment with hypomethylating agent or allogeneic stem cell transplant, while this benign bone marrow failure syndrome showed good response to immunosuppressive therapy with good long-term outcome, possibly a result of immune pathophysiology. Thus, bone marrow failure syndrome with del(13q), which is reported in less than 2% of the cases, should be managed as idiopathic aplastic anaemia and should be eliminated from the cytogenetic intermediate risk group as defined by the IPSS-R. As a conclusion, cytogenetic is important in bone marrow failure syndrome to determine the prognosis and management and should be performed in every patient.

CASE SERIES/CASE REPORT (CLINICAL)

CC25 P190 BCR-ABL CHRONIC MYELOID LEUKEMIA: A CASE REPORT

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Background: The oncoprotein Bcr-Ab1 exhibits two primary isoforms, which are determined by the breakpoint in the BCR gene: p190Bcr-Abl (p190) and p210Bcr-Abl (p210). While p210 is the hallmark of chronic myeloid leukemia (CML), p190 is prevalent in majority of Philadelphia-positive acute lymphoblastic leukemia (Ph+ALL) cases. In CML, p190 is the exclusive Bcr-Abl isoform at diagnosis in only a small percentage of patients (1-2%). The presence of p190 is linked to an elevated risk of progressing to the lymphoid blast phase and a suboptimal response to 1st generation tyrosine kinase inhibitor (TKI) treatments. Here, we report a patient with p190 CML and her treatment and outcome.

Case Presentation: A 19-year-old girl was diagnosed with Pre-B acute lymphoblastic leukemia (Pre B ALL) in August 2007 at 3 years old and given chemotherapy BFM 95 protocol from 2007 until 2009 by paediatric haematologist. She experienced a relapse in 2010 where she received chemotherapy with ALL-BFM 95 relapse protocol which was completed in 2013. As part of the central nervous system prophylaxis, she also underwent cranial irradiation. Remarkably, she maintained hematological remission until 2019. During a routine follow-up in 2019, incidental findings of leucocytosis with a white cell count of 181 x 10^9/L and splenomegaly. Further investigation through bone marrow aspiration and trephine biopsy confirmed a diagnosis of myeloproliferative neoplasm, chronic myeloid leukemia (CML) in the chronic phase. Cytogenetic analysis indicated the presence of the standard Philadelphia translocation (9;22) and the molecular test showed p190 the minor transcript. Treatment commenced with imatinib at a daily dose of 400 mg in April 2019 and subsequently in October 2019 it was switched to Nilotinib at a dose of 400 mg bd due to treatment failure. Unfortunately, her response to nilotinib also proved unsatisfactory, as observed through serial Bcr-Abl monitoring. No ABL kinase domain mutation was detected. Subsequently, dasatinib 100 mg daily was commenced and showed a good response based on serial Bcr-Abl monitoring. However, after two years on dasatinib, left pleural effusion developed which is a known side effect. Consequently, dasatinib dosage was reduced to 50 mg daily resulting in a suboptimal response. The option of haploidentical stem cell transplant was discussed, and while on transplant work-up, the patient transitioned to third generation TKI, ponatinib at a daily dose of 30mg aim to achieve a good disease control before stem cell transplant.

Discussion / Conclusion: The occurrence of p190 BCR-ABL translocation is uncommon, manifesting in merely 1% to 2% of individuals with chronic myeloid leukemia. Individuals with p190 BCR-ABL CML tend to exhibit an inadequate and brief response to 1st generation tyrosine kinase inhibitor (TKI) therapy, as evidenced in our patient. Thus, it is crucial to recognize these patients as high-risk right from the start to maximize the potential for achieving a good molecular response. Individuals diagnosed with p190 BCR-ABL CML should receive initial treatment with second-generation TKI to reach treatment target promptly. TKI with Src inhibitory activity such as dasatinib or ponatinib may have better efficacy for this special entity.

CASE SERIES/CASE REPORT (CLINICAL)

CC26 DELIVERING A SMILE, EVEN WITHOUT "SMILE"

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Background: Extra-nodal natural killer (NK)/ T-cell lymphoma is an aggressive type of cancer. It is the most common subtype of NK/T-cell lymphoma particularly in Asia, with strong association with Epstein- Barr virus (EBV) infection. Current guidelines suggest a combination of intensive chemotherapy; most commonly L-asparaginase containing SMILE regime, plus radiotherapy. However, the toxicities associated with SMILE regime can pose a difficult challenge while managing the disease in certain groups of population. We report our experience of managing a patient with multiple co-morbidities, diagnosed with extra-nodal NK/T-cell lymphoma by using a less toxic L-asparaginase containing chemotherapy regime, yet still able to achieve a good outcome.

Case Presentation: A 58-year-old gentleman was referred to Haematology Unit, Hospital Sultanah Aminah, Johor Bahru in November 2020 for further management of extra-nodal NK/T-cell lymphoma (nasal type). The patient has multiple medical co-morbidities, which includes type 2 diabetes mellitus (T2DM), essential hypertension, stage 3b chronic kidney disease (CKD) with GFR 40 ml/min, as well as history of recurrent ischemic cerebrovascular accident (CVA) in 2014 and 2016, with a residual left hemiparesis; rendering him to be ECOG 3 at time of presentation. He first presented to district hospital with complaints of right nasal mass associated with fever, loss of appetite as well as unintentional weight loss. A subsequent excision biopsy of the right nasal mass was consistent with extra-nodal NK/T-cell lymphoma, and correlating with further investigations, categorising him into Ann-Arbor stage IIB. Baseline Epstein-Barr Virus polymerase chain reaction (EBV PCR) was 1205 IU/mL. Considering patients' co-morbidities and performance status, decision was made to proceed treatment with a less intense chemotherapy regimen GELOX (Gemcitabine, Oxaliplatin, L-asparaginase) rather than the more intensive SMILE regimen. Patient subsequently underwent 3 cycles of GELOX and then received IFRT (involved-field radiotherapy) (50Gy/25#/5weeks). Chemotherapy was then resumed with another 3 cycles of GELOX, the last cycle received in September 2021. End of therapy assessment at end of 2021 via means of nasal endoscopy as well as positron emission tomography-computed tomography (PET- CT) scan showed that patient achieved complete remission. The repeat EBV PCR post treatment was undetected. Surveillance visits up till October 2023 shows that patient is still in remission (up to 24 months post therapy).

Discussion / Conclusion: Historically, anthracycline-based chemotherapy such as CHOP was used, albeit with unsatisfactory outcomes. The discovery of L-asparaginase containing regimens, when given along with radiotherapy has improved disease outcomes over the past 2 decades. The most commonly employed chemotherapy regime is SMILE regime, incorporating 5 chemotherapy agents (dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide). However, this regime has been associated with significant treatment-related toxicities. A less intense GELOX regime has relatively comparable overall response rate and progression-free survival rate, with reduced toxicity rates as illustrated in this case report. Therefore, clinicians should weigh in patients' co-morbidities in the decision-making process for the treatment, as sometimes the most intense or commonly employed treatment may not be the most appropriate. Continuous research into the management of the disease is warranted, to further improve outcomes in the future.

CASE SERIES/CASE REPORT (CLINICAL)

CC27 WEATHERING A STORM IN HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS DRIVEN BY EBV INFECTION

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Background: Hemophagocytic Lymphohistiocytosis (HLH) is a rare and potentially a life-threatening syndrome. It is caused by immune dysregulation leading to hypercytokinaemia and macrophage activation. HLH can be classified as primary and secondary. Primary HLH is caused by mutations affecting lymphocyte cytotoxicity and immune regulation whereby secondary HLH is triggered by infections, malignancies, and autoimmune disorders. It is challenging to manage HLH, especially Epstein-Barr Virus (EBV)-driven HLH. Here, we described a case of EBV-driven HLH, which responded well with HLH-94 protocol and virostatic agent.

Case Presentation: A 25-year-old lady, with no known medical illness, presented with unresolving fever for 5 days. She also had bilateral lower limb rashes and gum bleeding. Abdominal examination showed splenomegaly (4 finger breadth). There was no hepatomegaly nor lymphadenopathy. Full blood count showed pancytopenia (TWC $0.90x10^9$/L, Hb 7.7g/dL, Platelet $32x10^9$/L). There were hyperferritinemia (14,873 ng/mL), hypofibrinoginaemia (1.09g/L) and transaminitis (TG 2.04mmol/L and AST 246 U/L, ALT 525 U/L). Bone marrow aspirate and trephine biopsy showed hemophagocytosis with no evidence of leukemia, lymphoma and malignancy. Blood culture was negative. EBV viral load was markedly raised with 740,100 copies/mil, while ANA, Hepatitis B, C and HIV were negative. NK cell activity and sCD25 were not sent as these tests were not offered at our centre. She was diagnosed with HLH and was immediately commenced on HLH-94 protocol with etoposide and steroid. She was also given Rituximab and intravenous immunoglobulin. Ganciclovir was given for 24 days until clearance of EBV viral load. She responded well with the treatment with fever resolved and spleen not palpable. Her full blood count normalized and EBV viral load remained below level of detection. Currently, her condition remains stable at 24 weeks of protocol HLH-94

Discussion / Conclusion: The diagnosis of HLH is always challenging as described in our patient who presented with unresolving fever. Her presentation mimicked infectious and autoimmune conditions. High clinical suspicion and rapid recognition for HLH are mandated in unresolving fever, splenomegaly and pancytopenia. Extremely high ferritin should prompt physicians to consider HLH as the differential diagnosis. Early recognition of HLH is imperative as prompt treatment of HLH may prevent irreversible organ damage and subsequent mortality. In our patient, HLH targeted treatment (HLH-94 protocol) was initiated promptly within 1 week of presentation. Rituximab was added in the treatment of our patient to deplete EBV- harbouring B cells. EBV resides in T cells or in NK cells. EBV infected B cells are hypothesized to potentially transfer EBV virus to T cells or NK cells. For patient with EBV-HLH, EBV viral load is useful to guide the duration of ganciclovir treatment and monitor the response to treatment. Patients with persistently high EBV viral load may eventually require allogeneic stem cell transplant as a cure of the disease. In conclusion, high clinical suspicion and rapid recognition for HLH are important as prompt treatment of HLH may prevent irreversible organ damage and mortality.

CASE SERIES/CASE REPORT (CLINICAL)

CC28 LOW DOSE EMICIZUMAB: A MALAYSIAN EXPERIENCE

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Background: Emicizumab, a humanized, bispecific, monoclonal antibody has proven efficacy as prophylaxis for patients with Haemophilia A. Owing to the disease burden, it is cost effective in managing patients with Haemophilia A with inhibitors compared to conventional agents. However, the cost remains high at conventional doses. We report our 5-year experience with emicizumab and at a reduced dose which is effective and potentially affordable for resource poor countries.

Case Presentation: A total of 10 Haemophilia A with inhibitors received emicizumab during this period with a maximum duration of treatment of 267 weeks. 8 of these patients received standard dose of emicizumab as per package insert initially and subsequently dose reduction done (treatment duration of 156-267weeks) whilst 2 of them received low dose emicizumab; without loading dose, from the outset (treated for 37 weeks & 45 weeks respectively). Prior to emicizumab, they were treated with bypassing agents on demand with an annualized bleeding rate of between 3 to 92.

Discussion / Conclusion: Even at reduced dose, emicizumab continues to demonstrate favourable efficacy and bleeding outcomes. This provides a cost-effective alternative for prophylaxis in Haemophilia A with inhibitors especially from resource limited countries.

CASE SERIES/CASE REPORT (CLINICAL)

CC29 A 10-YEAR REVIEW OF PEDIATRIC BURKITT LYMPHOMA IN UNIVERSITY MALAYA MEDICAL CENTER

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Background: Burkitt lymphoma (BL) is the commonest subtype of childhood non-Hodgkin lymphoma (NHL), corresponding to about 40% of all childhood NHL. However, despite its highly aggressive nature, reported outcomes for pediatric BL treated with intensive chemotherapy are excellent with 5-year overall survival (OS) of 90% in localized disease and up to 80% for late-stage disease. The aim of this study was to review the outcome for pediatric BL in our center. We conducted a retrospective analysis of children aged <18 years who met the diagnostic criteria for BL and were treated in UMMC between 2010 and 2020.

Case Presentation: Nineteen patients (16 boys) were seen. All were of Asian ethnicity, and none were HIV positive. Median age at diagnosis was 7.6 (range: 2 to 15) years. The majority of patients (84%) had stage III-IV disease. Disease locations include cervical lymphnodes (5), abdomen (4), jaw (3), bone marrow (3), sinonasal (2), mediastinum (1) and orbit (1). All patients were treated according to the BFM-NHL-2004 protocol. Urgent complications at initial presentation were superior vena cava obstruction syndrome in 1 patient and tumour lysis syndrome with acute renal impairment in 3 patients. There were 3 induction deaths due to sepsis, gastrointestinal bleeding, and veno-occlusive disease each. One patient with stage III disease was refractory to first-line therapy; he did not respond to a salvage regimen (R-ICE) and died of disease 8 months post-diagnosis. All remaining patients completed treatment and achieved complete remission. There were 5 (26%) relapses: systemic/nodal (3) and isolated CNS (2). Median time of relapse following treatment cessation was 4 weeks (range: 1 to 12). Three patients received salvage regimens, either with R-ICE or R-CYVE, while two opted for palliative care. Of the three patients who received salvage therapy, two (both with isolated CNS relapse) proceeded to myeloablative chemotherapy with autologous stem cell rescue. One patient is alive (> 7 years, likely cured) while the other died from progressive disease soon after treatment. With a median follow-up of 5 years, 11 patients remain alive. Thus, we report a 5-year OS of 53%, and a 5- year EFS of 47%. There were 9 (47%) deaths in total: 5 due to disease (4 relapse, 1 refractory), and 3 due to treatment toxicity at induction.

Discussion / Conclusion: Notably, 84% of our patients presented at an advanced stage with organ impairment and/or tumour lysis syndrome at first presentation; factors which may have contributed to the poorer results seen. Survival rate for relapsed disease was low at 20%, comparable to reported survival outcomes of 10-20% in this cohort. Patients with CNS relapse can still be salvaged. However, our analysis is limited by the small sample size and sourced from a single institution, precluding robust conclusions. This audit has highlighted several areas for improvement. These include: [1] enhancing parental cancer literacy to reduce delays in seeking medical attention; [2] upgrading of supportive care services to reduce therapy-related toxic deaths; and [3] strengthening healthcare systems to avoid disruptions in treatment intensity which increase relapse risk.

CASE SERIES/CASE REPORT (CLINICAL)

CC30 A CASE OF PANCYTOPENIA AS A SEQUELAE OF RENAL OSTEODYSTROPHY

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Background: Hyperparathyroidism is a precipitating factor to the development of bone marrow fibrosis causing pancytopenia. It is rare but it is important to be vigilant of this complication when investigating patients with pancytopenia especially in those with chronic renal failure.

Case Presentation: We present a case of a 62 year old male with underlying diabetes, hypertension and end stage renal disease, on peritoneal dialysis for 3 years now. He had been on regular hematinics and erythropoietin injections for renal anemia. He presented to us with recurrent peritonitis and was noted to have pancytopenia which persisted even after the resolution of infection. His full blood count is as follows, WBC 3.8x10^9/L, Haemoglobin 7.8g/dL, Platelet 58x10^9/L. Peripheral blood smear showed tear drop cells, mild neutropenia and thrombocytopenia. Other blood investigations revealed a raised calcium of 3.1mmol/L (NR 2.18–2.6) and a raised phosphate level of 1.71mmol/L (NR 0.78-1.65). Liver function test was normal except for a markedly raised alkaline phosphatase level of 821U/L (NR 46- 116). Intact parathyroid hormone levels were 17.30pmol/L (NR 1.58-6.03). A computed tomography scan of his neck, thorax, abdomen and pelvis was done, however it was unremarkable. A bone marrow trephine biopsy was then performed to investigate the cause of his pancytopenia and hypercalcemia which showed features comparable with renal osteodystrophy – prominent Howship's lacunae containing osteoclasts and tunnelling of fibrous tissue into bony trabeculae at subcortical bone region. The marrow was hypo-normocellular, with reduced erythropoiesis and megakaryopoiesis. Granulopoiesis appeared to be adequate with all stages of granulocytic maturation seen. There were no increase in plasma cells to support the diagnosis of multiple myeloma.

Discussion / Conclusion: We have described a case of pancytopenia due to bone marrow fibrosis secondary to renal osteodystrophy. The patient developed secondary hyperparathyroidism as a complication of his renal failure which then evolved to tertiary hyperparathyroidism due to inadequate optimization of calcium and control of phosphate levels. Hypercalcemia, osteopenia and osteolytic lesions in such patients may also be mistaken for multiple myeloma. The giveaway that differentiates renal osteodystrophy from multiple myeloma is a high alkaline phosphatase level which is usually not present in the latter. Literature search has shown that performing a parathyroidectomy in patients with secondary and tertiary hyperparathyroidism actually improves the anemia and requirement for exogenous erythropoietin therapy. However, marrow fibrosis associated with renal osteodystrophy may be irreversible.

CASE SERIES/CASE REPORT (CLINICAL)

CC31 TREATING DIFFUSE LARGE B-CELL LYMPHOMA IN THE ELDERLY PATIENT WITH RITUXIMAB- LENALIDOMIDE COMBINATION VERSUS R-MINI-CHOP: A SINGLE CENTRE EXPERIENCE

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Background: Diffuse large B-cell lymphoma (DLBCL) forms the bulk of non Hodgkin lymphoma cases encountered in clinical practice among the elderly. For the majority of cases of DLBCL patients, treatment comprising of Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone (R- CHOP) is suggested as first line chemotherapy. However, chemotherapy in the elderly population may be hampered by multiple factors, including reduced bone marrow reserves, significant comorbidities and greater side effects from chemotherapy. Dose reduction in R-CHOP, also called the R-mini-CHOP regime, is used in DLBCL patients above 75 years of age. Non – chemotherapy based treatments offer an alternative for the medically unfit DLBCL patient. Lenalidomide, an immunomodulatory drug has been shown to be beneficial in the relapsing- refractory DLBCL patient when given together with Rituximab (R2).

Case Presentation: Materials and Methods: A retrospective search of all DLBCL patients who have received treatment with R2 and R-mini CHOP in the University Malaya Medical Center's database was performed. Demographic data were collected from a review of patients' electronic medical records. Patients' treatment regimes and responses to therapy were assessed at interim and at end of treatment (6 cycles). Overall response rate (ORR) is defined as the proportion of patients achieving complete remission and partial remission based on the Lugano classification. Data gathered was analysed using SPSS version 27. Results: A total of 51 patients were identified from January 2017 till June 2023. 27 (52.9%) of the samples were male and 24 (47.1%) were female. The median age of the sample cohort was 77 years old. A majority of the samples had advanced stage lymphoma at initial diagnosis with 33 (64.7%) having stage III and IV disease, and the median IPI score at diagnosis was 3. 17 patients had received R2 and 34 had received R-mini- CHOP. Of the R2 cohort, 15/17 (88.2%) had it as second line treatment for relapsed-refractory disease and 2 (11.3%) had it as first line treatment. 33/34 of the sample who received R-mini-CHOP received it as upfront treatment, while the remaining patient had it after failing first line therapy. 8/17 (47%) of the R2 cohort and 30/34 (88.2%) of the R-mini-CHOP cohort completed at least 6 cycles of treatment. At end of treatment, 1 patient each from both R2 and R-mini- CHOP cohort were lost to follow up. 7/16 (43.7%) patients from the R2 cohort and 17/33 (51.5%) of the R-mini-CHOP cohort attained partial or complete remission. In terms of survival, the median number of months from treatment commencement to disease progression or death in the R2 cohort was 12 (IQR 26) and R-mini-CHOP 16 (IQR 27).

Discussion / Conclusion: Our study examined two approaches to treating DLBCL in a local geriatric population. Our ORR of treating relapsed-refractory DLBCL with R2 (43.7%) is comparable with the 30% response from other cohorts. However, our ORR of 51.5% in treating primary DLBCL with R-mini- CHOP is lower than other cohorts, which warrant further investigation. In summary, our study provides local Malaysian data on treatment of DLBCL in the elderly patient, hence improving our understanding of this expanding patient cohort.

CASE SERIES/CASE REPORT (CLINICAL)

CC32 GEOTRICHUM LYMPHADENITIS MIMICKING TUBERCULOUS LYMPHADENITIS IN A PATIENT WITH POST-ESSENTIAL THROMBOCYTHEMIA (ET) MYELOFIBROSIS TREATED WITH RUXOLITINIB

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Background: Primary Myelofibrosis is a chronic myeloproliferative neoplasm that may cause debilitating symptoms, which can be improved with the use of Ruxolitinib, a Janus Kinase 2 inhibitor. However, this agent has significant immunomodulatory effects which may increase the risk of opportunistic infection.

Case Presentation: This is a 54-year-old lady with intermediate 2 JAK2 positive post ET myelofibrosis diagnosed in 2018. She was started on Ruxolitinib 15mg BD due to progressive splenomegaly after 5 years treatment with conventional therapies including Hydroxyurea, Thalidomide and Danazol. Full blood count prior to Ruxolitinib commencement showed white blood cell of 6.5 x 10^3/µL, hemoglobin of 8.4 g/dL and platelets of 451 x 10^3/µL. Ruxolitinib dosage was titrated up to 25mg BD due to sub-optimal splenic response. She presented with bilateral painful neck swellings after 9 months of Ruxolitinib therapy. No fever or constitutional symptoms was reported. There were matted cervical lymphadenopathies bilaterally with the lymphadenopathy over the right (4cm x 5cm) larger than the left (3cm x 5cm). She was initially treated with intravenous antibiotic as presumed bacterial lymphadenitis. CECT revealed retropharyngeal abscess, left submandibular abscess and extensive lymphadenopathy over bilateral submandibular, cervical, intraparotid, supraclavicular, and right axillary. Biopsy over the right posterior nasal space (PNS) mass and bilateral cervical lymphadenopathy showed non-caseating chronic granulomatous inflammation. Hence Ruxolitinib was tapered and discontinued due to suspicion of Tuberculosis lymphadenitis. However further diagnostic workup including Ziehl- Nieelsen (ZN) staining, TB PCR, TB gene expert and MTB C&S on the biopsy sample were negative. Subsequently targeted therapy with Voriconazole was initiated as right PNS biopsy grew Geotrichum species, which is an environmental fungus. She demonstrated dramatic clinical and radiological resolution of retropharyngeal and submandibular abscess with residual isolated sub-centimeter cervical lymphadenopathies after 6 weeks of antifungal therapy.

Discussion / Conclusion: Ruxolitinib as a JAK2 inhibitor could potentially interfere with the normal immune response, hence account for the absence of caseating granuloma characteristic of tuberculosis. However, the negative result for ZN stains, GeneXpert, Multiplex PCR, and culture for tuberculosis makes the diagnosis for tuberculosis less likely. Although PAS and GMS staining showed no fungal bodies, the right PNS mass fungal culture identified Geotrichum species. This paired with the clinical improvement with Voriconazole supported the diagnosis of Geotrichosis fungal lymphadenitis. Opportunistic infections associated with Ruxolitinib use are increasingly reported in the literature. As JAK inhibitors gain broader application, clinician should be aware of the potential for immunosuppression so that with early recognition, they may prevent significant patient morbidity and mortality.

CASE SERIES/CASE REPORT (CLINICAL)

CC33 PRIMARY HEPATIC LYMPHOMA IN A RVD POSITIVE PATIENT

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Background: Primary hepatic lymphoma (PHL) is a rare malignancy that arises from the lymphatic tissues of the liver. It accounts for less than 1% of all lymphomas and less than 0.1% of all primary liver tumours. Lymphoma cells, like other cancer cells, exhibit hypercalcemia and the Warburg effect, a metabolic adaptation seen in cancer cells where they preferentially use glycolysis for energy production, even in the presence of oxygen, contributing to lactic acidosis and hypoglycemia.

Case Presentation: Here we describe a case of a 24 year old male, who presented with a two week history of increasing abdominal distension, right hypochondriac pain and jaundice for 2 days, and significant weight loss. On further history, he had sexual promiscuity with female partners in the past and a biological brother who was diagnosed with lymphoma. Physical examination revealed jaundice, firm non tender hepatomegaly of 20 cm, but no lymphadenopathy or splenomegaly. During admission, the patient had fever, recurrent asymptomatic hypoglycaemic episodes, hypercalcemia, and unexplained persistent lactic acidosis despite adequate hydration, appropriate antibiotic therapy and blood cultures showing negative growth. His blood results also revealed a marked increase in liver enzymes with an obstructive jaundice pattern, but normal levels of alpha-fetoprotein (AFP) and other tumour markers. Further blood tests detected the presence of HIV virus in his serum with a low Helper T Cell count. An Ultrasonography of the abdomen showed extensive hypoechoic liver lesions occupying the whole of the liver with intrahepatic duct dilatations. A Contrast Enhanced Computed Tomography (CECT) of his neck, thorax, abdomen and pelvis showed a grossly enlarged liver with multiple hypodensities of various sizes, some with necrotic centre. This was associated with dilated intrahepatic and common hepatic ducts, enlarged porta hepatis lymph nodes, cervical and abdominal lymphadenopathies. An Endoscopic Ultrasound guided liver biopsy was done and this revealed Diffuse Large B-cell lymphoma. Post liver biopsy, he was commenced on intravenous dexamethasone with gradual tapering dose and was discharged with Bactrim prophylaxis. Upon review in the outpatient clinic setting, the patient was started on Highly Active Antiretroviral Therapy and received prephase cyclophosphamide. He is planned for cyclophosphamide, hydroxy-doxorubicin, vincristine sulfate and prednisone chemotherapy regime with Rituximab.

Discussion / Conclusion: Besides malignant hypercalcemia, the Warburg effect with lactic acidosis is also an associated presentation and has been shown to have prognostic significance in lymphoma. The diagnosis of Primary Hepatic Lymphoma could be challenging. A biopsy is mandatory to differentiate it from other hepatic lesions for targeted treatment. This case report emphasizes the effective recognition of hypercalcemia and the Warburg effect in Primary Hepatic Lymphoma especially in an immunocompromised patient so that early aggressive treatment can be commenced for disease remission.

CASE SERIES/CASE REPORT (CLINICAL)

CC34 T-LYMPHOBLASTIC LYMPHOMA, HYPEREOSINOPHILIC SYNDROME TRANSFORMED: A CASE REPORT

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Background: Idiopathic Hypereosinophilic Syndrome (HES) is diagnosed after exclusion of secondary hypereosinophilia (HE) and primary causes like myeloid or lymphoid neoplasms. We are reporting a case of T-cell lymphoblastic lymphoma which developed after an initial diagnosis of idiopathic HES.

Case Presentation: A 37-year-old army with no known medical illness presented in January 2022 with worsening fluid overload symptoms for one week. There was bilateral pedal edema, bibasal lung crepitations with no hepatosplenomegaly and palpable lymph nodes. Full blood count (FBC) leukocytosis with predominant hypereosinophilia of $6.5x10^9$/L. Full blood picture (FBP) revealed bicytopenia with hypereosinophilia of 52% with some dysplastic cells (hypogranulation) and no blasts. Bone marrow aspiration and trephine (BMAT) revealed hypercellular marrow with 80% eosinophils. Leukemic translocation studies for PDGFRA, PDGFRB, BCR-ABL and molecular study for JAK2 and Caltreticulin mutation were negative. There were bilateral ventricles thromboses noted with global pericardial effusion and reduced ejection fraction (EF) on echocardiography. He was diagnosed with idiopathic HES complicated with bilateral ventricles thromboses and was started on tablet Prednisolone 1mg/kg, tablet Imatinib 200 mg daily and tablet Warfarin adjusted to therapeutic INR. His eosinophil count improved to $0.07x10^9$/L with repeated cardiac echography revealed thrombus resolution after six months of treatments. He unfortunately defaulted all subsequent follow ups and presented again one year later with intermittent fever for two months associated with multiple lymph node swellings. Physical examination revealed palpable supraclavicular, bilateral axillary and inguinal lymph nodes and hepatosplenomegaly. FBC revealed leukocytosis with predominant hypereosinophilia of $4.5x10^9$/L. BMAT done noted presence of 5% abnormal T cell population, hypercellular marrow with presence of abnormal lymphoid cells and an increased in eosinophils and its precursors. Repeated echocardiography revealed no ventricles clot recurrence. CT thoracic, abdomen and pelvis done noted diffuse neck, mediastinal, axillary, abdominal and inguinal lymphadenopathy with hepatosplenomegaly. Right axillary lymph node biopsy done was suggestive of Angioimmunoblastic T cell lymphoma. He was subsequently diagnosed with T-cell lymphoblastic lymphoma and restarted back on tablet Imatinib 400 mg daily and commenced on COEP (Cycophosphamide, Vincristine, Epirubucin and prednisolone) chemotherapy before deciding to convert to Methotrexate based chemotherapy Hyper CVAD A with the aim for peripheral blood stem cell transplantation (PBSCT) later on to achieve remission.

Discussion / Conclusion: Idiopathic HES is defined as persistent eosinophilia of $>1.5x10^9$/L after excluding other primary and secondary causes of HES. Our patient was initially diagnosed with idiopathic HES during the first presentation and clinically responded well with corticosteroids and imatinib treatments. Unfortunately, after a year of defaulted follow up and treatments, he presented again with presumably a new onset T-cell lymphoma. This case is possibly the first case of an idiopathic HES which had responded to initial treatments but later transformed into T-Lymphoblastic lymphoma. However, since there was no peripheral tissue biopsy done in the beginning, an initial concomitant HES and undiagnosed lymphoma is still possible. This case emphasized that after an initial diagnosis, regular monitoring is important for an early detection of progression to lymphoma, so that early specific treatment can be instituted.

CASE SERIES/CASE REPORT (CLINICAL)

CC35 DEADLY CUDDLE OF DIFFUSE LARGE B-CELL LYMPHOMA AROUND THE HEART

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Background: Cardiac involvement in Non-Hodgkin Lymphoma is extremely rare. Based on the 2015 WHO Classification (Tumours of the Heart and Pericardium),, primary cardiac lymphoma (PCL) represents 1% of primary cardiac malignancies and 0.5% of all extra-nodal lymphomas. These rapidly growing high grade tumours are almost exclusively Diffuse Large B-cell lymphoma (DLBCL), remaining 8.7-27.2% originate from disseminated lymphoma infiltrating the heart. Right atrium is the most common location of PCL, with the tumour being intrapericardial during diagnosis. This aggressive tumour is unusual among immunocompetent patients. Main presentation of PCL with cardiac tamponade only occurs in 20% of the cases.

Case Presentation: This report describes the clinical case of a 70-year-old immunocompetent female, previously healthy, with cardiac tamponade in shock and failure symptoms. Her underlying comorbidities are hypertension and dyslipidemia. Urgent echograph showed massive pericardial effusion with cardiac mass. After pericardiocentesis, she had staging Contrast Enhanced Computerised Tomography (CECT) done confirming hyperdense crescentic lesion within anterior and left pericardium with minimal mass effect onto the adjacent right lateral ventricle. Further histopathology studies via pericardial window biopsy were done, confirming the diagnosis of Primary Cardiac DLBCL (PC-DLBCL) of Ann Arbour stage IVe, International Prognostic Index National Comprehensive Cancer Network (NCCN-IPI) score of 5. A less intense protocol of chemotherapy was initiated for her under close monitoring of Cardiac Care Unit (CCU), planning for gradual dose escalation subsequently.

Discussion / Conclusion: This case highlights the importance of recognising presentations of PC- DLBCL, especially life-threatening as seen in this patient presenting with cardiac tamponade requiring urgent treatment. Its clinical presentation can be nonspecific, yet PCL-DLBCL is aggressive with grim outcomes. Definite diagnosis can be achieved through multimodality diagnostic imaging and/or pathological study. In our case, early echocardiography was a non-invasive simple yet crucial diagnostic tool aiding in diagnosis and relieving the patient's cardiac tamponade. The CTC team was able to localise the lesion percutaneously for tissue biopsy. Early recognition can guide management and treatment to improve a patient's overall outcome. Complication of PC-DLBCL includes heart failure, angina, pericardial effusion, tumour embolisation, direct infiltration/compression of coronary arteries and electrical conduction system. The latter manifests as electrographic (ECG) abnormalities such as atrial arrhythmias and atrioventricular blocks, risking sudden cardiac death. First-line treatment for PCL is a combination of chemotherapy. Myocardial cell necrosis and infiltration by lymphoma cells which lack intercellular cohesion can predispose patients to angina, myocardial dysfunction, arrhythmias, thrombosis or myocardial rupture. Hence, the patient requires multidisciplinary team monitoring from Cardiology and CTC. Despite advances in medicine, prognosis of patients with PCL is poor with median survival of 7 months. Although it has a high mortality rate, it can be cured with intense chemotherapy and post chemotherapy surveillance. The authors report this remarkable clinical case due to its rare entity in the absence of immunodeficiency context.

CASE SERIES/CASE REPORT (CLINICAL)

CC36 THROMBOCYTOPENIA IN CARDIOLOGY WARD: POINTS TO PONDER

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Background: Thrombocytopenia in patients with acute coronary syndrome (ACS) leads to greater mortality and morbidity, compared with those without thrombocytopeniaThere are no evidence based recommendations on antiplatelet therapy for thrombocytopenic patients, therefore it is challenging to find the aetiology of thrombocytopenia, and provide the appropriate management. We present a case of acute severe thrombocytopenia within 24 hours of Percutaneous Coronary Intervention (PCI).

Case Presentation: A 75 year-old lady with coronary artery disease and a history of bypass graft surgery in 2004, presented with persistent chest pain and dynamic electrocardiography changes. She was diagnosed with Non-ST elevated myocardial infarction. She was treated with dual antiplatelet therapy (cardiprin and clopidogrel) and subcutaneous fondaparinux before being transferred to a PCI centre for urgent coronary angiography. The study revealed complete total occlusions in all coronary vessels and 99% stenosis of the previous grafts. Decision was made by the Cardiology team to stent the diseased graft. Full blood counts (FBC) prior to procedure showed Haemoglobin of 12.4 gm/dL, total white counts (TWC) of $8x10^9$/L and platelet of 188 $x10^9$/L. A total of 9000 U intraarterial heparin was given throughout the procedure. Post stenting, the patient was given intracoronary injection of Tirofiban, then followed by continuous IV infusion. However, FBC taken at 16 hours after tirofiban infusion revealed Haemoglobin of 12.5 gm/dL, TWC counts of $7.3x10^9$/L and platelet of $1x10^9$/L. Following that, the intravenous tirofiban infusion, cardiprin and enoxaparin were stopped. The full blood picture revealed no fragmented cells, and reduced platelet counts with no clumping seen. Despite severe thrombocytopenia, the patient did not manifest any bleeding tendencies. Her Glasgow Coma Score was full, not septic and there was no sign of thrombosis or skin changes. We applied 4Ts Score, which revealed 3 points consistent with low probability of Heparin- induced thrombocytopenia (HIT) . The decision was made to start oral prednisolone at 1mg/kg and no platelet transfusion was given. The platelet counts improved within 72 hours, eventually reaching $134,000x10^9$/L. Clopidogrel was started and she was discharged well with tapering dose of prednisolone.

Discussion / Conclusion: Around the time that PCI are performed, the drugs most commonly associated with thrombocytopenia are the glycoprotein (GP) IIb/IIIa receptor inhibitors and heparin. Tirofiban is a glycoprotein IIb/IIIa inhibitor and is commonly used as an adjuvant therapy to PCI for the treatment of patients with ACS. Although the mechanism is unclear, it has been proposed that tirofiban-related thrombocytopenia is immune-mediated, that involve antibodies which react with platelets coated with the drug and cause their destruction. Tirofiban and heparin are often used together, hence, it is important to identify which drugs causing thrombocytopenia and stop it immediately. Serial platelet monitoring within 6- 24 hours of Tirofiban infusion can help recognise this complication as it can occur early.

CASE SERIES/CASE REPORT (CLINICAL)

CC37 IgG4 RELATED-DISEASE: AN ENTITY NOT TO BE MISSED

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Background: A diagnosis of immunoglobulin G4-related disease (IgG4-RD) can be easily missed if the clinical index of suspicion is low, as the disease has many mimickers. Hematologists need to recognize IgG4-RD as patients can present with common hematological manifestations such as lymphadenopathy, eosinophilia and polyclonal hypergammaglobulinemia. Here we present a case of IgG4-RD diagnosed from histological confirmation of a submandibular swelling biopsy.

Case Presentation: A 48-year-old male with a previous history of Hodgkin's lymphoma (mixed cellularity, stage IIIA) in complete remission for 1 year 3 months presented with new cervical lymphadenopathy, orbital swelling, and polyclonal hypergammaglobulinemia for one week. Physical examination revealed bilateral upper cervical nodes measuring 3cm x 4cm with firm consistency. He was suspected to have relapsed Hodgkin's lymphoma. A PET/CT scan revealed FDG-avid cervical, supra-diaphragmatic and infra diaphragmatic nodal disease. His white blood count was 5.0×10^9/L with absolute eosinophil count of 0.1×10^9/L. Serum protein electrophoresis showed a polyclonal hypergammaglobulinemia with increase in IgG of 25.44 g/L (normal values 5.4 - 18.22 g/L) and in IgE of 618 (normal value < 100Ku/L). Further evaluation with an ultrasound of neck demonstrated a heterogeneously enlarged and hypervascular right submandibular swelling, which was biopsied. The biopsy findings were suggestive of IgG4-RD: the salivary glandular tissue was infiltrated by a dense population of mature lymphocytes and plasma cells insinuating between acini. A nodular appearance imparted by fibrous bands was noted. The lymphoid infiltrate was polyclonal, and comprising CD3+, CD20+ and CD138+ cells. Numerous plasma cells were seen, with >25% of cells expressing IgG4. A diagnosis of IgG4-RD was made. The patient received four weekly cycles of intravenous Rituximab with no complication. He attained clinical remission after Rituximab infusion and was last followed up one month ago. He is currently stable on maintenance treatment of oral prednisolone 10mg daily and oral acyclovir 200mg BD.

Discussion / Conclusion: IgG4-RD is a rare chronic immune-mediated condition that can affect any organ system. Common presentations include salivary and lacrimal gland enlargement, orbital disease, autoimmune pancreatitis, retroperitoneal fibrosis, and tubulointerstitial nephritis. Although it is commonly associated with lymphadenopathy, eosinophilia and polyclonal hypergammaglobulinemia, histology findings from lymph node or bone marrow biopsies rarely demonstrate the three typical histopathological features of IgG-RD – a) dense, polyclonal lymphoplasmacytic infiltrate enriched with IgG4 plasma cells; b) storiform fibrosis; and c) obliterative phlebitis. Hence, histology confirmation, which is the gold standard of investigation, should be performed on affected organ. Early recognition of the disease is crucial as patients respond well to steroids or rituximab in the early stages of the disease, as illustrated in our patient.

CASE SERIES/CASE REPORT (CLINICAL)

CC38 A RARE CASE: ACQUIRED ISOLATED FACTOR VII DEFICIENCY WITH SUSPICIOUS TUBERCULOSIS OF COLON

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Background: Factor VII (FVII) or proconvertin is a clotting factor involved in the initiation of clotting cascade. Isolated FVII deficiency is a rare autosomal recessive disease that could result in congenital or acquired coagulopathy. The clinical presentation may vary from asymptomatic to major bleeding tendency. The degree of bleeding is normally unpredictable and it is not always linked to the FVII measurement level.

Case Presentation: We reported a case of a young man with a history of gastroesophageal reflux disease and appendicectomy for acute appendicitis. He presented in late November 2023 with 2-weeks history of left thigh and ankle swelling with superficial bruises. There was no major bleed in the joints and other organs. Clinical examination revealed that the patient was cachexic with ecchymoses over the left thigh and left ankle. The routine blood test showed an isolated prolonged prothrombin time (PT); (13.4 seconds) with normal activated partial thromboplastin time (aPTT); (32.8 seconds) and international normalized ratio (INR); (1.25). The PT mixing test showed partial correction with normal fibrinogen activity and mildly elevated d-dimer. His factor assay analysis showed mildly low FVII activity (46.4%) with the normal activity of factor assay for factor II, factor IX, and factor X. He had severe normochromic normocytic anemia with a normal white cell count and platelet count. Hepatitis B, hepatitis C, RVD, and syphilis screening turned out to be non-reactive. Renal function test, liver function test, anti-nuclear antibody, complement, and tumor markers were within normal parameters. His condition progressively worsened since mid of December 2023. Subsequently, he presented in early January 2024 with severe intrabdominal sepsis in septic shock with multi-organ failure and disseminated intravascular coagulation (DIVC). Contrast-enhanced computed tomography (CECT) abdomen showed features of a large bowel infection with a highly suspicious of TB colon. We were unable to proceed with confirmatory test as his condition further deteriorated. He then succumbed on day 2 of admission.

Discussion / Conclusion: Acquired FVII deficiency presented with bleeding tendency, isolated prolonged PT, and low FVII activity. This condition was commonly associated with infection, aplastic anemia, and malignancy. Otherwise, 14% of cases are idiopathic. This condition usually resulted in poor clinical outcomes with limited response to treatment.

CASE SERIES/CASE REPORT (CLINICAL)

CC39 A RARE OCCURRENCE OF BLACKWATER FEVER SYNDROME CAUSED BY PLASMODIUM KNOWLESI IN MALAYSIA

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Background: Haemoglobinuria is a rare complication of severe malaria and this indicates intravascular hemolysis. This usually occurs due to high malarial parasite burden and in the past was frequently documented with a high association with Plasmodium Falciparum. Here we report a rare case of a very high parasitic burden of Plasmodium Knowlesi causing severe intravascular hemolysis and severe acute kidney injury on presentation.

Case Presentation: A young 29-year-old gold miner presented with fever, vomiting and lethargic. On presentation he appeared pale and deeply jaundiced, his Glasgow coma scale was full in the first hour and very rapidly deteriorated, having a drop in GCS from 15 to 10 and went into respiratory distress. Soon he was intubated and required high ionotropic support. Blood film for malarial parasite came back positive for plasmodium knowlesi with a count of 164543/1089. IV Artesunate 2.4mg/kg was administered immediately. His full blood count showed a mild anemia of 11.7g/dL and a very low platelet count of 10 x 10^3/uL. Renal profile was deranged with raised urea of 77mmol/L and creatinine of 1136umol/L. Transminases were also mildly raised and showed severe hemolysis with a total bilirubin of 196 with indirect predominance. Other hemolysis markers such as lactate dehydrogenase were significantly raised. Coombs test was positive with direct IgG marker being positive. He required sustained low efficiency dialysis for a total of three cycles and one regular hemodialysis. He was subsequently extubated and went through a good recovery journey. His anaemia and jaundice improved without any steroid administration.

Discussion / Conclusion: In conclusion, a high suspicion of blackwater fever syndrome must be taken into consideration in a clinical presentation of fever with severe hemolysis and acute kidney injury. Prompt treatment delivery is of utmost importance here to provide the best recovery platform. Jaundice and kidney impairment took a longer recovery period to return to normal baseline however in this case it was completely reversible upon effective and complete antimalarial course.

CASE SERIES/CASE REPORT (CLINICAL)

CC40 DELAYED NEUTROPHIL AND PLATELET ENGRAFTMENT IN AN AUTOLOGOUS TRANSPLANT PATIENT WITH VERY HIGH CD34 + COLLECTION AND INFUSION - A CASE REPORT

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Background: Optimal stem cell dose for autologous stem cell transplant has been well established by American Society of Transplantation, being 3-5 x 10^6 CD34+ cells/kg and minimum of 2 x 10^6 CD34+ cells/kg. Though there is no consensus, stem cell more than the recommended dose (>15x10^6/kg) was associated with more rapid neutrophils or platelet engraftment, lesser transfusion and shorter hospital stay. Nevertheless, we report a case of delayed engraftment despite extraordinarily high stem cell dose in autologous stem cell transplant for relapsed diffuse large B cell lymphoma (DLBCL).

Case Presentation: We report a middle-aged gentleman with DLBCL who was managed in another institution in year 2012. He attained complete metabolic remission after 6 cycles of chemoimmunotherapy. Unfortunately, his disease relapsed at abdominal skin in year 2017 but he had refused treatment. The disease progressed at the end of year 2022 and he received salvage chemotherapy. He attained complete metabolic remission and was referred to our institution for mobilization chemotherapy using rituximab, dexamethasone, high dose cytarabine and carboplatin. Single stem cell harvest yielded 5884.5x10^6 CD34+ cells. He was admitted for autologous transplant using thiotepa, etoposide, cytarabine and melphalan (TEAM protocol) as conditioning chemotherapy. Total CD34+ cells infused was 68.18 x 10^6 cells/kg. Growth factor support was initiated on D5 post infusion. Neutroepenic fever was treated accordingly. He failed to engraft by day 28. Thrombopoietic mimetic agent (s/c romiplostim) and erythropoiesis stimulating agent (s/c epoetin beta, Mircera) were added in addition to blood transfusion support. His neutrophils finally engrafted by day 33 but with persistent thrombocytopenia. He was discharged uneventfully day 55 with elthrombopag. Follow up at day 100 demonstrated isolated improving thrombocytopenia but he was otherwise well. His blood count normalized by 6 months post autologous transplant and his disease remains in remission by the time of writing.

Discussion / Conclusion: Delayed or failed engraftment in autologous stem cell transplant is very rare with adequate stem cell dose. Delayed engraftment in our case despite extraordinarily high stem cell dose suggests other factors may be at play. Recent report from a single center highlighted some patients with extraordinary high stem cell yield (median of 66.8x10^6 CD34+ cells/kg) in single apheresis had delayed neutrophils engraftment despite adequate dose of infused stem cell (median infused cell dose 14.5x 10^6/kg). Many factors could affect engraftment which include quality of stem cells, stem cell storage, host factors, disease characteristic, infection and treatment received. Bone marrow reserve reflected by pre-transplant transfusion dependence and cell count and low stem cell dose were strong predictor of delayed engraftment, but these were not present in our patient. Case reports have reported autoimmune mechanism as rare cause of delayed engraftment which responded to steroid or cyclosporine. As a conclusion, studies are needed to examine factors that cause delayed engraftment and whether extraordinarily high stem cell dose adversely impact engraftment in autologous stem cell transplant. In the interim period, it is prudent not to infuse more than 15x 106/kg of CD 34 stem cells and store the remainder stem cells until engraftment is achieved.

CASE SERIES/CASE REPORT (CLINICAL)

CC41 UNDERLYING NEUROFIBROMATOSIS TYPE 1 WITH JUVENILE MYELOMONOCYTIC LEUKEMIA

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Background: Juvenile myelomonocytic leukaemia (JMML) is classified as a combined myeloproliferative/ myelodysplastic disease by the World Health Organization and accounts for less than 3% of all childhood hematologic malignancies. Children typically present at young age (median age at diagnosis: two years old) with hepatosplenomegaly, leucocytosis with absolute monocytosis and elevated HbF. JMML usually involves somatic and/or germline mutations in the genes of the RAS pathway, including PTPN11, NRAS, KRAS, NF1, and CBL in the leukemic cells in the absence of Philadelphia chromosome. Cytogenetic analysis usually reveals normal karyotype in ~65% of the cases. Almost all patients with JMML experience an aggressive clinical course, thus hematopoietic stem cell transplantation (HSCT) is the only curative treatment.

Case Presentation: We report a case of 2 years 5 months old boy with underlying clinically diagnosed neurofibromatosis Type 1 since 2022. He went to clinic multiple times for recurrent upper respiratory tract infection and unprovoked epistaxis. Due to worsening symptoms, he was admitted and noted to have hyperleukocytosis with absolute monocytosis (WBC:156.77x10^9/L, Monocyte: 26.47x10^9/L,) bicytopenia with Hb:8.9 g/dL and platelets count: 35x10^9/L. Physical examination revealed hepatosplenomegaly and presence of multiple café au lait spots on limbs and trunk. Peripheral blood picture revealed hyperleukocytosis and dysplastic granulocytic cells with presence of 4% circulating blasts. Bone marrow aspiration and trephine biopsy (BMAT) shows markedly hypercellular marrow, granulocytic hyperplasia and dysgranulopoiesis with no excess of blast. Hb analysis showed increased Hb F (44.8%). Meanwhile, flow cytometry revealed aberration of monocytes with reduced classical monocytes while increased non-classical monocytes. Type 1 hematogone was absence. Cytogenetic and molecular studies showed no abnormalities. In correlation with clinical history and laboratory investigations, features highly suggestive of MDS/MPN favoring JMML.

Discussion / Conclusion: Neurofibromatosis type 1 predispose to JMML via loss of function of the NF1 tumor suppressor gene and consecutive deregulation of RAS signal transduction pathway. The risk of developing JMML is reported to be 200-500 times occurring in children with NF1 and is invariably rapidly fatal if left untreated. Therefore, a complete laboratory investigation along with proper clinical history correlation are mandatory for a definite diagnosis of JMML as well as establishing a better treatment for the patient.

CASE SERIES/CASE REPORT (CLINICAL)

CC42 OPTIMIZING CLINICAL OUTCOMES: CONSOLIDATION AUTOLOGOUS TRANSPLANT FOR CNS LYMPHOMA – INSIGHTS FROM A SINGLE-CENTRE STUDY IN MALAYSIA

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Background: Central nervous system (CNS) lymphoma is rare and aggressive subtype of non Hodgkin lymphoma. Despite its clinical significance, there is a scarcity of data concerning the role of autologous stem cell transplantation in this specific patient population. Here, we describe our experiences with consolidation autologous transplant for the treatment of CNS lymphoma.

Case Presentation: A total of 5 patients included in this series, 3 patients with primary CNS lymphoma (PCNSL) and 2 patients with secondary CNS lymphoma (SCNSL). **Case 1**: A 47-year-old gentleman, diagnosed with PCNSL after presenting with headache and status epilepticus. Brain imaging revealed a left temporal enhancing lesion. He received de Angelis protocol, followed by modified MATRix protocol (without thiotepa) due to inadequate response. Treatment was consolidated with autologous transplant using BCNU thiotepa conditioning one year after diagnosis. Unfortunately, he relapsed and succumbed six months post transplant. **Case 2**: A 19-year-old female with history of abnormal behaviour and left sided weakness had right basal ganglia mass on her brain MRI. Right endoscopic biopsy was performed and confirmed the diagnosis of DLBCL. Modified MATRix protocol was administered since interim imaging showed unfavourable response after week 7 de Angelis protocol. She underwent autologous transplant consolidation using busulfan (oral), cyclophosphamide and thiotepa (BuCyTT) conditioning two years after diagnosis. After follow-up of 17 months, she is in good remission with residual left hemiparesis. **Case 3**: A 51-year-old lady with history of vomiting and left sided weakness, had brain MRI showing right parietal lobe and body of corpus callosum lesion. Biopsy of the lesion confirmed diagnosis of PCNSL. She received de Angelis protocol up to week 19 and later salvaged with high-dose methotrexate with ifosfomide after relapsed within 6 months. Currently, 11 months post autologous transplant with BuCyTT, she is in remission and has resumed to work. **Case 4**: A 45-year-old lady was diagnosed with DLBCL from gastric biopsy when she presented with abdominal pain and constipation. She has isolated cranial nerve 6 palsy, hence treated for secondary CNS lymphoma, and marrow lymphomatous infiltration. She completed 3 pairs for Block AB protocol followed by an autologous transplant consolidation using BuCyTT conditioning. After follow-up of 8 months post-transplant, she has no sign of recurrence. **Case 5**: A 42-year-old gentleman was diagnosed with composite lymphoma (mixture of Burkitt and Mantle cell lymphoma) when he presented with lower limb weakness, headache with right eye ptosis and abdominal pain. He had MRI brain which showed secondary CNS lymphoma. He received Rituximab-IDARAM (idarubicin, dexamethasone, cytarabine and methotrexate) regimen in view of aggressive disease. Treatment further consolidated with an autologous transplant and currently awaiting PET/CT assessment.

Discussion / Conclusion: In our preliminary study, the application of autologous transplant consolidation in CNS lymphoma patients demonstrated promising outcomes within a short follow-up period. The use of BuCyTT conditioning showed improvements in achieving complete response post transplant, suggesting potential advantages for enhancement treatment efficacy in our cohort.

CASE SERIES/CASE REPORT (CLINICAL)

CC43 CHALLENGES IN THE MANAGEMENT OF PSORIASIS FLARE IN ACUTE MYELOID LEUKEMIA: A CASE REPORT

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Background: Chemotherapy has been the standard treatment for acute myeloid leukaemia (AML). Granulocyte colony-stimulating factor (G-CSF), a haemopoietic growth glycoprotein is often given for chemotherapy-induced neutropenia to accelerate neutrophil recovery via peripheral mobilisation of blood stem cells. Psoriasis flare is a rare complication following GCSF administration. We present a psoriatic lady who was recently diagnosed with AML and developed psoriatic flare after receiving GCSF.

Case Presentation: A 23-year-old female with underlying well-controlled psoriasis on topical treatment, presented with 2 weeks of intermittent fever and unintentional weight loss of 4kg (9%). Her initial FBC showed TWC 84.4, Hb 8.9, PLT 136; bone marrow aspirate revealed 88% myeloblasts expressing HLADR+ and CD33+, with abnormal cytogenetic exhibiting t(11;19)(q23;p13.3). A diagnosis of AML with KMT2A-MLLT1 mutation was made, and the patient was commenced on induction chemotherapy with Daunorubicin and Cytarabine (DA 3+7). During the second week of chemotherapy, she developed febrile neutropenia and was subsequently given G-CSF when her ANC dipped to 0.0. Shortly following GCSF administration, she developed flares of psoriasis and was started on potent topical steroids, topical tars, and emollients. A Skin biopsy was done and histopathological examination is consistent with plaque psoriasis with no evidence of leukemic cutis or infection. Her lesions responded well with topical therapy and the patient was discharged home towards the 4th week. During her follow-up on D26 of chemotherapy, she received another dose of Filgrastim because of ANC 1.3. Within 3 days, there is an eruption of silvery scaly plaques concentrated around her torso with distal extension to peripheries. This time, however, the lesions failed to improve despite optimal topical therapy. She was eventually initiated on oral retinoids due to extensive plaque lesions >20% BSA involvement.

Discussion / Conclusion: Psoriasis is a chronic inflammatory disease thought to revolve around genetic susceptibility and immune dysregulation, with Interleukin (IL)-23/ Th17 being the most important pathway. Unlike GM-CSF which has been detected in higher levels from psoriatic lesions, the role of G-CSF in psoriasis is less established despite being recognised as a rare therapy-related complication. Our patient experienced severe psoriatic flare which coincides with Filgrastim administration. Other possible triggers in this case include chemotherapy, infections, psychological stress from the illness, or even the malignancy itself. Clinicians who are treating AML patients with psoriasis need to be mindful of the potential deterioration of skin disease when deciding to administer GCSF. Treatment of psoriasis flare in AML is challenging due to the immunosuppressive properties of most systemic agents available. Phototherapy like narrow band ultraviolet-B (NBUVB) or psoralens-ultraviolet A (PUVA) are proven to be safe and effective in the treatment of psoriasis - these are unfortunately not available at our center. G-CSF is a recognised cause of psoriasis flare in patients with hematological disorder. Prompt diagnosis and co-management with a dermatologist will ensure best control of both psoriasis and the underlying hematological disease.

CASE SERIES/CASE REPORT (CLINICAL)

CC44 SPLENIC MARGINAL ZONE LYMPHOMA WITH CONCOMITTANT HEPATOCELLULAR CARCINOMA IN A CHRONIC HEPATITIS B PATIENT: A CASE REPORT

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Background: Chronic Hepatitis B infection increases the risk of lymphoproliferative disorder, ranging from the commonest form of diffuse large B cell lymphoma (DLBCL) to rarer forms of splenic marginal zone lymphoma (SMZL). Hepatocellular carcinoma (HCC) is the major concern among chronic Hep B patients, but coexistence of HCC and SMZL is rare.

Case Presentation: 65 years old Chinese gentleman, presented to government health clinic in May 2023 with bilateral lower limb purpuric rashes for 1 weeks. Full blood count (FBC) noted lymphocytosis with bicytopaenia, white blood cell (WBC) 55.8 x 10^9/L, haemoglobin (Hb): 9.5g/dL, platelet 73 x 10^9/L. Physical examination noted massive splenomegaly, no lymphadenopathy. He was referred to HSIJBTRO haematological malignancy. Urgent peripheral blood film revealed presence of 73% of abnormal lymphoid cell, for which peripheral blood immunophenotyping (IPT) showed 86.9% abnormal B lymphoid population and suggestive of B-cell lymphoproliferative disorder (B-LPD). His viral screening came back as Hep BeAg negative chronic hepatitis B infection, with negative anti-hepatitis C and anti HIV. Ultrasound hepatobiliary system reported liver hyperechoic lesion and splenomegaly with tiny hypoechoic lesions.

Subsequent CT 4-phase liver and CT thorax, abdomen and pelvis found a large exophytic liver mass at segment IV measuring 6.7 x 6.7 x 5.0 cm, and another similar lesion at segment VIII measuring 6.4 x 6.5 cm. HCC was diagnosed based on characteristic CT findings and elevated alpha-fetoprotein at 61678.4ng/mL. Patient was referred to haematologist for the subsequent investigation of his lymphocytosis. A bone marrow aspiration and trephine biopsy was done which revealed hypercellular marrow, all three hematopoietic cell lineages reduced, diffused and interstitial infiltration of abnormal lymphoid cells, lymphoid cells small in size with clumped chromatin pattern and scanty cytoplasm, positive for CD79a, CD20, PAX5, CD23, negative for CD5, CD10, BCL 6 and cyclin D1. Ki-67 proliferation index is < 10%. Thus, a diagnosis of SMZL was made. Patient was planned for hepatitis B treatment and monitored under haematology for resolution of SMZL, prior to deciding for further chemotherapy. For hepatitis B and HCC, he was managed in multidisciplinary approach under gastroenterology, hepatobiliary, and oncology department. Patient was started on tenofovir. Transarterial chemoembolization (TACE) was deemed not suitable by hepatobiliary team. Patient was started on FOLFOX (folinic acid, fluorouracil and oxaliplatin) regime under oncology since November 2023, after he declined lenvatinib due to financial constraint.

Discussion / Conclusion: Prevalence rate of both viral hepatitis B and C was higher among SMZL patients and other indolent B-cell non-Hodgkin lymphoma. The proposed mechanisms of oncogenesis included integration of HBV DNA in the host genome, causing chronic antigenic stimulation & viral production, with the release of haematopoietic tumour growth factors leading to B-lymphoid cells proliferation. Antiviral therapy is among the therapeutic options for the curative purpose of SMZL in patients with concomitant chronic hepatitis B. To our knowledge based on literature review, concomitant SMZL with HCC underlying chronic hepatitis B is rare. This case report serves to increase the awareness to look for B-LPD as a complication of chronic hepatitis B, which may co-exist with HCC.

CASE SERIES/CASE REPORT (CLINICAL)

CC45 IMMUNOGLOBULIN LIGHT CHAIN (AL) AMYLOIDOSIS: IMPORTANCE OF COMPLETE HAEMATOLOGIC RESPONSE

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Background: Immunoglobulin light chain (AL) amyloidosis is a monoclonal plasma cell proliferative disorder characterized by deposition of fibrils of monoclonal light chains in heart, kidneys and other tissues, leading to organ dysfunction. We report a case of AL amyloidosis to highlight that depth of haematologic response is critical for clinical outcome and overall survival.

Case Presentation: In December 2017, a 64-year-old man, with hypertension and dyslipidaemia, presented with 5-month-history of bilateral leg swelling and progressive worsening of shortness of breath. He had chronic diarrhoea, symmetric lower extremity peripheral neuropathy and autonomic neuropathy (postural hypotension). He had percutaneous coronary intervention (PCI) to left anterior descending artery in September 2017. Echocardiogram showed global bi-ventricular hypertrophy, interatrial septal thickening, ejection fraction 50%. Cardiac magnetic resonance imaging (MRI) reported as infiltrative cardiomyopathy, highly suggestive of cardiac amyloidosis. Serum and urine protein electrophoresis showed paraproteinaemia (8.9 g/L, IgG lambda) with no paraprotein in urine. Serum light chain assay showed normal free kappa light chain (12.7 mg/L), elevated free lambda light chain (227 mg/L), kappa:lambda ratio of 0.06. In December 2017, he was diagnosed as systemic AL amyloidosis based on (1) amyloid-related systemic syndrome (heart, gastrointestinal tract, peripheral nerve involvement), (2) positive amyloid staining by Congo red in rectal biopsy, (3) evidence of monoclonal plasma cell proliferative disorder (presence of serum M protein, abnormal serum free light chain ratio, clonal plasma cells in bone marrow). He was non-transplant eligible and treated with 2 cycles of cyclophosphamide+thalidomide+dexamethasone and 7 cycles of melphalan+prednisolone (MP). After 9 cycles of therapy, the optimal response was not achieved. Bortezomib was added to MP (VMP). In March 2019, after 3 cycles of VMP, he achieved complete haematologic response. The same treatment regimen was continued. No organ response was achieved. In January 2023, he succumbed to decompensated cardiac failure.

Discussion / Conclusion: Our patient achieved complete haematologic response, however, no organ response was achieved. His overall survival was 62 months. Addition of bortezomib to melphalan+prednisolone resulted in achieving rapid and deep/ complete haematologic response, leading to good long-term clinical outcome with prolonged overall survival. Several clinical trials demonstrated poor survival outcome if no complete haematologic response was achieved in AL amyloidosis. Complete haematologic response rate was lower with conventional chemotherapy (melphalan + dexamethasone) compared to bortezomib-based therapy (bortezomib + melphalan + dexamethasone) in AL amyloidosis. In this era, paradigm shift with emerging treatment, i.e., addition of daratumumab to bortezomib-based therapy (daratumumab + bortezomib + cyclophosphamide + dexamethasone) resulted in deeper responses and delayed major organ deterioration in newly diagnosed AL amyloidosis (ANDROMEDA trial). However, clinical trials with novel agents are urgently needed to improve rapid, deep, durable haematologic response rate and organ response rate for better quality of life, with ultimate goal of cure in AL amyloidosis.

CASE SERIES/CASE REPORT (CLINICAL)

CC46 HUMAN IMMUNODEFICIENCY VIRUS – NEGATIVE PLASMABLASTIC MYELOMA: A CASE SERIES

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Background: Plasmablastic myeloma is a unique subtype of plasma cell neoplasm. This highly aggressive form of myeloma has been associated with Human Immunodeficiency Virus (HIV) positive patients. Here, we report two male patients with HIV negative plasmablastic myeloma with rapid progression after chemotherapy and autologous stem cell transplantation.

Case Presentation: Patient 1: A 55-year-old man who was previously well presented with anaemia, whole-body pain and lymphocytosis. There was no lymphadenopathy or organomegaly. Bone marrow aspirate and trephine biopsy revealed histopathology and immunohistochemistry features that were consistent with plasmablastic myeloma. Immunochemotherapy consisting of bortezomib, thalidomide and dexamethasone (VTD) was initiated. His condition relapsed one year after autologous transplantation and is currently under palliative care. Patient 2: A 47-year-old man presented with anaemia and renal impairment. There was no nodal involvement or organomegaly. Histopathological and other related examinations revealed a similar diagnosis of plasmablastic myeloma. Initial therapy consisted of dexamethasone and thalidomide but the patient progressed to CNS infiltration. Immunochemotherapy for relapsed/refractory disease consisting of dexamethasone, daily thalidomide, and 4 days of continuous-infusion cisplatin, doxorubicin, cyclophosphamide, and etoposide (DTPACE) was commenced.

Discussion / Conclusion: A regulatory subset of plasmablasts, called IL-10+ plasmablasts, emerges from naive B cells in disease contexts like autoimmunity and cancer. Plasma cell transcription factors BLIMP1 and IRF4/MUM1 control the differentiation of this specialized population. In addition, like short- lived plasmablasts, IL-10+ plasmablasts are CD19+, CD24–, CD38+, CD27+, and CD138–. These two plasmablast populations can be distinguished by their expression of CD20. IL-10+ plasmablasts express low to intermediate levels of the marker, whereas normal plasmablasts do not express it at all. Additional markers of plasmablasts include CD19, CD44, CD45, CXCR3, CXCR4, KLF4, MS4A1, TNFRSF17, and HLA-DR. Plasmablastic myeloma is a rare form of myeloma with poor prognosis. The pathogenesis and molecular features of this rare entity still remains largely unclear.

CASE SERIES/CASE REPORT (CLINICAL)

CC47 SUCCESSFUL MANAGEMENT OF HYPOFIBRINOGENEMIA IN PREGNANCY WITH HUMAN FIBRINOGEN CONCENTRATE IN A LIMITED RESOURCE SETTING

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Background: Fibrinogen plays a pivotal role in hemostasis. Disorders of fibrinogen such as afibrinogenemia or hypofibrinogenemia may result in both haemorrhagic and thrombotic manifestations. This case explores the challenges and management of this hematological disorder in an obstetric setting.

Case Presentation: Madam A is a 30-year-old lady who first presented in 2021 with complaints of occasional bruising and mild gum bleeding during tooth-brushing. Her ISTH bleeding score was 4. Fibrinogen was measured using Clauss functional assay and she was found to have persistently low plasma fibrinogen levels ranging 50-60 mg/dl. Aside from mildly elevated PT and PTT levels, D-dimer and factor VII studies were normal and autoimmune screening was negative. She was presumed to have hypofibrinogenemia but further testing i.e. genetic analysis was not available. Her family members do not have history of bleeding and have not been tested before. She was referred to our center at 23 weeks into her first pregnancy. Fibrinogen was in the 70-90 mg/dl range. She was not given fibrinogen antenatally as she has no bleeding tendencies from history, and she was not keen for any blood product. Fetal assessment revealed late-onset intrauterine growth restriction; hence she was planned for early induction of labour. A multidisciplinary team discussion was held to devise a treatment plan. The patient was admitted and induced for vaginal delivery at 36 weeks 5 days of gestation. PCA Fentanyl replaced epidural anaesthesia for pain management. Fibrinogen levels were checked daily and a thromboelastogram done on admission showed normal fibrinogen activity. Just prior to amniotomy, 2 vials of human fibrinogen concentrate (Fibryga) containing approximately 2g of fibrinogen were given. Fibrinogen levels raised post administration from 79 mg/dl to 140 mg/dl. The patient delivered a healthy baby girl weighing 2370g, with a minimal estimated blood loss of 200 ml. Fibrinogen level of the neonate taken at birth was 40 mg/dl. The neonate did not have any bleeding episodes. The patient was discharged well second day post-partum. She returned nine days post-delivery with sudden increased vaginal bleeding (estimated blood loss 500ml) and fibrinogen of 78 mg/dl. One vial of Fibryga was promptly administered and bleeding subsided. No packed cell transfusion was required as her hemoglobin was stable. A course of antibiotics was given for possible endometritis. There were no more bleeding events thereafter.

Discussion / Conclusion: Favourable maternal and fetal outcomes were achieved because of early identification of potential complications, vigilant monitoring, and timely administration of fibrinogen replacement therapy. The collaborative efforts of haematologists, obstetricians and other medical specialites were valuable in navigating the challenges. This marks the first reported case of using Fibryga for hypofibrinogenemia during pregnancy in Malaysia. The guideline recommends maintaining fibrinogen levels above 150 mg/dL. However, a one-size-fits-all treatment approach isn't suitable. We must consider the patient's bleeding history and strike a balance between the risks of bleeding and thrombosis.

CASE SERIES/CASE REPORT (CLINICAL)

CC48 PITUITARY APOPLEXY IN MULTIPLE MYELOMA: A CONUNDRUM OF ETIOLOGY BETWEEN PITUITARY PLASMACYTOMA AND LENALIDOMIDE INDUCED PITUITARY ARTERY THROMBOSIS

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Background: Pituitary apoplexy in multiple myeloma patients are not uncommon. It can occur with a concomitant neurological symptoms before the multiple myeloma diagnosis, during the course of treatment and after post stem cell transplantation. Reports on this condition are scarce even with current sophisticated imaging techniques. The symptoms mainly are headaches, blurring of vision and rarely seizures. The cause of pituitary apoplexy in multiple myeloma largely are not well understood. Plasmacytoma of the pituitary has been reported with assumptions but thalidomide induced pituitary artery thrombosis could not be excluded.

Case Presentation: A 54-year-old female with underlying hypertension with history of chronic headaches. The MRI of brain did not show any remarkable findings. Her haemoglobin level was 51g /L with normocytic hypochromic anemia. Her albumin globulin ration was reversed. Subsequent full blood pictures shows marked rouleaux formation. Her multiple myeloma work-up confirmed that she has IgA kappa multiple myeloma (serum paraprotein 51 g/L) with extensive vertebral bone involvement. Her renal function was normal and plasma cells in the marrow 41.8% plasma cells before they opted for chemotherapy. Her serum paraprotein was undetectable after cycle 3. At day 5 of 5th cycle of dexamethasone and Lenalidomide regime, she presented again with headache and visual disturbance. Her brain MRI head showed a cystic sellar lesion with non-visualisation of pituitary gland. She was managed as pituitary apoplexy, with IV Hydrocortisone at the presentation, followed by oral hydrocortisone replacement. However, her hormonal work-up shows normal results and the treatment was withheld. When the MRI was compared, we assume that this might be a pituitary plasmacytoma however lenalidomide thrombogenesis to the pituitary vessels could not be excluded entirely. The MRA only shows no arterial feed to the sellar region. As we fear of lenalidomide thrombogenic risk, we withheld the patients chemotherapy regime at 5th cycle and put her on mainteinance therapy. She was asymptomatic without hormonal replacement and shows excellent response to treatment with her paraprotein remains undetectable under our care.

Discussion / Conclusion: Although the diagnosis of pituitary plasmacytomas can be challenging, these tumors often exhibit responsiveness to chemotherapy treatment. Additionally, they may present with pituitary apoplexy, a potentially life-threatening endocrine disorder, can arise from either infarction or hemorrhage in the pituitary gland. Incidence rates vary widely, reported in studies ranging from around 1% to 26%. Patients experiencing pituitary apoplexy may exhibit symptoms such as headaches, altered sensorium, and visual defects, which can be mistaken for conditions like subarachnoid hemorrhage or meningitis. Imaging techniques like CT or MRI play a crucial role in diagnosis. Comparable outcomes have been observed in both conservative management and surgical intervention in more recent research. Long-term follow-up with hormonal evaluations is necessary to address hormone deficiencies.

CASE SERIES/CASE REPORT (CLINICAL)

CC49 CASE REPORT OF A RARE DISEASE ENTITY: CHRONIC NEUTROPHILIC LEUKAEMIA

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Background: Chronic Neutrophilic Leukaemia (CNL) is an uncommon subtype of myeloproliferative disorder, characterized by leucocytosis and splenomegaly. This case report explores the diagnostic challenge of a young adult presented with hyperleukocytosis who was eventually diagnosed with CNL but succumbed to complications of the disease within months of diagnosis.

Case Presentation: A 35-year-old male farmer with no history of smoking, alcohol consumption, or significant medical issues, presented with a two-month history of constitutional symptoms and abdominal distention. Clinical examination showed splenomegaly 8cm below costal margin. Initial full blood count showed Hb 5.1 g/dl, WCC 125 x 10^3/uL and platelet 151 x 10^3/uL. Peripheral blood film revealed hyperleukocytosis with left shift and 4% blast cells. His bone marrow displayed hypercellularity with all stages of granulocytic maturation, notably prominent myelocytes and neutrophils. No BCR- ABL1 fusion gene was detected in the initial RT-qPCR testing however breakpoint in micro BCR region was detected (p230, c3a3) during the extended panel of testing. Cytogenetic study was a challenge as there was only a few metaphases available for analysis. In view of typical clinical presentation and marrow morphology, a diagnosis of chronic myeloid leukaemia (CML) was made, and patient was started on Imatinib. For the subsequent month, despite switching to nilotinib and patient claiming to be compliant to medication, his white cell count remained elevated averaging between 200 to 300 x 10^3/uL. He had frequent admissions to hospital for symptomatic anaemia needing blood transfusions and unfortunately passed away due to recurrent sepsis. Posthumously, testing of the remaining blood sample via next-generation sequencing (NGS) revealed CSF3R gene mutations and ASXL1 frameshift alteration, revising the diagnosis to chronic neutrophilic leukemia instead, in accordance with histopathological criteria.

Discussion / Conclusion: CNL is an extremely rare entity about which little is known. Typically, it manifests as a clonal disorder in elderly adults, yet in our instance, the patient is notably younger. The initial detection of the micro BCR ABL variant in the molecular sample proved to be a red herring, given its rarity, and sometimes is associated with CNL as well as neutrophilic CML variant (CML-N). This case underscores the diagnostic challenges of CNL and the value of integrating clinical, laboratory criteria, and treatment response to differentiate it from similar yet distinct disease entities It also further highlights the importance of utilizing NGS with reasonable turnaround times in complex situations. Despite extensive research, treatment of CNL remains limited. Allogeneic stem cell transplantation offers potential cure but poses high treatment-related mortality. On the other hand, ruxolitinib has shown promising responses in CNL patients.

CASE SERIES/CASE REPORT (CLINICAL)

CC50 HYPERGAMMAGLOBULINEMIA MASQUERADING AS HODGKIN LYMPHOMA AND POLYMYOSITIS: A CASE SERIES OF THE MANY FACES OF HYPERGAMMAGLOBULINEMIA

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Background: Hypergammaglobulinemia is characterised by elevated immunoglobulins as a result of overproduction by the plasma cells. It is commonly associated with inflammatory disorders, autoimmune diseases, liver diseases, connective tissue disorders, neurological conditions, infections and neoplasms.

Here, we would like to report two case reports with hypergammaglobulinemia that were later diagnosed as Hodgkin lymphoma and polymyositis.

Case Presentation: Case 1 was a 29-years-old male, presented with 8 years history of progressive right- sided neck swelling and B symptoms. Initial few excisional biopsy were performed and the histopathological examination report demonstrated reactive lymphadenopathy, reactive lymphoid hyperplasia and IgG4 related disease in 2020, April 2022 and August 2022 respectively. Hematology team was referred for further investigation of the neck swelling and persistent high globulin ranging from 75g/L to 95g/L. Physical examination was unremarkable except a huge right neck swelling measuring 10x15cm. He has anemia with hemoglobin of 8.6g/L, mild leucocytosis with white cell counts of $13.63x10^9$/L and thrombocytosis with platelets of $559x10^9$/L. His renal function and calcium level is normal. Serum and urine protein electrophoresis showed absence of paraprotein and bone marrow examination was unremarkable. Computed tomography (CT) of the neck, thorax, abdominal and pelvis showed right cervical mass measuring 3x8x16cm and lung nodules. Repeated neck swelling biopsy demonstrated mixed cellularity of Hodgkin lymphoma. He received a total of 6 pairs of ABVD and he achieved complete remission. His globulin level normalised to less than 35g/L. Unfortunately his disease relapsed 9 months later as evidenced by recurrence of right sided neck swelling and raised globulin with reading of 60g/L. Repeated biopsy confirmed the diagnosis of relapsed Hogkin lymphoma. He commenced on salvage chemotherapy and achieved complete remission and currently awaiting hematopoietic stem cell transplantation.

Case 2 was a 59-years-old gentleman with no known medical illness presented with dysphagia, progressive left upper limb weakness for the past 2 weeks associated with neck pain. Physical examination demonstrated left lower motor neuron of 7th cranial nerve palsy, left hypoglossal nerve palsy and left C4 to C7 radiculopathy. Full blood count revealed leukopenia with white cell count of $3.2x10^9$/L, hemoglobin of 11g/dL and platelet of $144x10^9$/L. Peripheral blood film showed presence of rouleaux formation. He has persistent high globulin level ranging 80 to 90g/L and serum protein electrophoresis showed polyclonal immunoglobulin with no immunoparesis. Creatine kinase ranged from 800 to 900U/L. Otherwise, he has normal renal function and calcium level. Bone marrow examination was performed and it excluded the possibility of plasma cell neoplasms.. CT brain showed midbrain infarct with right post central gyrus chronic encephalomalacia and magnetic resonance imaging (MRI) cervical spine showed degenerative cervical disc disease with mild spinal canal stenosis at C4/C5 level. He was diagnosed as polymyositis after reviewed by neurologist . His neurological impairment improved and globulin level dropped to less than 40 g/L after initiation of steroids and methothexate.

Discussion / Conclusion: We demonstrate two case reports that have high globulin level but were then diagnosed as hematological malignancy and neurological disorder. This highlights the importance of high awareness of diverse causes of hypergammaglobulinemia in our daily practices.

CASE SERIES/CASE REPORT (CLINICAL)

CC51 SEEING THROUGH THE ECLIPSE – KIKUCHI DISEASE IN HODGKIN LYMPHOMA

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Background: Kikuchi-Fujimoto disease (KFD) is a histiocytic necrotizing lymphadenitis usually affecting women of Asian descent. Common complaints include fever, night sweats and painful lymphadenopathy with predilection of cervical lymph nodes. Due to its rare condition, this presentation will first raise suspicion for other infective causes, autoimmune and lymphoproliferative diseases. We reported a case of Hodgkin lymphoma with a concomitant KFD.

Case Presentation: A 62-year-old Malay lady with underlying lymphocyte-rich Hodgkin lymphoma (LRHL), who was in complete metabolic response for the past 7 years following BEAM high dose chemotherapy and auto-SCT, presented with painless cervical and axilla lymphadenopathies. Clinical examination revealed no other abnormalities. She had mild thrombocytopenia and lymphocytopenia with reactive lymphocytes. Unlike the cervical lymphadenopathy, the axillary nodes persisted despite a course of antibiotic. Excision biopsy of the axillary lymph node revealed scattered necrotizing foci consisting of histiocytes, karyorrhectic debris and fibrin consistent with KFD. Since the patient was asymptomatic, and KFD is expected to have a self-limiting course, she was put on surveillance. 4 months later, the lymphadenopathy became generalized, involving bilateral neck, axilla, inguinal nodes, and splenomegaly. They were associated with fever and constitutional symptoms. Her blood investigation showed pancytopenia and raised serum lactate dehydrogenase, 2246 IU/L. This raised a diagnostic dilemma between severe KFD and relapsed Hodgkin lymphoma. 18FDG PET/CT showed disseminated congregate chain of active lymphadenopathies involving both sides of the diaphragm and extra-nodal sites including disseminated active bony lesion of the spine and diffuse splenic activity. The largest active cervical node was biopsied, and she was empirically treated for severe KFD with Prednisolone. As early as a week following corticosteroid initiation, she reported resolution of fever and improvement in constitutional symptoms. The lymphadenopathy persisted while the spleen size reduced. The repeated cervical biopsy was concluded as relapsed Hodgkin Lymphoma, Lymphocyte Rich. Nonetheless, the Hodgkin cells expressed dim CD20 positivity interspersed among T cell and histiocytes population. In retrospect, these cells were rarely identifiable among more prominent T-cells and histiocytic population leading to an interpretation of KFD. Unfortunately, before further tests can be performed, she contracted COVID-19 and succumbed to death soon after.

Discussion / Conclusion: Severe KFD with extra-nodal involvement may mimic aggressive lymphoma by presenting with generalized lymphadenopathies, splenomegaly, and constitutional symptoms. Clinical improvement following glucocorticoid treatment was also suggestive of severe KFD. This case proved to be a diagnostic challenge. 18FDG PET/CT directed tissue sampling helped confirmed relapsed Hodgkin lymphoma, with atypical histological findings. This case highlights the importance of careful evaluation in cases of severe KFD.

CASE SERIES/CASE REPORT (CLINICAL)

CC52 BLOODLESS MANAGEMENT OF BREAKTHROUGH HAEMOLYSIS IN A PATIENT WITH PAROXYSMAL NOCTURNAL HAEMOGLOBINURIA

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Background: Paroxysmal nocturnal haemoglobinuria (PNH) is an acquired clonal haematopoietic stem cell disorder caused by a somatic mutation in the PIGA gene located on chromosome Xp22. It is characterized by the triad of intravascular haemolysis, thrombosis & bone marrow failure. The mutation results in reduced or complete absence of glycosylphosphatidylinositol (GPI) anchor proteins on the surface of blood cells, resulting in complement mediated haemolysis. Diagnosis of PNH is made by flow cytometry, particularly fluorescent aerolysin (FLAER) based assays. Thrombosis which may be arterial or venous, is the leading cause of death among PNH patients. The introduction of complement inhibitors has revolutionized the treatment of PNH. Patients with PNH can present with severe anaemia secondary to acute hemolytic episodes, necessitating hospitalization and frequently receive packed cell transfusions. Frequent blood transfusions carry many risks including infections, iron overload and transfusion reactions.

Case Presentation: Our patient is a 26-year old lady who was diagnosed with PNH in 2018 and is currently enrolled in a clinical trial investigating the use of C3 inhibitors in PNH. Her last episode of breakthrough haemolysis was in April 2023, which was precipitated by COVID-19 infection. She presented to Hospital Ampang in early August 2023 with lethargy, palpitations, presyncope, chest discomfort and tea coloured urine for two days. She denied fever or any other symptoms suggesting a source of infection. On examination, she was pale, jaundiced and tachycardic but afebrile and her blood pressure was normal. She was severely anaemic with haemoglobin (Hb) of 3.6 g/dL, associated with indirect hyperbilirubinaemia and markedly elevated lactate dehydrogenase (LDH) of 4100 U/L. She was given supportive care such as hydration & supplemental oxygen and treated with intravenous iron sucrose and folate. She was also started on empirical antibiotics to cover for possible occult infection and low molecular weight heparin for thromboprophylaxis. She did not receive any blood transfusion throughout her 12 day hospitalization. Her haemoglobin and other hemolytic parameters gradually improved throughout her stay. Her haemoglobin upon discharge was 8.7 g/dL, with normalization of indirect bilirubin and reduction in LDH to 1812 U/L.

Discussion / Conclusion: Patient Blood Management (PBM) is an evidence based, multidisciplinary approach which aims to promote a judicious approach towards blood transfusion. The first pillar of PBM is optimizing haematopoiesis. A significant proportion of PNH patients have concomitant iron deficiency anaemia as a result of chronic haemoglobinuria. Patients with chronic haemolysis also tend to develop folate deficiency. Thus, iron & folate supplementation is important in this group of patients. PNH patients also receive frequent blood transfusions during their acute haemolytic episodes, but blood transfusions are not without risks which include infections, transfusion reactions and alloimmunization. This case demonstrates the successful use of intravenous iron and folate, supportive therapy and avoidance of blood transfusion in a PNH patient presenting with severe acute hemolysis and provides an example of how the principles of PBM can be utilized in the management of patients with PNH.

CASE SERIES/CASE REPORT (CLINICAL)

CC53 IMMUNE HEMOLYSIS PRESENTING AS PURE ERYTHROID LEUKAEMIA

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Background: Pure Erythroid Leukaemia (PEL) is a rare form of acute myeloid leukaemia with predominant erythroid lineage proliferation. Based on the French-American-British (FAB) Cooperative group revised it is defined AML-M6 as a proliferation of more than 50% erythroblast and more than 30% of myeloblasts within non-erythroid cells.

Case Presentation: A 65-year-old female presented with reduce effort tolerance, jaundice and loss of appetite for 3 months. On examination, she was found to be afebrile with pallor and icterus. Abdominal examination revealed soft abdomen with hepatosplenomegaly. Her complete blood count (CBC) showed bicytopenia with haemoglobin (Hb) of 4.4 g%, white blood cell (WBC) count of 3.21 x 10^9/L and platelet count of 153 x 10^9/L. The peripheral smear showed hypochromic microcytic anaemia with no spherocytes. Serum bilirubin 143 µmol/L (90% indirect), serum LDH 1427 IU/L and reticulocyte production index 1.2. Direct antiglobulin test was positive; C3d one plus only. Urine haemoglobin and hemosiderin were negative. Flowcytometry for PNH study was negative. Iron studies were not suggestive of iron deficiency. Normal serum B12 and folate level. Marrow examination showed erythroid hyperplasia. Cytogenetic analysis showed 21% abnormal metaphase with two population consisting of solely monosomy 14 or monosomy 18 aberration. She was treated for autoimmune hemolytic anaemia with steroid. Despite therapy, she still required monthly red cell transfusion. In view of the existing cytogenetic abnormality, a repeat marrow was carried out. It showed erythroid precursors consisted of >80% of nucleated cells. The precursor cells showed E-cadherin, glycophorin A with scattered CD117 and CD34 positivity. Hence a diagnosis of pure erythroid leukaemia (PEL) was made. The repeat cytogenetic analysis was reported normal. Nevertheless, there were sole monosomy 8 and monosomy 18 in one metaphase each, not fulfilling criteria for clonal abnormality. Despite treatment with Azacitadine monotherapy, she still required monthly red cell transfusion and a repeat marrow analysis six months later did not show improvement. DAT was persistently positive, C3d+ hence combined prednisolone and azacitidine was attempted in which red cell transfusion requirement appeared reduced. Patient eventually decided not to continue with azacitidine. We continue to pursue on immunosuppressive therapy. She has since been maintained on oral prednisolone and azathioprine for the past 24 months. Her hemoglobin ranged between 9-10 g/dL. She has only been transfused once when she was admitted for community acquired pneumonia.

Discussion / Conclusion: PEL is extremely rare and poor prognosis. Median survival is expected to be around three months. This case illustrates the difficulty in differentiating PEL from chronic hemolysis with secondary marrow response. This confusion is further fuelled by abnormal marrow cytogenetics. Although monosomy 18 has not been reported in myeloid malignancy, it has been associated with colonic cancer. At the hindsight, although this patient fulfilled the marrow criteria for PEL, the natural history of this patient is more typical of chronic immune haemolysis.

CASE SERIES/CASE REPORT (CLINICAL)

CC54 SECONDARY ACUTE MYELOID LEUKAEMIA IN TREATMENT-NAÎVE PRIMARY TESTICULAR DIFFUSE LARGE B-CELL LYMPHOMA

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Background: Secondary acute myeloid leukaemia (AML) refers to cases of AML that develop after a prior myeloid hematologic disorder or as a result of previous chemotherapy or radiotherapy for a different disease. On the other hand, it is also not uncommon for lymphoid malignancies to relapse or progress into a leukaemic phase. However, in this particular case, we present a rare instance of secondary primary AML in a patient with no prior treatment, who had initially been diagnosed with extra nodal diffuse large B-cell lymphoma.

Case Presentation: A 58-year-old male presented with right testicular swelling, devoid of any constitutional symptom. The subsequent testicular tissue biopsy from right orchidectomy procedure revealed an extensive infiltration of atypical lymphoid cells, with immunohistochemistry confirming diffuse large B-cell lymphoma (DLBCL). CT scan staging showed a normal contralateral testis, with only subcentimeter inguinal, aortocaval, and paraaortic lymph nodes. Marrow assessment exhibited no lymphomatous infiltration. The diagnosis was primary testicular DLBCL stage 1E, with a favorable prognostic score. The patient, deemed fit for treatment, was recommended standard R-CHOP plus intrathecal chemotherapy. However, he declined treatment and was subsequently lost to follow-up. Five years later, he reappeared with a three-week history of generalized lethargy. No lymphadenopathy, organomegaly, or contralateral testicular swelling was observed. Initial blood tests revealed Hb 6.7 g/dL, WBC 58.7x10^9/L, and platelets 228x10^9/L, with 43% circulating blast cells. Bone marrow aspirate demonstrated 60% blast cells, expressing CD13, CD33, CD117, HLA-DR, CD64, and CD56, while being negative for CD34, MPO, and B and T markers. Conventional cytogenetics displayed a normal male karyotype. A re-staging CT scan disclosed multiple enlarged cervical, abdominal, and pelvic nodes, but too small for imaging-guided biopsy. The new diagnosis was acute myeloid leukaemia with monocytic differentiation (M5) in a relatively unfit patient due to multiple comorbidities, including type 2 diabetes mellitus, hypertension, chronic atrial fibrillation, and chronic kidney disease stage 4. Despite being planned for azacytidine plus venetoclax, the patient succumbed to disease progression during a bridging treatment with low-dose cytarabine.

Discussion / Conclusion: Distinguishing acute leukaemia from non-Hodgkin lymphoma in blastic phase is of utmost importance, underscoring the significance of flowcytometric immunophenotyping. It is noteworthy that secondary primary AML, although treated similarly to de novo AML, might not retain the same prognostic significance.

CASE SERIES/CASE REPORT (CLINICAL)

CC55 HAEMOGLOBIN H DISESASE WITH NEW ALPHA ZERO THALASSAEMIA DELETION: A CASE REPORT

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Background: Alpha (α)-thalassaemia is an inherited haemoglobin (Hb) disorder with reduced α- globin chains synthesis, usually caused by deletions of the α-globin genes. Deletion of three of four α- globin genes results in Haemoglobin H (HbH) disease. In HbH disease, Hb analysis would reveal the presence of HbH, with DNA analysis demonstrating compound heterozygosity for α+-thalassaemia from single (-α) alpha gene deletion and α0-thalassaemia from two (--) alpha genes deletion. We describe here a case of HbH disease resulting from a newly described α0-thalassaemia deletion.

Case Presentation: A Malay lady, then 25-years old, was incidentally noted in 2015 to have hypochromic microcytic anaemia with Hb of 9.0g/dL (12-15), mean corpuscular volume (MCV) of 52.3 fL (83-101) and mean corpuscular haemoglobin (MCH) of 16.1 pg (27-32). There was no jaundice nor any hepatosplenomegaly. Hb capillary electrophoresis in 2016 showed normal HbA (97.9%), low HbA2 (1.2%) and presence of 0.9% HbH, while high performance liquid chromatography (HPLC) revealed normal HbA2 (2%) and HbF (0.2%) with presence of pre-run peaks, compatible with HbH disease. DNA analysis in 2016 with multiplex GAP-PCR identified her as homozygous (-α3.7) gene deletions, inconsistent with her Hb analysis profile. Multiplex ARMS-PCR for non-deletional alpha-thalassaemia mutations did not detect any abnormalities. She went on to have 3 uneventful pregnancies for which she never required any transfusions, with Hb remaining >8g/dL. Considering the discrepancy between the Hb analysis and DNA analysis findings and the importance of genetic counselling, we further investigated the molecular basis of her HbH disease in 2022 using multiplex ligation-dependent probe amplification (MLPA). Multiplex GAP-PCR detected the -α3.7 deletion while MLPA revealed a rare --GB deletion.

Discussion / Conclusion: The --GB deletion is a newly described α0-thalassaemia deletion not identifiable using routine Multiplex GAP-PCR testing. In a study by Institute for Medical Research (IMR), Malaysia, the --GB deletion appears to be unique among Malay ethnicity in Malaysia. Our case highlights the need to recognise discrepant Hb analysis and DNA analysis findings, the need for additional testing, and the utility of MLPA in identifying novel, rare, or undescribed deletions when standard methods fail. This would allow accurate genetic diagnosis, crucial for appropriate genetic counselling.

CASE SERIES/CASE REPORT (CLINICAL)

CC56 LENALIDOMIDE MAINTENANCE FOR ELDERLY PATIENTS WITH HIGH GRADE B CELL LYMPHOMA

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Background: High Grade B cell lymphoma (HGBL) is an aggressive disease and the treatment at relapse is challenging especially in elderly. Lenalidomide maintenance therapy has shown to prolong progression-free survival (PFS) versus placebo in elderly patients with DLBCL responding to first line chemotherapy.

Case Presentation: We report a case series of three adult female with HGBL, who has completed first line chemotherapy and received lenalidomide maintenance for 2 years duration. Case 1: A 71 years old presented with abdominal pain and upper gastrointestinal bleeding, was diagnosed with stage IV HGBL. She received 6 cycles R-CEOP (rituximab, epirubicin, cyclophosphamide, vinblastine, prednisolone). PET CT assessment showed partial metabolic response with residual active lymphoma in lower stomach, hence lenalidomide maintenance was started at 10mg biweekly (adjusted to tolerance) for 2 years. PET CT at 9 months of lenalidomide showed stable response but repeated scan at end of therapy revealed complete metabolic response (CMR). Case 2: 81 years old female presented with multiple cervical, axillary and inguinal lymphadenopathy, and diagnosed as stage III HGBL. She achieved CMR following 6 cycles R-CEOP. Lenalidomide maintenance was started 4 months following chemotherapy at 10mg EOD adjusted according to tolerance. Interim PET CT after 4 cycles lenalidomide showed relapse disease, however lenalidomide was continued as patient was clinically well with no B symptoms. End of treatment PET CT showed active disease in the cervical, mediastinal and abdomino-pelvic region associated with constitutional symptoms in keeping with disease progression. She was salvaged with rituximab and bendamustine. Case 3: 64 years old lady presented with neck nodes and progressive pancytopenia. She was diagnosed with stage IV (lungs, marrow involvement) double expressors HGBL. She received 6 cycles R-EPOCH DA and achieved CMR. Lenalidomide maintenance was started and she tolerated at a dose of 10mg OD for 2 years. There is no clinical evidence of disease and she is due for end of treatment PET CT in February this year.

Discussion / Conclusion: Lenalidomide, an immunomodulator has emerged as an attractive therapeutic option. It can stimulate the innate immune system, which can be explained by its ability to inhibit tumor necrosis factor-a, vascular endothelial growth factor, and NF-kB in cancer cells. The efficacy of oral lenalidomide in the context of local population has not been studied. In this case series we demonstrated patients response similar to those reported. One patient in PR was able to achieve CMR with lenalidomide maintenance. The treatment was well tolerated but dose reduction was required, between 10mg biweekly and daily. Haematological toxicity such as neutropenia and cutaneous reaction are the common adverse event during treatment. In these three cases, no severe complication were observed. In conclusion, this case series reflects real world experience of lenalidomide and provide a foundation for clinical translation as maintenance therapy for B cell lymphoma in Malay population.

CASE SERIES/CASE REPORT (CLINICAL)

CC57 A PHYSICIAN'S NIGHTMARE: HYPERHEMOLYSIS SYNDROME IN TRANSFUSION DEPENDENT BETA THALASSEMIA

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Background: Hyperhemolysis syndrome is an uncommon but potentially fatal type of delayed. Hemolytic transfusion reaction characterised by a drop in hemoglobin to below the pretransfusion levels and reticulocytopenia.

Case Presentation: We report 6 cases of hyperhemolysis syndrome in transfusion dependent beta thalassemia patients at our centre. They presented with hemoglobin of 2.3-4.5g/dL 1-2 weeks post transfusion with elevated lactate dehydrogenase levels(LDH), indirect hyperbilirubinemia, low haptoglobin levels and reticulocytopenia. Direct antiglobulin test was positive in all these patients with a strong positive IgG in all 6 patients and concomitant C3d positivity in 3 patients.These patients were transfused with crossmatch compatible(antigen negative) blood prior to the incidence of hyperhemolysis. Antibody identification revealed clinically significant allo-antibodies Anti -E in 2 patients, Anti -C in 1 patient, Anti-c in 1 patient, Anti-Cw in 2 patients, Anti-K in 1 patient and 1 patient did not have alloantibody identified. Cold agglutination was seen in 3 out of these 6 patients. Transfusion was witheld temporarily and they were given IVIG(intravenous immunoglobulin) and methylprednisolone. Most patients responded to these 2 agents . However 1 patient received Rituximab and mycophenolate mofetil due to ongoing hemolysis. 2 patients who had been splenectomised before. 1 patient developed a cerebral venous sinous thrombosis and succumbed.

Discussion / Conclusion: Transfusion of antigen-negative cross-match compatible RBCs does not prevent hyperhemolysis. Bystander hemolysis, RBC alloimmunization, complement regulation dysfunction, incomplete IgA antibodies and hemolysis due to HLA antigen and antibody reaction by hyperactive macrophages in addition to suppression of erythropoiesis can lead to this syndrome. Reducing transfusion burden using erythrocyte maturation agent such as Luspatercept, enrollment into a clinical trial or splenectomy in these patients would help to prevent another episode of hyperhemolysis which is life threatening.

CASE SERIES/CASE REPORT (CLINICAL)

CC58 RETROSPECTIVE ANALYSIS OF THE RESPONSE OF LUSPATERCEPT AMONG A SMALL COHORT OF TRANSFUSION DEPENDENT BETA THALASSEMIA PATIENTS IN HOSPITAL AMPANG

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Background: Luspatercept has been shown to act as a ligand trap, selectively suppressing the deleterious effects of GDF11 that blocks terminal erythroid maturation, restoring normal erythroid differentiation and improving anemia in Beta Thalassemia and MDS with ring sideroblast.

Case Presentation: We analysed the use of Luspatercept in 4 patients with transfusion dependent beta thalassemia at our centre. We targeted a certain group of patients with Beta Thalassemia who had difficulty achieving pre transfusion hemoglobin levels due to alloimmune antibodies or hypersplenism. Of these patients, 1 patient had hypersplenism, 2 had alloimmune antibodies and the other had neither of these problems. Genotypically 2 of them have beta zero thalassemia and 2 have HbE Beta Thalassemia. All these patients were given the standard 1mg/kg and subsequent dose increment to 1.25mg/kg according to recommendation. We analysed the average increment in hemoglobin concentration after initiation of Luspatercept. The median hemoglobin concentration over 24 weeks before initiation of Luspatercept was compared to the median hemoglobin concentration on optimal dose of Luspatercept for 24 weeks. The average hemoglobin increment for the patients with beta zero thalassemia was 1-1.5g/dL and for the patients with HbE beta thalassemia the average increment was 2.0-2.4g/dL. With this we were able to either reduce the number of packed cells transfused or increase interval of transfusion.

Discussion / Conclusion: We can therefore conclude that the use of Luspatercept has resulted in an increment in hemoglobin levels in all the patients analysed. In this series of 4 patients analysed, patients with HbE Beta thalassemia seem to fare better with a greater hemoglobin increment and subsequent reduction in transfusion burden.

CASE SERIES/CASE REPORT (CLINICAL)

CC59 A CASE SERIES: MEASURABLE RESIDUAL DISEASE (MRD) ASSESSMENT IN NEWLY DIAGNOSED NUCLEOPHOSMIN-1 (NPM1) ACUTE MYELOID LEUKEMIA (AML): HOW DOES IT AFFECT OUR TREATMENT DECISIONS?

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Background: Acute myeloid leukemia (AML) with Nucleophosmin-1 (NPM1) gene mutation is a distinct entity, due to its unique biological and clinical features. It accounts for approximately 30% of de novo AML. The evaluation of NPM1 and FMS-like tyrosine kinase internal tandem duplication (FLT3- ITD) status represents a major pillar of the European Leukemia Net (ELN) genetic-based risk stratification model. NPM1 molecular transcripts are particularly suitable for assessing MRD since they are frequent, stable at relapse, and do not drive clonal hematopoiesis. Here, we present 4 cases in which the utilization of MRD assessment aided long-term therapeutic decisions.

Case Presentation: **Case 1** A 30-year-old lady was diagnosed with AML with an isolated NPM1 mutation. Her presenting white cell count was $72x10^9$ /L, and she had normal cytogenetics. She was treated with a '7 + 3' regimen followed by 3 cycles of high-dose cytarabine-based consolidation. She has achieved MRD negative following each treatment cycle and remained as such during her surveillance marrow assessment. Her ability to achieve early MRD-negative status precludes the need for an allogeneic stem cell transplant. **Case 2** A 62-year-old lady was diagnosed with AML with NPM1 and FLT3-ITD mutation. Her treatment of a '7 + 3' regimen followed by 3 cycles of high-dose cytarabine based consolidation has resulted in the achievement of undetectable NPM1 transcripts after 2 cycles of treatment. She declined an allogenic transplant as a consolidation. During surveillance, she had an early molecular relapse with an NPM1 level of 26% which was followed by a morphological relapse 2 months later. She was salvaged with fludarabine, cytarabine, and filgrastim (FLAG) regimen with Midostaurin and was able to achieve MRD negative once again allowing an allogeneic stem cell transplant from a matched related donor to be performed. She remains in molecular remission 4 months post-transplant. **Case 3** An 85-year-old gentleman with a poor performance status presented with pancytopenia. A bone marrow examination confirmed the diagnosis of AML with NPM1 mutation A with wild-type FLT3 status and a normal male karyotype. He was treated with Venetoclax and hypomethylating agent (HMA) azacitidine. After 2 cycles his molecular transcript level was positive at 0.05%. He completed a total of 7 cycles of treatment but eventually progressed and succumbed to his illness. Case 4 A 63-year-old man with hyperleukocytosis (white blood count of 299 $x10^9$ /L) was diagnosed with NPM1 (type A) and FLT3-ITD mutated AML. He received a '7 +3' induction, followed by another three cycles of cytarabine-based consolidation while achieving an undetectable NPM1 transcript after 2 and 4 cycles of treatment. He had initially declined a haploidentical stem cell transplant. 3 months later, he had a detectable NPM1 transcript from the bone marrow at 229%, while remaining in morphological remission. He was pre-emptively treated with a hypomethylating agent (HMA) azacitidine, venetoclax, and gilteritinib combination and achieved molecular remission after 3 cycles.

Discussion / Conclusion: The inability to achieve early MRD-negative remission and early detection of molecular relapse reliably predicts subsequent hematological relapse/progression. It represents an important tool to aid MRD-guided therapeutic interventions in NPM1-mutated AML patients.

CASE SERIES/CASE REPORT (CLINICAL)

CC60 CHALLENGES IN MANAGEMENT OF AML IN PREGNANCY

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Background: Acute myeloid leukaemia (AML) in pregnancy is a rare occurrence with an estimated incidence of 1 in 75,000 pregnancies. Management of AML poses unique challenges due to the need to balance the health of both the mother and the developing fetus. Nevertheless, chemotherapy should not be withheld nor delayed as it may be associated with poor maternal and fetal outcome. We present a case of AML in a pregnant lady with successful pregnancy who opted for conservative management and subsequently achieved complete remission following chemotherapy post-delivery.

Case Presentation: A 42 year-old Malay lady, G3P1+1 presented at 15 weeks gestation with easy bruising and epistaxis for one week duration. There were leucocytosis, 41 $x10^9$/L (90% blast), anaemia and thrombocytopenia. She refused bone marrow examination. Hence, diagnostic work-up was confined to peripheral blood examination. Flowcytometry consistent with AML. She and her husband were counselled regarding disease and treatment options whereby termination of pregnancy and chemotherapy was preferred. However, they decided to continue with the pregnancy and considered supportive treatment. Due to severe thrombocytopenia, she had weekly full blood count and 2 weekly fetal scan assessment. Her platelet transfusion trigger was set at 5 $x10^9$/L and in total she received 8 units of platelet transfusion. Her white cell count range between 40-90 $x10^9$/L without cytoreductive therapy. Haemoglobin maintained between 8-10g/dL without transfusion. At 27 weeks of pregnancy, she developed severe sepsis secondary to pneumonia requiring mechanical ventilation. Emergency caesarean was conducted and delivered a morphologically normal baby girl with weight of 900 gm. The baby was admitted to intensive care unit and discharge well after 2 months of hospitalization. At one month postpartum, she agreed for definitive treatment. Diagnostic BMAT was consistent with AML with 90% blast and cytogenetic analysis was positive for deletion 9. She required two cycles of standard induction chemotherapy (daunorubicin and cytarabine) to achieve marrow remission. She then received three cycles of high dose cytarabine consolidation followed by maintenance chemotherapy. The patient remained in complete remission and is planned for allogeneic stem cell transplant from a matched sibling donor. Her baby is almost 2 years of age with normal development.

Discussion / Conclusion: AML is an aggressive disease and is fatal unless promptly treated. In pregnancy, it poses an immediate threat to the lives not only the mother but also for the fetus. When it involves a pregnant patient, management is a challenge. There is no specific guideline as the incident is very rare. Generally, in early pregnancy the advice is for termination of pregnancy followed by chemotherapy. Delay in treatment is not advisable, as the longer one waits, more genetic lesion is acquired increasing disease risk leading to poorer treatment outcome. However, a mother's emotional demand often overrules all other arguments. In this case, in the spirit of shared decision making, we respected the patient's wish, providing her the necessary treatment until she was ready. Hope still prevailed.

CASE SERIES/CASE REPORT (CLINICAL)

CC61 SECONDARY HEPATIC IRON OVERLOAD IN ACUTE MYELOID LEUKEMIA: A COMPLICATION NOT TO BE MISSED

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Background: Anaemia in patients with acute myeloid leukaemia (AML) is due to the disease itself or to chemotherapy-induced myelosuppression and requires supportive treatment with transfusions of blood products. Although iron overload commonly occurs in thalassaemia major and severe aplastic anaemia, it is also reported in cancer patients requiring blood transfusions. We report a young patient with severe transaminitis following induction chemotherapy, which was later found to be contributed by secondary iron overload.

Case Presentation: A 15-year-old male presented with a two-week history of malaise associated with fever and fatigue. Physical examination revealed multiple cervical lymphadenopathies without hepatosplenomegaly. Complete blood count showed pancytopenia with white blood cell count of $1.5x10^9$/L, haemoglobin of 8.6g/dL, platelet count of $99x10^9$/L and absolute neutrophil count of $0.1x10^9$/L. Peripheral blood film showed pleomorphic medium-sized blasts with prominent nucleoli. Bone marrow aspiration confirmed the diagnosis of AML with 55% blasts. He received daunorubicin and cytarabine induction, which was complicated by neutropenic sepsis and myelosuppression requiring prolonged antibiotic therapy and multiple blood transfusions. He achieved complete remission. On day 23 of the first consolidation with high- dose cytarabine, he developed impaired liver function with total bilirubin (TB) of 14 mol/L, alanine transaminase (ALT) of 61U/L, aspartate transaminase (AST) of 25U/L and alkaline phosphatase (ALP) of 138U/L with normal coagulation profile. He was taking prophylactic itraconazole during this time and had received amphotericin B two months prior to this event. All potentially hepatotoxic medications were discontinued. Liver function deteriorated progressively over a 2-month period with highest TB of 60 mol/L, ALT 2732U/L, AST 1713U/L and ALP 309U/L. He was asymptomatic, had no signs of hepatic encephalopathy and was haemodynamically stable. Comprehensive investigations for viral and autoimmune causes of hepatitis were negative. An ultrasound examination of the hepatobiliary system was normal. Since the diagnosis of AML, he had received a total of 25 units of packed cells. Serum ferritin was 20,882 ng/mL. The liver T2* value on MRI was between 4.6 and 5.5ms, indicating mild iron overload of the liver. Liver biopsy was performed and showed moderate brownish pigment deposits in the hepatocytes and portal tract. Perl staining showed moderate iron granule deposits in the hepatocytes and portal tract, indicating moderate hepatitis with excess iron. Histopathological examination results in combination with imaging and serum ferritin levels confirmed the diagnosis of transfusion-related iron overload of the liver. Deferiprone 500mg three times daily was commenced and his liver function normalized within two weeks. He was able to resume subsequent consolidation chemotherapy for AML and liver function remained normal throughout treatment.

Discussion / Conclusion: This case illustrates iron overload as one of the causes of transaminitis in a young AML patient. Although the T2* MRI showed only mild iron overload of the liver, the liver biopsy already revealed moderate hepatitis with excess iron. Severe transaminitis in AML patients therefore requires urgent investigations to clarify the aetiology. Timely initiation of iron chelators and good patient compliance are important as we have to balance the need for future blood transfusions with the complications of severe iron overload.

CASE SERIES/CASE REPORT (CLINICAL)

CC62 SPINAL CORD COMPRESSION: A RARE PRESENTATION OF CHRONIC LYMPHOCYTIC LEUKAEMIA OR SMALL LYMPHOCYTIC LYMPHOMA

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Background: Chronic Lymphocytic Leukaemia (CLL) or Small Lymphocytic Lymphoma (SLL) is an indolent malignancy. Patients are often asymptomatic at the initial presentation when a routine Full Blood Count reveals incidental finding of abnormal lymphocytosis. The primary disease sites include peripheral blood, bone marrow, spleen and lymph nodes. We present a case of newly diagnosed CLL/SLL with bone and spine involvement presented with spinal cord compression.

Case Presentation: A 51-year-old male with newly diagnosed Chronic Lymphocytic Leukaemia RAI 1 Binet A, on watchful observation. He presented with sudden onset of upper and lower limb weakness for 1 day, starting with sudden stabbing pain in his neck and upper back after waking up from sleep. Subsequently, he was unable to move both upper and lower limbs, associated with numbness. He had intermittent neck pain for the last 3 weeks. No B symptoms. He had diabetes mellitus, hypertension, dyslipidaemia, ischaemic heart disease with triple vessel disease (CABG done). On examination, he was alert, and conscious. Cardiovascular, respiratory and abdominal examinations were normal. There was no cervical/axillary/inguinal lymphadenopathy. There was tenderness at the cervical region. Neurological examination showed the best neurological level at C4 with reduced motor power and sensation below C4. Both bilateral upper limb and bilateral lower limbs were hypotonia and hyporeflexia with bilateral upper limb power 2/5 (below C4) and bilateral lower limb power 0/5. Babinski equivocal. Anal tone lax. Urgent MRI whole spine showed C4 and C5 pathological fracture with soft tissue component and dural enhancement resultant in spinal cord compression as well as possible focal spinal cord infarct. Emergency operation (anterior corpectomy and posterior instrumentation) was performed. Histopathological examination of C4 & C5 bone consistent with Small Lymphocytic Lymphoma (SLL). Bone & tissue C&S positive for Staphylococcus aureus. The comprehensive diagnosis was Spinal Cord Compression secondary to CLL/SLL Stage IV with bone and spine involvement and MSSA Spondylodiscitis. He was started on IV Cephazolin 2 g TDS. He was also on intensive limb physiotherapy post op, with good neurological recovery in which both power bilateral upper & lower limbs gradually improved to 4/5. He received Radiotherapy to spine C2-T1 (20Cy/5F) after recovery post surgery. Subsequently, upon completion of antibiotic for 12 weeks, he was counselled for CLL/SLL treatment. Due to financial constraint, novel agents such as Bruton Tyrosine Kinase inhibitor is not an option for him. Currently, he is undergoing chemoimmunotherapy with Rituximab, Fludarabine & Cyclophosphamide.

Discussion / Conclusion: Bone and spinal involvement in CLL/SLL is rare. It should be considered in patients with neck or back pain and neurologic symptoms who had been diagnosed with this form of leukemia in the past. Differentiation with infectious spondylodiscitis can be difficult. Histology is necessary to confirm diagnosis. In the era of novel agents, such as Bruton's Tyrosine Kinase inhibitor and BCL2 inhibitor, the treatment landscape for CLL/SLL has changed. These agents lead to improved outcomes in patients with CLL/SLL even among those with high risk features. However, financial constraint is the issue that needs to be addressed to access the novel agents.

CASE SERIES/CASE REPORT (CLINICAL)

CC63 NIVOLUMAB-INDUCED INTERSTITIAL PNEUMONITIS IN A PATIENT WITH RELAPSED HODGKIN LYMPHOMA

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Background: Immune checkpoint inhibitors like Nivolumab have revolutionized cancer treatment by enhancing the immune system's ability to combat cancer cells. They work by inhibiting the PD-1 pathway, but a notable challenge is the unpredictable immune-related toxicities that may occur, affecting organs like the endocrine glands, lungs, skin, and gut. Lung inflammation is a particularly important concern. Recognizing and managing these toxicities is crucial, requiring a multidisciplinary approach. Ongoing research aims to improve safety, efficacy, and early detection of adverse events associated with these groundbreaking cancer therapies.

Case Presentation: In this case report, a 29-year-old woman with a history of relapsed Hodgkin Lymphoma 2B, post-autologous transplantation of hematopoietic stem cells, developed interstitial pneumonitis as a side effect of Nivolumab treatment. She presented with a prolonged dry cough and left pleuritic chest pain, along with left lower zone opacities seen on a chest x-ray. Despite negative microbial assessments, she was empirically treated with antibiotics. To address immune checkpoint inhibitor-induced pneumonitis, she received oral Prednisolone at 1mg/kg daily. She did not require oxygen supplementation and continued Nivolumab treatment for four cycles despite ongoing chest symptoms. Eventually, Nivolumab therapy was discontinued, and at a follow-up visit two weeks later, the patient reported feeling well with the resolution of her prolonged cough.

Discussion / Conclusion: Nivolumab has gained approval for use in relapsed classic Hodgkin's lymphoma after autologous transplantation of hematopoietic stem cells and treatment with brentuximab, functioning as monotherapy. It is crucial to regularly screen and monitor for adverse events both before and during nivolumab therapy. Early detection and prompt treatment of side effects are essential when utilizing nivolumab and other checkpoint inhibitors. To establish consistent terminology for treatment- related adverse events, the National Cancer Institute's CTCAE (Common Terminology Criteria for Adverse Events) is employed to grade the severity of pneumonitis symptoms. Early identification and effective management of immune-related toxicities play a vital role in improving patient outcomes and enhancing overall quality of life during cancer treatment.

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CASE SERIES/CASE REPORT(LABORATORY)

CL1 "Insignificant Antibodies": Case Report Of In Vitro Cross Reactivity With The Commercial RBC Reagents And Concurrent Non Specific Cold Antibody

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Background: The basic serological assays, such as direct Coombs test, indirect Coombs test with and without potentiators, autocontrol, and antibody screening are utilized to predict the safety of blood transfusion in-vitro.

Case Presentation: We reported a case of 82-years-old man, admitted for acute urinary retention secondary to benign prostatic hyperplasia with urinary tract infection. Patient had no history of blood transfusion or transplantation. He required two unit of packed cells transfusion for bleeding due to traumatic bladder catheterization and anemia with Hb 9.1g/dL. The blood grouping performed by Column agglutination technology (CAT) using the Bio-Rad DiaMed reagent with fully automated Immunohematological Equipment IH500 showed an ABO discrepancy in which forward grouping showed 3+ reaction with anti-B while reverse grouping showed extra reaction at B cells. Hence, the entire ABO and Rhesus (Rh) grouping was repeated with conventional tube technique (CTT) using antisera from CSL. ABO discrepancy was resolved via CTT and patient's blood group was concluded as B RhD positive. Antibody screening was performed by CAT using commercially available cell panel (Biorad ID-DiaCell I-II-III Asia) at room temperature showed pan-positivity (4+) reaction with positive autocontrol (2+). Repeated antibody screening using a pre-warmed, and 4°C sample also showed similar findings. Antibody identification using (Biorad ID-DiaPanel and ID-DiaPanel-P) by CAT method revealed pan-positivity (4+) reaction with untreated reagent red cells and enzyme-treated reagent red cells. The Direct Coomb's test performed by CAT using the polyspecific anti IgG/C3d was positive for anti-complement and negative for anti-IgG likely due to presence of cold antibody. The Biorad red cells panel was then suspended in saline solutions and centrifuged. The supernatant was discarded and the red cells pellet was re-suspended. Antibody screening with the washed cell panel showed negative results. This preclude the presence of possible antibodies against reagent in the panel cell. Thus, the antibody identification was repeated using Panocell-10 reagent by CTT method which showed negative result at 37°C and AHG phase with weak (1+) pan-reactivity at 4°C. Subsequently, cold auto-absorption test was done in which the eluate revealed negative reaction. Therefore, we concluded that there was no clinically significant alloantibody. The usage of alternative reagent of Panocell-10 had gave greater help in resolving pan-reactivity results in both antibody screening and identification.

Discussion / Conclusion: There are few possibilities that needs to be excluded when pan-positivity result are obtained during antibody screening/identification which are; antibody against high frequency antigen, antibody against reagent in the panel cells, and cold antibody which enhanced in AHG phase . In this case, we identified two antibodies which are non-specific cold auto-antibody and possible antibody toward chemical in Bio-Rad reagent red cells. These antibodies are not clinically significant but otherwise can interfere with the pre-transfusion testing. In such situations, alternative reagent can be used to resolve it. For this patient, crossmatched compatible packed cell at 37 degree Celcius/AHG phase can be safely supplied and close monitoring is required during transfusion process. It becomes imperative to be aware of their existence in order to promptly identify, managed and to meet the patient transfusion demands.

CASE SERIES/CASE REPORT(LABORATORY)

CL2 SYSTEMIC MASTOCYTOSIS ASSOCIATED WITH HAEMATOLOGICAL NEOPLASM : AN INTRIGUING ASSOCIATION – A CASE REPORT

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Background: Mastocytosis is characterized by excessive mast cell accumulation in one or multiple tissues. Systemic mastocytosis associated with haematological neoplasm (SM-AHN) is considered a distinct entity in the WHO classification with 5% of them associated with myeloid malignancies. The most common AHN in adults is chronic myelomonocytic leukemia. Interestingly, Acute Myeloid Leukemia with t(8;21) has an increased incidence of systemic mastocytosis. Immunophenotyping and immunohistochemistry plays an integral role in the detection of mast cells. The presence of numerous blasts could mask the presence of mast cells. We present such a case whereby the patient who was in his early adolescence is diagnosed with SM-AHN focusing more on the morphology and laboratory aspects.

Case Presentation: Our case is a 13-year-old-boy, who initially presented with fever, lethargy, and gum-bleeding for two months. On examination, he does not have any organomegaly or lymphadenopathies. Full blood counts revealed haemoglobin of 3.3g/dL, WBC of 51.6 X 109/L and platelet of 7 X 109/L. Peripheral blood film reveals 79% blasts which are medium in size with irregular nuclear outline, open chromatin pattern of nuclei and conspicuous nucleoli with presence of Auer rods. Bone marrow aspirate, trephine biopsy, and immunophenotyping show evidence of Acute Myeloid Leukemia. He was started with induction chemotherapy and a repeated bone marrow aspirate was not in remission with presence of 15-25% mast cells detected. >25% of the mast cells show atypical and immature morphology with abundant cytoplasm containing densely packed metachromatic granules and oval, bilobed, kidney shaped nuclei, and occasional spindle-shaped cells. No immunophenotyping sample was sent at this point of time. Trephine biopsy findings revealed scattered increase in blasts with aggregates of mast cells. He was then given salvage chemotherapy. However, the mast cells persist in subsequent bone marrow examination. Thus, an immunophenotyping was performed using the bone marrow aspirate sample which showed presence of 0.2% mast cells with aberrant CD25. However, no serum tryptase was sent. Cytogenetic and molecular studies revealed t(8;21) with RUNX1::RUNX1T1 fusion gene and D816V (Realtime PCR) mutation detected in c-KIT gene. A diagnosis of Systemic Mastocytosis associated with haematological neoplasm was made (SM-AHN). Unfortunately, patient's family refused further chemotherapy and eventually succumbed to the disease.

Discussion / Conclusion: This case exhibits the rare entity of SM-AHN. High degree of suspicion is needed in a case of increased mast cells. Any presence of mast cells in the bone marrow should prompt further analysis with immunophenotyping and/or immunohistochemistry. Presence of numerous blasts could mask the mast cells especially in the early presentation as in our case. Hence, careful examination of bone marrow/trephine together with molecular studies are crucial in detecting the cKIT mutation and assist in the classification of the disease. SM-AHN is an aggressive pathology; thus, prompt diagnosis is imperative for initiation of therapy.

CASE SERIES/CASE REPORT(LABORATORY)

CL3 HETEROZYGOUS Hb YOUNGSTOWN WITH OVERLAPPING CLINICAL AND HAEMOGLOBIN ANALYSIS FINDINGS WITH HETEROZYGOUS Hb RUSH

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Background: Hb Youngstown is a rare unstable haemoglobin with only handful of published case series and report. Point mutation at HBB:c.305A>C causes substitution of glutamic acid with alanine at codon 101. It was first described as Hb St Mary back in 1998. In heterozygous state, it causes chronic haemolysis.

Case Presentation: A six-year-old girl with mixed ethnicity (Malaysian Chinese-Indonesian Javanese) was initially referred to the ophthalmology clinic for left eye swelling. She was later diagnosed with left eye lympangioma supported by Magnetic Resonance Imaging. During the hospitalization, she was noted to be pale and anaemic work up was sent. Her full blood count showed moderate anaemia (Haemoglobin 84 g/L, MCV 74 fl, MCH 22.3 pg), with reticulocytosis of 8%. She was also having high ferritin (931.7 ug/L), bilirubin (35 umol/L) and lactate dehydrogenase (565 U/L). Physical examination showed no evidence of hepatosplenomegaly, and her growth was at 10th centile. Peripheral blood film showed many basophilic stippling, pappenheimer bodies, irregularly contracted red cells and abnormally shaped red cells. Supravital stain demonstrated many Heinz bodies. Hb analysis run with High Performance Liquid Chromatography (HPLC) Bio-Rad Variant II Hemoglobin showed HbA (52.4%), Hb F (1.5%), HbA2 (4.2%) and Hb variant (36.7%) eluting at S window at retention time 4.6 minute. Second method with Capillary Electrophoresis (CE) Sebia CAPILLARYS 3 OCTA revealed HbA (52.4%), HbA2 (3.8%) and variant Hb at Zone 8 (43.8%). Interestingly, on alkaline agarose gel electrophoresis (PH 8.5), three distinct bands were seen: first was HbA, second in between A and F (hybrid tetramer), and third slightly cathodal to F. In acid agarose gel (PH 6.0), two bands were seen at A and S zone. Beta globin gene sequencing showed heterozygous point mutation for HBB:c.305A>C, while Alpha globin gene analysis by Multiplex ligation-dependent probe amplification (MLPA) did not show any common Alpha thalassaemia deletion.

Discussion / Conclusion: Observation of hybrid tetramer in alkaline gel raised initial high suspicion of Hb Rush in view of evidence of chronic haemolysis and almost identical HPLC and CE findings that are commonly illustrated in Hb Rush (eluting at S window on HPLC and zone 8 on CE). Other than Hb Rush and Youngstown, Hb Ypsilanti, Alberta, British Columbia, and Radcliffe have tetrameric hybrids that dissociate very slowly and, thus, remain intact long enough to be visualized at the end of the electrophoresis procedure. For the first time, Hb Youngstown is run and captured at zone 8 with CE method and found to form hybrid tetramer in alkaline agarose gel. Clinical and haemoglobin analysis findings of Hb Youngstown (HBB: c.305A>C) are overlapping with Hb Rush (HBB: c.304G>C), both are mutations occurring at the same codon 101. Differentiating Hb Youngstown and Hb Rush in this case is not possible without Beta globin gene sequencing to confirm the diagnosis at molecular level.

CASE SERIES/CASE REPORT(LABORATORY)

CL4 A CASE REPORT OF COEXISTENCE JAK2 V617F IN BCR/ABL1 POSITIVE CHRONIC MYELOID LEUKEMIA

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Background: BCR-ABL1 and JAK2 V617F coexistence in myeloproliferative neoplasms (MPN) has been described as concomitant or sequential events and it is rare. Little is known regarding the effect of these coexistence about the complications and the response to treatment. Here we report a case of BCR-ABL1 and JAK 2 positive MPN.

Case Presentation: A 64 years old Chinese male with complaint of left ankle pain and treated as acute gouty arthritis. Full blood count noted incidental finding of persistent marked thrombocytosis 1642 x 10^9/L with mild leukocytosis WBC 15.4 x 10^9/L, ANC 11.6 x 10^9/L, and moderate anemia. Hb 9.5g/dL. He had mild splenomegaly. Peripheral blood film showed leukocytosis with neutrophilia and marked thrombocytosis suggestive of MPN. No leucoerythroblastic features or circulating blasts. Bone marrow aspirate showed hypercellular marrow with haemodiluted cell trails. Granulocytes seen with mainly neutrophils and one percent blasts. Hypolobated megakaryocytes and some dwarf form are seen. Trephine biopsy was hypercellular, granulocytes seen in all stage of maturation with no excess of blasts. Megakaryocytes are increased, arranged in loose cluster and no significant megakaryocytic atypia. In view of marked thrombocytosis, JAK2 V617F mutation was send and detected. Prior starting the treatment molecular genetic analysis done to exclude BCR-ABL1 positive Chronic Myeloid Leukemia (CML) and the result came back positive for major fragment. He was diagnosed as coexistence JAK2 V617F in BCR/ABL1 positive CML in chronic phase. Patient was started on Tablet Hydroxyurea 500mg once daily and Tablet Imatinib 400 mg once daily. The latest full blood count showed Hb 7.9 g/dL, WBC 12.1 x10^9/L and Platelet 1071x10^9/L.

Discussion / Conclusion: Discussion: The atypical presentation in peripheral blood film where lack of significant leukocytosis, no increase of myelocytes and marked thrombocytosis mimicking Essential Thrombocythemia (ET). Meanwhile the bone marrow morphology displayed hypercellularity with dwarf megakaryocytes, no significant megakaryocytic atypia and increased fibrosis less favor of ET. The qualitative polymerase chain reaction (PCR) of the peripheral blood identified JAK2 V617F mutation and presence of the BCR-ABL1 fusion gene is important in order for us to classify the MPN. Conclusion: It is important to be aware of this potentially confounding genetic combination, in order to avoid these features be misinterpreted as resistance to therapy or disease progression, considerations that could lead to inappropriate management. Thus, it is likely necessary to revise the MPN diagnostic criteria of the World Health Organization to take into consideration the potential existence of this “double mutation” disease, which might be a novel clinical entity.

CASE SERIES/CASE REPORT(LABORATORY)

CL5 A CASE OF ISOLATED THROMBOCYTOPENIA WITH Inv (3) (q21.3;q26.2): FROM CCUS TO AML?

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Background: The structural changes involving the long arm of chromosome 3 in the forms of inversion and translocation in myeloid neoplasms have long been recognized and the most common form are inv(3) and t(3;3). These rearrangements cause the translocation of an enhancer of the GATA2 gene located at 3q21, to the MECOM locus at chromosome 3q26.1 leading to an activated MECOM oncogene and GATA2 haploinsufficiency. Patients with inv(3) (q21q26) or t(3;3)(q21;26) present an aggressive course with short overall survival and poor response to conventional therapy, regardless of the pathology.

Case Presentation: A 70-year-old man underlying Stage IV hepatocellular carcinoma (HCC) was investigated for unexplained thrombocytopenia. He has been on Lenvatinib as part of HCC treatment since July 2020. His platelet count showed a progressive decline, from 70 x 10^9/L in September 2020 to 16 x 10^9/L in September 2022 with no baseline platelet count recorded. His thrombocytopenia was initially thought to be attributed to Lenvatinib; nonetheless, his platelet count did not ameliorate after cessation of the medication. Trials with eltrombopag and steroids showed no positive results. A bone marrow examination performed in October 2022 demonstrated hypercellularity with active granulopoiesis and suppression of megakaryocytopoiesis, suggestive of acquired amegakaryocytic thrombocytopenia (AAMT). Bone marrow karyotyping shows a male karyotype with the presence of inv(3) (q21.3q26.2) in all 20 metaphases. Six months later, his routine full blood count showed a worsening in thrombocytopenia and anaemia, with the presence of circulating blasts. Clinically, he experienced fatigue and bleeding tendencies, and a physical examination detected hepatomegaly. A follow-up bone marrow examination done in April 2023 demonstrated hypercellularity with granulocytic hyperplasia, dysgranulopoiesis, dysmegakaryocytopoiesis, abnormal localization of immature precursors (ALIP), and increased blasts of 10 to 15%.

Discussion / Conclusion: The initial bone marrow examination identified a clonal chromosomal aberration with the presence of cytopenia in the absence of dysplasia or blasts. Based on the revised 4th WHO classification of hemolymphoid tumours, inv(3) was one of the cytogenetic abnormalities that defined myelodysplasia (MDS). However, the latest 5th WHO edition replaced this entity with clonal cytopenia of undetermined significance (CCUS), whereas MDS is defined as persistent cytopenia with at least 10% of cells being morphological dysplasia. Therefore, the initial bone marrow examination findings indicate CCUS and not MDS. The revised 4th WHO edition also stated that the diagnosis of AML with inv(3) or t(3;3) requires the presence of a 20% peripheral blood or bone marrow blasts, whereas cases with a blast count less than 20% are classified as MDS with excess blasts (MDS-EB). Recent studies discovered that individuals with MECOM rearrangement and blast counts below 20% exhibit clinical features resembling those with higher blast counts. Hence, the current 5th WHO edition stated otherwise, AML with MECOM rearrangement is considered to be among the AML with defining genetic abnormalities and does not require a blast threshold. This case illustrates the significance of clonal chromosome 3q aberration in a patient with persistent cytopenia, which has preceded the evidence of morphological dysplasia and excess blasts. It highlighted the strong association of inv(3) with myeloid malignancies, especially in MDS and AML.

CASE SERIES/CASE REPORT(LABORATORY)

CL6 ROLE OF ANTI-HUMAN LEUKOCYTE (HLA) ANTIBODY IN DIAGNOSIS OF FETAL AND NEONATAL ALLOIMMUNE THROMBOCYTOPENIA: A CASE REPORT

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Background: Fetal and neonatal alloimmune thrombocytopenia (FNAIT) is a possible cause of thrombocytopenia in term neonates with incidence of one in every 1,000 live births FNAIT is caused by cross-reactivity of maternal antibodies against antigens expressed on paternally inherited fetal platelets. Thus, thrombocytopenia results from antibodies that cross the placenta damaging the fetal platelets Human platelet antigens (HPA) and human leukocyte antigen (HLA) class I are both expressed by platelets. Although anti-HPA antibodies are thought to be the primary cause of FNAIT, it is not unusual for antibodies against HLA class I to cause FNAIT FNAIT presents in a spectrum from mild asymptomatic thrombocytopenia to marked thrombocytopenia resulting in spontaneous intracranial haemorrhage.

Case Presentation: We present a case of a baby boy who was born at 36 weeks 3 days period of gestation (POG) via emergency lower segment Caesarean section (EMLSCS) due to fetal distress. He was born with low birth weight (LBW) of 1.93 kg with no bleeding tendency. His mother had 2 episodes of previous preterm deliveries, no history of miscarriage or stillbirth and no other significant medical history. Maternal platelet counts remained normal throughout her pregnancy. Clinically, baby was well, not septic looking with no evidence of bleeding such as petechiae or bruises and no organomegaly. His platelet count was persistently low, ranging from 61 to 117 x 10^9/l from day one till day seven of life. A full blood picture showed true thrombocytopenia with occasional giant platelets seen. Other blood parameters were normal and non-suggestive of infection. A platelet immunology test was done in which anti-HLA Class 1 antibody was detected from mother's serum, thus diagnosis of FNAIT was made. Subsequently, his platelet count increased without intervention and he was discharged well without complications.

Discussion / Conclusion: The case demonstrates that despite being anti-HPA negative, the presence of anti-HLA antibodies may be a cause of FNAIT. In addition to that, our case reported an association between HLA class I antibodies and low birth weight in FNAIT. Moreover, anti-HLA positivity has been shown to present with a wider range of severity in FNAIT. In contrast to our case, some had reported neonates with severe NAIT caused by maternal anti-HLA antibodies resulting in mucosal bleeding and respiratory distress requiring mechanical ventilation, multiple platelet transfusions and gamma globulin infusions. In conclusion, the presence of anti-HLA antibodies is an important tool in the absence of anti-HPA antibodies in diagnosing FNAIT. It may also be used as a prognostic measure in determining FNAIT severity and its complications. Further studies may be warranted in establishing the role of anti-HLA antibodies as a prognostic marker for the clinical severity of FNAIT.

Keywords: Neonatal Alloimmune Thrombocytopenia, anti-Human Leukocyte Antigen Antibody

CASE SERIES/CASE REPORT(LABORATORY)

CL7 INFANTILE PYKNOCYTOSIS: A RARE CAUSE OF NEONATAL NON-IMMUNE HEMOLYTIC ANEMIA

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Background: Non-immune neonatal hemolytic anemia can be cause by hereditary (e.g. red cells membrane disorder or red cell enzymatic defect) or acquired disorder. These causes will lead to premature destruction of red cells. Infantile Pyknocytosis is a rare cause of acquired non-immune hemolytic anemia in neonatal period. Here we described a case that was diagnosed on peripheral blood film.

Case Presentation: A baby boy, born term at 38 weeks with birth weight of 2.58kg. Antenatally, mother had Gestational Diabetes Mellitus on diet control and iron deficiency anemia. The baby was intubated at 8 hours of life for meconium aspiration syndrome and was extubated after 20 hours. He developed neonatal jaundice at day 2 of life (DOL) and given phototherapy. At 7 DOL, he was treated for nosocomial infection for new onset respiratory distress and rebound hyperbilirubinemia. The jaundice persisted at 14 DOL (serum bilirubin level 329µmol/L), thus investigations for prolonged jaundice were sent. The investigations showed dropping of hemoglobin level from 15.8g/dL at birth, to 7.8g/dL. Clinically, patient was pale, jaundiced, good perfusion and afebrile. On examination, noted systolic murmur with mild hepatosplenomegaly. Other investigations were as follows; red blood cell 2.43x10^12/L, MCV 94.7fL, MCH 32.1pg, platelet 677 x10^9/L, reticulocytes count 5.3% and absolute reticulocytes 128 x10^9/L. Direct anti-globulin test was negative. Glucose-6-phosphate dehydrogenase screening was normal at birth. Maternal and baby blood group were B positive and O positive, respectively. Blood culture and sensitivity was negative. Urinalysis and thyroid function test were normal. C-reactive protein levels decreased from 35.25mg/L to 1.67mg/L since birth. Urgent peripheral blood film requested. Initial peripheral blood film (PBF) report was described as present of spherocytes, schistiocytes, microspherocytes with polychromasia, suspected microangiopathic haemolytic anemia. However, it was not consistent with patient clinical conditions. Second opinion PBF was sent to tertiary hospital and it was reported as numerous pyknocytes, few schistiocytes, occasional microspherocytes, target cell and polychromasia. These findings were suggestive of Infantile Pyknocytosis. Packed red cell was transfused once. Post transfusion hemoglobin was 11.3g/dL. Follow up at 2 months of age, patient was well with normal development milestone. His hemoglobin dropped to 8.7g/dl and was optimized using oral supplements. However, patient had defaulted the subsequent follow up.

Discussion / Conclusion: Infantile Pyknocytosis is a rare cause of hemolytic anemia in neonatal period. It was first described by Tuffy et al. as transient neonatal hemolytic anemia with presence of pyknocytes. Pyknocytes was described as much distorted, completely irregular, densely stained erythrocytes, usually appreciably smaller than undistorted cells and having from several to many spiny projections on peripheral blood film. The etiology of Infantile Pyknocytosis is still unknown. Patient usually presented with jaundice and negative direct antiglobulin test with hemolytic anemia which peak at third to fourth week of life. The anemia is usually severe with hemoglobin level of less than 8 g/dL. It is a self-limiting conditions and treatment is mainly supportive with phototherapy and blood transfusion. Due to its rarity, it requires high index of suspicion and experiences pathologist to review the red cells morphology.

CASE SERIES/CASE REPORT(LABORATORY)

CL8 A CASE REPORT OF POST-MORTEM DIAGNOSIS OF ACUTE PROMYELOCYTIC LEUKAEMIA (APL)

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Background: Acute promyelocytic leukaemia (APL), was defined in 1957 as a rapidly deteriorating clinical condition with characteristic severe bleeding tendency. The outcome is tremendously improved following breakthrough in treatment. Nonetheless, without timely diagnosis and intervention, outcome remains poor and can be fatal. Molecular confirmation of PML-RARA translocation is mandatory in reaching a definitive diagnosis, but not feasible in acute setting whereby urgent management are often initiated based on clinical suspicion and peripheral blood smear. Diagnosing APL solely on morphological inspection can be challenging, even for the experienced eye and further complicated if the sample received is "aged".

Case Presentation: We report a case of post-mortem diagnosis of acute promyelocytic leukaemia (APL) in a 48-year-old man who was found unconscious with oral and nasal bleeding, approximately 2 hours prior to the pronounced time of death. Blood sample from subclavian vein was taken about 22 hours after death for testing. Full blood count showed haemoglobin: 7.3 g/dL, MCV: 127.4 fl, MCH: 34.4 pg, white blood cell count (WBC): 4.0 x 10^9/L, absolute neutrophil count: 1.5 x 10^9/L and platelet 24 x 10^9/L. Peripheral blood film (PBF) showed presence of 42% abnormal promyelocytes/ blasts. They were medium to large with open chromatin, moderate to ample granular cytoplasm, some with bilobed nuclear outline, open chromatin pattern and prominent nucleoli with Auer rods. Occasional Faggot cells seen. Degenerative changes were observed, namely cytoplasmic and nuclear vacuolation, pyknosis, abnormal nuclear outline, nuclear disintegration and cytoplasmic blebbing in the nucleated cells. Peripheral immunophenotyping flow cytometry (IPT) showed presence of 43% abnormal promyelocytes/ blasts which are positive for MPO (bright), CD117, CD13, CD64, while negative for CD34 and HLA-DR, consistent with APL.

Discussion / Conclusion: For sample stored in ethylenediaminetetraacetic acid (EDTA), quality of blood cell morphology deteriorates with time and is usually compromised 6 hours post sampling even with storage at 4 °C. Similarly, blood cells also exhibit variable degenerative changes in relation to post mortem interval. Jet at al reported that RBC remains intact up to 18-24 hours interval but becomes grossly dysmorphic after 12-24hours with loss of central pallor after 18 hours. Dysmorphic changes can be seen in WBC after 6 hours of death. Study by Deepak et al, observed pyknosis post 6-12 hours, cytoplasmic and nuclear vacuolation post 12-18 hours, nuclear fragmentation post 16-24 hours and disintegration post 36 hours in WBCs, apart from lymphocytes which is more resistant to degradation. These changes hold true for our case. However, examination of blasts cells or leukemic cases were not included in the afore mentioned studies. In this case, blasts showed variable findings which are similar with WBC changes reported by Deepak et al. It is noteworthy that morphology of the Auer rods was preserved and the open chromatin pattern of most of the intact blasts are still recognizable. This case highlights the degenerative morphological changes of bloods cells, as well as illustrates the importance in integrating these features in reaching a haematological diagnosis in a post-mortem case.

CASE SERIES/CASE REPORT(LABORATORY)

CL9 DOUBLE PHILADELPHIA CHROMOSOMES IN DE NOVO PEADIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: A CASE REPORT

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Background: Philadelphia(Ph) chromosome is the result from reciprocal translocation t(9;22) (q34;q11) generating fusion transcripts BCR::ABL1 gene. It presences defined a specific subgroup of B- lymphoblastic leukemia(Ph+ALL), accounting for 3–4% of childhood ALL. Additional chromosomal abnormalities(ACAs) are found in 60%–70% of Ph+ALL. Among which are additional copies of Ph chromosome(+der(22)t(9;22)), described as double Ph chromosome. It was a characteristic of CML in blast crisis, very rarely observed in de novo ALL. Here we report a rare case of double Ph+ALL in a 1- year-old girl.

Case Presentation: A 1-year-2-months-old girl presented with low grade fever, submandibular and inguinal swelling, abdominal distension and loss of appetite for 3 weeks. She had been transfused prior to referral to our center with packed cells and platelets due to severe anaemia (haemoglobin(Hb):3.1g/dl) and thrombocytopenia(platelets: $10x10^9$/L). Examination revealed lymphadenopathy and hepatosplenomegaly. Blood picture revealed bicytopenia (Hb: 7.4g/dL, TWBC: $8.6x10^9$/L, platelets: $57x10^9$/L), leucoerythroblastic picture and presence of abnormal mononuclear cells. Bone marrow aspiration(BMA) was suboptimal due to hemodilution. Nonetheless, blast cells were evident at 12% of the nucleated cells and immunophenotyping analysis showed presence of 16% B- lymphoblasts expressing aberrant marker of CD58, CD38 and CD66c suggesting of B-ALL. Trephine biopsy was diffusely displaced by blast cells, confirmed the diagnosis of B-ALL. Chromosomal analysis revealed a female karyotype with complex chromosomal abnormalities, reported as 46,XX,t(9;22)(q34.1;q11.2),-10,-13,+mar1,+mar2[4]/46,sl,del(9)(p22)[4]/47,sl,+der(22)t(9;22)(6)/46,XX[16].

Three abnormal cell lines were observed, with double Ph chromosomes were evident. Additional deletion of short arm of chromosome 9[del(9)(p22)], monosomy 10 and 13 were also observed. FISH analysis confirmed the BCR::ABL1 fusion in 41% cells with additional extra fusion signal was observed in 9% of the cells, indicating the presence additional derivative chromosomes 22, consistent with double Ph chromosomes observed in karyotyping analysis. She received EshPALL chemotherapy protocol in which Imatinib was included in the treatment regime. To date, post induction 1A BMAT assessment showed that she was in morphological remission.

Discussion / Conclusion: ACAs in CML confer further disease stratification which often signify risk of disease progression. Little was discussed on their implication in Ph+ALL. +der(22),-9/9p-,-7/7p-,+8,+21 and +X is the most frequent abnormalities identified. Presence of additional copies of Ph chromosome is extremely rare in ALL but characteristic in some cases of CML in blast crisis, hence postulated to represent advancement of the disease. The incident of Ph+ALL itself rather frequently observed in older age group compared to our patient's age. Moreover, leucocytosis which often seen in Ph+ALL was not evident in our case. Nevertheless, CD66c aberrancy was evident as described in literature as among common associated marker on flowcytometric analysis. Significant co-occurrence of double Ph chromosome with both abnormal 9p and a complex karyotype as observed in our patient has been reported in adult Ph+ALL. Overall, a consistent conclusion has not been reached regarding the prognostic significance of ACAs in Ph+ALL. Variable outcomes were reported between its dismal event to insignificant different between the groups with and without ACAs. Further studies will be needed to verify the impact of specific ACAs on patient's outcomes. We highlight the awareness of this rare cytogenetic event in a case of paediatric Ph+ALL.

CASE SERIES/CASE REPORT(LABORATORY)

CL10 A RARE CASE OF MARROW INFILTRATION BY PLASMABLASTIC NEOPLASM

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Background: Plasmablastic lymphoma (PBL) is an uncommon and very aggressive B-cell lymphoma, frequently associated with Human Immunodeficiency Virus (HIV) infection. The most common site of PBL involvement is the oral cavity. The diagnosis is not straightforward in view of the variability and overlapping morphology and immunophenotypic features of several other plasmablastic differentiation lymphoma and myeloma. Herein, we reported a rare case of PBL infiltration to the bone marrow.

Case Presentation: A 33-year-old man with underlying HIV infection, presented with epistaxis, lethargy and reduced effort tolerance for 1 month. He was previously on Highly Active Antiretroviral Therapy (HAART) but defaulted follow-up. Full blood count showed pancytopenia with WCC: 2.1x109/L, Hb: 7.8g/dL, PLT: 17x109/L. Renal profile and calcium levels were normal. Full blood picture showed leucoerythroblastic picture with occasional plasma cells (<1%). Bone marrow aspirate showed hemodiluted smear with more than 90% abnormal plasma cells. They are medium to large cells exhibited round to oval shape, clumped chromatin and moderate amount of basophilic cytoplasm with perinuclear hof. Flowcytometry immunophenotyping revealed neoplastic cells with CD45 dim to moderate, positive for CD38, CD56 and CD117 (dim) while negative for CD138 and CD19. Cytogenetic analysis showed hyperdiploidy with complex chromosomal abnormalities. Trephine biopsy showed diffuse infiltration by abnormally large plasma cells, round nuclei, prominent nucleoli, coarse chromatin and scanty cytoplasm with background of starry sky appearance. They were positive for CD138 and MUM1 and negative for CD3, CD20 and CD79a. The proliferative index ki-67 was more than 90%. Computed Topography of Thorax, Abdomen and Pelvis (CT-TAP) revealed left retroperitoneal/perinephric mass and multiple intraabdominal lymphadenopathies. He underwent an interventional radiology-guided biopsy of perinephric mass in which the tissue biopsy was consistent with PBL. Epstein-Barr virus (EBV) in-situ hybridization test showed the malignant cells were positive for EBV. Patient was started on IV Methotrexate, but succumbed to death due to sepsis.

Discussion / Conclusion: PBL is a rare type of lymphoma composed of late B cells that express plasma cell markers (CD138), rather than the pan-B cell markers found in diffuse large cell lymphomas (CD20 and CD79a). In view of plasma cell differentiation of these tumors, the differential diagnosis of anaplastic or plasmablastic myeloma should be considered. Plasmablastic myeloma is characterized by the presence of serum and urine paraproteins, hypercalcemia, bone lytic lesions, anemia, and infiltration of bone marrow by plasma cells. PBL most frequently presents as a mass in extra nodal mass with gastrointestinal tract is common site. The immunophenotype of plasmablastic myeloma and PBL is remarkably similar, and all patients with both diseases show positivity for CD38, CD138, MUM1 with high Ki67 but are negative for CD20. In situ hybridization for EBER is positive in 60%-75% of PBL cases. MYC translocation has been identified in approximately 50% of PBL cases. A history of immunodeficiency and presence of EBV positive are useful in establishing the diagnosis of PBL which will be positive in almost all cases of PBL and negative in myeloma. Other factor such as lymphadenopathy or extramedullary lesion in the absence of myeloma-defining symptoms were used to favor the diagnosis of PBL. The diagnosis of this rare entity is not only depending on the histopathological features, but also on the integration of the clinical history, radiologic studies, and laboratory tests.

CASE SERIES/CASE REPORT(LABORATORY)

CL11 CLEFTED LYMPHOCYTES AND SMUDGE CELLS IN PERTUSSIS: A CASE SERIES

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Background: The incidence of pertussis infection in Malaysia has dramatically increased. To diagnose pertussis is always challenging as it is typically begin with mild catarrhal stage of respiratory symptoms. Morphologic examination of peripheral blood smears may provide some important findings that can lead to the early diagnosis of pertussis. We experienced two cases of lymphocytosis with the presence of clefted nuclei lymphocytes and smudge cells in Bordatella pertussis infection.

Case Presentation: Case 1: A 1 year old boy with no known medical illness presented to our hospital with fever, cough and reduce oral intake for three weeks. Documented temperature was 38.2ºC. He was severely tachypnoeic upon arrival, hence requiring oxygen support. Full blood count results (FBC) revealed a white blood cell (WBC) count of 89.77 x 10^9/L with predominantly lymphocytes (61.48 x 10^9/L). Respiratory Pathogen Genome Detection was positive for Bordatella Pertussis, Human Enterovirus/Rhinovirus and Parainfluenza 3. He was treated with IV Cefuroxime and IV Azithromycin, responded well to the treatment and was discharged on day 10 of admission.

Case 2 : A day 25 of life neonate presented with cough for one week, associated with facial congestion. Upon examination, patient was mildly tachypnoeic with minimal chest recession. He was subsequently put on nasal prong 2L/min. His WBC was 32.50 x 10^9/L, with predominance of lymphocytes (27.70 x 10^9/L). Polymerase chain reaction (PCR) testing for Bordetella pertussis, carried out on a nasopharyngeal swab, was positive. He was treated with IV Penicillin, IV Gentamycin and Syrup Azithromycin. He was discharged well after treatment. Morphologic examination of the peripheral blood smear for both patients revealed marked lymphocytosis which the lymphocytes were mature looking with scant cytoplasm, condensed chromatin and some showed clefted nuclei. There were also presence of smudge cells.

Discussion / Conclusion: Lymphocytosis in paediatric patients with distinctive lymphocytes morphology can support early diagnosis of Bordatella pertussis infection. The presence of both clefted lymphocytes and smudge cells in peripheral blood smear may provide a clue to paediatrician as one additional findings of suspecting pertussis infection. Few studies have been reported correlating the presence of clefted lymphocytes in peripheral blood smear with pertussis. However, presence of smudge cells are rarely seen in pertussis but can be found in viral infection i.e Epstein-Barr viral infection. Therefore, further studies is needed to explore the diagnostic significance of smudge cells in pertussis infection.

CASE SERIES/CASE REPORT(LABORATORY)

CL12 CONCURRENT COLD AUTOIMMUNE HEMOLYTIC ANEMIA (AIHA) IN A NEWLY DIAGNOSED PAEDIATRIC B-LYMPHOBLASTIC LEUKAEMIA (B-ALL): A CASE REPORT

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Background: Cold autoimmune hemolytic anemia (AIHA) is an acquired hemolytic disease due to autoantibodies against RBC. It is known as a complication of many malignancies, primarily lymphoid malignancies, B-lymphoproliferative Disorder (B-LPD) among which Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia (CLL) are the common primary diseases. The incidence in Acute Lymphoblastic Leukemia (ALL) is extremely rare. Here we report a rare incidence of Cold AIHA that emerged upon diagnosis of B-ALL.

Case Presentation: A 3-year-5-month-old girl, presented with fever associated with cough, runny nose, and abdominal discomfort for two days. Examination showed hepatosplenomegaly, lymphadenopathies and hyperpigmented skin lesions. Peripheral blood film (PBF) revealed pancytopenia (Hb 4.7g/dL, ANC $0.28x10^9$/L, Platelet $36x10^9$/L) with 22% abnormal mononuclear cells. RBC agglutinations were evidenced hence diagnosis of cold AIHA was made. Forward blood grouping showed A-positive with additional positive reaction seen in reverse A1 cell which was resolved after prewarming. Direct Coombs' test was positive for anti-IgG(+) and anti-complement C3d(3+). Nonetheless, elution study was not done. Bilirubin was mildly raised (21.3 umol/L), LDH was elevated (563.2 U/L). Bone marrow aspiration trephine biopsy (BMAT) and immunophenotyping were consistent with B-ALL. Cytogenetic analysis was normal. Infectious screening for Epstein Barr Virus (EBV) and Mycoplasma pneumonia were negative but revealed positive for Rhinovirus and Bacillus cereus. Treatment regimen UKALL protocol was started. In addition, packed cell transfusions were commenced for severe anemia. AIHA was resolved one week following treatment. Follow up BMAT shows she remains in complete remission.

Discussion / Conclusion: The incidence of Cold AIHA in concomitant with ALL, in contrast to B-LPD particularly CLL is extremely unusual. When this occurs, it is almost always described following treatment or post-transplant. This case presents Cold AIHA upon diagnosis of B-ALL, which to the best of our knowledge, has not been reported so far. Recent study elucidated the pathogenesis behind AIHA may either through the possible modification of RBC surface antigens, molecular mimicry, or in case of LPD owing from the production of autoantibodies by the clonal B cells. The possibility of malignant CLL cells acting as antigen-presenting cells (APCs) that activate T helper cells directed against RBC autoantigen has been described to explain the striking association of CLL and AIHA. B-ALL is a disease of the precursor B-cell in which it involves maturation arrest of the B-cells, hence anticipating the suppression of immune development. This may explain the low frequency of autoimmune manifestations including AIHA among patients with ALL. To date, no biological studies have established a pathogenic relationship between the two diseases. Whether or not the occurrence of the two disorders was merely coincidental or represented common underlying pathologic process as described in other hematological malignancies remains to be defined and warrants further insight to describe its biological link. Furthermore, our patient also had concomitant infections. Even though it is typically associated with Mycoplasma pneumoniae or EBV infection, rarely other specific infections may cause Cold AIHA. We highlight the awareness of this rare autoimmune incidence in a case of B-ALL.

CASE SERIES/CASE REPORT(LABORATORY)

CL13 SECRETLY ON MOM'S GENE FOR A DECADE: A CASE REPORT ON DELAYED DIAGNOSIS OF MODERATE HAEMOPHILIA B

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Background: Haemophilia B is an X-linked bleeding disorder characterised by deficiency of coagulation factor IX. Incidence is rare in Malaysia. People with severe haemophilia B typically develop bleeding symptoms during infancy. Moderate haemophilia B individuals may present with occasional spontaneous bleed or prolonged bleeding after minor trauma/surgery; they are usually diagnosed before age five to six years. Diagnosis of haemophilia B is easily made by demonstrating a prolonged activated partial thromboplastin time (aPTT), that is corrected on mixing test, and a reduced factor IX level below normal. The impact of missing this diagnosis can be detrimental, as people with moderate to severe haemophilia are at risk of life-threatening bleeding and musculoskeletal deformities if not treated properly. This case report illustrates an unusual late presentation of a schoolchild with newly diagnosed moderate haemophilia B.

Case Presentation: A 10-year-old boy was referred to our hospital for anaemia treatment. Two weeks earlier, he bled excessively after an uneventful tooth extraction in private clinic. The bleeding lasted for 2 weeks until his parents brought him for medical consultation due to pallor. His parents reported recurrent epistaxis since young, but otherwise he had no bruising or painful joint swelling. He completed his vaccination and suffered no complications. He was involved in sports activities as usual. His mother and eldest sister had similar epistaxis bleeding but were never investigated before. Physical examination showed a pale child with normal stature. Full blood count revealed severe hypochromic microcytic anaemia and thrombocytosis. Blood film reported features of iron deficiency, which was consistent with low serum ferritin of 5.06 µg/L. Haematinic therapy was started and he was transfused with one packed red cell unit during hospitalisation. His coagulation profile showed prolonged aPTT of 69.4 seconds (reference range: 28-45 seconds) with normal prothrombin time. Mixing test demonstrated correction of aPTT into normal range. Factor IX activity was 1% and factor VIII level was 223%. Similar results were obtained on repeated testing after one week. Genetic testing on F9 gene using polymerase chain reaction and Sanger sequencing detected point mutation at codon 88 of exon 1 causing missense effect, confirming diagnosis of haemophilia B. His mother was found to be a carrier of similar genetic mutation. He was given on-demand plasma-derived factor IX concentrate 1000 units daily for 3 days to alleviate his bleeding.

Discussion / Conclusion: This case highlights the need to improve general knowledge about bleeding disorders among healthcare workers and the community. Our patient bled for two weeks after tooth extraction and was not diagnosed with haemophilia B until admission for anaemia. This case also emphasises on the importance of obtaining a good bleeding history prior to invasive procedures, including details of family history and previous postsurgical bleeding. Further investigations should subsequently be performed if bleeding history is significant. Available case reports with genetic mutation similar to our case had severe haemophilia B phenotype, but our case had milder-than- expected severity. This difference could possibly be explained by innate differences in genetic factors that control other haemostatic and fibrinolytic pathways.

CASE SERIES/CASE REPORT(LABORATORY)

CL14 HAEMOGLOBIN TITUSVILLE: A CASE REPORT OF A RARE ALPHA GLOBIN GENE MUTATION

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Background: Haemoglobin disorders are heterogeneous hereditary disorders of the globin chain with impaired synthesis or structure or both. Although some haemoglobin disorders may demonstrate significant symptoms of disease, some may remain asymptomatic without treatment. Hence correct diagnosis is therefore important to avoid unnecessary investigations, treatments and anxiety to patients. We present a case of a child presented with decreased oxygen saturation on pulse oximeter as a result of haemoglobin Titusville.

Case Presentation: A 6 years old boy was initially hospitalized for COVID 19 infection. Despite being asymptomatic, the child's oxygen saturation measured by pulse oximeter was persistently decreased in room air, with range of 85% to 90%. He otherwise appeared well with no sign of hypoxia and other vital signs were normal. Cardiovascular and respiratory examinations were unremarkable. He was an adopted child with no marked family history of blood, lungs or cardiac disease. Upon admission to ward, he received oxygen supplement via nasal cannula and subsequently treated as COVID 19 Category 4A with atypical pneumonia. A series of antibiotics given to treat suspected infection was ceased following 72 hours of negative blood culture. Multiple investigations were conducted including series of full blood count which demonstrated normal counts, series of blood gas which showed normal partial pressure of oxygen in arterial blood and normal findings of chest X-ray, electrocardiography and lungs CT scan. Blood film was reported normal. Eventually, haemoglobin analysis identified a presence of Hb variant at Zone 7. DNA analysis was subsequently performed revealing a mutation of a1-globin gene on codon 94 with amino acid substitution from aspartic acid (GAC) to asparagine (AAC) which is a diagnostic of hemoglobin Titusville.

Discussion / Conclusion: Haemoglobinopathies involving structural globin chain defect may result in high oxygen affinity disorders such as Hb M Boston, Hb Ypsilanti or low oxygen affinity disorders like Hb Titusville or Hb Bassett. We reported a case of a Haemoglobin Titusville which is a rare, inherited alpha variant mutation. It involves a single nucleotide change from G to A at codon 94 of the alpha globin gene that results in amino acid substitution from aspartic acid (GAC) to asparagine (AAC). It is a mildly unstable variant associated with decreased oxygen affinity resulting in spurious oxygen saturation on pulse oximeter despite maintaining adequate oxygen delivery to tissues. Generally, no treatment is needed. However, an early diagnosis is crucial to avoid unnecessary investigations and treatment.

CASE SERIES/CASE REPORT(LABORATORY)

CL15 PREGNANCY-ASSOCIATED THROMBOTIC MICROANGIOPATHY: A CHALLENGING CASE OF THROMBOTIC THROMBOCYTOPENIC PURPURA WITH INTRAUTERINE FETAL COMPLICATIONS

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Background: Pregnancy-associated thrombotic microangiopathy (TMA) is a rare but serious condition characterized by microvascular thrombosis leading to organ damage. It encompasses disorders such as HELLP syndrome (Haemolysis, Elevated Liver enzymes, Low Platelet count), atypical haemolytic uremic syndrome (aHUS), and thrombotic thrombocytopenic purpura (TTP). These conditions share common features like microangiopathic haemolytic anaemia and thrombocytopenia and can result in complications for both the mother and foetus. The pathophysiology involves abnormalities in the complement system, endothelial injury, and platelet activation. Early recognition and intervention are crucial for optimal outcomes.

Case Presentation: This case involves a 32-year-old pregnant woman at 28 weeks of gestation who developed pregnancy-associated thrombotic microangiopathy secondary to atypical pneumonia. Characterized by fever, disorientation, and a rapid decline in platelet count (from 15 x 10^9/L to 5 x 10^9/L), she exhibited severe manifestations of microangiopathic haemolytic anaemia (MAHA). The presence of peripheral schistocytes was accompanied by the positive haemolysis markers including elevated level of lactate dehydrogenase, bilirubin and reticulocytes as well as low level of haemoglobin. Her Direct Coombs' was negative. She was treated with six cycles of plasmapheresis and immunosuppressive medication. Unfortunately, the patient experienced an intrauterine fetal death during intubation. After a month, a subsequent analysis on patient's sample taken on onset of symptoms revealed a complete absence of ADAMTS-13 activity with a significant inhibitor level of 36.5U/mL, confirming the diagnosis of TTP.

Discussion / Conclusion: This case underscores the challenges in managing TTP during pregnancy, emphasizing the need for prompt recognition and intervention to mitigate potential complications. TTP poses challenges in diagnosis during pregnancy due to overlapping symptoms with normal pregnancy- related conditions. Symptoms such as fatigue, thrombocytopenia, and mild renal dysfunction may be attributed to pregnancy itself. Additionally, distinguishing TTP from other pregnancy related complications like preeclampsia and HELP syndrome can be complex. The reliance on clinical manifestations, biochemical haemolysis markers and other haematological findings is crucial in deciding to start plasmapheresis, while the ADAMTS13 activity levels will only be known later. Timely recognition is essential, as untreated TTP can lead to severe complications for both the mother and the foetus.

CASE SERIES/CASE REPORT(LABORATORY)

CL16 IS IT LUPUS ANTICOAGULANT HYPOPROTHROMBINEMIA SYNDROME (LAHPS)? : A CASE REPORT

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Background: Lupus anticoagulant (LA) is an antiphospholipid antibody that inhibits phospholipid dependent clotting without inhibiting the activity of coagulation factors, and often leads to thrombotic events. It is rarely accompanied by hemorrhagic diathesis unless it is associated with a second coagulation abnormality such as thrombocytopenia or hypoprothrombinemia. Lupus anticoagulant hypoprothrombinemia syndrome (LAHPS) is a rare entity, characterized by bleeding and thrombosis in patients with autoimmune diseases or infections.

Case Presentation: We present a case of a 67-year-old gentleman with underlying diabetes mellitus and hypertension who presented with left sided body weakness and slurring of speech for a month that preceded with a fall. He had no family history of bleeding disorders or autoimmune disease. Upon initial neurological assessment, his GCS was E4V4M6 however dropped to E1V1M4 (6/15) hence intubated for cerebral protection. Brain imaging done showed posterior circulation and brainstem infarct with CT Angiogram findings consistent with total occlusion of basilar artery. Stroke protocol was activated and subsequently he was thrombolysed chemically with Alteplase. While staying in intensive care unit for ventilation support, he had multiple hospital acquired infection requiring antibiotics cocktails. He also had episodes of hematuria and bleeding from ETT tube and thus subcutaneous clexane and oral aspirin were withheld. Full blood count showed haemoglobin level of 6.3 g/dL, white cell count of $11.9x10^9$/L and platelet of $423x10^9$/L. A serial coagulation profiles taken and showed prolonged PT and APTT. Mixing test were done and showed correction for PT mixing test but APTT mixing studies show significant prolongation after immediate mixing. At this time, we suspected presence of lupus anticoagulant antibody with hypoprothrombinaemia. Factor assays were performed and showed mildly reduced factor XII and factor II (prothrombin) activities. Additionally, factor VIII activity was high, while factor V, IX, X, XI were normal. Lupus anticoagulant test was positive whereas anticardiolipin antibody and anti beta 2 glycoprotein were negative.

Discussion / Conclusion: The isolated acquired factor II deficiency can be occasionally observed in patients with LA. This association is known as LAHPS, a rare syndrome that normally has been reported to be related to certain situations such as primary antiphospholipid syndrome, infection and occasionally drugs, but mostly due to systemic lupus erythematosus (SLE). This case highlights the possibility of LAHPS in a patient with suspected LA who had bleeding manifestation. However, the dilemmas in this case are 1) the diagnosis of LA was not well established as the LA test was not yet repeated after 12 weeks and 2) the bleeding events could be due to anticoagulant given or LAHPS. 3) Besides, the reduction of factor II and XII can be due to acquired causes such as increased consumption (in the case of bleeding) and sepsis. However, it is worth to include LAHPS as one of the differential diagnosis in patient with prolonged PT and APTT which mixing test show correction for PT but not APTT after immediate mixing. An early diagnosis of this clinical entity and a quick initiation of immunosuppressive treatment, as well as a diagnosis of the underlying disease determines patient's clinical development.

CASE SERIES/CASE REPORT(LABORATORY)

CL17 THOMSEN-FRIEDENREICH ANTIGEN ACTIVATION IN A CASE OF STREPTOCOCCUS PNEUMONIAE-ASSOCIATED HEMOLYTIC UREMIC SYNDROME

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Background: Ninety percent of hemolytic uremic syndrome (HUS) is secondary to Shiga toxin producing bacteria, also known as post-diarrheal or typical HUS. Atypical HUS on the other hand encompasses all the other rarer causes characterized by dysregulation of complement. Streptococcus pneumoniae is the commonest cause for atypical HUS. We present a case of Streptococcus pneumoniae-associated HUS (Sp-HUS) with laboratory confirmation of Thomsen-Friedenreich antigen (T-antigen) activation.

Case Presentation: A four-year-old girl was referred from a secondary hospital for further management of necrotizing pneumonia with empyema. She required intubation and developed acute kidney injury, pancytopenia and microagiopathic hemolytic anemia (MAHA). Direct antihuman globulin test (DAT) was positive (IgG 2+, C3d weak). Minor crossmatch showed polyagglutination with adult but not cord blood plasma. Positive reactions were seen with peanut (Arachis hypogaea) and soy (Glycine soja) lectin test. ADAMTS-13 level was mildly low (20.5%) without evidence of inhibitor. Polymerase chain reaction from pleural fluid was positive for S. pneumoniae. All evidence is suggestive of classical T activation. The patient was treated with ceftriaxone, prednisolone and hemodialysis. Two cycles of total plasma exchange (PE) were performed, with first cycle using 5% human albumin and the second cycle with 5% albumin:fresh frozen plasma (60%:40%). After one month of hospitalization, she is discharged home with a normalized renal function and resolution of MAHA.

Discussion / Conclusion: T-antigen is cryptic and normally hidden by a terminal sialic acid. It is found on erythrocytes, platelets, glomerular capillary endothelium and renal tubular epithelium. Neuraminidase from S.Pneumoniae cleaves the terminal sialic acid, exposing the T-antigen. Anti-T is a naturally occurring IgM antibody that starts to develop around two to six months of age after exposure to gut flora with structural similarities with T-antigen. Binding of preformed anti-T to the exposed T-antigen leads to the cascade of events in Sp-HUS. T-activation is necessary, but not sufficient to cause Sp-HUS; Activation of alternate pathway of complement may also play a role. The unavailability of commercial lectin reagent in our centre stimulated attempts to extract peanut and soy lectin from raw seed, according to AABB technical manual. These “home-made” lectin extracts were found to yield satisfactory results and further confirm T-antigen activation in this case. The strategy of only transfusing washed cellular products and avoidance of plasma to prevent further anti-T exposure is previously accepted and still widely practiced. Newer insights on the underlying pathogenesis of Sp-HUS question the necessity of this approach. Although controversial, PE with 5% albumin or low titer anti-T plasma has been found beneficial by removing the circulating antibodies and pathogenic neuraminidase. Sp- HUS is an uncommon complication with S. pneumoniae infection. Nonetheless, it should be suspected if associated with HUS and a positive DAT, especially in young pediatric population. Minor crossmatch with adult and cord blood plasma can be done in most blood banks to support T-antigen activation. Saline extract from peanut and soy can be used if commercial lectin reagents are not available for the confirmation

CASE SERIES/CASE REPORT(LABORATORY)

CL18 A CHALLENGING BEHAVIOUR OF AN INDOLENT LYMPHOMA: PRIMARY CARDIAC MARGINAL ZONE LYMPHOMA

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Background: Primary cardiac lymphomas are rare extranodal lymphomas that involve the heart and/or pericardium. They account for 2% of cardiac malignancies and less than 1% of extranodal lymphomas. The reason behind this is that there is no lymphoid tissue in the heart.The common symptoms associated with primary cardiac lymphomas are shortness of breath, chest tightness, chest pain and arrhythmias.

Case Presentation: We report a case of a 47 year old gentleman with underlying chronic Hepatitis B infection who presented to a district hospital in May 2021 with shortness of breath and was noted to have global pericardial effusion. He was referred to the cardiology team and a pericardiocentesis was done. Pericardial fluid analysis was unremarkable. He was empirically treated with anti TB.A CECT Thorax in July 2021 showed minimal pericardial effusion.He presented again in May 2022 with progressive shortness of breath and recurrent hemoserous pericardial effusion. A CECT thorax in May 2022 revealed an enhancing infiltrating mass from left cardiac chamber to superior mediastinum compressing the left heart chamber and encasing the ascending aorta, main pulmonary trunk and main pulmonary artery.He however refused a cardiac biopsy at that point. He then presented again in November 2023 with similar symptoms and CECT showed worsening mediastinal insinuating mass which involves the entire mediastinum from thoracic inlet till inferior thoracic apertureand encasement of the heart and major vessels. A left anterolateral thoracotomy and left pleuropericardial window plus cardiac biopsy was done. The HPE showed atypical lymphoid cells that were small to medium in size with focal plasmacytic differentiation with low mitotic activity. Immunohistochemistry confirmed that these cells were positive forCD20, BCL2, CD79a, PAX-5, IgM, IgD with predominant Kappa ISH light chain (ratio (8:1) and negative for CD5, cyclin D1 and CD23 which was suggestive of Marginal Zone lymphoma with plasmacytic differentiation.Serum protein electrophoresis showed a monoclonal IgM kappa paraproteinemia of 10.7g/L. Unfortunately a bone marrow examination was not done as patient was not able to lie flat. MALT-IPI score was intermediate (1:stage). He has just completed 2 cycles of Rituximab-Bendamustine each cycle 28 days apart as per recommendation for indolent lymphomas to which he has clinically responded favorably. Also this regime was preferred in order to avoid anthracycline-related cardiotoxic effects.

Discussion / Conclusion: The rarity of this condition calls for more awareness and extensive application of combined imaging like echocardiography and cardiac MRI for early diagnosis. The difficulty and risk associated with obtaining sample for diagnosis may play a role in delayed diagnosis . Most cases of cardiac lymphoma were diagnosed by autopsy as the alarming symptoms are often late.The indolent slow growing behaviour of Marginal Zone lymphoma has led to a diagnosis 2 years after the onset of symptoms.The patient's response will be objectively reassesed with a cardiac MRI and echocardiography later.

CASE SERIES/CASE REPORT(LABORATORY)

CL19 ACUTE PROMYELOCYTIC LEUKAEMIA WITH FLT 3-ITD AND RUNX1 MUTATIONS: A CASE REPORT

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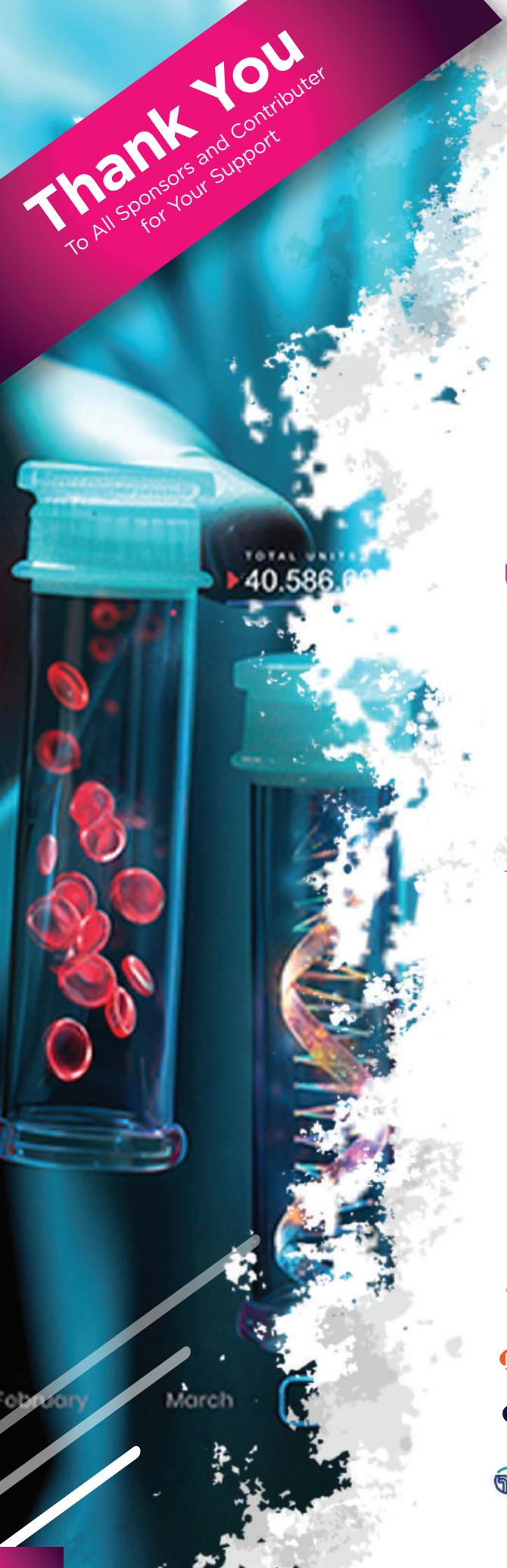
Background: Acute Promyelocytic Leukaemia (APML) is a subtype of Acute Myeloid Leukemia (AML) arising from a balanced reciprocal translocation between chromosomes 15 and 17. The fusion between promyelocytic leukemia (PML) and retinoic acid receptor alpha (RARα) genes results in the PML::RARα rearrangement t(15;17)(q24;q21), leading to the disruption of the RARα-regulated maturation of myeloid progenitors at the promyelocytic stage. In Malaysia, APML comprises less than 10% of AML and it constitutes approximately 2.8% of all leukaemia cases. In APML, several concurrent genetic mutations can occur alongside PML::RARA. The most common concurrent gene in APML is FLT3 (FMS-like tyrosine kinase 3). These mutations can have implications for disease prognosis and treatment response. For other concurrent genes such as RUNX1 in APML, it is considered rare and not many cases have been reported.

Case Presentation: A 47-year-old male patient was diagnosed with APML in 2021 and was given Idarubicin induction and consolidation at that time but then defaulted on the treatment. In February 2023, he presented to the hospital with prolonged fever and lethargy. Complete blood cell count showed leukocytosis (80×109/L), normal haemoglobin level (13.9g/dL), and thrombocytopaenia (platelets of 32×109). Peripheral blood revealed 89% abnormal promyelocytes characterized by bilobed nuclei with scanty basophilic cytoplasm and numerous Auer rods. At the time of relapse, the molecular screening test using multiplex polymerase chain reaction (PCR) showed the presence of PML::RARα fusion gene with short isoform bcr-3 subtype. Further testing using the Next Generation Sequencing platform by AmpliSeq™ for Illumina® Myeloid Panel identified FLT3-ITD which has a very high allelic ratio of 69.93 (measured by PCR) and another concurrent gene, RUNX1 mutation was also detected. He was given a second Idarubicin induction and later Arsenic Trioxide for the relapsed episode but the patient passed away in December 2023.

Discussion / Conclusion: Since the introduction of all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) for the treatment of APML, the overall survival rate has improved significantly. However, relapse/refractory patients showing resistance to ATRA and/or ATO still occur. The association of FLT3- ITD and RUNX1 with poor outcomes in AML is widely known as recommended in European LeukaemiaNet 2022. However, its significance in APML is less established. Additionally, short isoform bcr-3 subtype was also reported in some cases of relapsed APML. Concurrent genetic aberrations at initial diagnosis such as FLT3-ITD likely predispose patients to relapse or treatment resistance which suggests that patients carrying this mutation might benefit from treatment with FLT3 inhibitors. While RUNX1 mutations are not commonly associated with APML, there is a possibility this gene might worsen the outcome of APML patients. In this case, we could not confirm the presence of these concurrent genes at diagnosis due to the limited availability of NGS test thus, the possibility of genetic evolution cannot be excluded. The importance of reliable mutation screening at diagnosis and the onset of relapse is very crucial to assist clinicians in disease stratification and treatment intervention.



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