中華民國血液病學會 第184次聯合學術研討會

時間:113年9月21日(星期六)13:00-17:00 地點:三軍總醫院(內湖院區)B1第一演講廳 會長:三軍總醫院戴明燊主任

時間	演講題目
12:30-13:00	報到
13:00-13:05	會長 戴明桑主任 致歡迎詞
13:05-13:10	中華民國血液病學會 柯博升理事長 致開幕詞
時間	會員演講(I) Malignant Hematology
13:10-13:20	⁰¹ Clonal Dynamic Changes during the Progression of Myelodysplastic Syndromes to
	Secondary Acute Myeloid Leukemia: A Paired-Sample Comparison
	歐哲瑋 林口長庚紀念醫院內科部血液腫瘤科
13:20-13:30	⁰² Initial Hematopoietic Dynamics with Epcoritamab in Heavily Pretreated Large B-Cell
	Lymphoma Patients – Real World Experience in a Single Center
	楊庭瑋 國立臺灣大學醫學院附設醫院內科部血液科
13:30-13:40	⁰³ Dasatinib Related Pulmonary Hypertension – Case Sharing
	陳康盈 高雄醫學大學附設醫院血液腫瘤科内科
13:40-13:50	⁰⁴ Hemophagocytic Lymphohistiocytosis (HLH)
	林于傑 高雄醫學大學附設醫院血液腫瘤內科
13:50-14:00	⁰⁵ Nontuberculosis Mycobacteria Infection Associated Hemophagocytic
	Lymphohistiocytosis 古佐夫」专业英联盟人 计联点列
14:00-14:10	⁶⁰ Lyse or Not to Lyse? Typical and Atypical Presentation of Cold Agglutinin Syndrome
	(CAS) IN a Patient with Gastric Cancer and Another with Lymphoma 随建在上升信公应中公驳险加购公成做款加购投估到
	保廷廷[和后宿留十八 酉阮細肥冶療與针細肥移植杆
吐用	市 55 法 注(1)
時間	專題演講(I)
時間 14:10-14:45	專題演講(I) AML Overview: Evolving Disease Classification and Treatment (Virtual) Prof Harry Gill The University of Hong Kong, Hong Kong
時間 14:10-14:45 14:45-14:55	專題演講(I) AML Overview: Evolving Disease Classification and Treatment (Virtual) Prof. Harry Gill The University of Hong Kong, Hong Kong Open Discussion
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時間 14:10-14:45 14:45-14:55 14:55-15:15 時間 15:15-15:25 15:35-15:45 15:45-15:55 15:55-16:05 16:05-16:15	專題演講(I)AML Overview: Evolving Disease Classification and Treatment (Virtual) Prof. Harry Gill The University of Hong Kong, Hong KongOpen DiscussionCoffee Break會員演講(II) MPN, Benign Disease, 小兒血液學07Efficacy and Safety of Myelofibrosis Patients Treated with Ruxolitinib: Real-World Clinical Data from Single Institution 黃翊翔 三軍總醫院內科部血液腫瘤科08080909Eltrombopag Induced Cerebral Venous Thrombosis 林伐緯 馬偕紀念醫院血液腫瘤科10A Single Center Experience of 4 Patients of Acquired Hemophilia 林彧德 衛生福利部雙和醫院血液腫瘤科11111414151516161718181911111212131414151516171818191911111213141415151617171818191911111213141415151617181919191111111211141516 </td

時間	會員演講(III) Transplantation and cell therapy
16:15-16:25	¹³ Extracorporeal Membrane Oxygenation Support in Pediatric Patient with Malignancies or Haematopoietic Stem Cell Transplant History: Outcomes of a Single Center Cohort 黃韻融 臺北榮民總醫院兒童醫學部
16:25-16:35	¹⁴ Experience with Maribavir for Ganciclovir-Intolerant Cytomegalovirus Infections in Allogeneic Stem Cell Transplantation: A Case Report 李珩 臺北榮總內科部
16:35-16:45	¹⁵ Salvage of Resistant-Relapsed Pediatric Diffuse Large B-Cell Lymphoma by Bridging Chimeric Antigen Receptor T-cells and Multimodal Regimens Followed by Consolidative HLA-Haploidentical Peripheral Blood Stem Cell Transplantation: A Case Report 陳榮隆 和信治癌中心醫院小兒血液腫瘤科
16:45-16:55	¹⁶ Transplant-Associated Thrombotic Microangiopathy (TA-TMA), with Secondary Atypical Hemolytic Uremic Syndrome (aHUS) and Posterior Reversible Encephalopathy Syndrome (PRES) Successfully Salvage with Eculizumab 劉家豪 台大癌醫血液腫瘤部
16:55-17:00	中華民國血液及骨髓移植學會 李啟誠理事長 致閉幕詞
備註:	
專講演講:每題	9.45分鐘,其中包括35分鐘「演講」、10分鐘「討論」。
30	分鐘鈴響一聲,35分鐘鈴響兩聲,請結束演講。

- 會員演講:每題10分鐘,其中包括8分鐘「演講」、2分鐘「討論」。
- 7 分鐘鈴響一聲,8 分鐘鈴響兩聲,請結束演講。
- 主辦單位:中華民國血液病學會、中華民國血液及骨髓移植學會、三軍總醫院
- 贊助單位:台灣協和麒麟股份有限公司、台灣必治妥施貴寶股份有限公司、嬌生股份有限公司
- 教育學分:中華民國血液病學會甲類5分、中華民國血液及骨髓移植學會5分、其他學會(TBD)。

Curriculum vitae

Name : Dr. Gill Harinder Singh, Harry

Academic Qualifications:

M.B.,B.S. (H.K.)	2006	P.Dip.I.D. (HK)	2009	M.R.C.P. (UK)	2009
F.H.K.C.P.	2013	F.H.K.A.M. (Medicine)	2013	F.R.C.P. (Edin)	2018
F.R.C.P. (Glasg)	2018	F.R.C.P. (Lond)	2019	F.R.C.Path.	2019
M.D. (H.K.)	2020	Fellow in Genetics and Genomics (Medicine) (HKCP)	2023		

Previous positions held:

House Officer, Queen Mary Hospital, Hong Kong (1 July 2006 – 30 June 2007).

Medical Officer, Department of Medicine, Queen Mary Hospital, Hong Kong (1 July 2007 – 30 June 2014). Clinical Assistant Professor, Department of Medicine, the University of Hong Kong (1 July 2014 – 30 June 2023).

Present positions:

Honorary Associate Consultant, Department of Medicine, Queen Mary Hospital, Hong Kong (1 July 2020 – present) Honorary Associate Consultant, Palliative Medical Unit, Grantham Hospital, Hong Kong (1 July 2020 – present).

Honorary Associate Consultant, Department of Medicine, the University of Hong Kong-Shenzhen Hospital (1 March 2023-present) Clinical Associate Professor, Department of Medicine, the University of Hong Kong (1 July 2023 – present)

Previous relevant research work:

- 1. Clinical and Genomic Registry of Myelodysplastic Syndrome (MDS) and Secondary Acute Myeloid Leukaemia (AML) in Asia (ClinicalTrials.gov Identifier: NCT03169296).
- 2. The Acute Promyelocytic Leukaemia Asian Consortium (APL-AC) Project (ClinicalTrials.gov Identifier: NCT04251754).
- 3. Frontline Oral Arsenic Trioxide-based Induction in Newly Diagnosed Acute Promyelocytic Leukaemia in Adults a Multicentre Phase 2 Study (ClinicalTrials.gov Identifier: NCT04687176).
- 4. Phase 2 Study to Assess the Safety and Efficacy of Bomedemstat (IMG-7289) in Combination With Ruxolitinib in Patients With Myelofibrosis (ClinicalTrials.gov Identifier: NCT05569538)
- 5. Efficacy and Safety of Ropeginterferon Alfa-2b for Pre-fibrotic Primary Myelofibrosis and DIPSS Low/Intermediate-1 Risk Myelofibrosis (ClinicalTrials.gov Identifier: NCT04988815)

Publication record (89 original peer-reviewed articles; 3 books edited; 32 conference papers): Section A:

Five most representative publications in recent five years

- 1. **Gill H**, Yung Y, Chu HT, Au WY, Yip PK, Lee E, Yim R, Lee P, Cheuk D, Ha SY, Leung RY. Characteristics and predictors of early hospital deaths in newly diagnosed APL: a 13-year population-wide study. **Blood Adv**, 2021;5(14):2829-38. **(2021 Impact Factor: 7.637)**
- Gill H, Yim R, Kumana CR, Tse E, Kwong YL. Oral Arsenic Trioxide, ATRA and Ascorbic Acid (AAA) Maintenance Following First Complete Remission in Acute Promyelocytic Leukemia - Long-Term Data and Unique Prognostic Indicators. Cancer, 2020; 126(14): 3244-3254. (2021 Impact Factor: 6.921)
- 3. **Gill H**, Yim R, Pang HH, Lee P, Chan TSY, Hwang YY, Leung GMK, Ip HW, Leung RYY, Yip SF, Kho B, Lee HKK, Mak V, Chan CC, Lau JSM, Lau CK, Lin SY, Wong RSM, Li W, Ma ESK, Li J, Panagiotou G, Sim JPY, Lie AKW, Kwong YL. Clofarabine, cytarabine, and mitoxantrone in refractory/relapsed acute myeloid leukemia: High response rates and effective bridge to allogeneic hematopoietic

stem cell transplantation. Cancer Med, 2020; 9(10): 3371-3382. (2021 Impact Factor: 4.711)

- Gill H, Kumana CR, Yim R, Hwang YY, Chan TSY, Yip SF, Lee HKK, Mak V, Lau JSM, Chan CC, Kho B, Wong RSM, Li W, Lin SY, Lau CK, Ip HW, Leung RYY, Lam CCK, Kwong YL. Oral arsenic trioxide incorporation into frontline treatment with all-trans retinoic acid and chemotherapy in newly diagnosed acute promyelocytic leukemia: A 5-year prospective study. Cancer, 2019; 125(17): 3001-3012. (2021 Impact Factor: 6.921)
- Gill H, Yim R, Lee HKK, Mak V, Lin SY, Kho B, Yip SF, Lau JSM, Li W, Ip HW, Hwang YY, Chan TSY, Tse E, Au WY, Kumana CR, Kwong YL. Long-term outcome of relapsed acute promyelocytic leukemia treated with oral arsenic trioxide-based re-induction and maintenance regimens: A 15year prospective study. Cancer, 2018; 124(11): 2316-26. (2021 Impact Factor: 6.921)

Section B:

Five representative publications beyond the recent five years

- Gill H, Man CH, Ip AH, Choi WW, Chow HC, Kwong YL, Leung AY. Azacitidine as post-remission consolidation for sorafenib induced remission of Fms-Like Tyrosine Kinase-2 internal tandem duplication positive acute myeloid leukemia. Haematologica, 2015; 100(7):250-3. (2021 Impact Factor: 11.047)
- Seto WK, Chan TS, Hwang YY, Wong DK, Fung J, Liu KS, Gill H, Lam YF, Lie AK, Lai CL, Kwong YL, Yuen MF. Hepatitis B reactivation in patients with previous hepatitis B virus exposure undergoing rituximab-containing chemotherapy for lymphoma: a prospective study. J Clin Oncol, 2014; 32(33): 3736-43. (2020 Impact Factor: 50.717)
- Gill H, Au WY, Cheung WW, Kwong YL. Oral arsenic trioxide based regimen as salvage treatment for relapsed or refractory mantle cell lymphoma. Ann Oncol, 2014; 25(7): 1391-7. (2021 Impact Factor: 51.769)
- Man CH, Lam SS, Sun MK, Chow HC, Gill H, Kwong YL, Leung AY. A novel tescalcinsodium/hydrogen exchange axis underlying sorafenib resistance in FLT3-ITD⁺ AML. Blood, 2014; 123 (16): 2530-9. (2021 Impact Factor: 25.476)
- Gill H, Ip AH, Leung R, So JC, Pang AW, Tse E, Leung AY, Lie AK, Kwong YL. Indolent T-cell large granular lymphocyte leukaemia after haematopoietic SCT: a clinicopathologic and molecular analysis. Bone Marrow Transplant, 2012; 47(7): 952 – 6. (2020 Impact Factor: 5.174)

專題演講(I)

AML Overview: Evolving Disease Classification and Treatment

Prof. Harry Gill The University of Hong Kong, Hong Kong

Abstract

The aim is to provide a comprehensive review of the current treatment landscape and emerging therapies for the treatment of acute myeloid leukemia (AML). It is the most common type of acute leukemia in adults and is associated with poor long-term survival and a high relapse rate, mainly due to relapse and resistance to available therapies. The recent advancements in the technologies for genomic profiling have enabled the identification of recurrent and novel genetic mutations implicated in the pathogenesis of AML. Therefore, treatment for AML has evolved rapidly over the last decade as improved understanding of cytogenetic and molecular drivers of leukemogenesis refined survival prognostication and enabled development of targeted therapeutics. In addition, one approach towards preventing relapse in AML is to use maintenance therapy in patients, after attaining remission. Allogeneic hematopoietic stem cell transplantation (HSCT) is an effective post-remission therapy that has been proven to reduce the risk of relapse. However, in patients who are ineligible for HSCT or have a high risk of relapse, other effective measures to prevent relapse are needed. This session will provide the advantages of current novel therapeutic approaches for AML treatment, discuss their limitations, and focus on a practical guide to navigating these options, tailored to individual patient needs. As we look towards 2024 and beyond, the spotlight on AML illuminates a path of continual discovery and innovation.

Clonal Dynamic Changes during the Progression of Myelodysplastic Syndromes to Secondary Acute Myeloid Leukemia: A Paired-Sample Comparison

骨髓分化不良症候群進展至次發性急性骨髓性白血病過程中的克隆動態變化:成對檢體的比較

<u>Che-Wei Ou</u>¹, Hsiao-Wen Kao¹, Tung-Liang Lin¹, Ming-Chung Kuo^{1,2}, Jin-Hou Wu¹, Hung Chang^{1,2}, Lee-Yung Shih^{1,2}

歐哲瑋1、高小雯1、林棟樑1、郭明宗1,2、吳金和1、張鴻1,2、施麗雲1,2

¹Division of Hematology-Oncology, Department of Internal Medicine, Chang Gung Memorial Hospital at Linkou, Taoyuan, Taiwan; ²School of Medicine, Chang Gung University, Taoyuan, Taiwan ¹林口長庚紀念醫院內科部血液腫瘤科、²長庚大學醫學系

Background:

Myelodysplastic syndromes (MDS) composed of a heterogeneous group of clonal hematopoietic blood cell disorders characterized by cytopenia, ineffective hematopoiesis, and a risk of progression to secondary acute myeloid leukemia (sAML). Over the past decade, advances in gene sequencing technology have elucidated the genetic landscape of MDS. Previous studies on the paired samples at both MDS and sAML were very rare. This study aimed to investigate the genetic changes during the progression from MDS to sAML by comparing both phases of MDS at diagnosis and sAML in the same individuals.

Methods:

Eighty-two paired matched samples of MDS at diagnosis and sAML phase were examined for 33 gene mutations commonly occurring in myeloid neoplasms, including epigenetic regulators, cohesin complex, spliceosome complex, signaling pathway, tumor suppressors, transcription factors, and NPM1 by next-generation sequencing.

Results:

The acquisition of gene mutations involving signaling pathway and transcription factors was significantly more frequent during the progression to sAML compared to other groups of genes. Mutations involving epigenetic regulators, cohesin complex, and spliceosome complex were generally stable or expanded when disease progressed. Loss of gene mutations was rare, and all mutations showed no apparent decline in their variant allele frequencies except STAG2 mutation. RUNX1 mutations were characterized by acquisition or clonal expansion with no loss or decline during disease progression.

Conclusion:

Our results demonstrated a distinct pattern of clonal changes in different groups of gene mutations during the progression from MDS to sAML.

Keywords: Myelodysplastic syndromes, secondary acute myeloid leukemia, gene mutations, paired-sample analyses

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Initial Hematopoietic Dynamics with Epcoritamab in Heavily Pretreated Large B-Cell Lymphoma Patients – Real World Experience in a Single Center Epcoritamab 於難治性與復發性瀰漫大 B 細胞淋巴癌患者之應用與對血球的影響: 單一醫學中心之臨床經驗

Tyng-Wei Yang^{1,2}, Yu-Wen Wang³, Tai-Chung Huang¹

楊庭瑋、王好文、黄泰中

¹Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; ²Department of Hemato-Oncology, Cathay General Hospital, Taipei, Taiwan; ³Department of Pharmacy, National Taiwan University Hospital, Taipei, Taiwan

¹國立臺灣大學醫學院附設醫院內科部血液科、²國泰綜合醫院內科部血液腫瘤科、³國立臺灣 大學醫學院附設醫院藥劑部

Purpose:

T-cell-engaging bispecific antibodies represent a novel therapeutic approach for various malignancies, including acute lymphoblastic leukemia, multiple myeloma, and lymphoma. Epcoritamab, a subcutaneously administered CD3xCD20 bispecific antibody, has demonstrated remarkable efficacy in clinical trials involving patients with relapsed or refractory CD20+ large B-cell lymphomas. This study reports real-world experiences of epcoritamab administration under a compassionate use program.

Methods:

Patients with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) at our institution who had received at least one dose of epcoritamab were included in this study. Epcoritamab treatment continued until death or disease progression. Laboratory data, including complete blood count (CBC), white blood cell differential count (DC), and lactate dehydrogenase (LDH) levels, were recorded before the first dose and after the last dose of epcoritamab.

Results:

From November 2023 to April 2024, 12 patients with R/R DLBCL were included in this cohort. The median age was 63.5 years, with a male-to-female ratio of 7:5. This cohort consisted of heavily pretreated patients, with lymphomas refractory to at least 3 to 8 lines of treatment, and half of the patients had an Eastern Cooperative Oncology Group (ECOG) performance status ≥2. Seventy-five percent of the patients had been exposed to CHOP-based regimens, and 25% had undergone autologous stem cell transplantation. Patients received up to four cycles of epcoritamab, resulting in a 25% response rate, including complete and partial responses. The median overall survival (OS) was 16.6 months. Comparison of laboratory data before and after epcoritamab treatment showed no significant differences in LDH, hemoglobin (Hb), platelet count (PLT), white blood cell (WBC) count, and absolute neutrophil count (ANC). However, significant decreases in lymphocyte and monocyte counts were observed.

Conclusions:

Epcoritamab proves to be an effective treatment option in challenging clinical scenarios. Although the treatment did not result in anemia, thrombocytopenia, or neutropenia, the observed decreases in lymphocyte and monocyte counts are of concern and warrant further investigation.

Keywords: Epcoritamab, Diffuse large B cell lymphoma (DLBCL)

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Table 1. Patient Characteristics (N=12)						
Male Sex	7 (58.3%)	Treatment demographics				
Median Age, years (range)	63.5	Lines of therapies, median	4.5 (3-8)			
	(48-82)	(range)				
		CHOP based	9 (75%)			
ECOG	Gemcitabine based 6 (5		6 (50%)			
0-1	6 (50%)	Autologous stem cell transplant	3 (25%)			
>=2	6 (50%)	Epcoritamab treatment lines,	4.5 (3-8)			
		median (range)				
		Epcoritamab doses, median	5 (2-10)			
		(range)				
Staging and risk		Epcoritamab cycles, median	1 (1-4)			
		(range)				
Ann Arbor stage IV	9 (75%)	Best response to epcoritamab				
IPI Score	3/3	CR	2 (16.7%)			
(Median/Average)						
Median OS, months	16.6 (10.1-	PR	1 (8.3%)			
(range)	77.7)					
		SD	0 (0%)			
		PD	6 (50%)			
		Not evaluable	3 (25%)			

Table 2. Patient's lab data (N=12)							
	1st Epcoritamab	Last Epcoritamab	p value				
Median LDH (IU/L, range)	354.5 (149-1136)	256.5 (153-1408)	0.671				
Median Hb (g/dL, range)	8.5 (6.6-12)	8.6 (6.7-13.8)	0.84				
Median WBC (/mm3, range)	3950 (1200-16970)	3835 (120-12340)	0.713				
Median Platelet (1000/mm ³ , range)	59 (17-247)	52.5 (2-218)	0.713				
Median ANC (/mm3, range)	2269.9 (828-11641.4)	3251.6 (9.6-12093.2)	0.755				
Median ALC (/mm3, range)	1041 (146.2-2083.1)	266.8 (0-1752.1)	0.017				
Median AMC (/mm3, range)	467.34 (84-3394)	172.5 (0-1951.6)	0.024				



Dasatinib Related Pulmonary Hypertension – Case Sharing Dasatinib 相關的肺高壓:案例分享

Tan Kang Ying

<u>陳康盈</u>

Division of Hematology & Oncology, Department of Internal medicine, Kaohsiung Medical University Hospital

高雄醫學大學附設醫院血液腫瘤科内科

Abstract

Pulmonary hypertension is one of the rare complications of dasatinib, a TKI commonly used in patients with CML. Here we presented 3 cases of dasatinib induced pulmonary hypertension and sharing the experience of clinical diagnoses, management and prognosis of this rare complications.

Keywords: CML, dasatinib

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Hemophagocytic Lymphohistiocytosis (HLH) 噬血症候群

<u>Yu-Chieh Lin</u>, Yuh-Ching Gau, Shih-Feng Cho, Tsung-Jang Yeh, Jeng-Shiun Du, Hui-Ching Wang, Min-Hung Wang, Chien-Tzu Huang, Chieh-Yu Hsieh, Ming-Hui Lin, Jui-Feng Hsu, Hui-Hua Hsiao, Yi-Chang Liu <u>林于傑</u>、高育青、卓士峯、葉宗讓、杜政勳、王慧晶、王閔宏、黃千慈、謝絜羽、林明慧、許 瑞峰、蕭惠樺、劉益昌

Division of Hematology and Oncology, Kaohsiung Medical University Hospital 高雄醫學大學附設醫院血液腫瘤內科

Abstract

Hemophagocytic lymphohistiocytosis (HLH) is an uncommon hematologic disorder, life-threatening disease of severe hyperinflammation caused by uncontrolled proliferation of benign lymphocytes and macrophages that secrete high amounts of inflammatory cytokines. It is classified as one of the cytokine storm syndromes. Initial signs and symptoms of HLH can mimic common infections: fever of unknown origin, hepatitis, or encephalitis.

We will present a case of 27-year-old male, who presenting EBV (Epstein-Barr virus)-positive T-cell lymphoma with hemophagocytic lymphohistiocytosis, complicated with bicytopenia, AKI (acute kidney injury), impaired liver function, hyperbilirubinemia, coagulopathy. Ever received 1st chemotherapy of Etoposide (100mg) for 2 days, and further corticosteroid treatment.

Traditional HLH-2004 criteria requires molecular testing consistent with HLH, or 5 of 8 of the following criteria, including fever, splenomegaly, cytopenias affecting ≥2 lineages, hypertriglyceridemia and/or hypofibrinogenemia, hemophagocytosis (in bone marrow, spleen, or lymph node), hyperferritinemia, impaired NK cell function, and elevated soluble CD25. The diagnosis of HLH is particularly challenging because the symptoms are nonspecific and many features overlap with other causes of severe illness including sepsis and hematologic malignancy. Importantly, these same disorders can trigger HLH, further complicating the diagnosis. Early recognition is crucial and without prompt treatment HLH is often fatal.

HLH treatment aims to halt triggers and control immune dysregulation. Etoposide-based chemotherapy, which inhibits topoisomerase II, selectively depletes activated T cells, was effective in lymphoma-associated HLH, is standard, and often combined with steroids for enhanced suppression of hypercytokinemia. Allogeneic HSCT offers a potential cure, particularly for refractory or relapsed HLH, replacing the dysfunctional immune system. Further studies are required to improve our understanding of the optimal treatment of HLH in adults.

Keywords: Hemophagocytic lymphohistiocytosis (HLH), T-cell lymphoma, EBV (Epstein Barr virus), hyperferritinemia

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Nontuberculosis Mycobacteria Infection Associated Hemophagocytic Lymphohistiocytosis 非结核分枝桿菌感染相關噬血细胞性淋巴组織细胞增多症

<u>Woei-Yau Kao</u>^{1,5}, Mu-Chun Yang¹, Chung-Tai Yue^{2,5}, Ching-Chi Chang¹, Po-Ping Hung³, Shiou-Chi Cherng^{4,5}, Her-Shyong Shiah¹, Ching-Liang Ho¹

高偉堯^{1,5}、楊牧俊¹、余忠泰^{2,5}、張靖媒¹、洪伯斌³、程紹智^{4,5}、夏和雄¹、何景良¹ Division of Hematology-Oncology, Taipei Tzu Chi Hospital Division of Infection, Taipei Tzu Chi Hospital Division of Pathology, Taipei Tzu Chi Hospital Division of Nuclear Medicine, Taipei Tzu Chi Hospital Department of Medicine, Medical College, Tzu Chi University

臺北慈濟醫院 1 血液腫瘤科、2 病理科、3 感染科、4 核子醫學科、5 慈濟大學醫學系

Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a devastating disorder of uncontrolled immune activation with distinct clinical hallmarks including fever, cytopenia, splenomegaly and systemic inflammatory-like syndromes. In contrast to children, HLH in adults presents predominantly as secondary syndrome triggered by infections, malignancies, or autoimmune disorders. Here, we present our experience treating a rare case of nontuberculosis mycobacteria (NTM) infection associated HLH presenting with persistent fever, pancytopenia, splenomegaly, pleural effusion, lymphadenopathy.

Case Presentation: A 62 years old female was referred to our emergent room with the chief complaints of intermittent fever and headache with severe leukopenia and severe thrombocytopenia on June 26, 2024. Bone marrow biopsy on June 17 revealed normocellularity for age with three cell lineages are present with normal maturation. She suffered from acute onset of shortness of breath since June 19 and chest X-ray film showed Rt pleural effusion. Pig-tail drainage of the effusion was done and exudative effusion was concluded. CT chest on June 21 showed multiple enlarged nodes in Rt lower neck, paratracheal space, and subcarinal space; splenomegaly (13 cm) and one enlarged nodes in Lt paraaortic space (3.5x2.2 cm). Malignant lymphoma was highly suspected. Pathological examination of excised lymph node revealed proliferation of fibroblasts, chronic inflammation and one nodule full of histiocytes engulfing cell debris. Fever, severe neutropenia and severe thrombocytopenia persisted in spite of medication with various antibiotics. Patient symptoms and signs fulfilled the HLH-2004 criteria for a diagnosis of HLH, including fever, cytopenia, splenomegaly, hyperferritinemia and hemophagocytosis. The patient was put on intravenous dexamethasone 10mg/m²/day for 14 days since June 28 according to modified HLH-94 treatment guideline. Her fever subsided quickly and severe neutropenia and severe thrombocytopenia progressively improved. The white blood cell count rose up to 2950/dL on July 10. Unexpectedly, pleural fluid TB culture revealed growth of nonmycobacterium tuberculosis complex isolated/acid-fast positive bacilli. Klarcid 500 mg po bid was recommended by infection doctor. She was discharged on July 13, 2024. The rare association of NTM and HLH has been sporadically reported in the literature. The strategy in treating the scenario will be presented in the meeting.

Discussion and Conclusion: There are limited cases of NTM-associated HLH reported in the literature. Quick diagnostic work-up and high alert for the HLH diagnosis can avoid lethal condition. And effort put on searching the etiology is crucial in choosing subsequent management of the syndrome. In our experience, the severe neutropenia, severe thrombocytopenia, dyspnea and fever progressively resolved after initiating steroid therapy. NTM are being increasingly isolated in clinical prectice. The pathogen should be considered as a trigger of HLH. Although the treatments reported in the literature varied, the overall prognosis of NTM-associated HLH appears promising. Clinicians' knowledge and awareness of this may result in the appropriate investigations needed to ensure diagnosis and proper treatment.

Keywords: Hemophagocytic Lymphohistiocytosis (HLH); Nontuberculosis Mycobacteria (NTM) 著作權授權同意書:本人不同意將本次投稿主題之會員演講幻燈片掛網。

Lyse or Not to Lyse? Typical and Atypical Presentation of Cold Agglutinin Syndrome (CAS) in a Patient with Gastric Cancer and Another with Lymphoma

溶或不溶? 冷凝集素症之不典型表現

Chien-Ting Chen, Tran-Der Tang

陳建廷、譚傳德

Department of Cell Therapy and Stem Cell Transplant, Koo Foundation Sun Yat-Sen Cancer Center 和信治癌中心醫院細胞治療與幹細胞移植科

Abstract

Cold agglutinin syndrome (CAS) is characterized by pathogenic antibodies, that agglutinates and destroys red cells via complement-mediated extra-vascular hemolysis. CAS associated more with infection, aggressive lymphoma, and rarely with solid tumors. Here, we present two cases of CAS with distinct manifestation of hemolysis, and literature as well as reviewed.

Keywords: Hemolysis, cold agglutinin syndrome, solid tumors, complement inhibitor 著作權授權同意書:本人同意將本次投稿主題之會員演講幻燈片轉成 PDF 檔格式後,掛於血 液病學會網站上供該會會員瀏覽下載。

Efficacy and Safety of Myelofibrosis Patients Treated with Ruxolitinib: Real-World Clinical Data from Single Institution ruxolitinib 治療骨髓纖維化患者的療效及安全性:單一機構的真實世界臨床數據

草稿

<u>Yi-Hsiang Huang</u>, Yu-Guang Chen, Shiue-Wei Lai, Ren-Hua Ye, Jia-Hong Chen, Tzu-Chuan Huang, Yi-Ying Wu, Ping-Ying Chang, Ming-Shen Dai, Yeu-Chin Chen <u>黄翊翔</u>、陳昱光、賴學緯、葉人華、陳佳宏、黃子權、吳宜穎、張平穎、戴明燊、陳宇欽 Division of Hematology and Oncology, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan 國防醫學中心 三軍總醫院 血液腫瘤科

Keywords: Myelofibrosis, ruxolitinib, JAK1/2 inhibitor, treatment outcome, splenic reduction 著作權授權同意書:本人不同意將本次投稿主題之會員演講幻燈片掛網。

Von Willebrand Disease: A Clinical and Laboratory Cohort of 48 Cases 類血友病臨床和實驗室表現 48 例病例研究

Chien-Yuan Chen

<u>陳建源</u>

National Taiwan University Hospital, HsinChu 新竹台大醫院內科部血液科

Purpose:

von Willebrand disease is a common inherited bleeding disorder but rarely reported in Taiwan. **Materials & Methods:**

We retrospectively reviewed of medical records of 374 patients with iron deficiency anemia. 136 patients enrolled who checked with comprehensive laboratory tests including factor VIII clotting activity, von Willebrand factor (vWF) antigen assay, vWF: ristocetin cofactor activity (vWF:RCo), vWF Glycoprotein Ib binding assay and platelet function analyzer (PFA)-100 closure times. **Results:**

48 (35.2%) of 136 patients were diagnosed with vWD, including 22 with type I, and 26 with type II. 22(16.2%) patients need to follow up due to have low ratio (<0.7) of vWD RCo/ vWD Ag and borderline vWD Ag level. 66(48.5%) patients were less like vWD by laboratory profile. vWD is a common disease but easy to miss the diagnosis. vWD activity can significantly change during stress and need to follow up for definite diagnosis.

A 28-year-old woman has recurrent hypermenorrhea since 14-year-old, she is treated as iron deficiency anemia without definite diagnosis. Recurrent and refractory iron deficiency anemia (low Hb:4~6 g/dl) causes significant symptoms of weakness, fatigue, and exertional dyspnea, and cardiomegaly at plain chest film. Accurate diagnosis could improve the quality of life and cardiovascular risk in patients with vWD, and potentially reduce the risk of surgery.

Conclusions:

The female patients with iron deficiency anemia since young age are high risk of vWD, early identify this disease could improve the quality of life, cardiovascular complication and surgery risk in patients with vWD.

Keywords: von Willebrand disease, Anemia

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Eltrombopag Induced Cerebral Venous Thrombosis Eltrombopag 導致的腦靜脈血栓

<u>林佾緯</u>

<u>l-Wei Lin</u>

Mackay Memorial Hospital, Hematology and Oncology Department 馬偕紀念醫院血液腫瘤科

Abstract

Thrombopoietin receptor agonists such as eltrombopag have been used as second line treatment for Immune Thrombocytopenia Purpura (ITP) by promoting platelet production. Cerebral venous thrombosis is a rare side effect caused by eltrombopag. We reported a case of cerebral venous sinus thrombosis after eltrombopag use.

A 20-year-old woman was diagnosed with ITP in May 2023. Despite treatment with steroids, the patient still had thrombocytopenia with gum bleeding and petechiae. Eltrombopag 50 mg daily was given since 2023/09/26. Platelet count was up to 589000 uL in October 2023. Nevertheless, the patient developed a headache with nausea after two weeks of Eltrombopag use. Magnetic Resonance Venography revealed cerebral venous thrombosis so we discontinued eltrombopag. Her symptoms resolved after treatment with enoxaparin. After re-treatment with eltrombopag 25 mg daily, cerebral venous thrombosis recurred. Eltrombopag was permanently discontinued thereafter but platelet count declined again (lower than 20000 uL). The patient refused splenectomy and she received Rituximab 500 mg weekly for 2 doses in December 2023 and kept cyclosporine and mycophenolate mofetil with moderate response at Out-Patient Departments.

Cerebral venous sinus thrombosis must be considered in differential diagnosis in ITP patients treated with thrombopoietin receptor agonists when neurologic symptoms such as unexplained headache, nausea or vomiting developed.

Keywords: Eltrombopag, Immune Thrombocytopenia Purpura, Cerebral venous sinus thrombosis **著作權授權同意書:**本人同意將本次投稿主題之會員演講幻燈片轉成 PDF 檔格式後,掛於血液病學會網站上供該會會員瀏覽下載。



- Poor enhancement in the straight sinus, right transverse & sigmoid sinus

- Small focal filling defect in the superior sagittal sinus, suspicious of thrombus



A Single Center Experience of 4 Patients of Acquired Hemophilia 單一中心後天型血友病案例報告

Yu-Te Lin, Tsu-Yi Chao, Jacqueline Whang-Peng, Yao-Yu Hsieh 林彧德、趙祖怡、彭汪嘉康、謝燿宇 Division of Hematology and Oncology, Department of Internal Medicine, Taipei Medical University-Shuang Ho Hospital, New Taipei City 235, Taiwan. 衛生福利部雙和醫院血液腫瘤科

Introduction:

Acquired hemophilia is a rare bleeding disorder characterized by the sudden onset of bleeding in individuals with no prior history of bleeding disorders. The clinical presentations are diverse, ranging from mild to life-threatening bleeding. Prompt diagnosis and treatment are crucial for managing this condition. Immunosuppressive therapy remains the cornerstone of treatment to eradicate inhibitors, while hemostatic agents are essential for controlling acute bleeding episodes. The cases presented highlight the variability in response to treatment and the need for individualized management strategies.

Case Presentation:

We retrospectively reviewed the records of adult patients diagnosed with Acquired Hemophilia at a single academic medical center over the past 10 years between January 1, 2014, and July 12, 2024. **Results:**

Four patients were treated for four episodes of Acquired Hemophilia. The cohort was entirely male (100%, n=4), with a median age of 57 years and a median weight of 65 kg upon admission. None of the patients had a family history of bleeding disorders. All patients presented with Factor VIII (FVIII) levels of less than 1%, and the median anti-FVIII antibody titer was 399.3 Bethesda Units (BU). Recombinant factor VIIa was administered as the first-line bypassing agent for all patients, with a median treatment duration of seven days. No thrombotic events were observed following the diagnosis of acquired hemophilia. Two episodes (50%) were treated with a combination of prednisone and cyclophosphamide, while one episode (25%) was treated with prednisone and oral azathioprine. During the follow-up period, no patient experienced a relapse, and there were no deaths.

Conclusions:

Acquired hemophilia is a challenging condition that requires a multidisciplinary approach for effective management. Early diagnosis, appropriate use of hemostatic agents, and tailored immunosuppressive therapy are key to achieving favorable outcomes. We report on four episodes of acquired hemophilia successfully treated at a single academic medical center between 2014 and 2024. Recombinant factor VIIa was consistently used as the first-line bypassing agent. Immunosuppressive therapy, including prednisone with either cyclophosphamide or azathioprine, effectively eliminated autoantibodies in all patients. The cohort experienced no significant infections, thrombotic events, or deaths during the follow-up period.

Keywords: Acquired hemophilia, factor VIII inhibitors, immunosuppressive therapy, bleeding disorders, case series

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The Efficacy of Haploidentical Donor-Derived BK Virus-Specific T Cell Therapy in One Child With Diffuse Large B Cell Lymphoma and Refractory BK Virus Infection HLA 半相合捐贈者 BK 病毒 T 細胞療法 在患有彌漫性大型 B 細胞淋巴瘤 BK 病毒感染兒童中的療效

<u>Chia-Yu Cheng</u>, Chun-Yao Yang, Hsi-Che Liu, Jen-Yin Hou, Sung-Nian Chang, Won-Shin Yen, Fang-Ju Wu, Chong-Zhi Lew, Ting-Chi Yeh

<u>鄭佳祐</u>、楊鈞堯、劉希哲、侯人尹、張崧年、顏婉欣、吳芳儒、劉充智、葉庭吉 ¹Division of Pediatric Hematology-Oncology, MacKay Children ¹馬偕兒童醫院 小兒血液腫瘤科、²台寶生醫股份有限公司

Purpose:

To report the use of haploidentical donor-derived BK Virus-specific T cell therapy in a child with lymphoma and refractory BK virus infection.

Patient & Methods:

An 11-year-old male child diagnosed with combined immunodeficiency due to a SOCS1 gene c.464 T>C mutation presented with autoimmune hemolytic anemia, Cytomegalovirus viremia with retinitis, and BKV viremia with hemorrhagic cystitis. He subsequently developed stage IV diffuse large B cell lymphoma with tumors in the left subclavicular and axillary regions, along with bone marrow metastasis. He received six cycles of R-CHOP chemotherapy. During chemotherapy, his blood BK viral load reached a maximum of 1,708,00 IU/ml, and treatment with cidofovir and intravenous immunoglobulin was ineffective. Due to the onset of clinical signs of chronic kidney disease in his blood and urine tests, the patient began preparation for BK Virus-specific T (VST) cell therapy after completing lymphoma chemotherapy. Six potential donors underwent HLA testing and BKV IgG testing to determine the most suitable donor for lymphocyte donation. The CliniMACS[®] Prodigy cytokine capture system was used to manufacture BK Virus-specific Cytotoxic T Lymphocytes via in vitro BK large T-antigen (LT) and VP1 capsid protein (VP1) stimulation. During the manufacturing process, the expression of interferon-gamma (IFNy) indicated whether the cytotoxic T cells had been activated by BK antigens.

Results:

A total of six potential donors were evaluated, including the father, mother, two younger brothers, aunt, and uncle. His father was chosen as the lymphocyte donor due to being HLA haploidentical with weakly positive BKV Immunoglobulin G. The father's peripheral blood mononuclear cell showed positive results in an in vitro stimulation assay, as the percentage of IFN γ + cells among CD3+ cells increased more than 2-fold under BK LT and VP1 stimulation. We harvested 15.21 and 7.19 × 107 cells/kg of CD3+ cells and produced 4 units containing 5 × 104 cells/kg of qualified BKV VST product. Starting on May 22, 2024, the patient received BKV VST cell therapy every 2-3 weeks, for a total of four treatments. Following the BKV VST injection, the patient's blood BKV viral load decreased significantly. Three months after the treatment, the viral load dropped to below 10³ IU/mL, and by eight months post-treatment, it became undetectable(Figure 1A). Blood creatinine, and the ratio of urine protein to urine creatinine declined after BK VST therapy (Figure 1B). **Conclusions:**

In children with cancer who suffer from refractory BKV infection leading to chronic kidney disease, BKV VST therapy may be considered after the failure of cidofovir treatment or the ineffectiveness of temporarily discontinuing immunosuppressors. Haploidentical donor-derived BKV VST cell the **Keywords:** Diffuse Large B Cell Lymphoma, BK Virus-specific T (VST) cell therapy (BK VST), Haploidentical Donor, Interferon-gamma (IFNy) cells among CD3+ cells

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Figure 1 (A) Four doses of BKV VST injection on 5/22, 6/9, 7/1, 7/26(arrows)

Piladelphia-Positive / DEK-NUP214 Rearranged Acute Myeloblastic Leukemia: An Adolescent Case Sharing 費城染色體陽性之急性骨髓性白血病伴有 DEK-NUP214 轉位:青少年病例分享

草稿

<u>Ke-Xin Chang</u>¹, Fang-Liang Huang¹*, Chi-Yen Chen¹, Jui-Ju, Tseng¹, Chiung-Wen Liang² 張可歆¹、黃芳亮¹*、陳其延¹、曾瑞如¹、梁瓊文²

¹Department of Pediatric Hematology-Oncology, ²Department of Nursing, Taichung Veterans General Hospital, Taichung, Taiwan

臺中榮民總醫院 1 兒童醫學中心血液腫瘤科、2 護理部

Introduction:

Acute myeloid leukemia (AML) with the translocation DEK-NUP214 (t(6;9)(p23;q34)) is a rare subtype present in 1-2% of AML patients. This translocation is associated with poor clinical outcome, resistance to chemotherapy and remains poorly characterized. We present the case of a rare case of acute myeloid leukemia (AML) with the translocation DEK-NUP214 (t(6;9)(p23;q34)), compounded by the presence of BCR-ABL1 mutation and Philadelphia chromosome.

Case Presentation:

A previously healthy 16-year-old boy with initial presentation of low grade fever up to 38 degree Celsius and dry cough in Sep.2018. Poor activity and body weight loss were also mentioned. The initial blood test showed WBC over 200000/uL. The peripheral blood smear showed blast 30%. The phenotype compatible with acute myeloid leukemia. The genetic mutation revealed DEK-NUP214 traslocation and BCR-ABL1 (M-bcr, p210) mutation. The chromosome study showed positive for Philadelphia chromosome. He received therapy as TPOG-AML-97A protocol since Oct.11.2018 with Imatinib use since Oct.30.2018 . Remission was noted on Dec.17.2018 according to bone marrow biopsy. Three courses of chemotherapy was performed after remission. He received allogeneic hematopoietic stem cell transplantation with 10/10 matched unrelated donor on Apr.24.2019. Grade 1 acute graft versus host disease with skin and intestines presentation were noted. We titrated up the dosage of cyclosporine. Imatinib was slowly tappered since Nov.21.2019, with 1 tab every 2 days now. Currently, The patient presented with stable condtion.

Conclusion:

In conclusion, we have presented a rare case of acute myeloid leukemia (AML) with the translocation DEK-NUP214 (t(6;9)(p23;q34)), compounded by the presence of BCR-ABL1 mutation and Philadelphia chromosome. This genetic profile is associated with aggressive disease behavior and poor response to conventional chemotherapy. Through a multidisciplinary approach involving intensive chemotherapy, targeted therapy with Imatinib, and ultimately allogeneic hematopoietic stem cell transplantation from a well-matched unrelated donor, we achieved initial remission and managed subsequent challenges including acute graft versus host disease. The patient is currently in stable condition. This case highlights the evolving landscape of treatment options and challenges in managing rare subtypes of AML, emphasizing the need for continued research to improve outcomes in this challenging patient population.

Keywords: Piladelphia Chromosome -positive, Acute myeloblastic leukemia, DEK-NUP214 translocation, Case sharing

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Extracorporeal Membrane Oxygenation Support in Pediatric Patient with Malignancies or Haematopoietic Stem Cell Transplant History: Outcomes of a Single Center Cohort 體外循環膜肺維生系統在兒童癌症或造血幹細胞病人的使用:單一醫學中心的經驗

<u>Yun-Jung Huang</u>^{1,2*}, Wei-Yu Chen^{1,2}, Ming-Hsin Hou^{1,2}, Cheng-Yin Ho^{1,2}, Ting-Yen Yu⁴, Chih-Ying Lee^{1,2}, Giun-Yi Hung^{1,2}, Chia-Sui Chou^{1,2,3}, Pei-Chen Tsao^{1,2,3}, Yu-Sheng Lee^{1,2,3}, Mei-Jy Jeng^{1,2,3}, Hsiu-Ju Yen^{1,2}

黃韻融^{1,2*}、陳威宇^{1,2,3}、侯明欣^{1,2}、何正尹^{1,2}、余廷彦⁴、李致穎^{1,2}、洪君儀^{1,2}、周佳穗^{1,2,3}、 曹珮真^{1,2,3}、李昱聲^{1,2,3}、鄭玫枝^{1,2,3}、顏秀如^{1,2}

¹Division of Pediatric Hematology and Oncology, Department of Pediatrics, Taipei Veterans General Hospital, Taipei, Taiwan; ²Faculty of Medicine, School of Medicine, National Yang-Ming Chiao-Tung University, Taipei, Taiwan; ³Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan; ⁴Department of Pediatrics, Far Eastern Memorial Hospital, New Taipei City, Taiwan

¹臺北榮民總醫院兒童醫學部、²國立陽明交通大學醫學院、³國立陽明交通大學醫學院急重症 醫學研究所、⁴醫療財團法人徐元智先生醫藥基金會亞東紀念醫院

Purpose:

There is still a debate on the use of extracorporeal membrane oxygenation (ECMO) support in pediatric patients with malignancies. In this retrospective cohort study, we aim to discuss the outcome of ECMO use in these patients.

Materials & Methods:

We retrospectively analyzed the hemato-oncology patients who had been admitted to pediatric intensive care unit (PICU) and received ECMO support at Taipei Veterans General Hospital from January 2008 to December 2023.

Results:

Total nineteen patients (9 males and 10 females) were included in the 15-year period, with mean age of 42 months (IQR 8-44). Eleven patients (58%) with history of hematological malignancies and 9 with history of solid tumors. Six patients had undergone hematopoietic stem cell transplantation (2 autologous and 4 allogenic HSCT). Six patients had achieved complete remission before ECMO use, while 13 patients were still under cancer treatments. Among these patients, 47% (n=9) received veno-arterial ECMO (VA ECMO) and 53% (n=10) received veno-venous ECMO (VV-ECMO). The main reason for VA ECMO was septic shock (n=3), and the main reason for VV-ECMO was acute respiratory distress syndrome (ARDS) (n=9). All patients received vasopressor treatment before and during ECMO use, and 89% (n= 17) patients received continuous renal replacement therapy (CRRT). Six patients (31.6%) survived ECMO in PICU and all survived to hospital discharge, the average duration of ECMO use was 13.5 days. Bleeding was the most common ECMO related complications (n=9, 47%). Association factors for survival to hospital discharge were analyzed, and revealed shorter duration of PICU stay before ECMO use and ARDS were associated with better survival of statistical significance.

Conclusions:

In our experience, ECMO is a treatment option in pediatric hemato-oncologic patients, especially those suffered from acute onset ARDS episode.

Keywords: Extracorporeal membrane oxygenation support, Pediatrics, malignancy, hematopoietic stem cell transplantation

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Experience with Maribavir for Ganciclovir-Intolerant Cytomegalovirus Infections in Allogeneic Stem Cell Transplantation: A Case Report Maribavir 用於無法忍受 Ganciclovir 副作用的人類巨細胞病毒感染: 異體造血幹細胞移植個案報告

Heng Lee, Wen-Chun Chen, Sheng-Hsuan Chien*, Chia-Jen Liu, Liang-Tsai Hsiao 李珩、陳玟均、簡聖軒*、劉嘉仁、蕭樑材

Division of Transfusion Medicine, Department of Medicine, Taipei Veterans General Hospital Division of Hematology, Department of Medicine, Taipei Veterans General Hospital 臺北榮總內科部輸血醫學科、臺北榮總內科部血液科

Abstract

Maribavir is a novel therapy for refractory or resistant cytomegalovirus (CMV) infection, targeting the UL97 kinase. According to the SOLSTICE study, maribavir significantly improves CMV viremia clearance rates and causes fewer hematological toxicities and instances of renal failure. We presented a case of Epstein-Barr virus (EBV)-positive diffuse large B-cell lymphoma with CMV infection and secondary engraftment failure after autologous hematopoietic stem cell transplantation. The patient was successfully rescued using compassionate maribavir and allogeneic hematopoietic stem cell transplantation.

Keywords: Cytomegalovirus, autologous hematopoietic stem cell transplantation, allogeneic hematopoietic stem cell transplantation

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Salvage of Resistant-Relapsed Pediatric Diffuse Large B-Cell Lymphoma by Bridging Chimeric Antigen Receptor T-cells and Multimodal Regimens Followed by Consolidative HLA-Haploidentical Peripheral Blood Stem Cell Transplantation: A Case Report CAR-T 及多模式療程橋接鞏固型 HLA 半套相合周邊血幹細胞移植搶救兒童 B 大細胞淋巴瘤抗 藥性復發:一病例報告

Yu-Ju Chao, Ming-Yuan Lee, Yu-Chun Tsai, Ting-Yu Lin, Li-Hua Fang, Yun-Hsin Wang, Rong-Long Chen¹ 趙郁如、李明媛、蔡玉真、林庭瑜、方麗華、王芸馨、<u>陳榮隆</u>¹

Departments of ¹Pediatric Hematology and Oncology, Koo Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan

和信治癌中心醫院小兒血液腫瘤科

Purpose: Although relapses of children with B-cell non-Hodgkin lymphoma in modern immunochemotherapy era are rare, the outcome is poor once the lymphoma progresses early after treatments. The outcome is even more dismal for those who have failed the standard of care pathway. An effective salvage strategy is urgently needed.

Case Report: An 11-year-old female was diagnosed stage III, R2 (LDH 372 IU/L) diffuse large B-cell lymphoma (DLBCL) in March 2022 shortly after presenting with intermittent abdominal pain and approximately an 8% loss of body weight within the year. Diagnostic positron emission tomographycomputer tomography (PET-CT) revealed tumor involvement of bilateral kidneys, multiple lymph nodes in the central and right upper abdomen, right pelvic and right upper cervical regions. Pathology from kidney biopsy indicated diffuse infiltration of medium to large-sized lymphoid tumor cells positive for CD20, Bcl2, Bcl6, CD10, and MUM1 by immunohistochemistry. Other relevant markers were negative for EBER-1, CD30, or ALK, with 5-10% of tumor cells showing positive staining for PD-L1 expression. She completed rituximab and an anthracycline-containing chemotherapy regimen from March to June 2022, achieving a partial to good response noted on PET-CT in May 2022. However, progressive lesions were detected in the right pelvic, para-aortic regions and right upper abdomen involving the ascending colon, confirmed by colon biopsy in August 2022. Treatment with three cycles of rituximab and ICE (ifosfamide, carboplatin, etoposide) failed, with progression noted on PET-CT evaluation in December 2022. Thereafter, she received a total of 4 x 10e6/kg autologous CD19 chimeric antigen receptor (CAR) T-cells (UWELL Biopharma) in January 2023, maintaining stable lymphoma status five weeks post-infusion. In addition, she underwent four cycles of RB-POLA (consisting of rituximab, bendamustine, and polatuzumab vedotin, an antibodydrug conjugate (ADC)), combined with involved-site radiotherapy from March to June 2023. Metabolic minimal residual disease was detected before she received non-myeloablative HLAhaploidentical peripheral blood stem cell transplantation (PBSCT) in July 2023. She has recovered from prolonged hypogammaglobulinemia and remains free from relapse and graft-versus-disease more than one year after PBSCT.

Conclusions: Bridging novel therapeutics, including CAR T cells and ADCs, with combined-modality regimens followed by timely haploidentical PBSCT successfully salvages the resistant-relapsed DLBCL, which was previously associated with dismal outcomes.

Keywords: Antibody-drug conjugate, chimeric antigen receptor T-cells, diffuse large B-cell lymphoma, HLA haplo-identical transplantation, childhood, peripheral blood stem cell transplantation

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Transplant-Associated Thrombotic Microangiopathy (TA-TMA), with Secondary Atypical Hemolytic Uremic Syndrome (aHUS) and Posterior Reversible Encephalopathy Syndrome (PRES) Successfully Salvage with Eculizumab

移植相關性血栓性微血管病合併次發性非典型溶血性尿毒症候群和可逆性後腦病變症候群 成功以 Eculizumab 救援

<u>Liu Jia Hau</u>¹, Fan Yu Chen¹, Chao Pon¹, Kevin Ko^{1,2} 劉家豪¹、范玉珍¹、趙芃¹、柯博升^{1,2}

¹Department of Hemato-Oncology, National Taiwan University Cancer Center; ²Department of Internal Medicine, National Taiwan University Hospital ¹台大癌醫血液腫瘤部、²台大醫院內科部

Abstract:

We report a 24 year-old woman with refractory NK/T cell lymphoma and underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT) from her HLA 10/10 full matched sister. She experienced grade III gastrointestinal graft-versus-host disease (aGVHD) two months after allo-HSCT. During the steroid and multiple drug treatments for aGVHD, she had the complications of cytomgelovirus viremia, retinitis and colitis. Two months after aGVHD treatment, rapidly progressive acute kidney injury occurred. Progressive thromcytopenia was also noted. Renal ultrasound showed severe decreased of bilateral renal flow. Peripheral blood smear found schistocytosis. Generalized tonic seizure (GTC) attacked 4 days later. She became comatous and intubated. Brain MRI showed posterior reversible encephalopathy syndrome (PRES). ADAMT-13 was normal. aGVHD and CMV viremia was subsided at the onset of GTC. Despite therapeutic plasma exchange (TPE) given for 16 times, intravenous immunoglobulin (IVIG) for more than 4 g per kg, and rituximab 600 mg, she remained in deep coma and anuria requiring hemodialysis. Eculizumab 600 mg was given for one dose on 18th days after onset of GTC. The urine output increased and hemodialysis stopped two weeks after administration of Eculizumab. Her conscious recovered and follow up brain MRI showed the resolution of PRES. She was transferred to ward and discharged with normal conscious and renal function 2 and 3 months after Eculizumab, respectively. She is disease-free and GVHD-free now at OPD 1.2 year after allo-HSCT.

Keywords: Transplant-Associated Thrombotic Microangiopathy (TA-TMA), atypical hemolytic uremic syndrome (aHUS), posterior reversible encephalopathy syndrome (PRES), Eculizumab 著作權授權同意書:本人同意將本次投稿主題之會員演講幻燈片轉成 PDF 檔格式後,掛於血液病學會網站上供該會會員瀏覽下載。