Acute Myeloid Leukaemia (AML) with *KMT2A* rearrangement presented with haemophagocytic lymphohistiocytosis (HLH)

Ke Xu (1,2), Elisabeth Nacheva (2,3)

1. Department of Haematology, University College London Hospitals NHS Foundation Trust, University College London, London, UK
2. Specialist Integrated Haematology Malignancy Diagnostic Service, Health Services Laboratories, University College London Hospitals NHS Foundation Trust, University College London, London, UK
3. UCL School of Life and Medical Sciences, London, UK

Corresponding author: Ke Xu

Ke.xu @nhs.net

Department of Haematology, University College London Hospitals NHS Foundation Trust, 250 Euston Road, London NW1 2PG, UK

Phone: (+44) 02034567890

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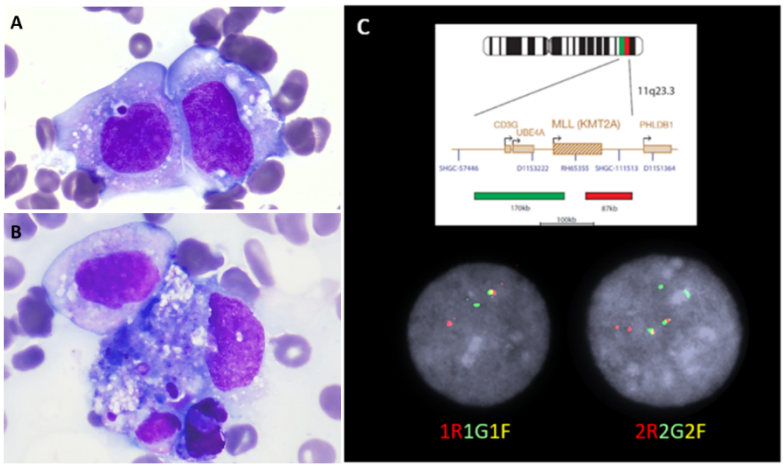

Figure 1. (A, B) Bone marrow aspirate (May-Grünwald-Giemsa stain x100 objective); (C) Fluorescence *in situ* hybridization (FISH) (100x objective, DAPI staining) carried out on interphase cells using the break-apart *KMT2A* probes (Cytocell). Out of 100 cells analysed 17 showed *KMT2A* rearrangement and 13 showed *KMT2A* rearrangement with concurrent amplification.

A 22-year-old female, presented with fever and worsening pancytopaenia (Hb 83 g/L, WBC 0.17 x10^9/L, Platelet 16 x10^9/L). Clotting screen showed prothrombin time 12 seconds (reference range 10-12 seconds), activated partial thromboplastin time 28 seconds (reference range 25-37 seconds), fibrinogen 1.03 g/L (reference range 1.5-4.0 g/L). Ferritin 35775 µg/L (reference range 13-150 µg/L), triglyceride 2.1 mmol/L (reference range 0.4-2.3 mmol/L). She developed hyperpyrexia and increasing oxygen requirement with haemodynamic instability and was

transferred to intensive therapy unit (ITU) for treatment for haemophagocytic lymphohistiocytosis. She underwent extensive investigation for infective drivers but no clear causes found. Bone marrow aspirate showed large monoblasts with no Auer rods (Figure 1.A) and haemophagocytosis (Figure 1.B). By flow cytometry these cells were positive for HLADR, CD33, CD15, cytoplasmic myeloperoxidase (cMPO); weakly positive for CD13, CD56; and negative for CD34, CD117. Targeted FISH showed *KMT2A* rearrangement in 17% cells analysed and *KMT2A* rearrangement with concurrent amplification in 13% cells analysed (Figure 1.C), while molecular karyotyping detected trisomy of chromosome 8. Next generation sequencing (NGS) (Archer Fusionplex Pan-Heme panel) identified *KMT2A* rearrangement (*KMT2A-MLL10*) and *PTPN11* E69K mutation (variant allele frequency (VAF) 33%). Trephine sample was largely effaced by large blasts with myelomonocytic morphology. The blasts were positive for CD33, CD15, and negative for CD34, CD117, CD3, CD79a, terminal deoxynucleotidyl transferase (TdT). A small minority appear MPO positive.

She was diagnosed with acute myeloid leukaemia with *KMT2A* rearrangement which was the presumed driver for HLH. She responded well to HLH directed therapy with methylprednisolone and anakinra, and was commenced on Fla-Ida (fludarabine, cytarabine, idarubicine) for high-risk AML. Her bone marrow biopsy post induction showed morphological complete remission, minimal residual disease negativity of AML and no evidence of HLH. Her blood counts recovered well and HLH treatment was wean off. She received second cycle of Fla-Ida followed by allograft transplant.

This case highlighted the importance of rapid diagnosis and risk stratification of driver disease of HLH to enable timely initiation of definitive treatment [1].

Reference:

1. Bozgul SMK, Ak G, Soyer NA, Barutcuoglu B, Mercan E, Acar C, Yetişken M, Hekimgil M, Bozkurt D. Biomarker diversity in increased inflammation: Secondary hemophagocytic syndrome vs. systemic inflammatory response syndrome. Int J Lab Hematol. 2023 Apr;45(2):213-220.