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Research Letter

Acute Myeloid Leukemia with Myelodysplasia-related Cytogenetic/Genetic-defined Abnormalities Masquerades as Acute Undifferentiated Leukemia

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A 71-year-old man was admitted for complete heart block and anemia, neutropenia with more than 15% undifferentiated-looking blasts. He had no prior hematological diseases. He had approximately 100 lbs of weight loss during the last year. The computed tomography scan of chest, abdomen, and pelvis showed no lymphadenopathy or splenomegaly. Blood tests showed: leukocytes, 8.9×10^9/L; neutrophils, 1.34×10^9/L; blasts, 1.83×10^9/L; hemoglobin, 71 g/L; mean corpuscular volume, 90.9 fL; platelets, 489×10^9/L, reticulocytes 77×10^9/L. Peripheral blood (PB) film demonstrated more than 20% of blasts. The blasts were of medium to large size, with a high nuclear/cytoplasm (N/C) ratio, open chromatin, and conspicuous nucleoli. In addition, dysplastic granulocytes were present (hypo-granular neutrophils/bands). The bone marrow aspirate revealed hypercellular bone marrow with over 70% blasts, which had a high N/C ratio and conspicuous nucleoli. No obvious Auer rods were observed. Megakaryopoiesis was markedly dysplastic with mono/hypo-lobated megakaryocytes and those with separate lobes (Fig. 1a, May-Grunwald-Giemsa stain, original magnification × 40, red arrows). Granulopoiesis and erythropoiesis were suppressed but mild dysplastic features could be observed including hypo-granular neutrophils and bands and dysplastic erythropoiesis including irregular nuclear contour, karyorrhexis, poor hemoglobinization, *etc*. No obvious lymphocytosis, plasma cells, or non-hematopoietic cells were observed. Flow cytometry immunophenotyping of the bone marrow aspirate illustrated that the blasts were positive for $CD34^+$, Tdt^+, $HLA\text{-}DR^+$, partial $cCD79a^{+/-}$ and partial $CD36^{+/-}$, but were negative for $CD117^-$, cytoplasmic MPO^-, $CD13^-$, $CD33^-$, $CD14^-$, $CD16^-$, $CD56^-$, $CD64^-$, $CD235^-$, cytoplasmic $CD3^-$, $CD1a^-$, $CD2^-$, $CD4^-$, $CD5^-$, $CD7^-$, $CD8^-$, $CD19^-$, $CD20^-$, $CD10^-$, and cytoplasmic $CD22^-$, suggesting acute undifferentiated leukemia (AUL). The bone marrow biopsy revealed hypercellular marrow with sheets of blasts with conspicuous nucleoli (Fig. 1b, hematoxylin and eosin stain, original magnification ×40), dysplastic megakaryopoiesis and suppressed granulopoiesis/erythropoiesis. A comprehensive immunohistochemistry panel demonstrated that the blasts were positive for $CD34^+$, Tdt^+, $CD43^+$ (Fig. 1c, original magnification ×40), partial $CD79a^+$, partial $PAX5^+$ and partial $lysozyme^+$, but were negative for $CD117^-$, MPO^-, $E\text{-}CAD^-$, $CD71^-$, Factor 8^-, and B cells and T cells lineage markers such as $CD19^-$, $CD10^-$, $CD20^-$, $CD3^-$, $CD4^-$, $CD8^-$, $CD56^-$, $CD68^-$ and $CD123^-$, confirming the diagnosis of AUL. Cytogenetics unveiled 45,X,-Y,[11]/89~91,XX,-Y,-Y,-2,del(5)(q15q33),+21[cp9], a complex karyotype with 5 chromosome aberrations including loss of Y, loss of 2, trisomy of 21, deletion of 5q and the ploidy aberration (Fig. 1d). Genome-wide molecular tests demonstrated multiple genetic mutations including *ASXL1*, *RUNX1*, *U2AF1*, *KMT2A*, *KRAS*, *NRAS*, *SH2B3* and *ZRSR2*. A final diagnosis of acute myeloid leukemia, myelodysplasia-related (AML-MR) was rendered following the 5th Edition of the World Health Organization (WHO) Classification and International Consensus Classifications (ICC).[1,2] The patient decided to receive supportive care only with regular red cells transfusion and was followed up by hematologists.

The 5th Edition of the WHO Classification and ICC eliminates the AML with myelodysplasia-related changes (AML-MRC).[1,2] Instead, AML-MR and AML, and MDS/AML with myelodysplasia-related gene mutations are created. AUL is classified as acute leukemia of ambiguous lineage (ALAL),[1–6] it is extremely rare with a dismal prognosis.[1] The blasts lack morphological myeloid differentiation, and express CD34, HLA-DR, Tdt, but without myeloid, monocytic, B-cell and T-cell lineage specific markers. Interestingly, CD43, an early hematopoietic stem cell marker is diffusely expressed in our case.[7,8] CD43 is known to be expressed in cases of myeloid leukemia cutis, and myeloid sarcoma.[9,10] Its role in AUL is not fully studied, which might provide an additional marker for the diagnosis of AUL. The 5th Edition of the WHO Classification, ICC, and some other studies advocate that ALAL (including AUL) with myelodysplastic syndrome defining cytogenetics/genetic abnormalities be classified as AML-MR, as exemplified in this case.[1,2,5,6] We believe this is the first reported case of AML-MR masquerading as AUL with CD43 expression.

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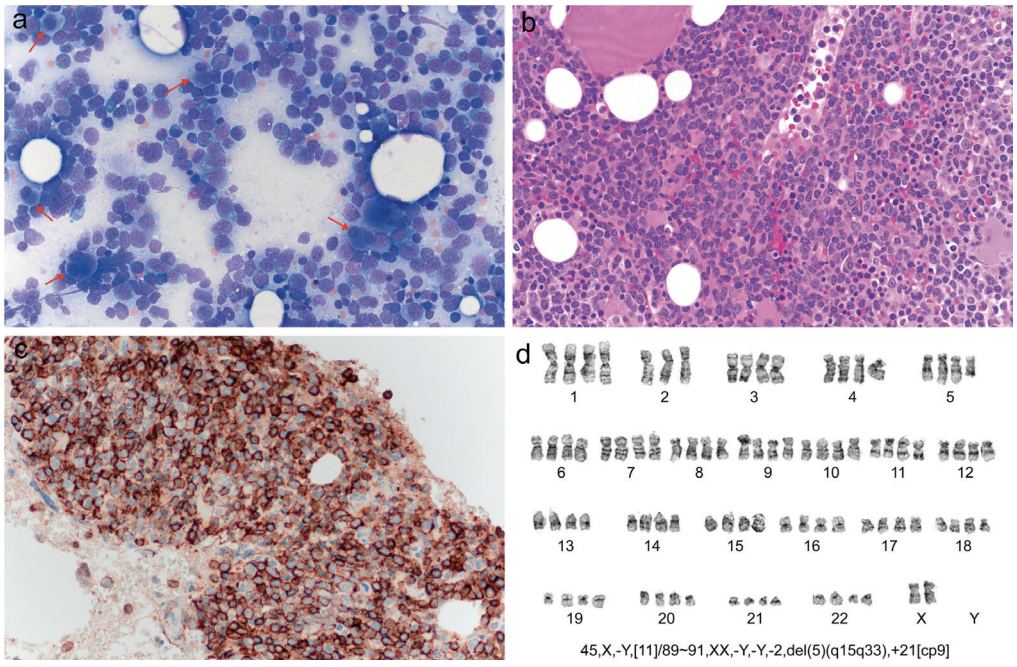

Fig. 1. (a) Bone marrow aspirate showing dysmegakaryocytes, red arrows. May-Grunwald-Giemsa stain, original magnification ×40, red arrows; (b) Bone marrow biopsy, hematoxylin and eosin stain, original magnification ×40; (c) CD43, original magnification ×40; (d) Karyotype.

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

ZDX was responsible for the diagnosis of the disease. RM was responsible for the cytogenetic diagnosis. ZDX wrote the manuscript.

Ethical statement

This case report involves a retrospective analysis of a clinical case and is not considered human research according to the U.S. federal policy [and institutional review board (IRB) regulations of Royal Jubilee Hospital]. An IRB approval was thus deemed unnecessary. This study was performed in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for the publication of this case report and the accompanying images.

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