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Title	Distinct cytomorphological features in DUX4-rearranged B-ALL
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Abstract

A 35-year-old man presented with dizziness, exertional dyspnoea and palpitations for 1 month without fever. Complete blood count showed anaemia (haemoglobin, 4.0 g/dL), leucopenia (3.70×10^9/L) and neutropenia (1.60×10^9/L) with occasional circulating blasts on the peripheral blood smear.

Bone marrow examination was performed. The bone marrow aspirate showed 91% medium-sized blasts with around half of them showing "cup-like" nuclei and around a third of them showing cytoplasmic and/or nuclear blebs. Some of the blasts showed both features. Some leukaemic cytoplasmic fragments were also noted in the background. Flow cytometry showed B-lymphoblasts which were positive for CD34, CD19, CD79a (cytoplasmic), CD10 (weak), CD13 (weak) and HLA-DR. The B-lymphoblasts showed co-expression of CD2 and CD371. Karyotype was normal (46,XY). Targeted next-generation sequencing showed IKZF1 partial deletion (exons 4 to 7), PTPN11 pathogenic variant (p.G503V) and multiple NRAS pathogenic variants (p.G12A, p.G12D, p.G12S, p.G13D). Targeted RNA sequencing showed presence of IGH::DUX4 fusion, confirming the diagnosis of B-lymphoblastic leukaemia/lymphoma (B-ALL) with DUX4 rearrangement. The patient was given paediatric-inspired intensive chemotherapy and achieved complete remission. He was planned to have allogeneic hematopoietic stem cell transplantation.

B-ALL with DUX4 rearrangement is a new provisional entity in the 5th edition of the World Health Organization Classification of Haematolymphoid Tumours which is more common in children, adolescents and young adults and is associated with good prognosis. DUX4 rearrangements in B-ALL are usually cytogenetically cryptic. Co-expression of CD2 and CD371 in B-ALL is strongly associated with DUX4 rearrangement. Yet, morphological description of this entity is scarce. "Cup-like" nuclei in blasts are known to be associated with acute myeloid leukaemia with NPM1 and/or FLT3-ITD mutations but are less recognized in B-ALL. Moreover, cytoplasmic and nuclear blebs are hitherto not described as a distinctive feature in any specific subtype of B-ALL. The distinct cytomorphological features of the disease may hint a diligent search for the underlying DUX4 rearrangements as they are often cytogenetically cryptic. Further study on the link between the morphological and molecular features of B-ALL with DUX4 rearrangement cases would be of value.

References:

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