blood work
images in hematology

Cuplike nuclei in B-cell acute lymphoblastic leukemia with *DUX4* rearrangement

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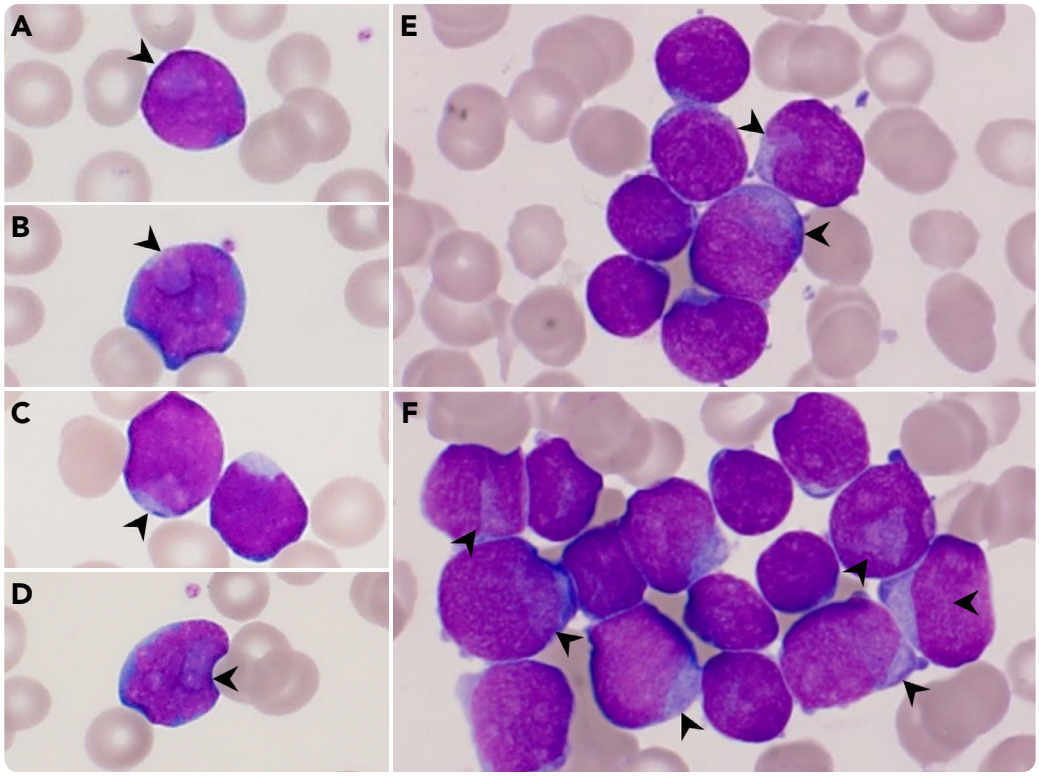

An 11-year-old girl presented with a 1-month history of weakness, headaches, and fever episodes. Complete blood count showed anemia (hemoglobin, 41 g/L), leukopenia (3.44 × 10^9/L), neutropenia (0.77 × 10^9/L), and 25% blasts with frequent (80%) cuplike nuclei (panels A-D; arrowheads; original magnification ×1000; May-Grünwald-Giemsa stain). Flow cytometry showed coexpression of CD19, CD10, and CD34 consistent with a common B-cell acute lymphoblastic leukemia (B-ALL). Bone marrow aspiration showed 90% lymphoblasts with a less conspicuous and less frequent (40%) cuplike nuclei than in blood (panels E-F; arrowheads; original magnification ×1000; May-Grünwald-Giemsa stain). Karyotype was normal (46,XX). Targeted next-generation sequencing showed pathogenic variants in *IKZF1* (p.R213Stop), *FLT3* (p.M578delinsIP), and *TP53* (p.R248W). Moreover, *IKZF1* and *ERG* deletions were found leading to highlight an *IGH*::*DUX4* fusion by targeted RNA sequencing.

DUX4-rearranged B-ALL is an oncogenic subgroup with good prognosis. In 30% of cases, *IKZF1* alterations are associated, without affecting the prognosis. However, the presence of a *TP53* mutation can negatively impact outcome regardless of *DUX4r*. There are few morphological data on this entity. Blasts with cuplike nuclei are well recognized in acute myeloid leukemia associated with *NPM1* and/or *FLT3-ITD* mutations but are uncommon in B-ALL. A recent study reported that cuplike B-ALL frequently harbored *IKZF1* deletion, the abnormality present in our patient. Additional observations will undoubtedly be necessary to better clarify the link between each of these molecular abnormalities and the observed morphology.

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https://doi.org/10.1182/blood.2022017662