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Acute myeloid leukemia with NPM1 and FLT3 ITD mimicking acute promyelocytic leukemia

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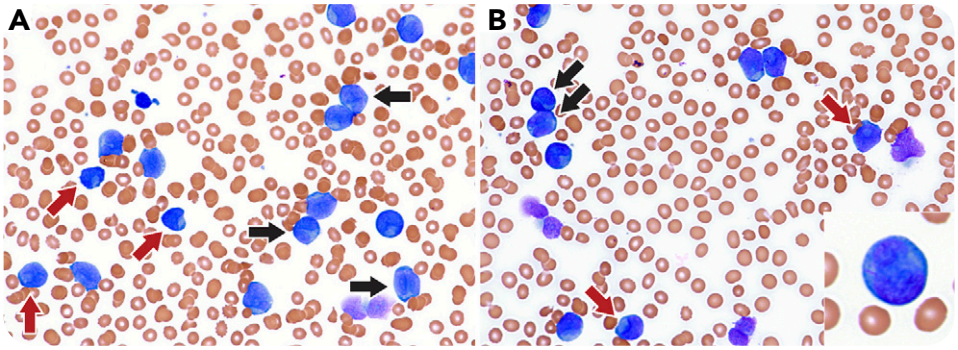

A 58-year-old man presented with a white blood cell count of 126 × 10^3/μL, hemoglobin of 10.7 g/dL, a platelet count of 45 × 10^3/μL, and a D-dimer of 12.01 μg/nL fractional excretion of urea. A peripheral smear revealed 97% blasts, demonstrating prominently cleaved nuclei with fine chromatin, prominent nucleoli, Auer rods, and occasional cup-like nuclei (panels A-B: black arrows, cleaved nuclei; red arrows, cup-like nuclei; Wright-Giemsa stain; original magnification ×400; inset, blast with Auer rod, original magnification ×400). Flow cytometry revealed abnormal myeloid blasts expressing myeloperoxidase, CD13, CD33, CD117, CD38, CD64, CD4, and lacking CD34, CD11B, and HLA-DR. Cytogenetics showed a normal 46,XY karyotype, and there was no evidence of promyelocytic leukemia/retinoic acid receptor α (*PML-RARA*) by fluorescence in situ hybridization (FISH) or real-time polymerase chain reaction. Next-generation sequencing revealed pathogenic variants in nucleophosmin 1 (*NPM1*; c.860_863dup), DNA methyltransferase 3A (*DNMT3A*; c.1054delA), isocitrate dehydrogenase 2 (*IDH2*; c.419G>A), and an *FLT3* internal tandem duplication (ITD).

Although the cleaved nuclei and lack of CD34 and HLA-DR are suggestive of acute promyelocytic leukemia (APL) with hypogranular morphology, acute myeloid leukemia (AML) with mutated *NPM1* and/or *FLT3* ITD often shows loss of CD34 and HLA-DR and presents with a high D-dimer. In some cases, such as this one, the nuclear features mimic APL, although some blasts show the distinctive cup-like nuclei of AML with mutated *NPM1* and/or *FLT3* ITD. Therefore, it is important to consider AML with *NPM1* and/or *FLT3* ITD in cases that have features suggestive of APL but are negative for *PML-RARA* by FISH and/or molecular methods.

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