blood work
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Cryptic insertion of *KMT2A*, a rare t(9;11) variant

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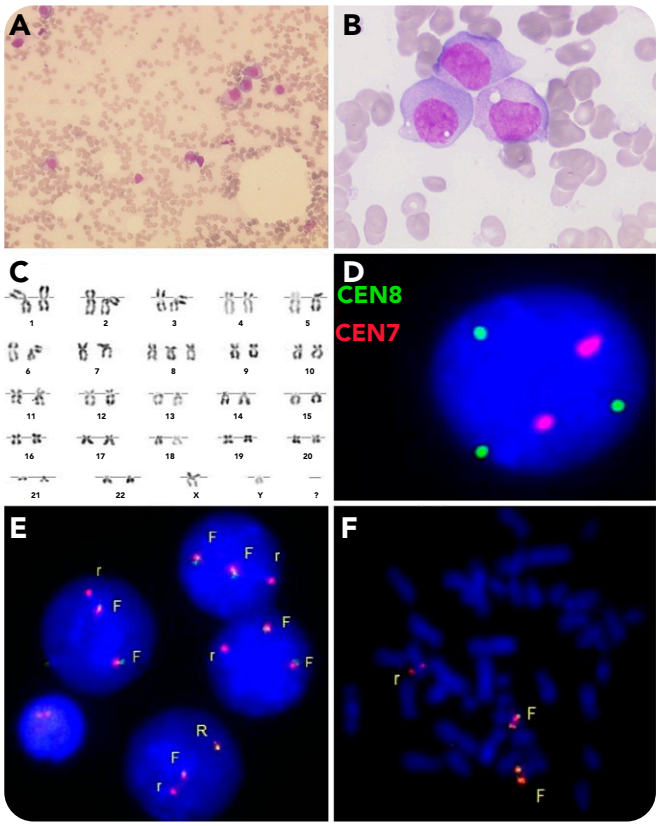

A 77-year-old man presented for the investigation of recent pancytopenia in peripheral blood. Bone marrow (BM) aspirate showed a hypocellular marrow infiltrated by large blasts with abundant cytoplasm and fine azurophilic granules, round to lobulated nuclei, open chromatin, and prominent nucleoli (panels A-B; original magnification ×500 [A], ×1000 [B]; Wright-Giemsa stain), expressing CD34 and negative for CD3, CD4, CD13, CD33, CD45, CD19, CD20, CD45, and myeloperoxidase by flow cytometry. BM karyotype revealed trisomy 8 (panel C; R-banding karyotype, 47,XY,+8[12]), confirmed by fluorescence in situ hybridization (FISH) using dual-color, centromere enumeration probes for chromosomes 7 and 8 (panel D; D-FISH C7/C8 probes; C7, red; C8, green). Break apart D-probes, targeting *KMT2A*, indicated its 5′ portion insertion into the p arm of chromosome 9 or 10 (panels E-F; D-FISH *KMT2A*; 5′*KMT2A*: red; 3′*KMT2A*: green; F, fusion; r, dim red signal). Because of poor cellularity, identification of the partner chromosome for acute myeloid leukemia (AML) risk stratification (t(9;11) intermediate or t(9;10) adverse group) was done using next-generation sequencing, revealing a *KMT2A* (intron 8)-*MLLT3* (intron 5) fusion resulting from a cryptic deletion of 5′*KMT2A* and insertion into chromosome 9, validated by quantitative polymerase chain reaction.

This is the first reported variant of t(9;11)(p22;q23) involving *KMT2A* deletion and insertion into cytogenetically normal chr11. This case emphasizes the importance of *KMT2A* FISH reflex testing of intermediate-risk AML for proper stratification.

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