blood work
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Acute leukemia of ambiguous lineage with *BCL11B* rearrangement

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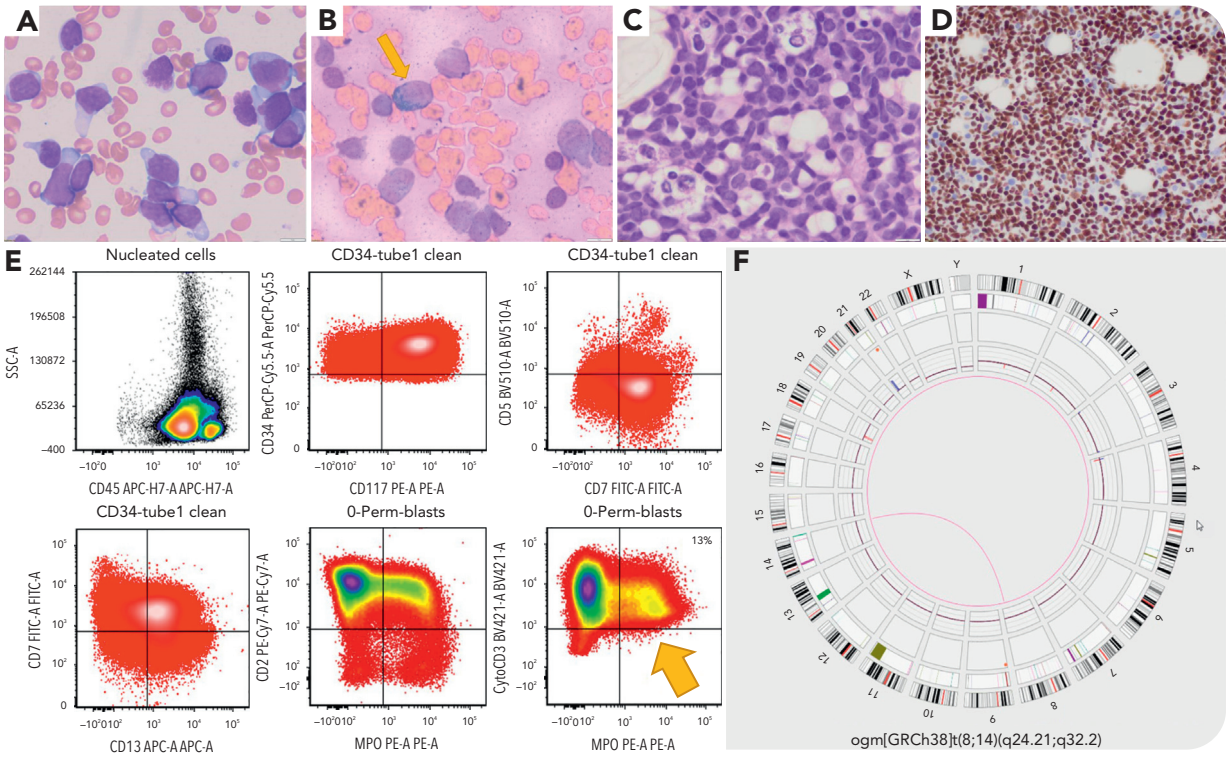

A 66-year-old man presented with abnormal complete blood count (white blood cell count 28.4 × 10^9/L, hemoglobin 6.9 g/dL, platelets 54 × 10^9/L) with 81% blasts. The bone marrow (BM) aspirate showed 79% blasts (panel A, Wright-Giemsa stain, 100× objective), with a subset positive for myeloperoxidase (panel B, 100× objective). The BM biopsy showed sheets of blasts (panel C, hematoxylin and eosin stain, 100× objective). Blasts had a T/myeloid phenotype (panel E, flow cytometry) positive for CD2, cCD3, CD7, CD13, CD33, CD34, CD117, CD123, CD133, HLA-DR, MPO (13%), TDT, and negative for CD1a, sCD3, CD5, CD8. This prompted additional immunohistochemical staining for BCL11B, which was diffusely positive (panel D, 40× objective). Sequencing identified *FLT3* internal tandem duplication and *TET2* (R1465*) and *RAD21* (L193fs) mutations. Optical genome mapping showed t(8;14)(q24.21;q32.2) with *CCDC26*::*SET3* putative fusion gene (panel F), previously shown to lead to *BCL11B* deregulation due to enhancer hijacking.

Acute leukemias (ALs) with *BCL11B* deregulation can manifest with various phenotypes including undifferentiated myeloid, T/myeloid, early T precursor (ETP), or near-ETP AL. *BCL11B* deregulation is driven by 14q32 rearrangements juxtaposing *BCL11B* to super-enhancers or amplifications generating superenhancers from non-coding elements distal to *BCL11B*. These frequently co-occur with *FLT3*, *WT1*, and epigenetic mutations and are important to recognize as they may be sensitive to FLT3 or JAK/STAT inhibition. This patient's neoplasm would be classified as AL of ambiguous lineage with *BCL11B* rearrangement or mixed phenotype AL with *BCL11B* activation in the World Health Organization, 5th Edition and International Consensus Classification, respectively.

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