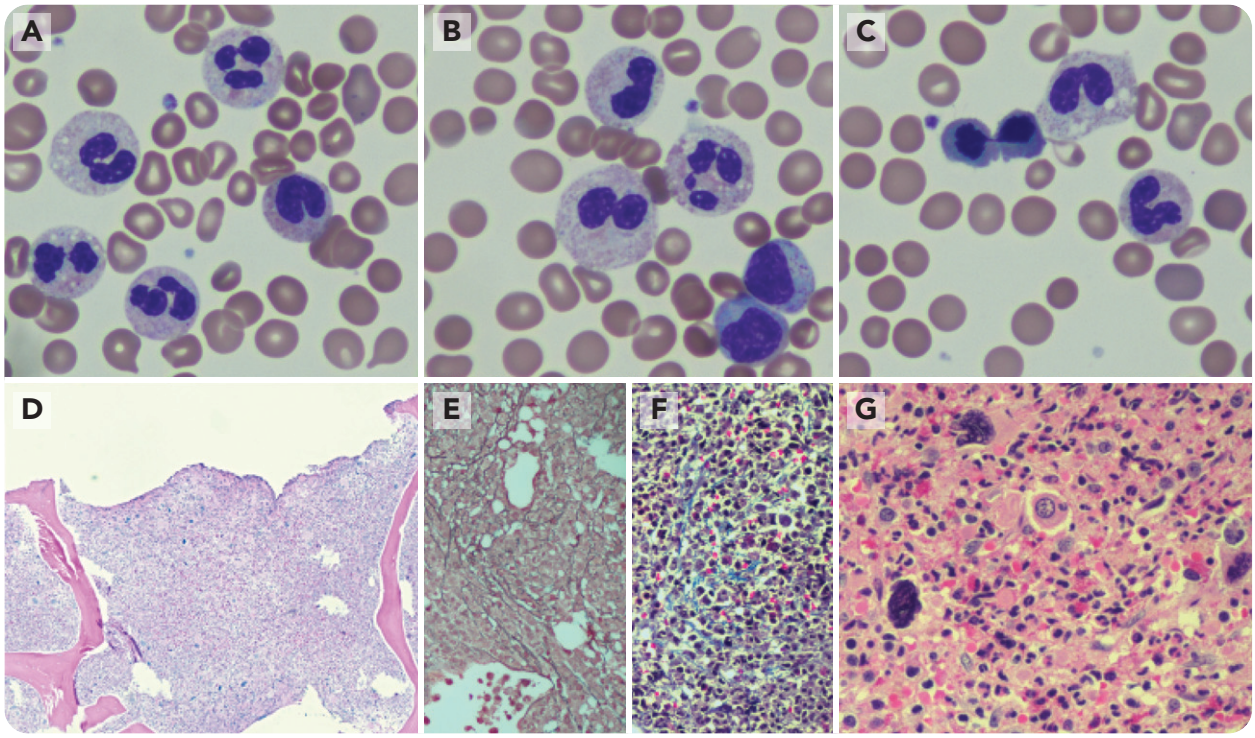
blood work
images in hematology

Atypical CML with mutated SRSF2, ASXL1, CSF3R, and MPL

Ann Tran, University of British Columbia; and Michelle Wong, Surrey Memorial Hospital



A 70-year-old, previously healthy woman presented with splenomegaly, anemia (98 g/L), thrombocytopenia (119 × 10^9/L), and leukocytosis (142.6 × 10^9/L). Differential abnormalities included 53% neutrophils, 45% neutrophil precursors, and 1% blasts. Eosinophil, basophil, and monocyte counts were normal. Blood film examination showed dysplasia with hypogranular and hyposegmented neutrophils with abnormal chromatin clumping, and occasional hypogranular platelets and dysplastic erythroid precursors (panels A-C; Wright-Giemsa, 50× objective, ×500 original magnification). The bone marrow aspirate demonstrated an elevated myeloid:erythroid ratio (25:1), and the trephine was hypercellular with increased granulopoiesis. (panel D; hematoxylin and eosin [H&E], 4× objective, ×40 original magnification). Focal fibrosis (panels E-F; reticulin and Masson trichrome, respectively, 40× objective, ×400 original magnification), and megakaryocytes with hyperchromatic nuclei and hypolobation were present (panel G; H&E, 40× objective, 400× original magnification).

Her karyotype was normal. By fluorescence in situ hybridization, *BCR-ABL1*, *PDGFRA*, *PDGFRB*, *FGFR1*, and *JAK2* rearrangements were excluded. Next-generation sequencing identified mutations, in descending order by variant allele frequency (VAF), in *SRSF2* P95H (VAF 50.0%), *ASXL1* c.1934dupG (VAF 40.3%), *CSF3R* T618I (VAF 37.9%), *MPL* S505N (VAF 37.2%), and *JAK2* V617F (VAF 1.9%). Not fulfilling criteria for other entities and with dysplasia, atypical chronic myeloid leukemia (aCML) was diagnosed. This is a rare and prognostically poor diagnosis. Although mutations in *JAK2*, *CALR*, *MPL*, and *CSF3R* are classically associated with other myeloid neoplasms, their occurrence has been reported in aCML.

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