blood work
images in hematology

Constitutive STAT5 activation in precursor B-cell acute lymphoblastic leukemia with *P2RY8*::*CRLF2* fusion

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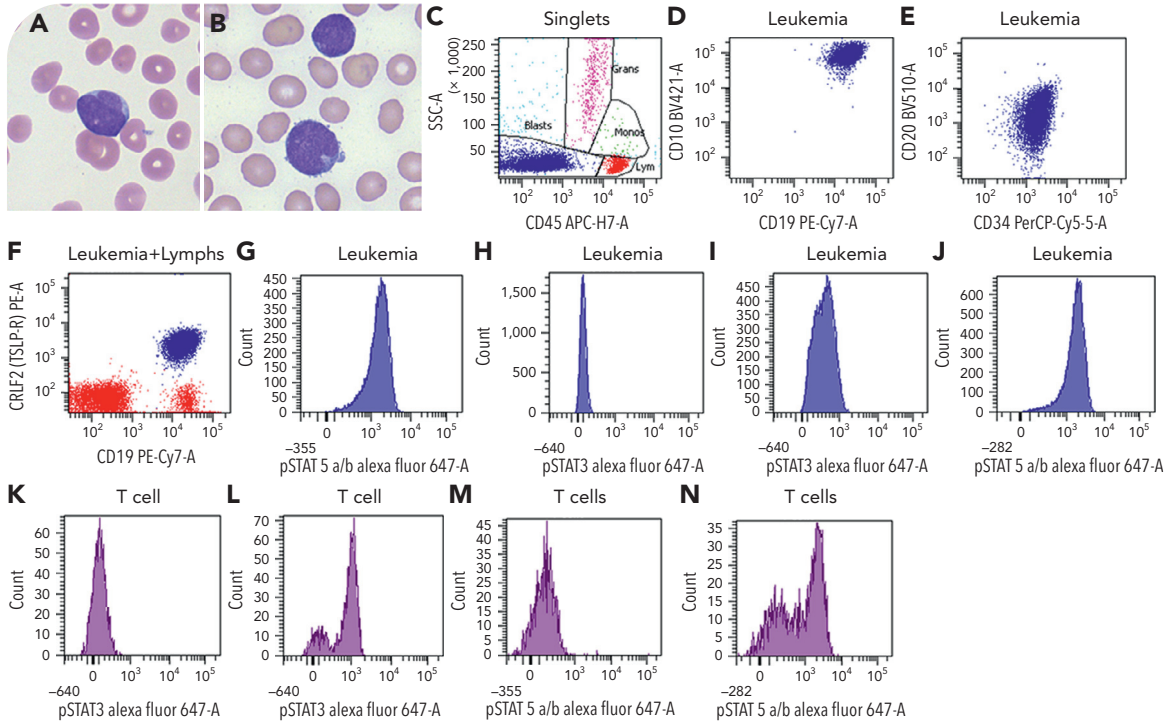

A 3-year-old girl presented with fever, petechiae, and bruising. Laboratory tests revealed pancytopenia (hemoglobin 5.1 g/dL, platelets 12 × 10^9/L, neutrophils 0.59 × 10^9/L) and 19% medium-sized blasts in peripheral blood (panel A: Wright stain, original magnification ×1000). Bone marrow aspirate revealed 75% blasts with similar morphology (panel B: Wright stain, original magnification ×1000). Flow cytometry analysis revealed a $CD45^-CD19^+CD10^+CD34^+CD20^+$ blast population (blue, panels C-E) consistent with precursor B-cell acute lymphoblastic leukemia (B-ALL). The unstimulated leukemia cells showed CRLF2 overexpression (panel F) and phosphorylation of STAT5 (panel G) but not STAT3 (panel H). There were no significant differences in protein levels of STAT3 and STAT5 (not shown) or stimulated phosphorylation of STAT3 (by interleukin-6) and STAT5 (by interleukin-2) (panels I-J) compared with internal T cells (panels K and M: non-stimulated; panels L and N: stimulated). Conventional cytogenetic study revealed 46,XX,i(9)(q10). Fluorescence in situ hybridization analysis revealed deletion of the 3′ *P2RY8*, indicating *P2RY8*::*CRLF2* fusion, which was confirmed by reverse transcription polymerase chain reaction. The patient received blinatumomab in combination with chemotherapy per AALL1731 and achieved complete remission with a negative measurable residual disease by flow cytometry assay (sensitivity 0.01%) at the end of induction.

This case directly demonstrates the dysregulation of the JAK-STAT signaling pathway in B-ALL with *P2RY8*::*CRLF2* by flow cytometry. It highlights the therapeutic potential of targeting the JAK-STAT pathway in this subtype of B-ALL.

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