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Pseudo–Chédiak-Higashi inclusions in *BCR::ABL1*-like B-lymphoblastic leukemia with *IGH::EPOR* rearrangement

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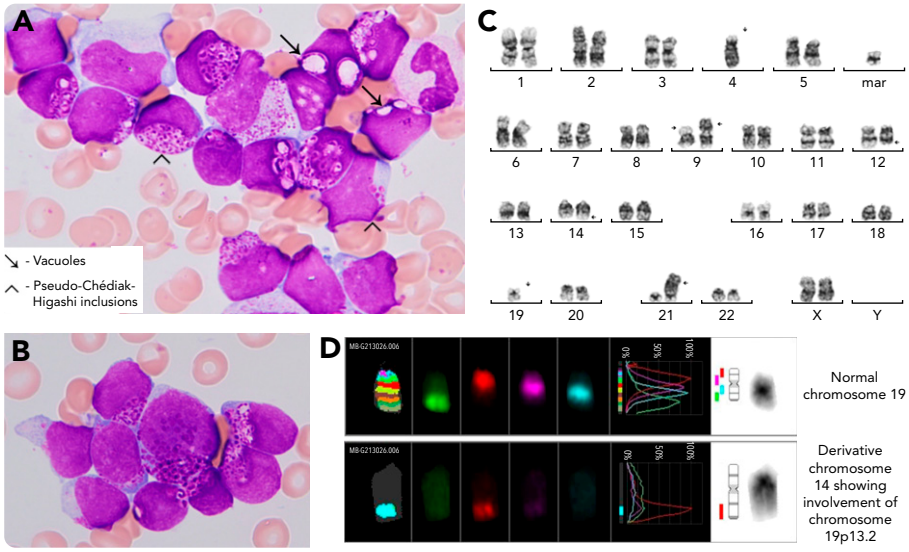

A 21-year-old woman presented with 6 weeks of progressive exertional dyspnea. Initial testing showed normocytic anemia (hemoglobin, 56 g/L) and 14% circulating blasts, with normal neutrophil and platelet counts. Bone marrow aspirate revealed an excess of medium-sized blasts with a high nucleus-to-cytoplasm ratio, fine nuclear chromatin, inconspicuous nucleoli, frequent large vacuoles, and prominent azurophilic inclusions resembling pseudo–Chédiak-Higashi granules (panels A-B; Wright-Giemsa; original magnification x1000). Flow cytometry demonstrated a blast population expressing CD19, CD22, CD24, CD10, CD34, and CD38, but no myeloid or T-cell markers. Karyotyping revealed 45,XX,-4,add(9)(p24),add(9)(p12),add(12)(q13),add(14)(q32),-19,der(21)t(4;21)(q13;p11.2),+mar1[8/20] (panel C). Fluorescence in situ hybridization showed nuc ish(CDKN2Ax1,D9Z3x2)[76/200]/(IGHx2)(3′IGH sep 5′IGHx1)[115/200], indicating loss of 1 CDKN2A signal per cell in 76 of 200 cells and IGH signal rearrangement in 115 of 200 cells. Whole-genome sequencing revealed *IGH::EPOR* rearrangement; copy number loss of *IKZF1*, *CDKN2A*, *CDKN2B*, *PAX5*, and *BTG1*; and no changes consistent with t(4;21)(q13;p11.2). Multicolor banding confirmed der(14)t(14;19)(q32;p13.2), corresponding to *IGH::EPOR* (panel D). *BCR::ABL1*-like B-lymphoblastic leukemia (B-ALL) was diagnosed based on the *IGH::EPOR* rearrangement. The patient remained in complete remission at 6 months after diagnosis following commencement of chemoimmunotherapy.

Pseudo–Chédiak-Higashi granules are characterized by large azurophilic cytoplasmic inclusions, similar to those in granulocytes of Chédiak-Higashi syndrome. The combination of prominent vacuolation and pseudo–Chédiak-Higashi inclusions in lymphoblasts in this case is unique, as neither finding has been described in either pediatric or adult patients with the uncommon variant of *BCR::ABL1*-like B-ALL with *IGH::EPOR* rearrangement.

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