



# Lymphoblasts with Engulfed Red Blood Cells Mimicking Pseudo-Chediak–Higashi Inclusions in a Case of B-Lymphoblastic Leukemia

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We herein report a case of B-lymphoblastic leukemia with the rare finding of pink amorphous cytoplasmic structures that resemble Chediak–Higashi inclusions (often referred to as pseudo-Chediak–Higashi [PCH] inclusions) within lymphoblasts. We further present images that strongly suggest their nature as engulfed red blood cells (RBCs).

A 3-year-old girl presented with fever, leg pain, and easy bruising. She was found to have anemia, leukocytosis, and thrombocytopenia (white blood cells [WBCs] =  $21.6 \times 10^3/\mu\text{L}$ , hemoglobin = 3.7 g/dL, platelets =  $6 \times 10^3/\mu\text{L}$ ). Examination of peripheral blood smear showed 37% blasts. Stained bone marrow aspirate smears showed similar blasts constituting 91% of marrow cells. The blasts were small to medium sized with scant light blue cytoplasm, irregular to clefted nuclei, smooth chromatin, and small nucleoli. Nuclear and/or cytoplasmic small vacuoles were seen in some blasts, but no cytoplasmic granules or Auer rods were noticed. Some blasts, however, showed round pink myeloperoxidase-negative inclusions (►Fig. 1). These inclusions were variable in size, from close to RBC size (►Fig. 1A) to smaller round inclusions, resembling PCH inclusions (►Fig. 1B–D). Despite the variable size, they all had color and staining similar to RBCs, but with variable degrees of dissolution. A diligent search showed rare examples of partial dissolution where an upper crescentic

portion of the ingested RBC has an RBC-like color, and the rest is partially dissolved into a less distinct appearance (►Fig. 2).

Flow cytometry showed blasts expressing CD10, CD19, CD22, CD34, CD58, CD45 (dim), and CD38 with negative myeloperoxidase (MPO), CD117, and CD11b. There was no aberrant myeloblast population. Cytogenetic analysis showed evidence of *ETV6-RUNX1* (12p13; 21q22). The patient was started on a B-lymphoblastic leukemia treatment protocol and is in complete remission 2 years after the diagnosis.

Similar PCH inclusions have been reported in myeloblasts in acute myeloid leukemia (AML),<sup>1,2</sup> chronic myeloid leukemia (CML),<sup>3</sup> and myelodysplastic syndrome.<sup>4</sup> In the context of myeloid neoplasia, reports have described them as pink azurophilic (►Fig. 3A–C) or having a vacuolated appearance and MPO positive.<sup>2,5</sup> They resemble the inclusions described originally in Chediak–Higashi syndrome (►Fig. 3D), a rare autosomal recessive disorder characterized by partial oculocutaneous albinism, recurrent pyogenic infections, and platelet dense granule deficiency.<sup>1</sup> Two mechanisms have been proposed for the PCH formation of myeloblasts: aberrant fusion of primary granules and lysosomes or lysosome-derived organelles, or fusion of granules with cell organelles forming a giant autophagic granule.<sup>6,7</sup>

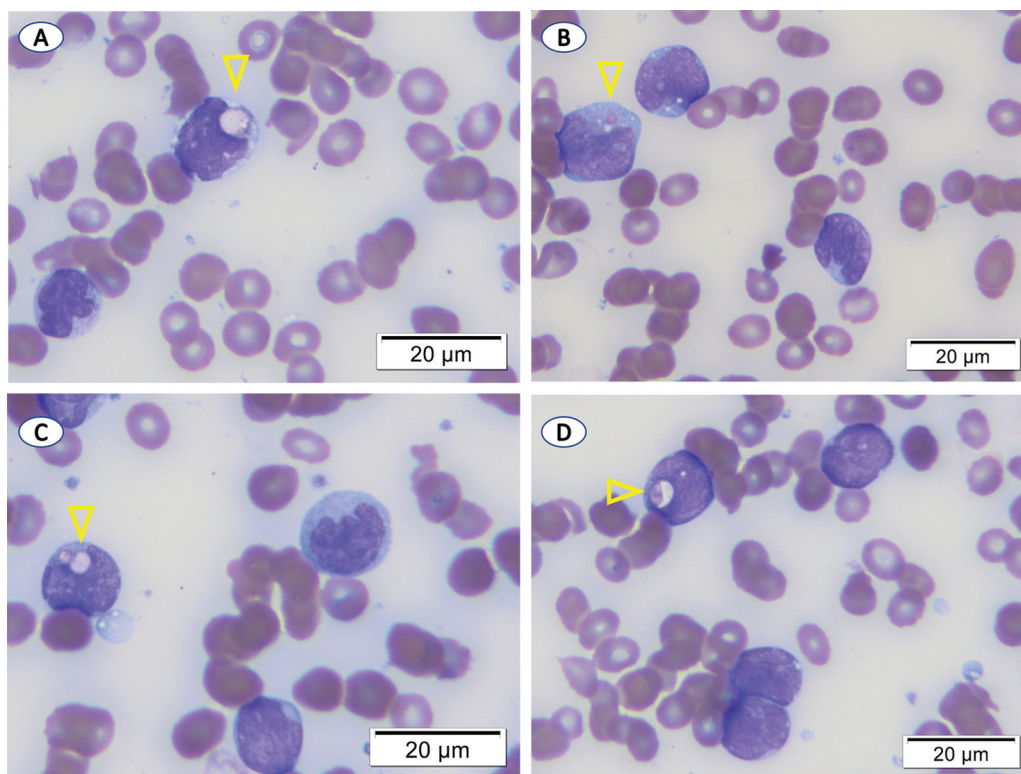
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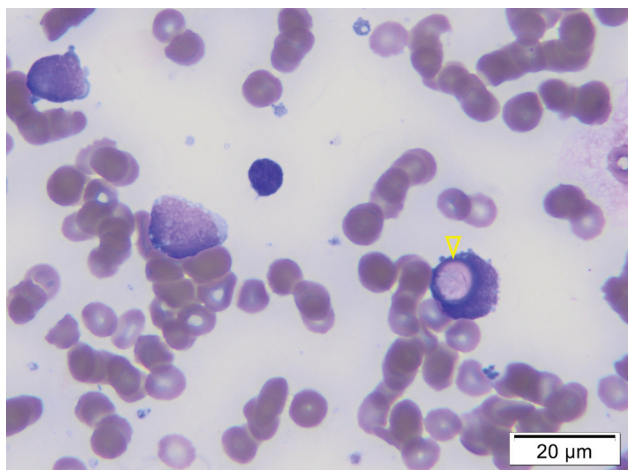
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**Fig. 1** Selected images from bone marrow aspirate showing lymphoblasts with (A) ingested red blood cells (RBC) (arrowhead) and (B–D) RBC fragments (arrowheads). Giemsa stain, 100X oil magnification.



**Fig. 2** A lymphoblast showing a rather recently ingested red blood cell (RBC) retaining a partial crescentlike RBC appearance (arrowhead: upper crescent).

Inclusions similar to those described herein have been described in lymphoblastic leukemia, with only rare cases reported in the literature.<sup>8</sup> The nature of PCH inclusions in this context was not elucidated with certainty.<sup>9,10</sup> In our case, the morphologic appearance is more consistent with engulfed RBCs showing variable degrees of degradation. The negative staining of blasts for MPO supports this presumption and helps separate them from those seen in myeloblasts.

Due to variable degrees of ingested RBC degradation, it was not possible to further prove the nature of inclusions by immunohistochemical staining. The visual resemblance, however, is compelling.

Cancer cells are known to engulf patient's native cells—including their RBCs—a phenomenon referred to in the medical literature as “cannibalism.”<sup>11</sup> This phenomenon further contributes to peripheral blood cytopenia seen in cancer patients.

In conclusion, we described a very rare case of B-lymphoblastic leukemia with engulfed RBCs mimicking the PCH inclusions. They represent morphological curiosities that may be encountered in practice and should not be confused with those seen in AML.

#### Author's Contributions

S.B.K. made the diagnosis, wrote the first draft of the manuscript, and prepared the photographs. J.W. reviewed and edited the manuscript.

#### Compliance with Ethical Principles

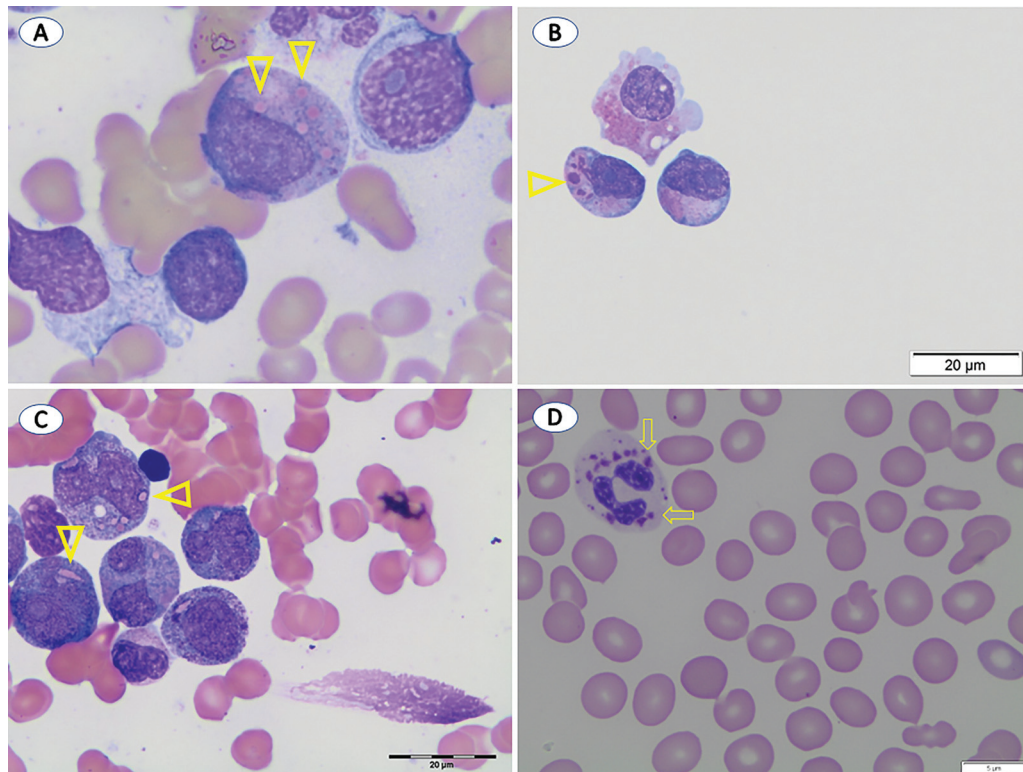
This manuscript and related work was performed under full compliance with all medical ethical principles.

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None.

#### Conflict of Interest

None declared.



**Fig. 3** (A–C) Pseudo-Chediak–Higashi inclusions from a case of acute myeloid leukemia (*arrowheads*) compared to (D) a neutrophil from a child with Chediak–Higashi disease exhibiting the classic rust-colored inclusions (*arrows*).

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