



Letters to the Editor

Mixed-phenotypic acute leukemia: cytochemically myeloid and phenotypically early T-cell precursor acute lymphoblastic leukemia

TO THE EDITOR: Early T-cell precursor acute lymphoblastic leukemia (ETP-ALL) is characterized by the specific immunophenotype of CD1a⁺, CD8⁺, and CD5^{weak/-} with stem cell or myeloid marker expression. This leukemia presents a particular flow cytometric diagnostic challenge, as it frequently exhibits sufficient myeloid-lineage differentiation to be classified as mixed-phenotype acute leukemia (MPAL). The 2008 World Health Organization classification has established new strict criteria for the diagnosis of MPAL; however, the exact MPO positivity cut-off percentage required for establishing a myeloid lineage was not mentioned. Herein, we report a case of ETP-ALL with trisomy 4 and t(6;14)(q27;q22) in a 25-year-old man, the final diagnosis of which was MPAL (T/Myeloid) due to the morphologic presence of Auer rods and myeloperoxidase staining, despite exhibiting a flow cytometric ETP-ALL phenotype. To the best of our knowledge, this is the first report on a case of ETP-ALL with Auer rods.

INTRODUCTION

Early T-cell precursor acute lymphoblastic leukemia (ETP-ALL) is characterized by the specific immunophenotype of CD1a⁺, CD8⁺, and CD5^{weak/-} with stem cell or myeloid marker expression [1]. This leukemia is associated with increased genomic instability, a high remission failure frequency, and hematological relapse. ETP-ALL patients also represent a distinct molecular T-ALL subgroup with a low frequency of *NOTCH1* mutations and a high frequency of *FLT3* mutations. ETP-ALL with *FLT3* mutation has also been described as a new ETP-ALL subgroup with unique immunophenotypic features and high levels of CD2, myeloid antigen CD13, and CD117 expression, indicating a stem cell phenotype [2]. Mixed-phenotypic acute leukemia (MPAL), T/Myeloid subtype is rarely suspected from mor-

phology, except in a small subset of cases, which have a distinct dual-blast population with both lymphoid and myeloid features. Therefore, final diagnoses of MPAL are based on flow cytometric immunophenotyping. Common cytogenetic abnormalities associated with MPAL include t(9;22) and *MLL* rearrangements, which may be restricted to B-Myeloid cases, whereas T-myeloid cases exhibit generally non-recurring chromosomal abnormalities [3]. Herein, we report a case of MPAL (T/Myeloid) with trisomy 4 and t(6;14)(q27;q22) in a 25-year-old man, the diagnosis of which was directed by the morphological presence of Auer rods and myeloperoxidase (MPO) staining, despite exhibiting a flow cytometric ETP-ALL phenotype.

CASE

A 25-year-old man presented with multiple bilateral neck swelling along with a nasal vocal intonation, weight loss, and low-grade fever since 1 month. He was externally evaluated via neck ultrasonography and nasal endoscopy, which revealed bilateral cervical lymphadenopathy and nasopharyngeal lymphoid hyperplasia, respectively. The results of fine needle aspiration of a cervical lymph node were suggestive of a hemato-lymphoid malignancy, and the patient was referred to our hospital for further evaluation. Upon examination, he presented with bilateral cervical lymphadenopathy and splenomegaly. His lactate dehydrogenase level was elevated (1,703 U/L; reference range, 313–618 U/L) and liver and renal functions were normal. Hematological parameters revealed a hemoglobin level of 55 g/L, total leukocyte count of 193.8×10^9 cells/L, and platelet count of 40×10^9 cells/L. A peripheral blood smear revealed a blast frequency of 88%; these were large with scant light blue agranular cytoplasm, open nuclear chromatin, and 1–2 indistinct nucleoli. The bone marrow showed near total replacement by blasts. Most blasts exhibited the previously described morphology, but few had moderate amounts of granular cytoplasm, fine nuclear chromatin, and 2–3 prominent nucleoli, and occasional blasts contained Auer rods (Fig. 1A). Myeloperoxidase (MPO) cytochemistry revealed approximately 3% MPO-positive blasts, including an occasional Auer rod (Fig. 1B). Flow cytometric immunophenotyping revealed that the blasts were positive for CD45;

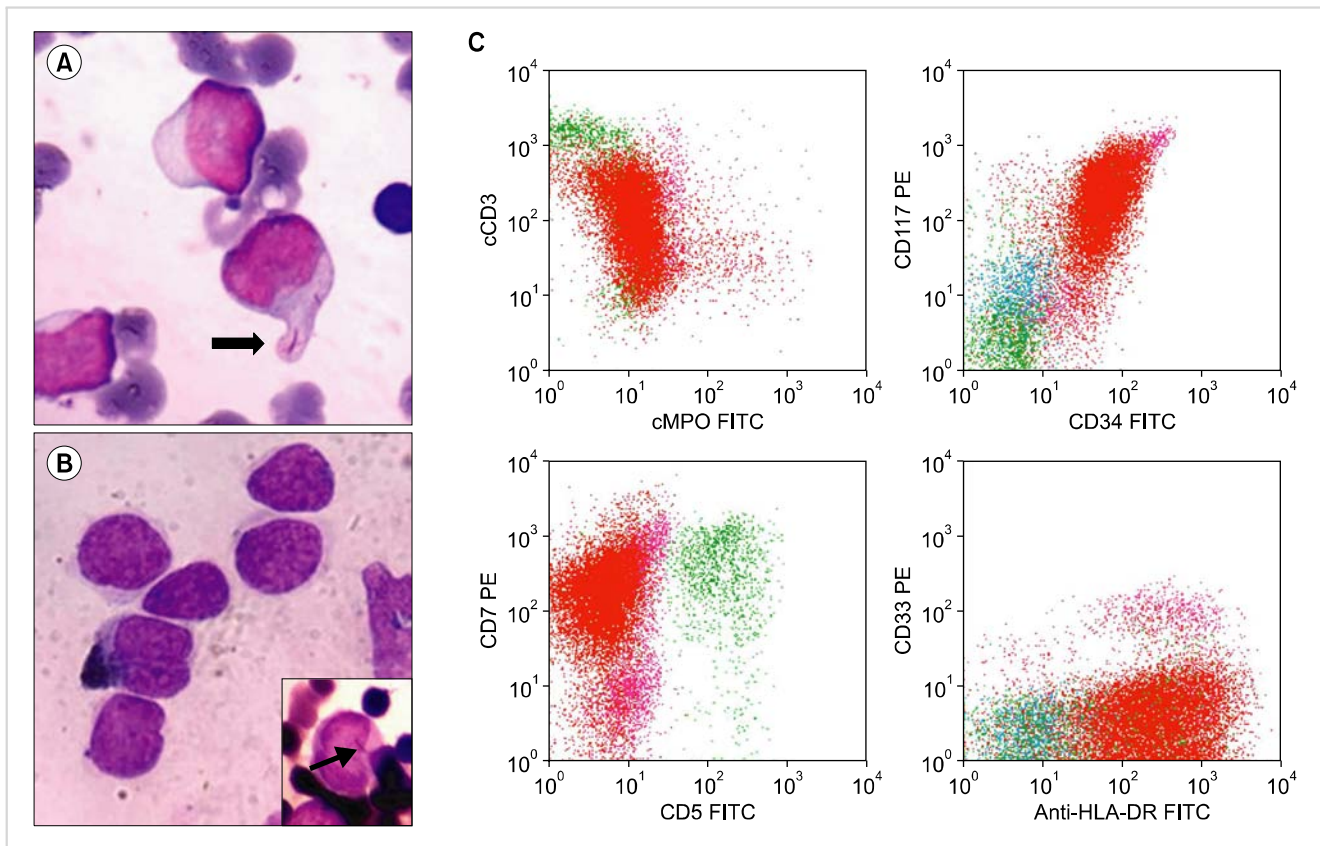


Fig. 1. (A) Bone marrow aspirate showing blasts with a single Auer rod (thick arrow; Giemsa, $\times 100$). (B) Few myeloperoxidase (MPO)-positive blasts; inset shows an MPO-positive Auer rod (thin arrow; MPO, $\times 100$). (C) Blasts are cCD3, CD34, CD117, and CD7 positive and cMPO, CD5, and CD33 negative.

the T cell markers cCD3, CD2, and CD7; and the myeloid/stem cell markers CD34, CD117, CD13, HLA-DR, CD123, and CD99, but were negative for CD1a, CD8, and CD5 as well as CD19, CD10, CD4, sCD3, CD64, CD14, CD20, CD33, CD56, CD16, CD66b, CD15, CD11b, and MPO, suggesting a diagnosis of ETP-ALL (Fig. 1C). Given the morphological presence of MPO-positive Auer rods and the flow cytometric ETP-ALL phenotype, a final diagnosis of MPAL (T/Myeloid) was made. Conventional karyotyping revealed 47, XY, +4, and t(6;14)(q27;q22). The real-time polymerase chain reaction analysis was positive for *FLT3-ITD* mutation and negative for *NPM1* mutation.

DISCUSSION

The 2008 World Health Organization (WHO) classification established new and strict criteria for the diagnosis of MPAL [4]. The WHO definition of MPAL, T/Myeloid was based on the expression of specific T-cell (cytoplasmic/surface CD3) and myeloid (MPO) antigens; the latter is determined using flow cytometry, cytochemistry, or immunohistochemistry and/or from clear evidence of monocytic differentiation. The newly identified entity ETP-ALL, which is not yet included in the WHO classification, presents a particular flow cytometric diagnostic challenge because it frequently presents with sufficient myeloid-lineage differ-

entiation to be classified as MPAL, T/Myeloid [5]. Recently, Borowitz [6] suggested that these 2 types of leukemia have more similarities than differences; however, they are treated differently because of the central importance of MPO in labeling a disease as myeloid and the manner, in which leukemia treatment protocols are structured. However, the exact MPO positivity cut-off percentage required to establish a myeloid lineage was not mentioned in the WHO classification. Our case fulfilled all the flow cytometric criteria for ETP-ALL, including MPO negativity [1]. However, an extensive light microscopic evaluation of the bone marrow revealed approximately 3% blasts with cytochemical MPO positivity and Auer rods (also positive for MPO); thus, this case was classified as MPAL, T/myeloid phenotype. To the best of our knowledge, this is the first case of ETP-ALL with Auer rods reported in the literature.

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Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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Leukemic manifestation of blastic plasmacytoid dendritic cell neoplasm: laboratory approaches in 2 cases

TO THE EDITOR: The blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare subtype of the myeloid neoplasm, with an incidence of 0.44% among all hematologic malignancies and characterized by clonal plasmacytoid dendritic cell presence [1, 2]. Patients with BPDCN typically display skin lesions and aggressive clinical features with rapid systemic dissemination, exhibiting bone marrow (BM) involvement in 60–90% of cases [3, 4]. However, leukemic presentation of BPDCN is rare, with a reported incidence of less than 1% among those with acute leukemia [5]. Moreover, BPDCN with leptomeningeal involvement has been reported to be more infrequent compared with lymph node or liver/spleen involvement, as only 4 of 43 BPDCN patients experienced cerebrospinal fluid (CSF) involvement in a large-scale multicenter study [1]. Herein, we report 2 patients with BPDCN who exhibited leukemic manifestation (1 with simultaneous leptomeningeal involvement) diagnosed by using immunohistochemical staining and flow cytometry analysis for CD4, CD56, and CD123.

CASES

The first case of BPDCN was observed in a 36-year-old woman who was admitted to the authors' institution for workup of a left cheek skin lesion that had developed 6 months previously. An incisional biopsy of the skin lesion

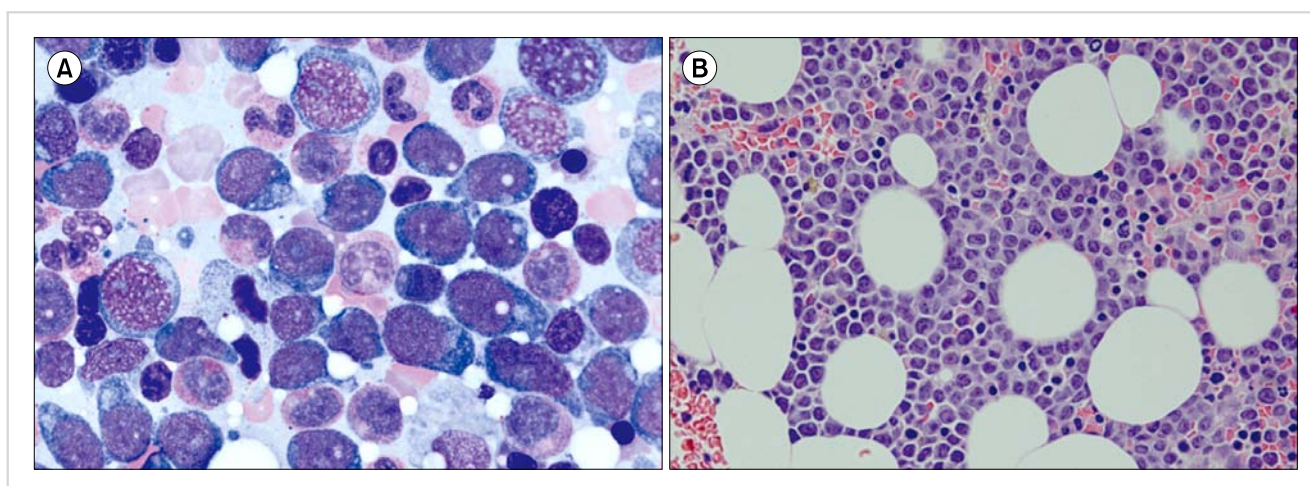


Fig. 1. Bone marrow (BM) aspiration and biopsy findings in the first case. BM aspiration showed the presence of neoplastic cells (27.8%) with oval to round nuclei, prominent nucleoli, and abundant amount of bluish cytoplasm (A, Wright staining, $\times 1,000$). The BM clot section also showed interstitial infiltration of neoplastic cells (B, hematoxylin and eosin staining, $\times 400$) positive for CD4, CD56, and CD123 on immunohistochemical staining.