Abnormal Lymphoid Cells in T-Cell Acute Lymphoblastic Leukemia/Lymphoma Resembling Burkitt Lymphoma Morphology

Burkitt Lenfoma Morfolojisine Benzeyen T-Hücreli Akut Lenfoblastik Lösemi/Lenfomada Anormal Lenfoid Hücreler

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To the Editor,

A 34-year-old female with chest tightness and shortness of breath for approximately 1 week was found to have an anterior mediastinal mass upon chest computed tomography. A routine full blood count on admission indicated hyperleukocytosis ($63.87x10^9$/L). A peripheral blood smear revealed a group of abnormal cells with cytoplasmic vacuoles, representing 10% of nucleated cells (Figure 1A). The bone marrow aspirate smear showed marked hypercellularity with 92% abnormally infiltrated lymphoid cells. These cells were of intermediate size and showed a high nuclear:cytoplasmic ratio, fine condensed chromatin, and no prominent nucleoli. Notably, cytoplasmic basophilia was evident along with abundant lipid vacuoles, exhibiting a Burkitt lymphoma-like morphology (Figure 1B). Cytochemical staining results with myeloperoxidase and periodic acid-Schiff were negative (Figures 1C and 1D). After considering these findings, a preliminary diagnosis of Burkitt's lymphoma (BL) was made.

However, immunophenotyping of the bone marrow aspirate by flow cytometry revealed a group of T-lineage-derived blasts representing 95% of nucleated cells, with the expression of CD7, CD8, CD4, CD2, CD38, CD99, CD45RO, and CD10; partial expression of CD5, cCD3, and CD3; and negativity for other markers (cCD79a, HLA-DR, cMPO, CD56, CD19, CD123, CD34, CD117, CD13, and CD33) (Figure 2). The bone marrow biopsy revealed hyperplasia with tumor cellularity of roughly 80% and MF-1 grade fibrosis (Figure 1E). Bone marrow immunohistochemistry results indicated negativity for CD20, with patchy positivity observed for CD2 and CD3. Fluorescence in situ hybridization analysis did not detect *MYC* rearrangement. Molecular analysis showed overexpression of the fusion gene *Hox11*. Next-generation sequencing identified *NOTCH1* (c.4799T>C and c.4775T), *PTEN* (c.738_739insGTGGG), and *PHF6* (c.969-1G>A) genetic mutations, which frequently occur in T-lymphoblastic leukemia/lymphoma. The final diagnosis was T-cell acute lymphoblastic leukemia/lymphoblastic lymphoma (T-ALL/LBL).

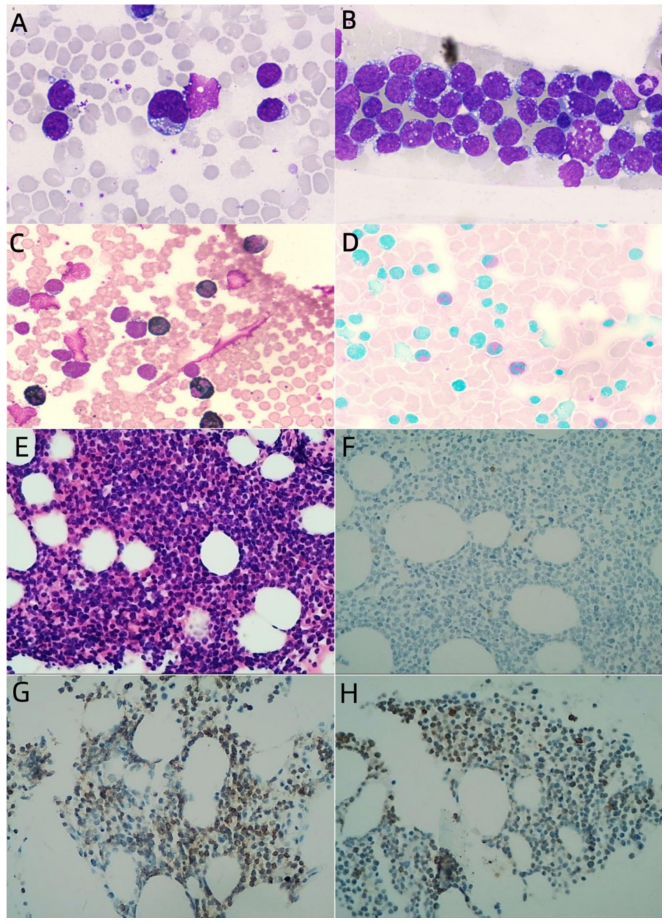

Figure 1. Peripheral blood and bone marrow morphology. Peripheral blood smear (Wright-Giemsa staining×1000) indicated the presence of medium-sized neoplastic lymphoid cells with basophilic cytoplasm and clear vacuoles (Figure 1A). The bone marrow aspirate smear (Wright-Giemsa staining×1000) showed similar lymphocyte morphology to the peripheral smear (Figure 1B). Cytochemical staining for myeloperoxidase and periodic acid-Schiff was negative for neoplastic lymphoid cells (Figure 1C-D). The bone marrow biopsy (Hematoxylin and eosin staining× 400, HE staining) revealed hyperplasia with a tumor cellularity of roughly 80% and MF-1grade fibrosis (Figure 1E). The bone marrow immunohistochemistry result(× 400) indicated negativity for CD20(Figure 1F), with patchy positivity observed for CD2(Figure 1G) and CD3(Figure 1H).

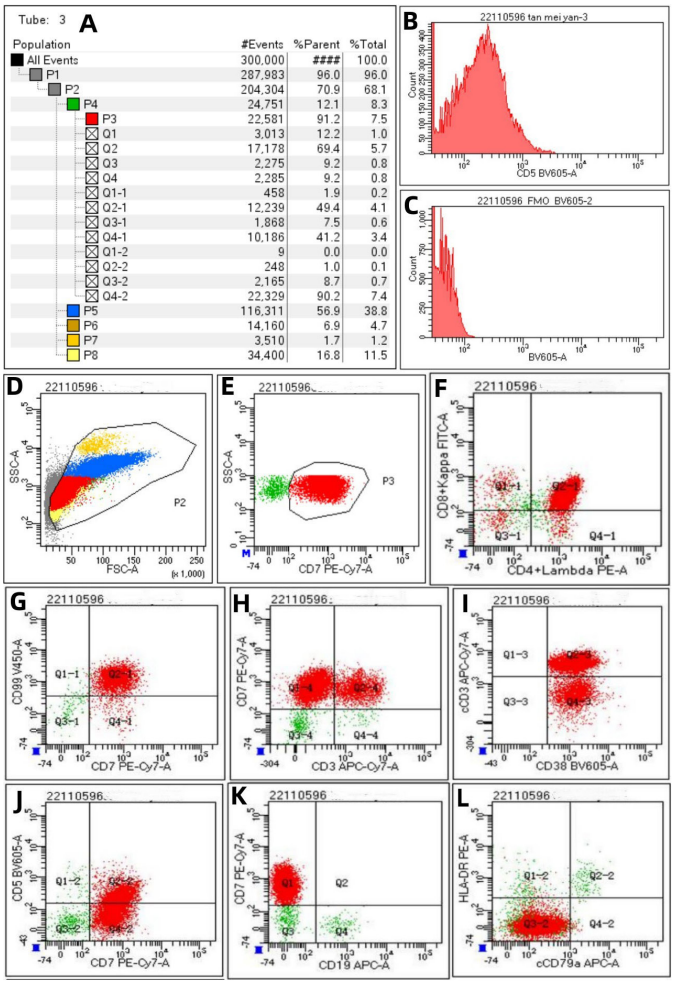

Figure 2. The unstained tube displayed viable cells of 204304((A); (B) and (C) displayed CD5 FMO; White blood cells were gated on SSC vs. FSC(D). Flow cytometry analysis of bone marrow revealed the presence of CD7+ T lymphocytes (E) that were positive for CD4 (F) and CD8 (F), as well as CD99 (G); Additionally, they were partially positive for cCD3 (I), CD3(H), and CD5(J), while negative for CD19(K) and cCD79a(L).

Despite the similarly aggressive natures of T-ALL/LBL and BL, the former has a poor prognosis while the latter is potentially curable with high-dose intensive chemotherapy [1]. In the case presented here, the morphological diagnostic process was suggestive of BL due to the presence of prominent cytoplasmic vacuolization. The markedly elevated level of lactate dehydrogenase (3124 U/L; reference range: 120-250 U/L) and the high tumor burden led us to consider the possibility of BL. The translocations involving the *c-MYC* proto-oncogene located on chromosome 8q24 are critical to the development of most cases of BL. While activation of *Notch1* signaling serves as a critical regulator that is strictly required for promoting the commitment of multipotent hematopoietic progenitors toward a T-cell lineage, the constitutive activation of *Notch1* signaling by various activating mutations is associated with T-cell leukemogenesis [2]. The abundant cytoplasmic vacuolation seen in BL indicates increased lipid synthesis associated with a high degree of proliferative activity, and we inferred that the similar cytology seen in our case may have also arisen from a highly proliferative tumor.

Indeed, the appearance of vacuolated cytoplasm in acute leukemia does not always imply BL. The diagnosis is initially based solely on morphological evaluation, followed by integrated multistep procedures, including morphological analysis (peripheral blood/bone marrow biopsy), cytochemistry, immunophenotyping, cytogenetics, and molecular genetics, to establish an accurate diagnosis, which is the prerequisite for treatment and disease management.

Keywords: T-Cell acute lymphoblastic leukemia/Lymphoma, Cytoplasmic vacuolization, Burkitt lymphoma-like morphology

Anahtar Sözcükler: T-hücreli akut lenfoblastik lösemi/Lenfoma, Sitoplazmik vakuolizasyon, Burkitt lenfoma benzeri morfoloji

Ethics

Informed Consent: Informed consent was obtained from the patient.

Authorship Contributions

Surgical and Medical Practices- X.C.; Concept- X.C.; Design- X.C.; Data Collection or Processing- Y.Y.; Analysis or Interpretation- X.C.; Literature Search- Y.Y.; Writing- Y.Y., X.C.

Conflict of Interest: No conflict of interest was declared by the authors.

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