Turk J Hematol 2023;40:68-81

A Novel Inclusion Body in Acute Promyelocytic Leukemia

Akut Promyelositik Lösemide Yeni Bir İnklüzyon Cisimciği

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To the Editor,

Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML) described in the French-American-British classification as AML-M3, and it accounts for approximately 4% to 20% of adult AML cases [1]. APL is characterized by rearrangements between the retinoic acid receptor-a (*RARa*) gene located on chromosome 17 and another transcription factor gene. The most common translocation associated with over 70%-90% of all APL cases is t(15,17), a fusion between the promyelocytic leukemia (PML) gene located on chromosome 15 and the *RARa* gene, encoding PML/RARa [2]. Morphologically, APL is characterized by rich hypergranular promyelocytes with immature bilobed nuclei that vary greatly in both size and shape, as well as cytoplasm containing abundant giant azurophilic granules. Numerous Auer rods can also be identified in the cytoplasm of promyelocytes [3,4]. A small group of APL cases is characterized by smaller azurophilic granules in blast cells [5,6]. Here, we describe a rare case of APL with highly unusual cytoplasmic granules.

A 41-year-old man was admitted to our hospital and diagnosed with APL based on laboratory examinations. A peripheral blood count revealed a white blood cell count of $1.6x10^9$/L and red blood cell count of $2.04x10^{12}$/L, with hemoglobin of 68 g/L and platelet count of $23x10^9$/L. Flow cytometry showed that the immature leukemia promyelocytes were strongly positive for CD13 and CD33 while being moderately positive for CD117, CD38, and myeloperoxidase (MPO); weakly positive for CD64; and negative for CD34, HLA-DR, and CD56 (Figures 1 and 2). The karyotype was 46,XY, t(15;17) (q24; q21). Cytogenetic analysis indicated that leukemic promyelocytes were positive for the *PML/RARa* fusion gene.

Under light microscopy, most blast cells appeared large and filled with thick azurophilic granules in cytoplasm. Most of the nuclei were eccentrically located, with butterfly shapes, and contained 1 to 3 fine nucleoli (Figure 3a). On cytochemical inspection, these blast cells were found to be positive for MPO, periodic acid-Schiff, and specific esterase staining (Figures 3b-3d). Transmission electron microscopy showed that most of the anomalous blast cells contained an abundance of primary granules, dilated rough endoplasmic reticulum, and aberrant electron-dense bodies rather than the typical cytoplasmic Auer rods (Figures 3e and 3f). The aberrant bodies were large with uneven electron densities and well-defined irregular membranes. In some cases, there were irregular protrusions on membrane surfaces that included a lumen or clear space. Some of these bodies contained both chambers and electron-dense material (Figures 3g and 3h). Bone marrow biopsy results showed hyperplasia and increased percentages of blast cells. There were also scattered granulocytes and mature erythrocytes (Figures 3i-3l). This is the first description of this type of ultrastructure in a patient with APL to date.

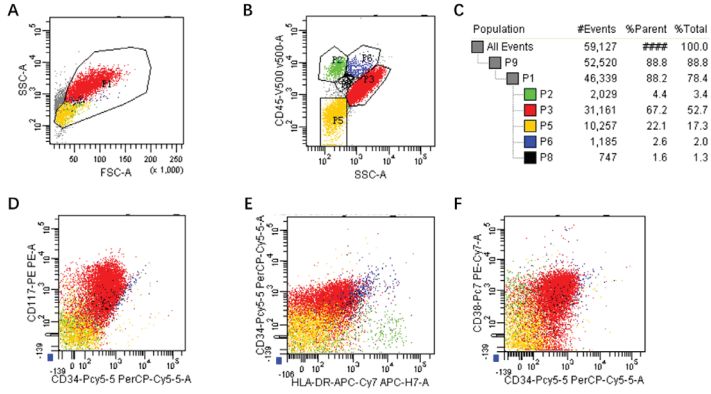

Figure 1. Flow-cytometry analysis of the patient. a) Total cells are calculated and the goal is set as P1. b) The cells in P1 are divided into several compartments and goals are set as P2, P3, P5, P6, P8. c) Cell compartments are listed. d) The cells in P3 were moderately positive for CD117 but negative for CD34. e) The cells in P3 were negative for CD34 and HLA-DR. f) The cells in P3 were moderately positive for CD38 but negative for CD34.

In this letter, novel cytoplasmic bodies with irregularly shaped structures and large volumes in a patient with APL are described. These bodies contained both chambers and dense material enclosed within a thick intact membrane. Some of the bodies showed membranous protrusions with irregular luminal spaces,

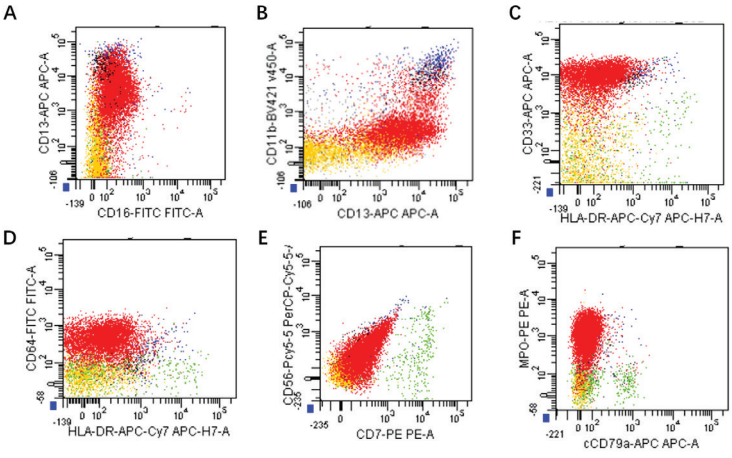

Figure 2. Flow-cytometry analysis of the patient. a) The cells in P3 are strongly positive for CD13 but negative for CD16. b) The cells in P3 are strongly positive for CD13 but negative for CD11b. c) The cells in P3 are strongly positive for CD13 but negative for HLA-DR. d) The cells in P3 are weakly positive for CD64 but negative for HLA-DR. e) The cells in P3 are negative for CD56 and CD7. f) The cells in P3 are moderately positive for MPO but negative for cCD79a.

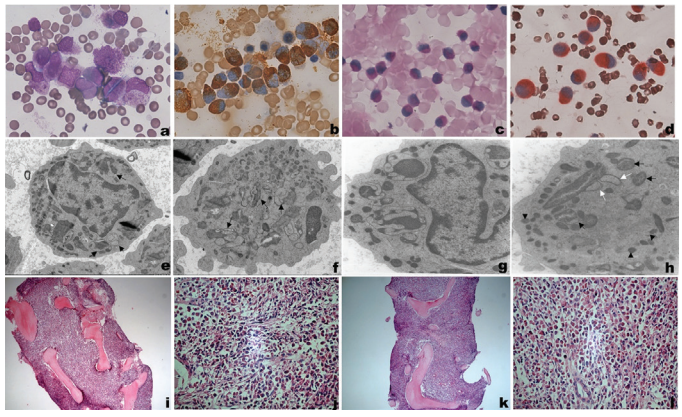

Figure 3. Morphology, cytochemical staining, and ultrastructural characteristics of promyelocytes in a case of acute promyelocytic leukemia. a) Giemsa-Wright staining, 1000^{x}. b) Myeloperoxidase staining, 1000^{x}. c) Periodic acid-Schiff staining, 1000^{x}. d) Specific esterase staining, 1000^{x}. e, f) Promyelocytes including numerous primary granules, dilated rough endoplasmic reticulum, and variant bodies (arrows), e: 4000^{x}, f: 6000^{x}. g) Variant bodies containing irregular electron-dense inclusions and lucent spaces in a dense envelope, 10000^{x}. h) Variant bodies in promyelocytes similar to mitochondria in shape (black arrows), with some accompanied by membranous protrusions (white arrows) (arrowheads indicate primary granules), 10000^{x}. 267x108 mm (72x72 DPI).

which differed from the regular structures and electron densities of Auer rods and primary granules. However, further research should be performed to analyze the structures and formation of these novel bodies.

Keywords: Acute promyelocytic leukemia, Variant bodies, Ultrastructure, Leukemia diagnosis, Transmission electron microscopy

Anahtar Sözcükler: Akut promiyelositik lösemi, Varyant cisimler, İnce yapı, Lösemi teşhisi, Transmisyon elektron mikroskobu

Authorship Contributions

Design: Y.R.; Data Collection or Processing: S.D., J.L.; Analysis or Interpretation: Y.R.; Literature Search: S.D., J.L.; Writing: S.D.

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

Financial Disclosure: The authors declared that this study received no financial support.

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Received/Geliş tarihi: June 23, 2022
Accepted/Kabul tarihi: December 27, 2022
DOI: 10.4274/tjh.galenos.2022.2022.0277