A Crumbled but Fatal Acute Leukemia

Parçalanmış ama Ölümcül Bir Akut Lösemi

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To the Editor,

A 54-year-old woman was admitted to our center for progressive anemia and thrombocytopenia (white blood cells $4.9x10^9$/L, hemoglobin 96.8 g/L, and platelets $62.3x10^9$/L). She had a past medical history of metastatic breast cancer treated with surgery and adjuvant chemoradiotherapy 10 years before. A bone marrow (BM) biopsy showed hypercellular marrow with dysplastic features and 7% myeloid blasts. Cytogenetic analysis revealed a complex karyotype: 44,X,-X,?del(5q),add(6p),-17, -20,+mar[8][20]. A diagnosis of therapy-related myelodysplastic syndrome (t-MDS) was made. The patient underwent four cycles of azacytidine, achieving hematologic recovery. A few weeks later, her blood cell count showed leukocytosis, anemia, and thrombocytopenia (white blood cells $18.1x10^9$/L, hemoglobin 92 g/L, and platelets $62.0x10^9$/L). Peripheral blood (PB) smear analysis showed several round, pale, basophilic fragments of cytoplasm (Figures 1A-1E, May-Grunwald-Giemsa, 100^x). BM aspiration showed many proerythroblasts (>60% of BM cells), often multinucleated (Figures 1F-1L, May-Grunwald-Giemsa, 100^x), with basophilic fragmented and vacuolated cytoplasm. Moreover, proerythroblasts with marked cytoplasmic fracture lines were evident: large areas of basophilic cytoplasm were evident, separate from the contours of the nuclei, and basophilic fragments of cytoplasm of different sizes were visible (Figures 1F-1L, May-Grunwald-Giemsa, 100^x). The cytoplasm showed intense periodic acid-Schiff staining (Figure 1M, periodic acid-Schiff, 100^x). Immunophenotype analysis by flow cytometry revealed that the BM cells were CD71+, CD235+, CD117+, CD34, and CD45-. Cytogenetic analysis could not be completed due to the absence of metaphases. Fluorescence in situ hybridization with a *TP53* locus-specific probe revealed 17p chromosome deletion. A diagnosis of secondary pure erythroid leukemia (PEL) was made. The patient died a few days later. Next-generation sequencing (NGS) analysis was performed on BM samples at the time of the t-MDS diagnosis and then the PEL diagnosis. The entire coding regions or specific exons of 26 target genes (*MPL*, *JAK2*, *CALR*, *DNMT3A*, *SF3B1*, *IDH1*, *IDH2*, *GATA2*, *KIT*, *TET2*, *NPM1*, *DDX41*, *ETV6*, *ANKRD26*, *EZH2*, *CBL*, *KRAS*, *NRAS*, *FLT3*, *SRSF2*, *CEBPA*, *ASXL1*, *RUNX1*, *ZRSR2*, *U2AF1*, and *TP53*) were analyzed. NGS revealed the presence of *TP53* gene mutation (p.R175H) in both samples. Considering the vacuolization in the cytoplasm of the erythroid cells, the *UBA1* gene hotspot mutational status was evaluated, revealing no mutation.

PEL is characterized by cytological abnormalities of the proerythroblasts and basophilic erythroblasts that dominate the morphological picture (i.e., giant multinucleated forms, megaloblastic and markedly dysplastic nuclei, and abundant basophilic and vacuolated cytoplasm with frequent protrusions) [1]. There are many morphologic mimics of malignant proerythroblasts that could complicate the diagnosis of PEL. Our case showed all the morphological PEL anomalies and the presence of numerous basophilic cytoplasmic fragments in the PB and BM, deriving from the breakdown of leukemic cells. These cytoplasmic fragments recall the lymphoglandular bodies often associated with lymphoid neoplasms [2]. The p.R175H *TP53* gene mutation has been related to exuberant necroptosis in epithelial cells [3]. We cannot exclude the role of the p.R175H *TP53* gene mutation in the cellular breakdown observed in our case.

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Keywords: Pure erythroid leukemia, Cytoplasmic fragments, Therapy-related myeloid neoplasms, Necroptosis

Anahtar Sözcükler: Saf eritroid lösemi, Sitoplazmik parçalar, Tedavi ilişkili myeloid neoplaziler, Nekroptoz

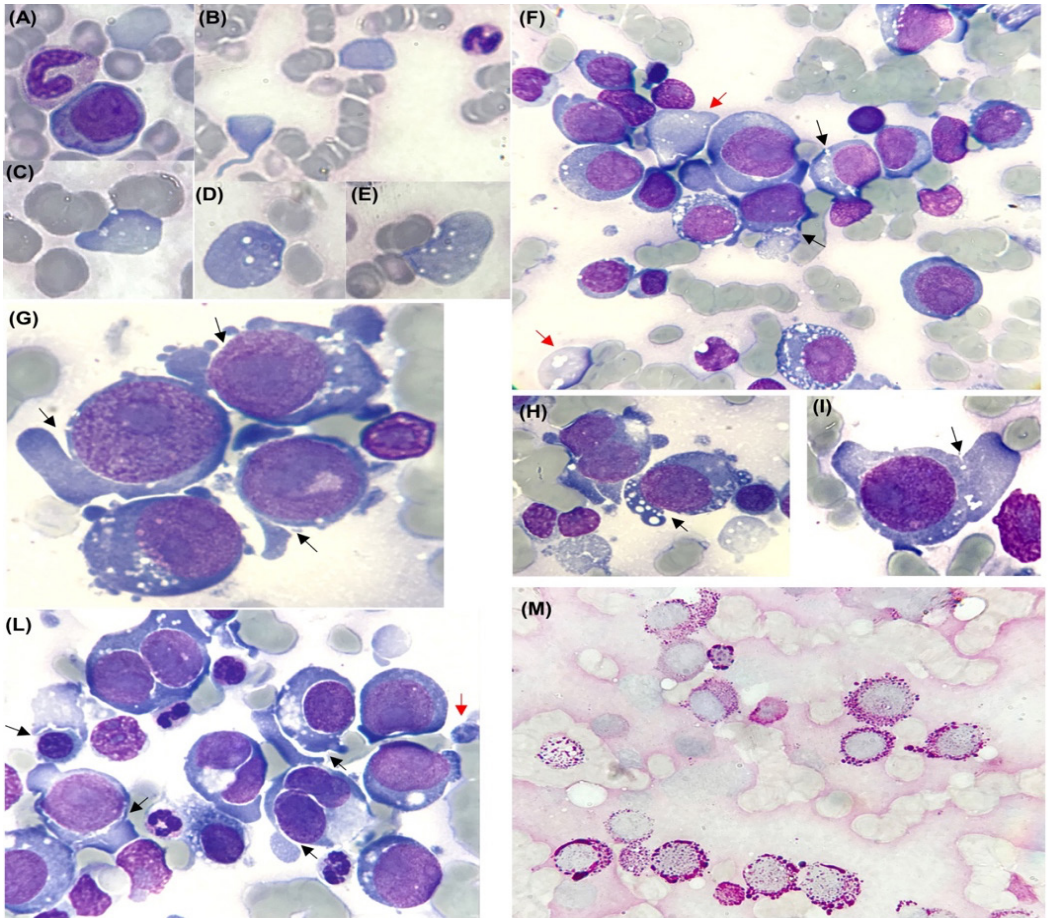

Figure. 1. A-E) Several round basophilic cytoplasm fragments of different sizes were observed in the peripheral blood smear (May-Grunwald-Giemsa, 100ˣ). **F-L)** Proerythroblasts and erythroid leukemic cells showed marked cytoplasmic fracture lines with large areas of basophilic cytoplasm, separate from the contours of the nuclei (black arrow), with evident basophilic fragments of cytoplasm of different sizes (red arrow) (May-Grunwald-Giemsa, 100ˣ). **M)** The cytoplasm of the erythroid leukemic cells showed intense periodic acid-Schiff staining (periodic acid-Schiff, 100ˣ).

Informed Consent: Obtained.

Authorship Contributions

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