LETTER TO THE EDITOR

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Basophils in Acute Promyelocytic Leukemia: Clonality or Reactiveness?

Akut Promiyelositik Lösemide Bazofiller: Klonalite mi, Reaktivite mi?

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To the Editor,

A 19-year-old female patient presented with ecchymoses of 2-3 cm in diameter on the skin of the right knee and right elbow without injury. On admission, a routine complete blood count showed a leukocyte count of $1.38x10^9$/L, hemoglobin of 63 g/L, and platelet count of $24x10^9$/L. A peripheral blood smear showed abnormal promyelocytes representing 13% of the nucleated cells (Figure 1A). A bone marrow aspirate smear showed 71% abnormal promyelocytes without Auer bodies (Figure 1B) and 5% basophils (Figures 1C and 1D), demonstrating positivity for myeloperoxidase staining (Figure 1E). The presumptive diagnosis was acute promyelocytic leukemia (APL).

Immunophenotyping of the bone marrow aspirate revealed 82% myeloid-derived leukemic cells expressing CD117, CD33, CD9, cMPO, and CD13, consistent with APL. Furthermore, we observed an increase of 4.78% in basophils expressing CD9, CD203, CD11b, CD13, CD33, and CD123. Subsequently, both reverse-transcription polymerase chain reaction and fluorescence in situ hybridization (FISH) confirmed the presence of the *PML::RARA* fusion gene. The karyotyping result was 46,XX,t(15;17) (q24;q21) [18]/46,XX[2]. Next-generation sequencing identified the p.S386* mutation in the *WT1* gene. FISH revealed the following signal patterns across the 62 cells analyzed for the identified *PML::RARA* fusion gene: 2G2R, 8.0%; 1G1R1F, 25.8%; 1G1R2F, 58.1%; 2G2R1F, 6.5%; and 1G2R, 1.6%. To ascertain whether the elevated basophils were clonal or reactive, we isolated basophils from bone marrow samples and subsequently evaluated them utilizing the *PML::RARA* probe. The final diagnosis was APL with clonal basophilia (Figure 1F). The patient received induction chemotherapy comprising all-trans retinoic acid (ATRA), arsenic trioxide (ATO), idarubicin, and venetoclax, followed by ATRA and ATO for consolidation therapy upon achieving molecular remission.

Various myeloid neoplasms have the potential to progress to acute myeloid leukemia (AML) with basophilia, such as chronic myeloid leukemia, atypical chronic myeloid leukemia, myeloproliferative neoplasms without *BCR::ABL1* fusion, and myelodysplastic syndrome. Furthermore, 44% of AML cases with *DEK::NUP214* exhibit basophilia [1]. Concomitant basophilia does not appear to have a specific correlation with the type of APL (i.e., whether classic or a variant). Some studies have shown that ATRA could hinder the differentiation of promyelocytes into eosinophils and basophils, whereas ATO does not show such an effect [2,3]. However, there have also been reports indicating basophilia among patients with APL following induction therapy with ATRA or ATO. In our case, the patient did not show basophilia after induction therapy. The relationship between differentiation-inducing therapy and eosinophil-basophil differentiation remains unclear, necessitating further investigation.

Another concern is whether the basophils present in APL are clonal or reactive. Clonal basophilia in APL diagnosis was previously supported by bone marrow findings (22% basophils, 28% promyelocytes) and FISH-confirmed t(15;17) in 44.5% of nuclei [4], with our study providing direct evidence of its clonal origin despite the heterogeneity that may exist in the origins of basophils after APL treatment [5,6]. It is worth noting that in all pertinent cases, the basophil count returned to normal following hematological remission.

Keywords: Basophils, Acute promyelocytic leukemia, Clonality, Reactiveness

Anahtar Sözcükler: Bazofiller, Akut promiyelositik lösemi, Klonalite, Reaktivite

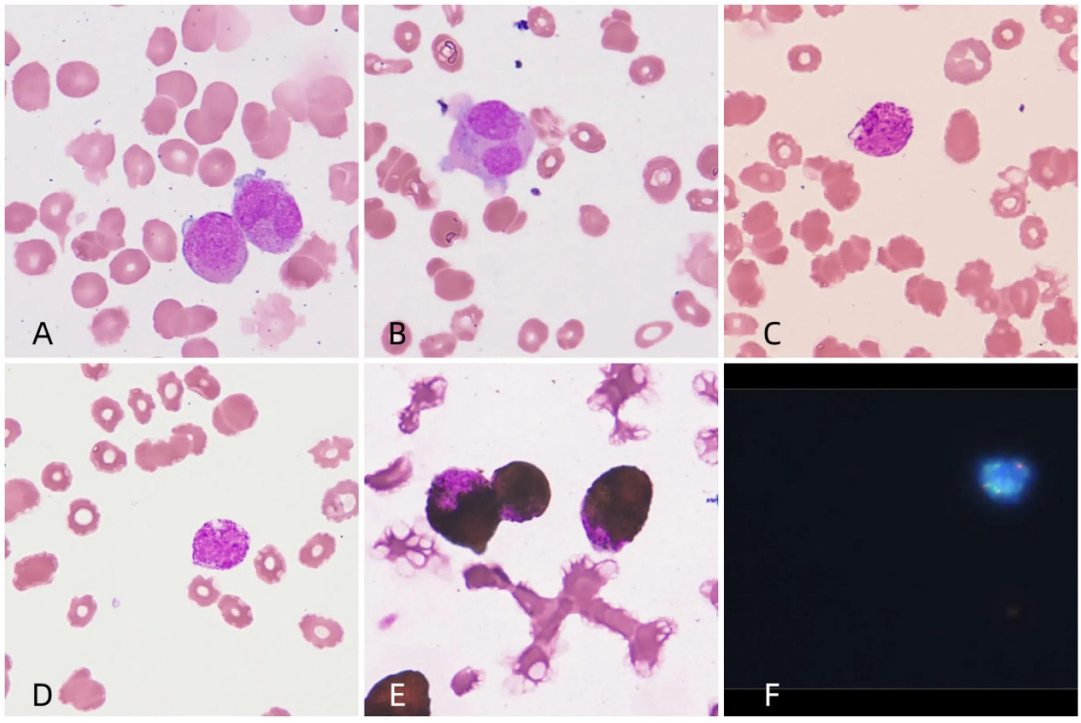

Figure 1. A, B) Abnormal promyelocytes are visible in the peripheral blood (A) and bone marrow aspirate (B), Wright-Giemsa (WG), 1000x. C, D) Basophils are present in bone marrow aspirate (WG, 1000x). E) Positivity for myeloperoxidase staining was observed (1000x). F) Basophils isolated from bone marrow samples were evaluated utilizing the *PML::RARA* probe (1000x).

Ethics

Informed Consent: Informed consent was obtained from the patient reported in this study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: P.Q.; Concept: B.Y.; Design: B.Y.; Data Collection or Processing: X.L., Q.Y., P.Q.; Analysis or Interpretation: X.L.; Literature Search: X.L., B.Y.; Writing: X.L., Q.Y., B.Y.

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

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