LETTER TO THE EDITOR
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The Basophils in Acute Promyelocytic Leukemia: Clonality or Reactiveness?

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To the Editor,

A 19-year-old female presented with ecchymoses 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 of 1.38 × 10^9/L, hemoglobin of 63g/L, and platelet of 24 × 10^9/L. A peripheral blood smear showed abnormal promyelocytes (Figure 1A) representing 13% of the nucleated cells. The bone marrow aspirate smear showed 71% abnormal promyelocytes(Figure 1B) without Auer bodies and 5% basophils(Figure 1C, 1D), demonstrating positivity for myeloperoxidase staining(Figure 1E). A 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 expressed CD9, CD203, CD11b, CD13, CD33 and CD123. Subsequently, both reverse-transcription polymerase chain reaction (RT-PCR) and Fluorescence in situ hybridization (FISH) confirmed the presence of the *PML::RARA* fusion gene. The karyotyping results were 46,XX,t(15;17) (q24;q21)[18]/46,XX[2]. Next-generation sequencing identified the p.S386* mutation in the WT1 gene. Fluorescence in situ hybridization(FISH) identified the *PML::RARA* fusion gene, revealing the following signal patterns across the 62 cells analyzed: 2G2R 8.0%,1G1R1F 25.8%,1G1R2F 58.1%,2G2R1F 6.5%,1G2R 1.6%.To ascertain whether the elevated basophils are clonal or reactive, we isolated basophils from bone marrow samples and subsequently detected 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 byATRA and ATO for consolidation therapy upon achieving molecular remission.

Multiple myeloid neoplasms have the potential to advance into 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 with *DEK::NUP214* exhibit basophilia [1]. Concomitant basophilia does not appear to have a specific correlation with the type of APL (whether classic or variant). Some studies have revealed that ATRA could hinder the differentiation of promyelocytes into eosinophils and basophils, whereas arsenic trioxide(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 this case, the patient did not show basophilia after induction therapy. The relationship between differentiation induction 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 is supported by bone marrow findings (22% basophils, 28% promyelocytes) and FISH-confirmed t(15;17) in 44.5% nuclei [4], with our study providing direct evidence of its clonal origin despite heterogeneity may exist in the origin 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.

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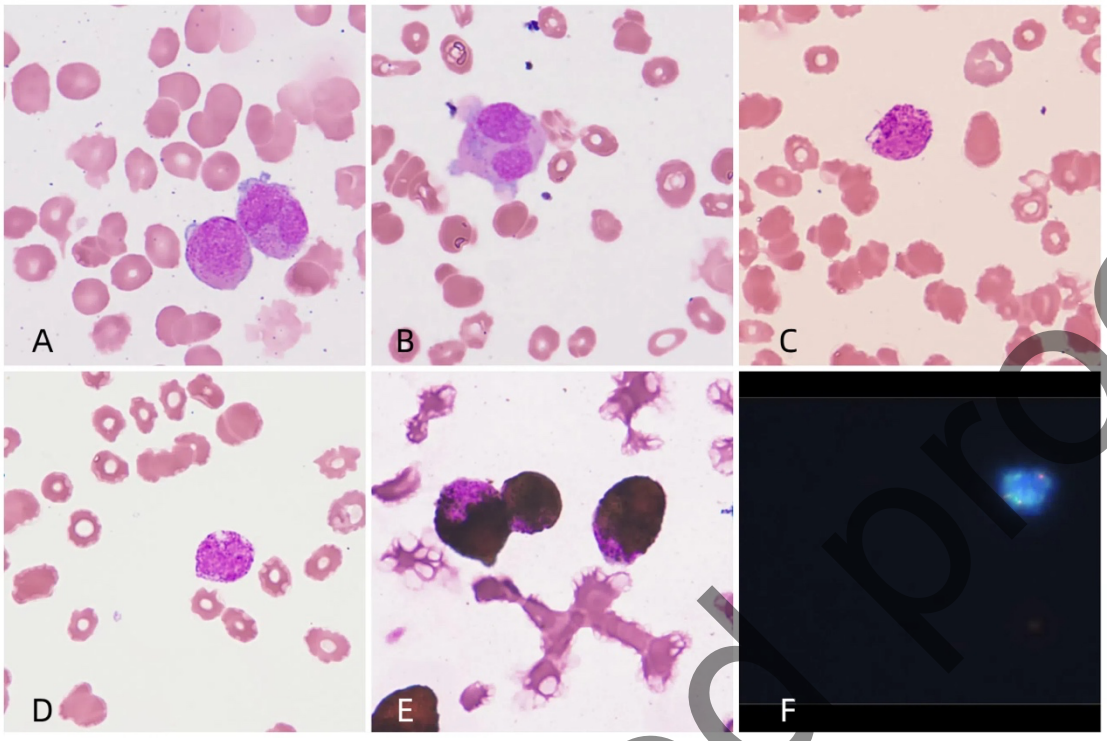

Figure 1. A Abnormal promyelocytes are visible in the peripheral blood smear. B Basophils are present in bone marrow aspirate. C The PML:: RARA fusion was identified in basophils using FISH, indicated by a yellow signal.