a total leukocyte count (TLC) of 2.9×10^9/L. On day 70, he completed his second phase of induction chemotherapy and was started on G-GSF therapy for severe neutropenia (TLC: 0.76×10^9/L). On day 73, his peripheral blood smear showed marked leukopenia with a predominance of lymphocytes and 2% blasts without any left shift or increased granulations. This lack of prototypical G-CSF response along with previous MRD positivity and presence of 2% blasts led to a suspicion of relapse, and bone marrow examination was advised. Marrow aspirate showed hypocellular marrow with 14% blasts, and focal areas showed up to 25% blasts (Fig. 1B), along with a lack of a maturing myeloid component, which suggested relapse. Trephine biopsy, in contrast, showed hypocellularity with only a few scattered CD34 positive blasts. This necessitated flow cytometric evaluation, where the blasts showed negativity for B lymphoblastic markers and expressed myeloid markers, including CD13, CD33, and CD34, suggesting that they were regenerating myeloblasts (Fig. 1C-F). No further therapy was administered and the patient was kept on close hematological follow-up. The counts recovered after 4 days, with the typical responses of a left shift and increased granulation. Follow-up marrow examination after complete recovery of blood counts, 10 days after discontinuing G-CSF therapy, revealed cellular marrow elements with 4% blasts (regenerating) and negative MRD (<0.01%).

Post-G-CSF blastocytosis is a problematic and confusing issue that is difficult to differentiate from disease recurrence and hemopoietic recovery. In our case, there were regenerating blasts (>20%) in the bone marrow, with an absence of telltale G-CSF-induced changes, such as presence of immature granulocytes, monocytosis, or prominent granulations on peripheral smear. To conclude, the regenerating blast percentage may increase after G-CSF therapy to >20%, without concomitant increases in other mature myeloid precursors.

The lag time before complete response to G-CSF therapy may be as long as 10 days, as seen in our case, posing potential problems in management and a challenge in therapeutic decisions. A careful morphological assessment of the blasts at the time of diagnosis, aided by awareness of these G-CSF-associated aberrant patterns and flow cytometric characterization can help guide management decisions.

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Authors' Disclosures of Potential Conflicts of Interest
No potential conflicts of interest relevant to this article were reported.

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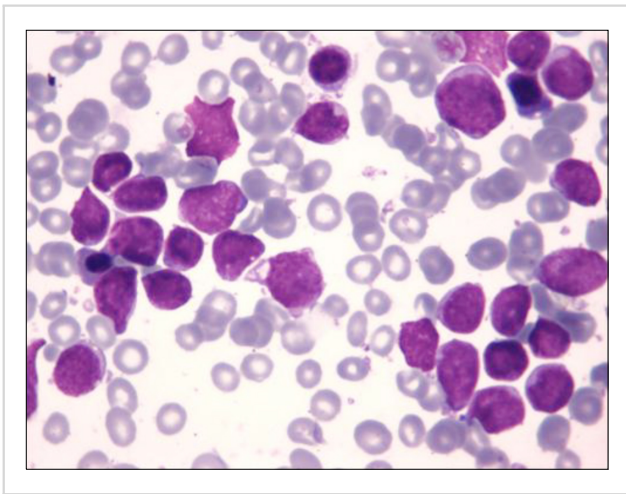
A case of pediatric ALL with t(16;21)(p11.2;q22) and *FUS-ERG* rearrangement

TO THE EDITOR: t(16;21)(p11.2;q22) is a non-random chromosomal translocation that occurs in acute myeloid leukemia (AML), myelodysplastic syndrome that evolves to AML, blast crisis of chronic myelogenous leukemia, and rare cases of Ewing's tumors [1]. AML cases harboring t(16;21)(p11.2; q22) are associated with poor prognosis and a high relapse rate. This translocation produces a fusion gene between the *FUS* (fused in sarcoma) gene on chromosome 16 and the *ERG* (erythroblast transformation-specific related) gene on chromosome 21. The *FUS* gene is highly related to the *EWSR1* (Ewing sarcoma breakpoint region 1) gene, and the FUS protein is an RNA binding protein. On the other hand, the *ERG* gene encodes an external transcribed spacer (ETS) family transcription factor. In the chimeric protein, the N-terminal FUS transactivation domain fuses to the C-terminal DNA binding ETS domain of ERG. The fusion protein seems to function as a transcriptional activator [2].

However, the occurrence of t(16;21) in acute lymphoblastic leukemia (ALL) is very rare. To our knowledge, it has been reported in only 13 ALL patients, including 10 adults and three children [3-6].

We herein describe the case of a 6-year-old boy who was admitted to our hospital owing to parotid enlargement and cranial nerve VII palsy. Physical examination revealed
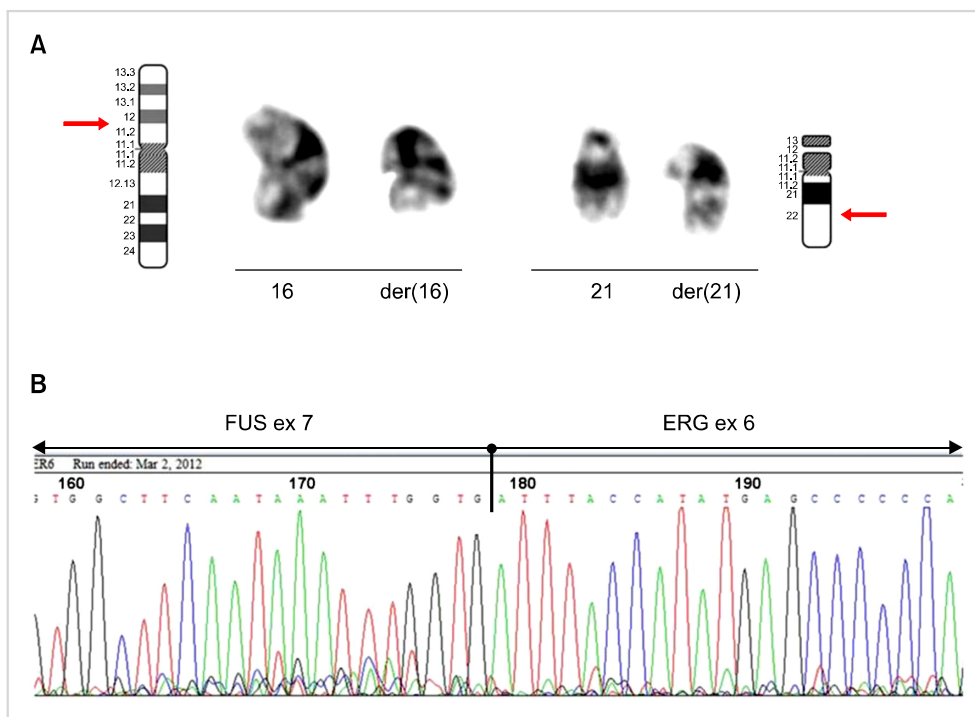
with high-dose methotrexate). MRD was also confirmed to be negative by quantitative real-time PCR at these time points (day 33 and week 12).

According to the Mitelman database and the literature, about 71 cases of t(16;21) have been reported to date, most of them in AML [9]. The rearrangement of the two chromosomes involved in such a translocation forms the *FUS-ERG* fusion gene.

In AML, four types of chimeric transcripts have been described, designated as types A, B, C, and D, which correspond to the 255-, 211-, 176-, and 349-bp chimeric products, respectively [2, 8]. These transcripts consist of *FUS* exons 1 to 6, 1 to 7, or 1 to 8 fused to *ERG* exons 7 to 17 or 9 to 17. Types A and C are out-of-frame fusion transcripts and likely to have been produced by alternative splicing. The other two in-frame transcripts, types B and D, have been shown to result from the fusion of *FUS* and *ERG* genes at different breakpoint positions in t(16;21). These two types of fusion were predicted to produce the FUS-ERG chimeric protein, which may function as the transcriptional activator responsible for the neoplastic process of several t(16;21)-AML cases. The prognosis of AML patients with this translocation is usually very poor owing to resistance to chemotherapy and a high rate of early relapse.

On the other hand, in ALL, a recent study of 256 adult patients reported that *FUS-ERG* fusion transcript was found in 14 cases, including 10 with t(16;21) identified by cytogenetic analysis. Unfortunately, no information regarding the sequencing of the *FUS-ERG* fusion gene and the follow-up of these patients was provided [3]. Furthermore, three pediatric cases of t(16;21) have been reported, but only two of them provide clinical information and results from RT-PCR and sequencing of the *FUS-ERG* fusion gene [4-6]. The case reported by Kanazawa et al. involved a 1-year-old boy with precursor B cell ALL that did not initially respond to ALL-oriented therapy, but the patient achieved complete remission with an AML treatment protocol. Moreover, Oh et al. described the case of an 8-month-old infant with precursor B cell ALL who achieved complete remission but relapsed 4 months after diagnosis. These patients and the one in our case had the same unusual chimeric transcript that consisted of *FUS* exon 7 at the 5' end fused with *ERG* exon 6 at the 3' end, which is different from those described in AML [5, 6]. It is worthy of note that despite having the same molecular rearrangement, the three patients had different responses to ALL-oriented treatment. Our patient achieved complete remission with a chemotherapy schedule for ALL, and he remained free of leukemia 31 months after diagnosis. Therefore, it is challenging to establish the prognostic value of t(16;21) in ALL patients, mostly owing to the small number of reported cases with this unusual abnormality, differences in patient age, treatment heterogeneity, and short follow-up periods.

In conclusion, the present case supports the possible association between ALL cases with t(16;21) and a specific type of *FUS-ERG* fusion transcript first suggested by Oh et al.

However, the role of this transcript in the leukemogenesis of ALL and its prognostic value remain uncertain. Therefore, an analysis of additional ALL cases with t(16;21)(p11.2;q22) and the *FUS-ERG* fusion chimeric transcript are needed to determine the significance of these findings.

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Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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Chronic eosinophilic leukemia with a *FIP1L1-PDGFRA* rearrangement: Two case reports and a review of Korean cases

TO THE EDITOR: According to the 2008 World Health Organization (WHO) guidelines, eosinophilia is associated with hematologic diseases such as chronic eosinophilic leukemia-not otherwise specified (CEL-NOS); idiopathic hypereosinophilic syndrome (HES) or idiopathic hypereosinophilia; and myeloid and lymphoid neoplasms with eosinophilia, and abnormalities of *PDGFRA*, *PDGFRB* or *FGFR1* [1]. CEL is diagnosed in cases with increased blasts or cytogenetic/clonal abnormalities. We report 2 cases of myeloid and lymphoid neoplasms (CEL) with the *FIP1L1-PDGFRA* rearrangement.

CASES

The first case, 27-year-old man was referred to our hospital for a dyspnea workup. The echocardiogram revealed severe tricuspid valve regurgitation and moderate mitral valve regurgitation. A valvuloplasty was performed and dizziness developed after the surgery. Brain magnetic resonance imaging revealed microbleeding in the right temporo-occipital lobe. He was referred to the hemato-oncology department for evaluation of eosinophilia. The laboratory findings were as follows: WBC count, 21.1×10^9/L (eosinophil count,
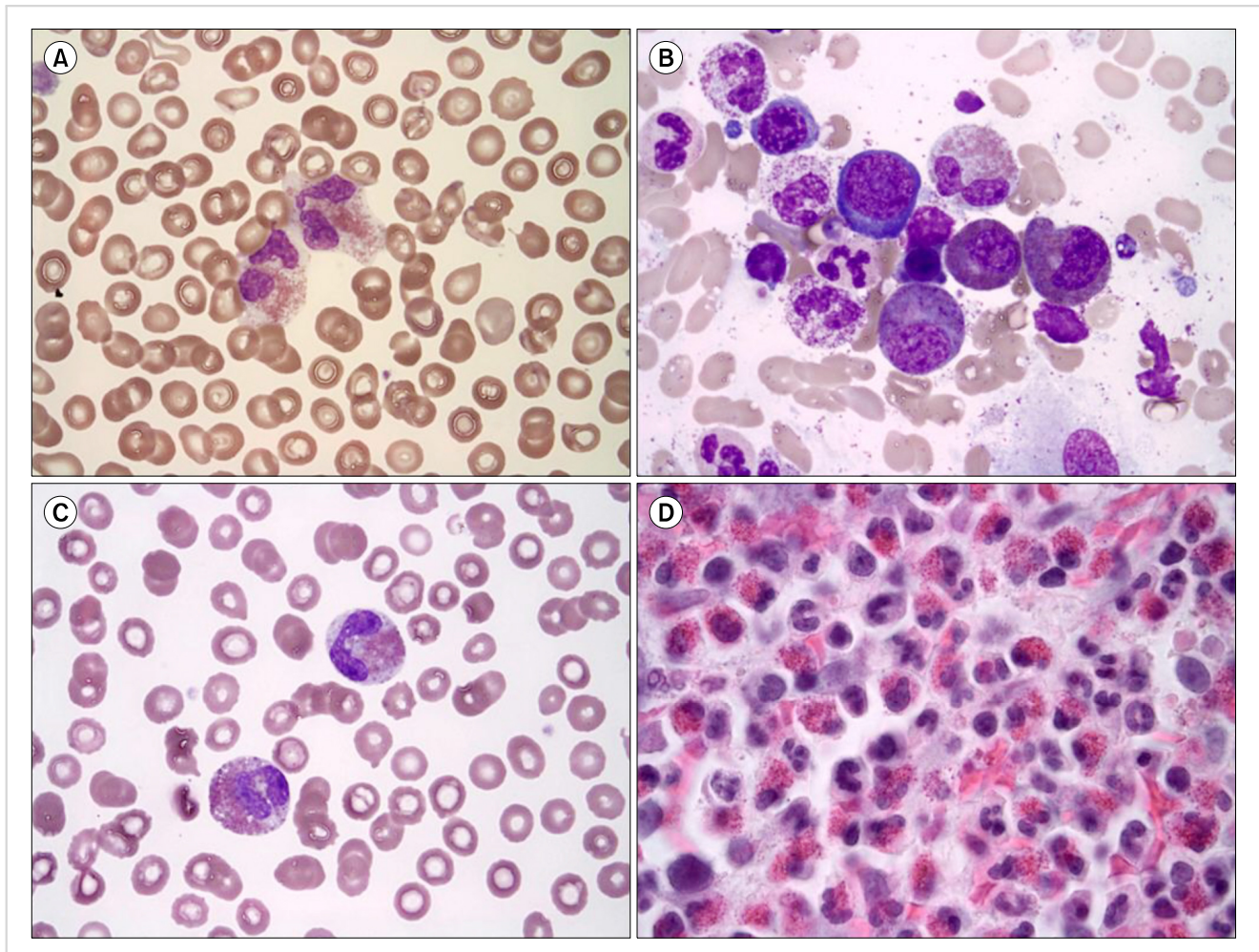
Fig. 1. Peripheral blood (PB) smear and bone marrow (BM) aspirate findings of first case **(A, B)** and second case **(C, D)**. **(A)** Eosinophilia (13.0×10^9/L) was observed in the PB (Wright-Giemsa, ×1,000). **(B)** Dysplastic eosinophils (sparse and mixed granules) were increased in the BM aspirate (Wright-Giemsa, ×1,000). **(C)** Eosinophilia (55.316×10^9/L) was observed in the PB (Wright-Giemsa, ×1,000). **(D)** The BM section was packed with eosinophils (hematoxylin-eosin, ×400).