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LETTER TO THE EDITOR

Acute myeloid leukemia with t(19;21)(q13;q22) and marked eosinophilia

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Dear Editor,

Translocation (19;21)(p13;q22) has only once been previously reported, in one case of radiation-associated acute myeloid leukemia (AML) [1]. Here, we report the first case of AML with t(19;21)(q13;q22) and marked eosinophilia.

A 58-year-old man was admitted because of severe anemia. His white blood cell (WBC) count was 6.7×10^9/L, with 42% eosinophils, 1% myeloblasts, and 1.5% erythroblasts (Fig. 1a). The hemoglobin concentration was 49 g/L, and the platelet count was 196×10^9/L. Bone marrow aspiration showed myeloid dysplasia with 4.8% myeloblasts and 22.4% eosinophils (Fig. 1b). The patient was diagnosed temporarily with myelodysplastic syndrome, unclassifiable (MDS-U). Cytogenetic analysis revealed the karyotype 45, X, -Y, t(19;21)(p13;q22) in 17/20 of the metaphases examined (Fig. 1c). Fluorescence in situ hybridization analysis showed three *RUNX1* signals and two *RUNX1T1* signals in 37% of cells, but no signals corresponding to *RUNX1-RUNX1T1* gene fusion (Fig. 1d). As the fusion transcript termed *RUNX1-AMP19* has been isolated from an AML patient with a t(19;21)(q13;q22) [2], RT-PCR of *RUNX1-AMP19* fusion gene was performed; however, the transcripts were not detected. As the patient's symptoms were improved by transfusions, he was discharged from hospital and closely monitored for disease progression. The peripheral blood (PB) eosinophil count diminished over time.

Two months later, anemia and thrombocytopenia progressed. Transformation to AML was confirmed by the increasing blast counts in the bone marrow (64%; Fig. 1e). After two courses of ineffective chemotherapy, pancytopenia and transfusion dependency remained because normal hematopoiesis was suppressed by increasing numbers of blasts. Thereafter, the patient developed septic shock due to *Klebsiella pneumonia* infection. His clinical condition recovered after intensive treatment for the infection, but, 2 weeks later, the patient died from pontine hemorrhage due to severe thrombocytopenia.

In the present case, because the duration from diagnosis of MDS to diagnosis of AML was very short (2 months), the marked eosinophilia could be considered one of the accompanying symptoms at the onset of AML. The decrease in the proportion of eosinophils observed thereafter could have been due to immature blasts outnumbering eosinophils.

Although *RUNX1-AMP19* fusion transcript was cloned from an AML patient with a t(19;21)(q13;q22) [2], this fusion gene was not detected in the present patient. Identification of chimeric gene in our case is an interesting subject in the future. Both the first reported case [1] and the present case showed loss of sex chromosome (LOS). LOS is one of the most common recurrent cytogenetic abnormalities observed in t(8;21) AML [3]. Several studies suggest that LOS leads to decreased expression of the GM-CSF receptor, located on the pseudoautosomal regions of the sex chromosomes, and is an additional event required for transformation to full-blown leukemia [4–6]. Thus, LOS could also be an important event for the leukemic transformation in t(19;21) AML. As interleukin (IL)-3Rα, GM-CSFRα, and IL-5Rα chain share a common β subunit (cβ) [7, 8], and IL-5 is a major regulator of eosinophils, it is feasible that insufficient expression of GM-CSFRα could induce greater occupation of the cβ by IL-5Rα,

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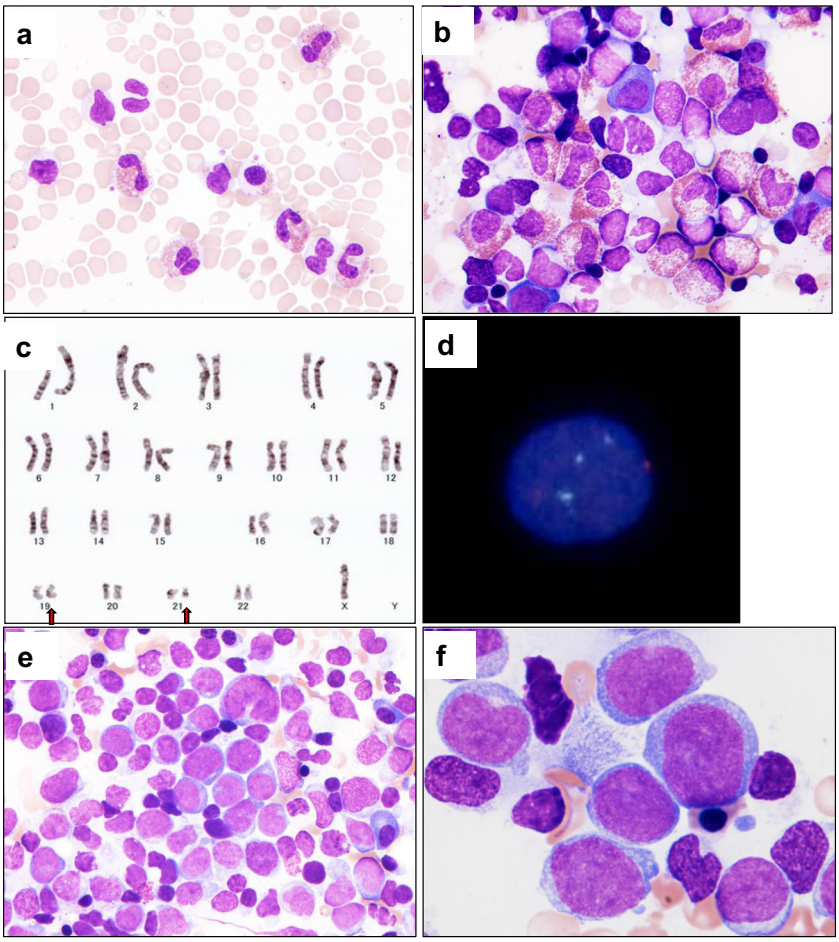

Fig. 1 **a**, **b** Morphology of peripheral blood and bone marrow samples at first admission. **a** May-Grünwald Giemsa staining of the peripheral blood (original magnification × 400). Eosinophilia, pseudo Pelger-Huët anomaly, and hypogranular neutrophils were seen. **b** May-Grünwald Giemsa staining of the bone marrow (original magnification × 500). **c** Karyotype at initial diagnosis demonstrating t(19;21)(q13;q22) and –Y. *Arrows* indicate abnormal chromosomes. **d** Fluorescence in situ hybridization analysis of the bone marrow cells using a *RUNX1/RUNX1T1* dual color, dual fusion translocation probe. Representative nucleus showing three green (*RUNX1*), and two orange (*RUNX1T1*) signals, indicating that a rearrangement of 21q22 had occurred with a gene located other than on 8q22. **e**, **f** Morphology of the bone marrow at the diagnosis of AML. May-Grünwald Giemsa staining of bone marrow aspirate (**e**, original magnification × 400; **f**, × 1000)

resulting in eosinophilic differentiation of leukemic cells. More cases are needed to elucidate the clinical behavior and prognosis of t(19;21) AML. It will also be interesting to ascertain whether this chromosomal rearrangement is involved in the development of eosinophilia.

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Compliance with ethical standards

Informed consent Informed consent was obtained from the patient.

Conflict of interest The authors declare that they have no conflicts of interest.

References

1. Hromas R, Shopnick R, Jumean HG, Bowers C, Varella-Garcia M, Richkind K (2000) A novel syndrome of radiation-associated acute myeloid leukemia involving AML1 gene translocations. Blood 95: 4011–4013
2. Hromas R, Busse T, Carroll A, Mack D, Shopnick R, Zhang DE, Nakshatri H, Richkind K (2001) Fusion AML1 transcript in a radiation-associated leukemia results in a truncated inhibitory AML1 protein. Blood 97:2168–2170
3. Sood R, Kamikubo Y, Liu P (2017) Role of RUNX1 in hematological malignancies. Blood 129:2070–2082
4. Kita K, Shirakawa S, Kamada N (1994) Cellular characteristics of acute myeloblastic leukemia associated with t(8;21)(q22;q22). The Japanese Cooperative Group of Leukemia/Lymphoma. Leuk Lymphoma 13:229–234
5. Jahns-Streubel G, Braess J, Schoch C, Fonatsch C, Haase D, Binder C, Wormann B, Buchner T, Hiddemann W (2001) Cytogenetic subgroups in acute myeloid leukemia differ in proliferative activity and response to GM-CSF. Leukemia 15:377–384
6. Matsuura S, Yan M, Lo MC, Ahn EY, Weng S, Dangoor D, Matin M, Higashi T, Feng GS, Zhang DE (2012) Negative effects of GM-CSF signaling in a murine model of t(8;21)-induced leukemia. Blood 119: 3155–3163
7. Kitamura T, Sato N, Arai K, Miyajima A (1991) Expression cloning of the human IL-3 receptor cDNA reveals a shared beta subunit for the human IL-3 and GM-CSF receptors. Cell 66:1165–1174
8. Tavernier J, Devos R, Cornelis S, Tuypens T, Van der Heyden J, Fiers W, Plaetinck G (1991) A human high affinity interleukin-5 receptor (IL5R) is composed of an IL5-specific alpha chain and a beta chain shared with the receptor for GM-CSF. Cell 66:1175–1184