



A Case of Acute Myeloid Leukemia With *inv(16)(p13.1q22);CBFB-MYH11* Presenting With Faggot Cells

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Dear Editor,

Unlike in other acute myeloid leukemias (AMLs), in acute promyelocytic leukemia (APL), bleeding is the most common cause of early death. Thus, prompt treatment of patients with APL is necessary, and a presumptive APL diagnosis should be made, with immediate administration of all-trans retinoic acid (ATRA), which induces promyelocyte differentiation and can thus prevent coagulopathy, lowering mortality rate [1]. Faggot cells are immature cells with Auer rod bundles in the cytoplasm, characteristic of APL but have rarely been found in other AML types, including myelodysplastic syndrome [2-6]. We report an AML case presenting with several faggot cells in the bone marrow, which had caused a prompt ATRA treatment but was later diagnosed as concurrent AML with *inv(16)(p13.1q22)*. The Institutional Review Board of Soonchunhyang University Hospital, Seoul, Korea, approved this study (IRB File No. 2020-05-020).

In January 2020, a 65-year-old woman complaining of sudden abdominal pain and diarrhea, was admitted to Soonchunhyang University Hospital. Initial complete blood counts were: Hb, 64 g/L (120–160 g/L); platelet count, $43 \times 10^9/L$ ($130\text{--}450 \times 10^9/L$); and white blood cell count (WBC), $7.4 \times 10^9/L$ ($4.0\text{--}10.0 \times 10^9/L$). Coagulation test results were within normal range, except for the slightly prolonged prothrombin time at 12.4 sec (9.3–11.6 seconds). The peripheral blood smear showed 9% blasts based on

all WBCs and bone marrow aspirate smear revealed 45.9% blasts, including 20.6% promonocytes, which have a morphologic picture resembling promyelocytes, based on ANCs. A variety of faggot cells (Fig. 1A, 1B, and 1C) were observed, with occasional observation of abnormal eosinophils. Most blasts were found to be positive for both myeloperoxidase and alpha-naphthyl acetate esterase on cytochemical staining.

Flow cytometric analysis (Navios EX Flow Cytometer and Kaluza Analysis Software, Beckman Coulter, Inc., Miami, FL, USA) demonstrated the presence of blasts expressing CD34, CD13, CD38, CD117, and HLA-DR and CD56 as an aberrant marker, consistent with AML, and being negative for CD11c, CD14, and CD64. Given the possibility of APL based on morphological diagnosis, ATRA was administered to the patient. The next day, however, sequential FISH (*CBFB/MYH11*- Translocation, dual fusion probe, designed by Cytocell, Cambridge, UK and Metafer/Zeiss system, Metasystems, Altlußheim, Germany) and reverse-transcription PCR (GeneAmp PCR System 9700, Applied Biosystems, Foster City, CA, USA) revealed *CBFB-MYH11* rearrangement (Fig. 1D) in the absence of *PML-RARA* rearrangement. Hence, ATRA was discontinued.

Cytogenetic analysis revealed $47,XX,inv(16)(p13.1q22),+22[17]/46,XX[3]$ (Fig. 1E). The p.Asp816His variant in *KIT* represented 32.0% of the total depth in targeted next-generation sequencing (Customized panel, designed by Celemics, Inc., Seoul,

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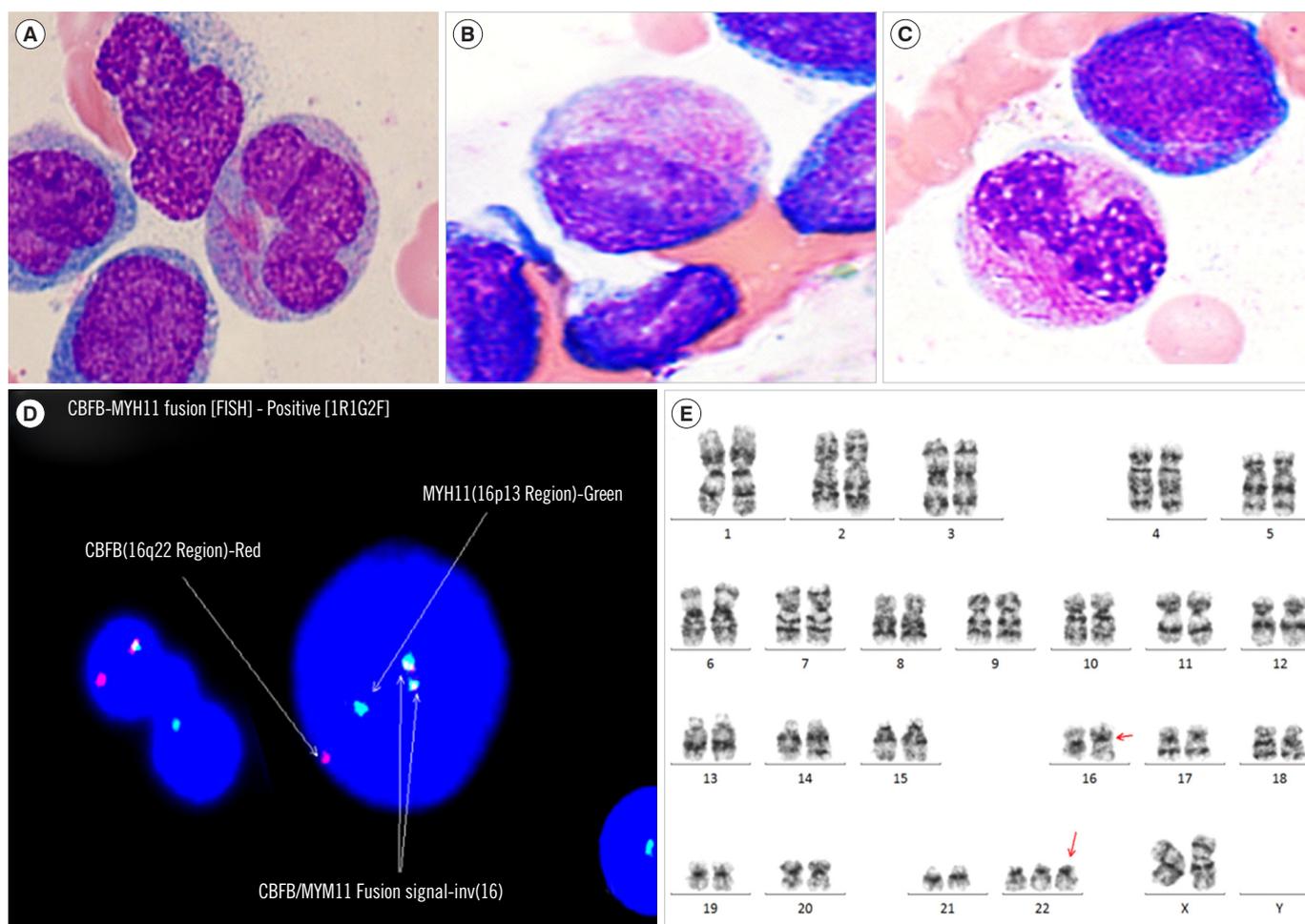


Fig. 1. Morphology, FISH, and cytogenetics of bone marrow. (A–C) Aspirate smears (Wright-Giemsa stain; magnification, 1,000 \times) showing a variety of faggot cells. (D) FISH analysis showing *CBFB-MYH11* gene rearrangement by *inv(16)* (white arrow). (E) Conventional cytogenetics showing 47,XX,*inv(16)(p13.1q22)*,+22. Abbreviation: CBF β , core-binding factor subunit beta.

Korea; NGS platform, Illumina MiSeq DX, San Diego, CA, USA). Based on these findings, the patient was diagnosed as having AML with *inv(16)(p13.1q22);CBFB-MYH11*, and a standard AML induction chemotherapeutic regimen, including idarubicin and cytarabine, was started. After a month of induction chemotherapy, bone marrow examination showed that the patient achieved complete hematologic and cytogenetic responses, without faggot cells. The patient is currently well and undergoing consolidation therapy.

Faggot cells presence in AML with recurrent genetic abnormalities (by 2017 WHO classification) other than APL has been mainly reported to accompany core binding factor (CBF) variants, especially, *t(8;21)* and *inv(16)* [4-7]. CBF variants cause CBF complex decomposition to block cell differentiation. In addition to ours, three AML cases with faggot cells accompanied by *inv(16)* have been reported [4-6]. Two cases were *de novo*

AML with *inv(16)* harboring a *KIT* variant, as in our case [4, 5], and the other case was therapy-related AML with *inv(16)(p13.1q22)* in a patient treated for HIV infection and Hodgkin lymphoma [6]. Clinical features and hematologic findings of these cases and ours are summarized in Table 1.

Faggot cells presence is not sufficient for APL diagnosis, but there is diagnostic value of faggot cell detection in APL for ATRA treatment in the early disease stage to prevent coagulopathy, since APL has a high mortality rate due to disseminated intravascular coagulation [8]. In line with our case, trisomy 22 in AML with *inv(16)* was reported to have favorable prognosis; however, presence of a *KIT* (p.Asp816His) variant in AML may have adverse prognostic significance [9]. To investigate the prognosis of non-APL AML with faggot cells, further studies may be needed.

In summary, we report a rare AML case with *inv(16)(p13.1q22)*;

Table 1. Characteristics of four AML cases with inv(16)(p13.1q22) with faggot cells

	*Present case	*Jerez <i>et al.</i> [4]	*Garrastazul-Sánchez <i>et al.</i> [5]	*Kim <i>et al.</i> [6]
Sex/age (yr)	F/65	M/32	M/36	M/12
Underlying disease	DM, colon adenoma	HIV infection, Hodgkin lymphoma	None	None
Initial CBC	WBC count $9.4 \times 10^9/L$ Hb 95 g/L Platelet count $37 \times 10^9/L$	WBC count $67.4 \times 10^9/L$ Hb 85 g/L Platelet count $10 \times 10^9/L$	WBC count $22.0 \times 10^9/L$ Hb 98 g/L Platelet count $42 \times 10^9/L$	WBC count $20.85 \times 10^9/L$ Hb 106 g/L Platelet count $55 \times 10^9/L$
Cytogenetic study	47,XX,inv(16)(p13.1q22),+22[17]/46,XX[3]	47,XY,+8,inv(16)(p13q22)[20]	inv(16) and hyperdiploidy of 52 chromosomes	47,XY,inv(16)(p13.1q22),+22[20]
Molecular study (rearrangement /variant)	<i>CBFB-MYH11</i> <i>KIT</i> (p.Asp816Val)	<i>CBFB-MYH11</i>	<i>CBFB-MYH11</i> <i>KIT</i> (p.Asp816Val)	<i>KIT</i> (p.Asp816Tyr)
Disease course	CR after induction CTx	CR after induction CTx	CR after induction CTx	Died two days after remission

*All cases did not present with DIC.

Abbreviations: DM, diabetes mellitus; CBC, complete blood count; CR, complete remission; CTx, chemotherapy; DIC, disseminated intravascular coagulation; F, female; M, male; WBC, white blood cell count; CBFB, core-binding factor subunit beta.

CBFB-MYH11, resembling APL due to faggot cell presence. While prompt treatment with ATRA is crucial for APL, final diagnosis should be made carefully. Accurate diagnosis based on a combination of additional laboratory findings is recommended, since AML subtypes differ in disease progress, treatment choice, treatment response, and prognosis.

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AUTHOR CONTRIBUTIONS

Park R conceived the study; Kim JA contributed to the interpretation of the results and initial drafting of the manuscript; and Shin WY, Kim J, and Bang HI contributed to the analysis and interpretation of the results. All authors contributed to writing the manuscript and approved the final version of the manuscript.

CONFLICTS OF INTEREST

None.

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