Letter to the Editor
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# *PCM1-JAK2* Fusion in a Patient With Acute Myeloid Leukemia

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Dear Editor,

Over 34 myeloid neoplasm cases with a *PCM1-JAK2* fusion have been reported worldwide since 1999, including one case reported in Korea [1, 2]. These cases share common features, such as splenomegaly, eosinophilia, myelofibrosis, and male predominance. Most cases have been diagnosed as myeloproliferative neoplasm or myelodysplastic/myeloproliferative neoplasm, in particular, as chronic eosinophilic leukemia and atypical chronic myeloid leukemia. However, acute myeloid/lymphoid leukemia cases have also been reported [1]. Therefore, the 2016 WHO revision recognized the *PCM1-JAK2* fusion gene as a provisional entity [3], joining the existing category of "myeloid and lymphoid neoplasms with eosinophilia and abnormalities of platelet-derived growth factor receptor α (*PDGFRA*), platelet-derived growth factor receptor β (*PDGFRB*), or fibroblast growth factor receptor 1 (*FGFR1*)."

A *PCM1-JAK2* diagnosis can be made with or without eosinophilia, if the presence of the genetic rearrangement is proven. However, identification of the genomic breakpoint in the *PCM1-JAK2* fusion is quite difficult because it varies by case; as many as 14 different fusion transcripts from 15 patients have been reported [2, 4-6]. Moreover, the genetic lesions involved in the rearrangement of the two genes are widely distributed, from exon 23 to exon 36 in *PCM1* and from exon 1 to exon 11 in *JAK2* [5]. Therefore, it is important to report cases of newly confirmed breakage sites where chromosomal assays offer the only indication of a *PCM1-JAK2* fusion. We report a case of acute myeloid leukemia with a *PCM1-JAK2* fusion that was not accompanied by eosinophilia. This study was approved by the institutional review board of Seoul St. Mary's Hospital, Korea, and informed consent was obtained from the patient. A 51-year-old woman was diagnosed as having acute myeloid leukemia at a tertiary hospital in September 2009. At diagnosis, a complete blood count revealed $1.8\times10^9$/L leukocytes, 66 g/L Hb, and $34\times10^9$/L platelets. A peripheral blood smear demonstrated a leukoerythroblastic reaction (nucleated red blood cells: 86/100 leukocytes; left shifted maturation pattern). A bone marrow (BM) biopsy showed hypercellularity with increased erythroid precursors (64% of all nucleated cells) and blasts (47% of non-erythroid cells). The blasts were positive for CD13, CD33, CD117, human leukocyte antigen–antigen D related (HLA-DR), and myeloperoxidase (MPO), and were weakly positive for CD64, CD56, and nuclear terminal deoxynucleotidyl transferase (TdT). A diagnosis of acute erythroid leukemia was made based on the 2008 WHO

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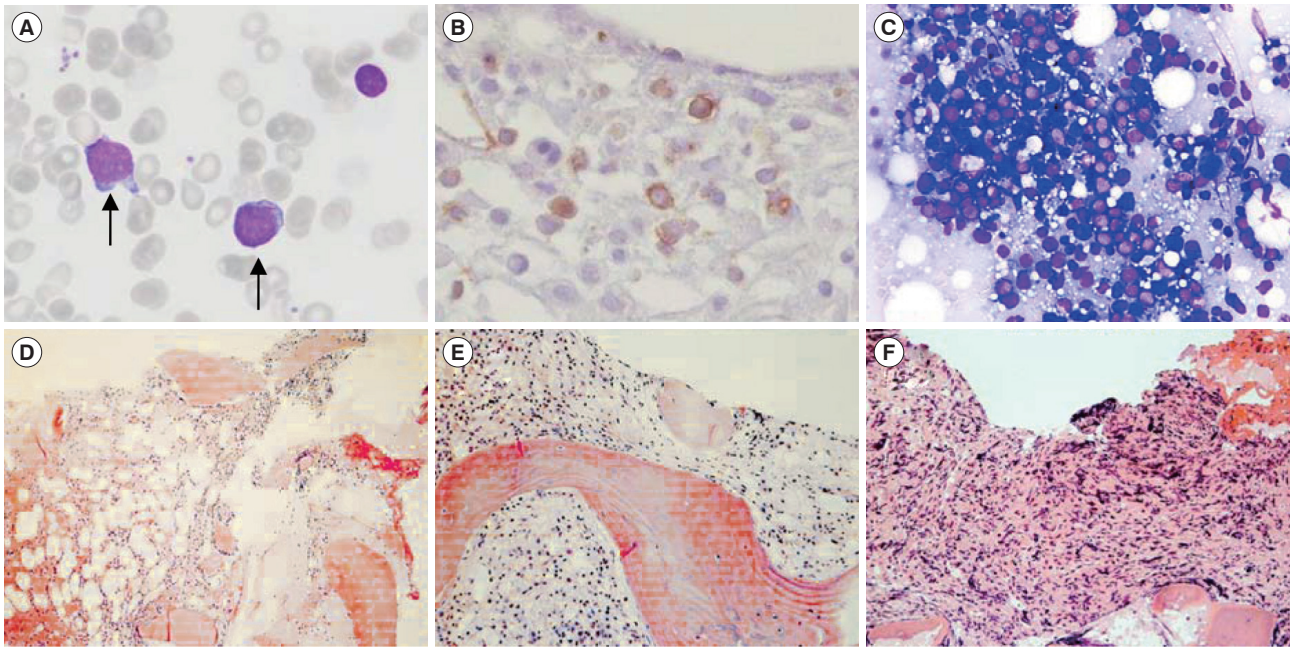


**Fig. 1.** Bone marrow (BM) findings. (A) Myeloblasts showing less cytoplasm and distinct prominent nucleoli at initial diagnosis (April 2011) (Wright stain, ×400); (B) CD34-positive myeloblasts in the BM biopsy (November 2011) (immunohistochemistry stain, ×400); (C) increased immature cells in touch preparation (March 2012) (Wright stain, ×400); (D–F) serial BM biopsies showing fibrosis progression (April 2011, November 2011, and March 2012, respectively) (hematoxylin & eosin stain ×200).

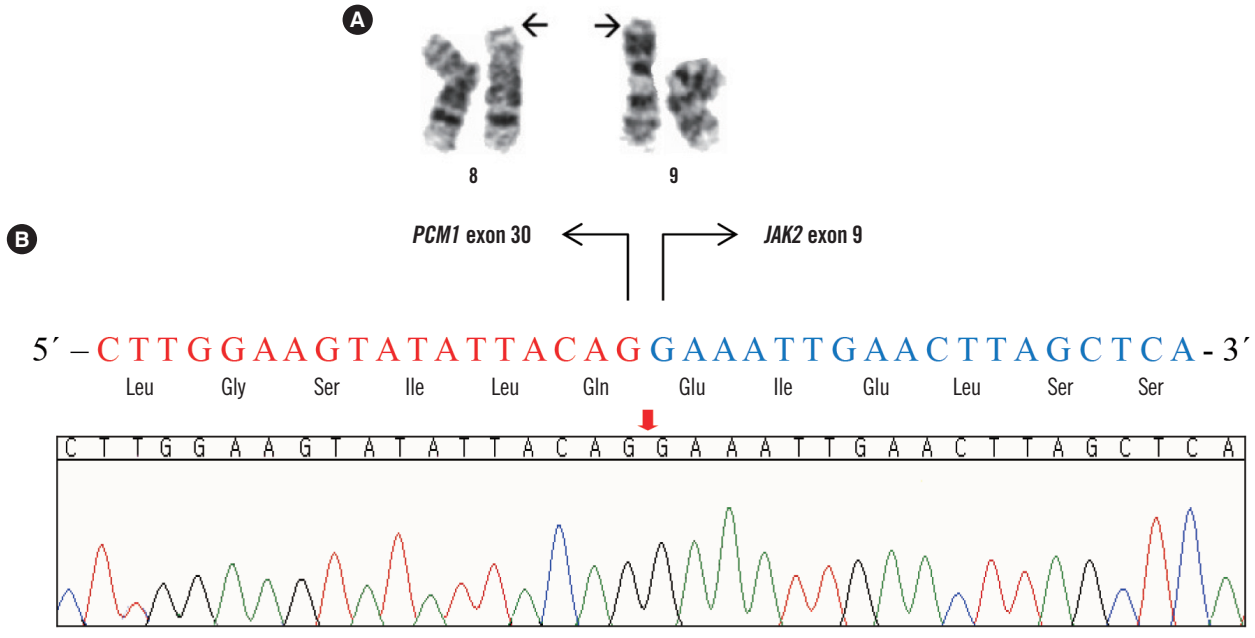


**Fig. 2.** The t(8;9)(p21;p24) translocations and *PCM1-JAK2* fusion gene. (A) Karyogram of BM showing 46,XX,t(8;9)(p21;p24), (B) Sequence of the chimeric *PCM1-JAK2* gene showing in-frame fusion between exon 30 of *PCM1* and exon 9 of *JAK2*.

classification [7]. A cytogenetic examination could not be performed successfully because of inadequate specimens. The patient experienced complete remission following induction chemotherapy with an idarubicin and cytosine arabinoside regimen and subsequently received three courses of high dose consolidation therapy with cytosine arabinoside. In April 2011, the pa-

tient re-developed pancytopenia, which lasted for three weeks; she was transferred to Seoul St. Mary's Hospital, and the BM biopsy confirmed increased myeloblasts (13%; Fig. 1A). The patient received re-induction chemotherapy (FLANG regimen; 30 mg/m$^2$/day fludarabine, 1 g/m$^2$/day cytosine arabinoside, 10 mg/m$^2$/day mitoxantrone, and 300 μg/day G-CSF for five days) twice because of persistent myeloblasts in the BM. After seven months, in November 2011, the BM revealed increased myeloblasts (8%; Fig. 1B). The patient received an allogeneic peripheral blood stem cell transplant from an HLA-matched unrelated donor. Unfortunately, her BM study revealed a relapse of acute myeloid leukemia at the 3-month follow-up post transplantation (myeloblasts 60%, Fig. 1C). In this case, well-known phenotypes of the *PCM1-JAK2* fusion, such as splenomegaly and eosinophilia, were not observed; however, myelofibrosis, a morphological feature that matches myeloid neoplasms with *PCM1-JAK2* was detected (Fig. 1D, 1E, and 1F). Chromosomal analyses of the specimen in November 2011, demonstrated abnormalities in the short arm of chromosome 8 and 9 (Fig. 2A): 46,XX,t(1;14)(p36.1;q11.2),t(2;6)(q35;p21.1),t(8;9)(p21;p24)[10]/46,XX[3]. We amplified the *PCM1-JAK2* fusion transcript from the BM specimen with the detected chromosomal rearrangement by reverse-transcription PCR with primers designed using PRIMER 3 (available from: http://primer3.sourceforge.net): *PCM1* exon 28 forward (5′-GAGCGTATGAAGACTG-3′) and *JAK2* exon 9 reverse (5′-GGCCATGACAGTTGCTTTGT-3′). Sanger sequencing also confirmed an in-frame fusion between *PCM1* exon 30 and *JAK2* exon 9 (Fig. 2B). Targeted next-generation sequencing, including 46 myeloid neoplasm-associated genes, identified a *DNMT3A* c.2644C>T, p.Arg882Cys mutation.

The *PCM1-JAK2* fusion, together with the *JAK2* V617F, *MPL* mutations, causes overexpression of the *JAK2* pathway [5]. Therefore, a *JAK2* inhibitor, ruxolitinib, could be used as a therapeutic agent; in fact, several cases with positive treatment efficacy have been reported [8, 9]. Because eosinophilia and myelofibrosis accompany 50–70% of myeloid neoplasms with *PCM1-JAK2* [10], careful genetic evaluation is necessary for adequate diagnosis and the application of targeted therapy, even when a patient does not manifest well-known characteristics.

## Authors' Disclosures of Potential Conflicts of Interest

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

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