



## Letters to the Editor

### Chronic eosinophilic leukemia with *FIP1L1-PDGFR*A rearrangement

**TO THE EDITOR:** We read an interesting paper by Shin *et al.* [1] in a recent issue of **Blood Research**, titled “Chronic eosinophilic leukemia (CEL) with a *FIP1L1-PDGFR*A rearrangement: Two case reports and a review of Korean cases”. To our knowledge, CEL with *FIP1L1-PDGFR*A rearrangement is very rare in Korea, and only 4 cases have been reported to date [1-3] (Table 1). In this letter, we report an additional rare case of CEL with *FIP1L1-PDGFR*A rearrangement and briefly discuss the possibilities of ethnical differences of this rare gene rearrangement, specifically in the Korean population.

#### CASE

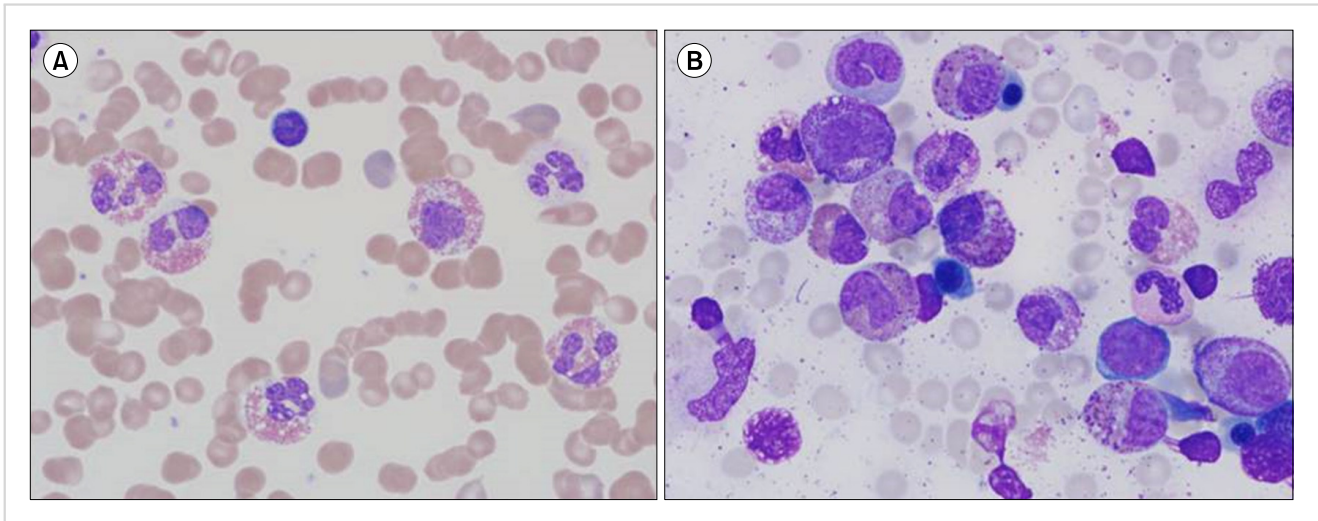
A 30-year-old Korean man was admitted to our hospital due to left flank pain associated with ureter stone. Initial complete blood count (CBC) showed a hemoglobin (Hb) level of 11.9 g/dL (reference range, 13–17 g/dL) and a platelet count of 127,000/ $\mu$ L (reference range, 150,000–350,000/ $\mu$ L)

with a white blood cell (WBC) count of 46,030/ $\mu$ L (reference range, 4,000–10,000/ $\mu$ L): 30.6% neutrophils, 7% lymphocytes, 3.9% monocytes, 55.7% eosinophils, and 1% basophils. Peripheral blood (PB) smear also showed increased number of eosinophils (Fig. 1A). Blood urine nitrogen (BUN) and creatinine levels were within reference ranges. Causes of eosinophilia due to allergy and parasite infections were excluded from further studies. Bone marrow examination was performed, showing hypercellular marrow with eosinophilic precursors, including mature eosinophils, being counting up to 36.2% (Fig. 1B). The chromosome study showed a normal karyotype; however, the *FIP1L1-PDGFR*A rearrangement was detected by fluorescence in situ hybridization (FISH) analysis (Fig. 2). Diagnosis of CEL with *FIP1L1-PDGFR*A rearrangement was made. Our patient was treated with daily administration of imatinib mesylate (100 mg) and followed up with CBC. After 1 year, the follow up CBC showed normalized leukocyte count of 8,170/ $\mu$ L with 3% eosinophils. Furthermore, eosinophil precursors were within reference range of bone marrow aspiration. FISH analysis using a *FIP1L1-PDGFR*A probe showed normal signal patterns (without deletion signals).

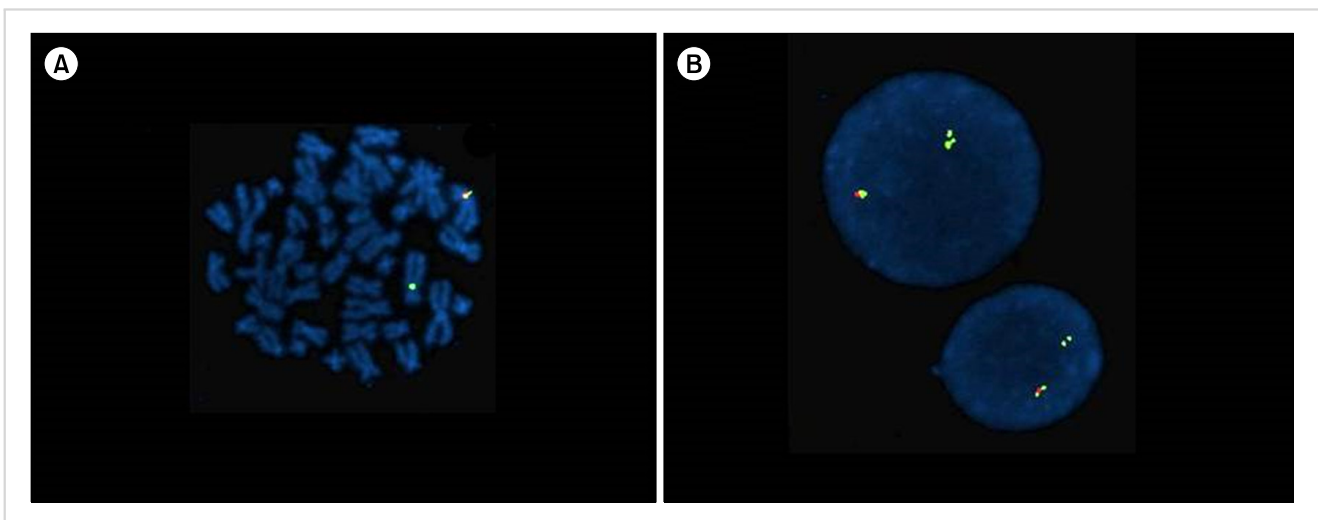
**Table 1.** Summary of Korean cases of chronic eosinophilic leukemia with *FIP1L1-PDGFR*A rearrangement.

	Patient 1 [1]	Patient 2 [1]	Patient 3 [2]	Patient 4 [3]	Present case
Age/Gender	27/M	23/M	30/M	49/F	30/M
Initial CBC					
Hb (g/dL)	9.1	10.1	10.5	10.0	11.9
Platelet ( $\times 10^9$ /L)	99	131	152	237	127
WBC ( $\times 10^9$ /L)	21.1	70.7	20.6	16.4	46.0
Eosinophils (%)	61.6	78.2	71.8	17.0	55.7
Clinical symptoms	Dyspnea, valve regurgitation	No	Hematuria, valve regurgitation	Proteinuria, edema	Left flank pain
Treatment	Imatinib mesylate	Imatinib mesylate	Imatinib mesylate	Imatinib mesylate with combination chemotherapy	Imatinib mesylate
Treatment response					
Eosinophils (%)	NA	NA	9.8	2.5	3.0

Abbreviations: M, male; F, female; CBC, complete blood count; NA, not available.



**Fig. 1.** Morphology in a patient of chronic eosinophilic leukemia with a *FIP1L1-PDGFRα* rearrangement. **(A)** The number of eosinophils increased (55.7%) in the peripheral blood (PB) smear (Wright-Giemsa,  $\times 1,000$ ). **(B)** The number of eosinophilic precursors and eosinophils was markedly increased, and equaled up to 36.2% in the bone marrow (BM) aspiration (Wright-Giemsa,  $\times 1,000$ ). Dysplastic eosinophils, including sparse granulation, nuclear hypersegmentation or hyposegmentation are shown in PB smear and BM aspiration **(A, B)**.



**Fig. 2.** Fluorescence in situ hybridization (FISH) for the *FIP1L1-PDGFRα* rearrangement. *CHIC2* is labeled in orange, *FIP1L1-PDGFRα* in green. Loss of orange signal suggests deletion of the 4q12 region on metaphase FISH **(A)** and interphase FISH **(B)**.

## DISCUSSION

Within the distinct disease entity of myeloid and lymphoid neoplasms with eosinophilia and abnormalities of *PDGFRα*, *PDGFRβ*, or *FGFR1*, *FIP1L1-PDGFRα* is the most common of three genetic abnormalities associated with CEL, although its incidence among the general population is fairly low. It also has a male predilection with male to female ratio of 17 : 1, and a median age of onset late in fifth decade of life [4].

Representative examples of ethnic differences among genetic abnormalities of hematologic malignancy include a higher incidence of acute promyelocytic leukemia in Chinese populations and the comparably low incidence of chronic lymphocytic leukemia among Asian ethnicity.

Interestingly, most CEL cases with *FIP1L1-PDGFRα* rearrangement in the Korean population were male patients in their early third and fourth decades of life, with the exception of a female patient in her forties, suggestive of an earlier onset among the Korean population. However, this conclusion is premature because there have only been five Korean cases reported, including our case. Nation-wide, multicenter research should properly assess the incidence and clinical characteristics, such as early onset and patients' responses to therapy.

Tae Hee Kim<sup>1</sup>, Hyun Jung Gu<sup>1</sup>, Woo-In Lee<sup>1</sup>, Juhie Lee<sup>2</sup>,  
Hwi-Joong Yoon<sup>3</sup>, Tae Sung Park<sup>1</sup>

Departments of <sup>1</sup>Laboratory Medicine, <sup>2</sup>Pathology, <sup>3</sup>Hematology-Oncology, School of Medicine, Kyung Hee University, Seoul, Korea

**Correspondence to: Tae Sung Park**

Department of Laboratory Medicine, School of Medicine, Kyung Hee University, 23 Kyungheedaero, Dongdaemun-gu, Seoul 02447, Korea  
E-mail: 153jesus@hanmail.net

Received on Jul. 28, 2015; Revised on Aug. 5, 2015; Accepted on Aug. 19, 2015  
<http://dx.doi.org/10.5045/br.2016.51.3.204>

### Acknowledgments

This work was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2014R1A1A1002797).

### Authors' Disclosures of Potential Conflicts of Interest

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

### REFERENCES

1. Shin SY, Jung CW, Choi DC, Lee BJ, Kim HJ, Kim SH. Chronic eosinophilic leukemia with a FIP1L1-PDGFR $\alpha$  rearrangement: Two case reports and a review of Korean cases. *Blood Res* 2015;50:58-61.
2. Jeung YJ, Lee JY, Lee GY, Oh MJ, Lee BJ, Choi DC. A case of idiopathic hypereosinophilic syndrome presenting with nocturia and dyspnea. *Korean J Asthma Allergy Clin Immunol* 2010;30:241-5.
3. Kim DW, Shin MG, Yun HK, et al. Incidence and causes of hyper-eosinophilia (corrected) in the patients of a university hospital. *Korean J Lab Med* 2009;29:185-93.
4. Swerdlow SH, Campo E, Harris NL, et al, eds. WHO classification of tumours of haematopoietic and lymphoid tissues. 4th ed. Lyon, France: IARC Press, 2008.

## A case of histoplasmosis in a patient with MDS/MPN-U

**TO THE EDITOR:** We would like to share the following intriguing case with readers of *Blood Research*. A 72-year-old HIV-negative man presented with a 2-month history of gradual-onset generalized weakness, low-grade fever, and loss of weight and appetite. On examination, he had pallor and hepatosplenomegaly. His hemogram findings revealed a nearly normal hemoglobin level (11.8 g/dL), leukocytosis ( $15.8 \times 10^9/L$ ), and thrombocytopenia ( $78 \times 10^9/L$ ). Differential counts showed 3% circulating blasts apart from 6% immature myeloid cells, 4% basophils, and 2% monocytes. A bone marrow aspirate was hypercellular with 5% blasts

along with dyserythropoiesis (36%, including 32% ring sideroblasts), dysgranulopoiesis (11%), and dysmegakaryopoiesis (40%). The trephine biopsy showed dyshemopoiesis along with World Health Organization grade 2 reticulin fibrosis. Tests for the detection of *BCR-ABL1* fusion gene and *JAK2* mutations were negative. A diagnosis of myelodysplastic syndrome/myeloproliferative neoplasm-unclassifiable (MDS/MPN-U) was made [1].

Subsequently, the patient was lost to follow-up, but 7 months later, he visited the emergency room with a high-grade fever with chills and rigors, altered sensorium, and irrelevant talking. On examination, he had neck rigidity, a positive Kernig sign, and right lower limb monoparesis along with hepatosplenomegaly. A computed tomographic scan of his head and cerebrospinal fluid examination were normal. Blood and urine bacterial cultures were sterile. At this time, the hemogram revealed anemia (hemoglobin level, 6.0 g/dL), thrombocytopenia ( $19 \times 10^9/L$ ), and leukocytosis ( $63.5 \times 10^9/L$ ) with a differential similar to that obtained 7 months previously. A bone marrow aspirate also revealed a picture similar to that of the previous marrow aspirate. The striking finding noticed at the time of peripheral blood and marrow evaluation was the presence of intracytoplasmic yeast forms (within neutrophils) conforming to *Histoplasma* species (Fig. 1). These were confirmed to be *Histoplasma capsulatum* based on fungal culture studies from peripheral blood (Fig. 1) as well as gene sequencing of the internal transcribed spacer region of the fungus. The patient died on the same day as the bone marrow procedure.

We present this case because this patient highlights an unusual morphological coexistence of a neoplastic and infective disorder [2]. A predisposing factor might have been the dysplastic neutrophils with defective phagocytic and microbicidal activity [3]. The case illustrates the importance of morphology in the era of genomics as well as the value of close interdisciplinary cooperation in diagnostic hematology. It also reinforces the dictum that hematopathologists must always stay on the alert for uncommon infections in unusual specimens, especially in tropical countries.

Pulkit Rastogi<sup>1</sup>, Prashant Sharma<sup>1</sup>, Narender Kumar<sup>1</sup>,  
Shivaprakash M. Rudramurthy<sup>1</sup>, Neelam Varma<sup>2</sup>,  
Subhash Varma<sup>2</sup>

Departments of <sup>1</sup>Hematology and Medical Microbiology, <sup>2</sup>Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India

**Correspondence to: Narender Kumar**

Department of Hematology, Level 5, Research Block A, Postgraduate Institute of Medical Education and Research, Sector 12, Chandigarh 160012, India  
E-mail: nkkalson@yahoo.co.in

Received on Jul. 16, 2015; Revised on Oct. 15, 2015; Accepted on Nov. 12, 2015  
<http://dx.doi.org/10.5045/br.2016.51.3.206>