Complete response of myeloid/lymphoid neoplasms with *PDGFRA* rearrangement presenting as leukemia/myeloid sarcoma to imatinib monotherapy

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To the Editor: The presence of FIP-1-like-1-platelet-derived growth factor receptor-α (*FIP1L1-PDGFRA*, *F/P*) fusion gene accounts for approximately 23% (3%–56%) of all eosinophilias.[1] From 2008, the World Health Organization (WHO) classification redefined this disease as "myeloid/lymphoid neoplasms with eosinophilia and *PDGFRA* rearrangement," now constituting a distinct type of hematopoietic disorders. *F/P* fusion is a tyrosine kinase and is therefore sensitive to tyrosine kinase inhibitors (TKIs). TKIs are recommended as the first-line therapy in the treatment of myeloid/lymphoid neoplasms with eosinophilia and *PDGFRA* rearrangement by the WHO guidelines.[2]

Until recently, most of the reported cases for eosinophilia with *F/P* fusion presented at a "chronic phase," with little or no increase of blasts in the bone marrow (BM). Rare cases have been reported presenting as more aggressive forms at disease onset, such as leukemia or sarcoma, with BM blasts meeting the criteria of 20% or presenting with extramedullary infiltrations. In such cases, whether imatinib would be a successful monotherapy or used in combination with chemotherapy/radiotherapy/hematopoietic stem-cell transplantation remains unclear. Here, we describe two patients carrying the *F/P* fusion gene and presenting as myeloid sarcoma or leukemia who responded well to imatinib monotherapy.

The first patient was a previously healthy 33-year-old man who was referred to our institute on January 13, 2016. One month earlier, he had palpated a mass on his chest that gradually increased in size. Positron emission tomography-computed tomography (PET-CT) revealed hypermetabolic lesions across the body, with the largest identified in the left chest wall (6.9 cm × 3.3 cm) and invading into adjacent tissues. Biopsy of the mass suggested a diagnosis of sarcoma with an immunohistochemical phenotype of myeloperoxidase$^+$, CD34$^+$, and CD117$^+$. Blood tests identified the presence of eosinophilia (3.86×10^9/L, 49.2% of white blood cell count [WBC]) with normal hemoglobin and platelet count. BM aspirates showed an infiltration of 22% eosinophils and reverse transcription-polymerase chain reaction (RT-PCR) revealed the presence of the *F/P* fusion gene (0.28%). A diagnosis of myeloid neoplasm with eosinophilia and *F/P* rearrangement was made.

After two cycles of chemotherapy, *F/P* transcripts lowered to 0.037%. However, the chest tumor did not shrink and PET-CT still showed multiple fluorodeoxyglucose hypermetabolic lesions. A standard dose of imatinib at 400 mg/d was started on March 11, 2016. Nine days later the chest mass had shrunk significantly. A BM test was repeated 1 month later and no *F/P* fusion transcripts were detected, indicating complete molecular remission (CMR) in this patient [Figure 1A]. Follow-up therapy consisted of imatinib at 200 mg/week and he is now in sustained CMR.

The second patient was a 25-year-old man who was admitted on December 25, 2016 with the main complaint of intermittent fever for 1 week. Blood tests detected the presence of eosinophilia (2.89×10^9/L, 20.6% of WBC count) with reduced hemoglobin (81 g/L) and platelet count (48×10^9/L). BM aspirate showed increased myeloblasts (27%), monoblasts (31%), and eosinophils (26%), together meeting the criteria of an acute myeloid leukemia (AML)-M4 diagnosis as per the French-American-British classification. Flow cytometry confirmed the existence of blasts with the phenotype CD34$^+$, CD123$^+$, CD33^{dim}, and CD13^{dim}. A diagnosis of AML-M4 with BM eosinophilia (AML-M4Eo) was suspected; however, subsequent RT-PCR did not detect the core-binding transcription factor β-myosin-11 (*CBF β-MYH11*) but did detect 4.6% *F/P* fusion transcripts. Thus, a diagnosis of

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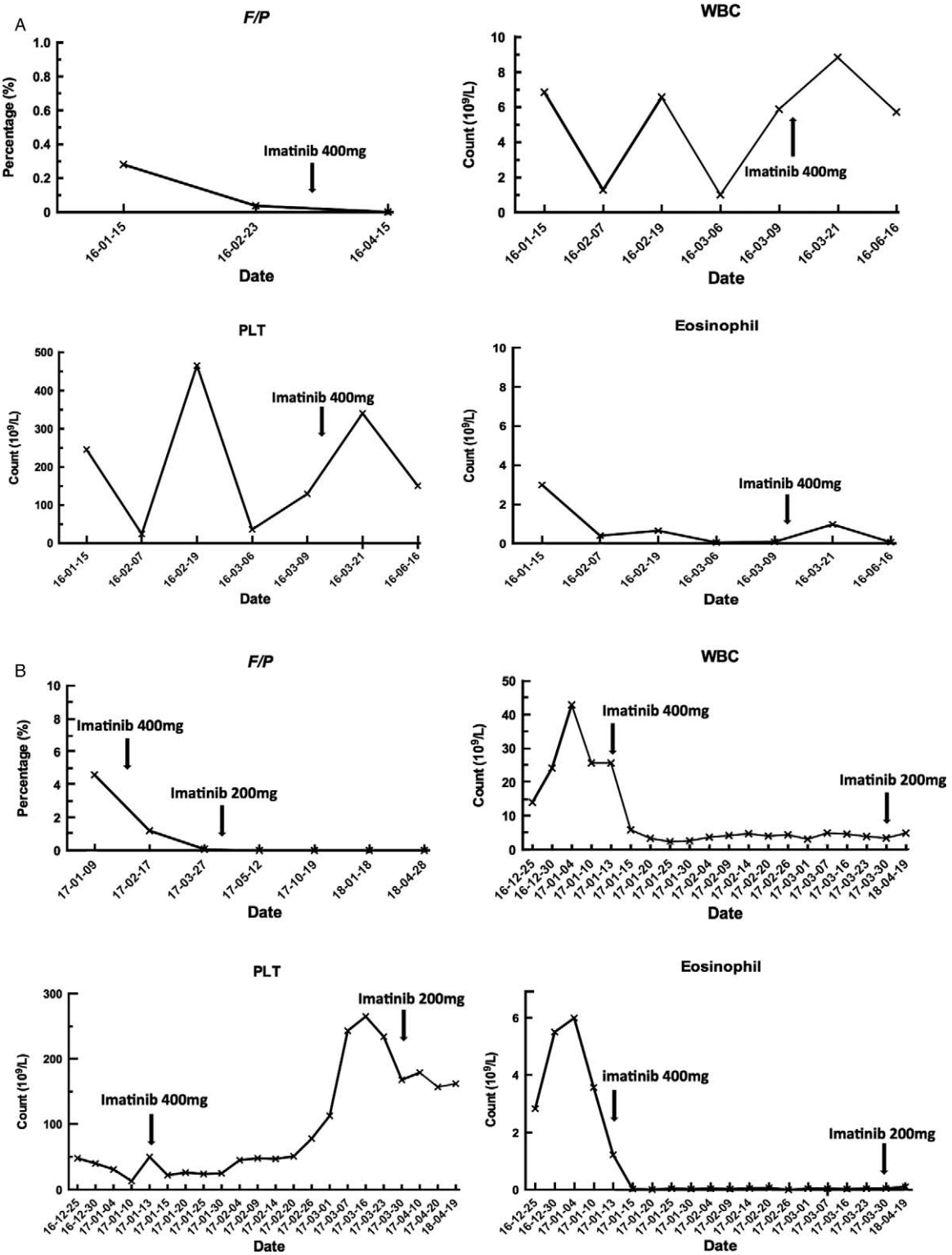

Figure 1: Changes of *F/P* transcripts, counts of WBC, platelet, and eosinophils for the reported patients during treatment. (A) Changes of parameters for Patient 1. (B) Changes of parameters for Patient 2. *F/P*: FIP-1-like-1-platelet-derived growth factor receptor-α; WBC: White blood cell; PLT: Platelet.

myeloid neoplasm with eosinophilia and *F/P* rearrangement was made.

Based on the successful therapy selection for our first patient, no chemotherapy was given and imatinib monotherapy was started instead on January 13, 2017 at a standard dose (400 mg/d). One month after diagnosis, the patient's eosinophils dropped to normal level. A BM test suggested a complete morphologic remission with negative minimal residual disease, as determined by

fluorescence-activated cell sorting. *F/P* transcripts had also lowered to 1.2%. Considering its significant effect, imatinib therapy was continued without addition of chemotherapy. Four months later, *F/P* gene testing was negative, and the patient had achieved CMR [Figure 1B]. This patient is currently being treated with imatinib monotherapy and has remained in CMR at the lower dose of 200 mg/d.

In conclusion, we reported two cases of myeloid neoplasms with *PDGFRA* rearrangement but presenting as AML/myeloid sarcoma and showed their successful response to imatinib, which was consistent with previous reports.[3-5] Due to this being a very rare disease and the heterogeneity of the selected treatment for each patient in literature, a clear conclusion on whether imatinib monotherapy is superior to combination therapy is yet to be determined. Moreover, extended follow-up would be needed for these patients to investigate long-term effect of imatinib monotherapy. Nevertheless, given that *F/P* positive eosinophilia could present as leukemias/sarcomas and that they respond positively to imatinib, screening for *F/P* fusion in leukemic patients with eosinophilia would be beneficial.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

None.

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