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CORRESPONDENCE

Chromosome 12 Rearrangement in an Adolescent with Primary Myelofibrosis

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Dear Editor,

Primary myelofibrosis (PMF) is a Philadelphia negative myeloproliferative neoplasm with bone marrow megakaryocytic and granulocytic proliferation along with fibrosis and extramedullary hematopoiesis. There is a sequential evolution in PMF from a prefibrotic to a fibrotic stage [1].

The patient was a 14 year-old-girl with thrombocytemia and the following complete blood count: white blood cell = 8000/μL, hemoglobin = 10.2 g/dl and platelet = 1,200,000/μL and treatment with anagrilide was started for her. Two year later, she complained of fatigue and abdominal fullness. Imaging workup revealed an enlarged spleen in sonography measuring 166 × 70 mm. Complete blood count showed leukocytosis, anemia and thrombocytopenia with a leucoerythroblastic change in peripheral blood smear (white blood cell = 15,800/μL, hemoglobin = 9 g/dl, platelet = 110,000/μL). Subsequently, she underwent bone marrow biopsy which showed grade 2 reticulin fibrosis along with megakaryocytic and granulocytic proliferation (Fig. 1a, b). Molecular evidence of calreticulin type 1 mutation was detected. Synchronized Bone marrow culture and subsequent giemsa-trypsin banding with a resolution of 350 bands per haploid set revealed an abnormal female chromosomal complement with rearrangement of chromosome 12q13 translocating to chromosomes 6 and 21 (Fig. 1c).

Cytogenetic study of primary myelofibrosis has some limitations such as insufficient bone marrow sampling, especially in fibrotic stage. In spite of these limitations, some studies have evaluated more than 600 cases of PMF including post polycythemia vera myelifobrosis and post essential thrombocythemia myelofibrosis. Prevalence of cytogenetic abnormality is estimated about 30–55% in primary myelofibrosis. The most common cytogenetic aberrations are del(20q), del(13q), trisomy 8, trisomy 9, and abnormalities of chromosome 1q [1].

In a recent comprehensive study, chromosome 12 aberrations were seen in 2% of Philadelphia negative myeloproliferative neoplasms, which were significantly more prevalent among myelofibrosis (86%) compared to other Philadelphia negative myeloproliferative neoplasms (hypereosinophilic syndrome 8%, polycythemia vera 3%, unclassified myeloproliferative neoplasms 3%). The most common aberrations were 12q13 as in the present case, 12q24, trisomy 12 and 12q25 in decreasing order of frequency [2]. There are similar reports in the literature that indicate chromosome 12 abnormalities in Philadelphia negative myeloproliferative neoplasms and its specific abnormalities in primary myelofibrosis [3–5]. It has been proposed that chromosome 12 rearrangement especially at bands 12q13, 12q15 and 12q24 affect NF-E2 transcription factor, HMGA2 and SH2B3 genes respectively and can lead to philadelphia negative myeloproliferative neoplasms [2, 6]. However, role of chromosome 12 structural abnormalities in pathogenesis of Philadelphia negative myeloproliferative neoplasms has not been entirely characterized

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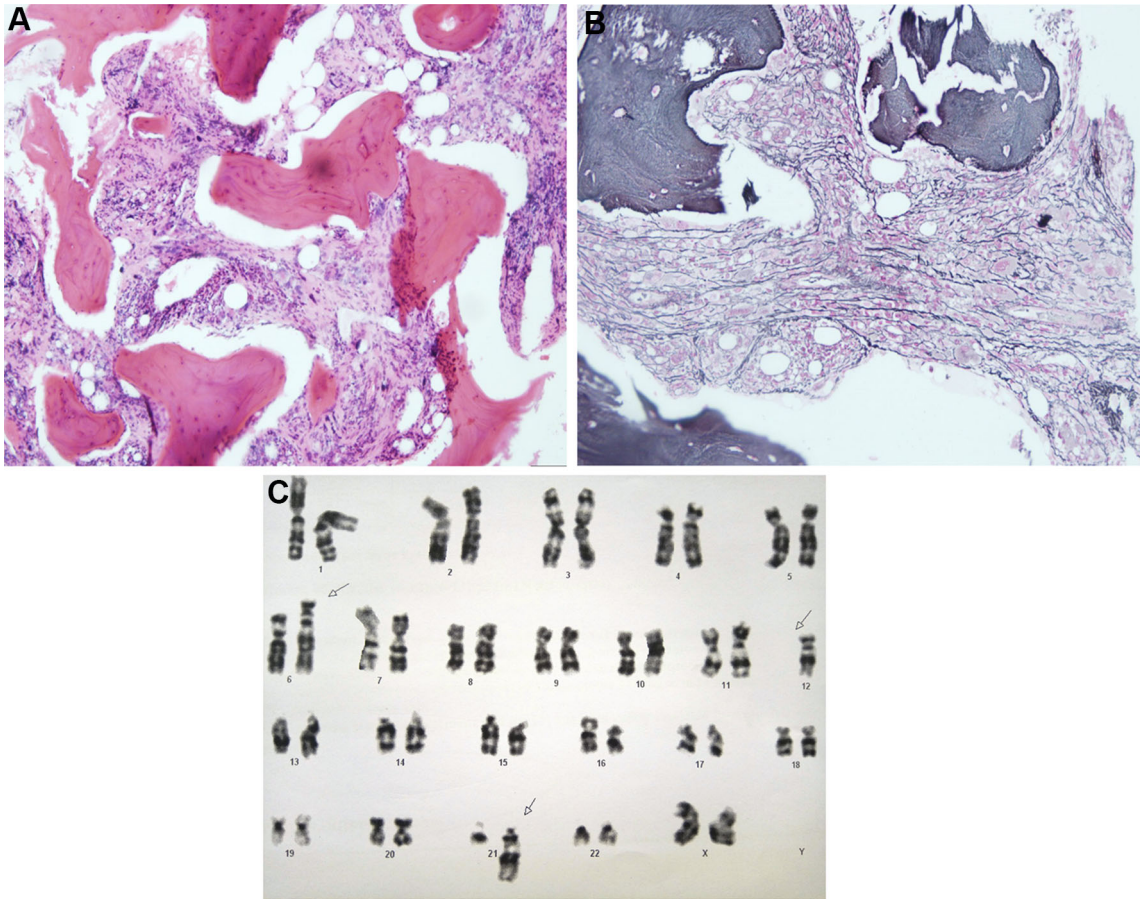

Fig. 1 **a** Bone marrow biopsy showed diffuse myelofibrosis with osteosclerosis (hematoxylin and eosin, magnification × 100). **b** Reticulin stain revealed grade 2 fibrosis in the marrow (magnification × 200). **c** Bone marrow cytogenetic study by giemsa-trypsin banding technique revealed breakage of chromosome 12 at q13 and translocation of the proximal part to short arm of chromosome 6 and the distal end to the chromosome 22

[2]. Some authors believe that chromosome 12q13–15 rearrangements are associated with disease progression in primary myelofibrosis and hematopoietic stem cell transplant should be considered as a therapeutic modality in these patients [6]. In contrary, other authors have not observed the more likelihood of myelofibrosis progression to acute myeloid leukemia in this cytogenetic abnormality [2]. In conclusion, chromosome 12 aberrations merit attention in bone marrow fibrosis and should be considered as a clue for diagnosis of primary myelofibrosis and its prognostic effect remains to be fully clarified in the future.

Compliance with Ethical Standards

Conflict of interest Authors declares that he/she has no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from individual participant included in the study.

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