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LETTER TO EDITOR Open Access

Rare gene fusion rearrangement SPTNB1-PDGFRB in an atypical myeloproliferative neoplasm

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Abstract

The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia recognizes a distinct class of myeloid and lymphoid tumors with eosinophilia-related proliferations associated with specific gene rearrangements, one of which involves rearrangements of platelet-derived growth factor receptor B (PDGFRB) gene. We report a case of a rare PDGFRB rearrangement with SPTNB1 (spectrin beta, nonerythrocytic 1) that presented as atypical myeloproliferative neoplasm.

Keywords: Myeloproliferative neoplasm, PDGFR mutation

Dear Editor,

The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia recognizes a distinct class of myeloid and lymphoid tumors with eosinophilia-related proliferations associated with specific gene rearrangements, one of which involves rearrangements of platelet-derived growth factor receptor B (*PDGFRB*) gene [1]. More than 30 fusion partners of *PDGFRB* gene have been reported [2]. Although uncommon, they are important for diagnosis and treatment [3–8]. We report a case of a rare *PDGFRB* rearrangement with *SPTNB1* (spectrin beta, nonerythrocytic 1) that presented as atypical myeloproliferative neoplasm.

A 76-year-old male presented with progressively worsening of dyspnea on exertion and complete blood count revealed macrocytic anemia (hemoglobin 8.3 mg/dl), monocytosis and lymphopenia. Etiology was not delineated at the time, but subsequently the patient became transfusion dependent. His bone marrow was consistent with myeloproliferative disease with hypercellularity and increased myeloid:erythroid ratio of 5:1 with a prominent granulocytic hyperplasia associated with eosinophilia (24%). Remarkably, peripheral blood (PB) eosinophil counts were normal. *BCR-ABL* rearrangement was not detected by fluorescence in situ hybridization (FISH) of PB.

Cytogenetic analysis of bone marrow revealed 16/20 cells to represent an abnormal clone with a (2;5) translocation: 46,XY,t(2;5)(p21;q33)[16]/46,XY [4] (Fig. 1a). Interphase FISH evaluation for *PDGFRB* rearrangement was performed with a PDGFRB Break Apart probe (Kreatech Diagnostics, Inc./Leica Biosystems, Buffalo Grove, IL) at 5q33; rearrangement was observed in 85/100 nuclei (Fig. 1b). Based on a single previous report of a t(2;5)(p21;q33) that was determined to represent an *SPTBN1/PDGFRB* fusion, FISH was performed to assess possible involvement of *SPTBN1*. Two BAC probes, RP11-378O10 and RP11-564H16 (Empire Genomics, Buffalo, NY) that together span a 310 kb region containing *SPTBN1* (Fig. 1d) were hybridized to both metaphase and interphase cells. Interphase FISH showed rearrangement (splitting) of RP11-5644H16 in 75/100 nuclei; metaphase FISH showed RP11-5644H16 to be split with signal on both the derivative 2 and the derivative 5, and RP11-378O10 to be translocated entirely to the derivative chromosome 5 (Fig. 1c). Thus, the chromosome 2 breakpoint is within the *SPTBN1* gene. To our knowledge, this is only the second report of an *SPTBN1/PDGFRB* rearrangement. Of note, rearrangement of *SPTBN1* with other partner genes also has been reported rarely [9, 10].

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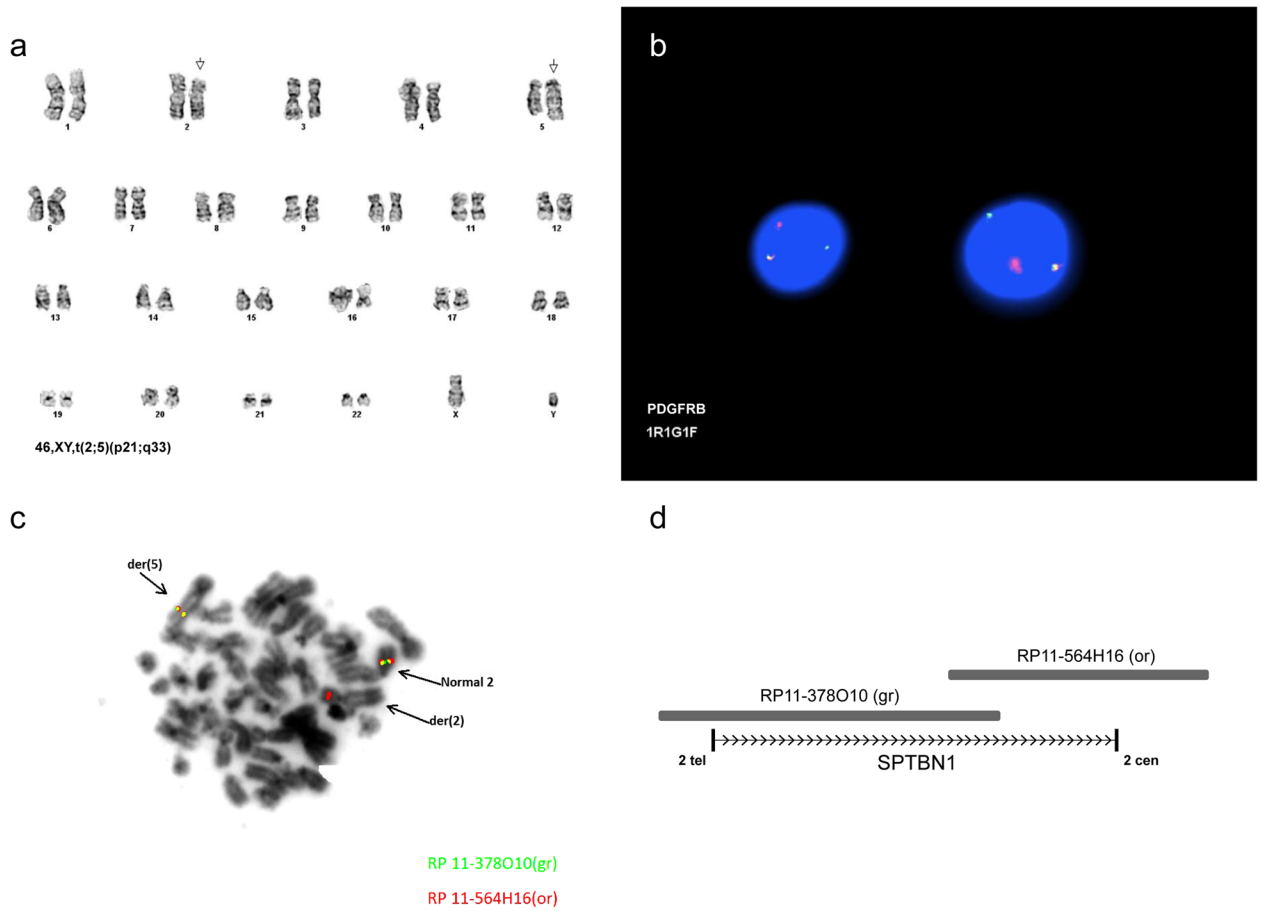

Fig. 1 **a** Karyogram showing translocation t(2;5)(p21;q33). **b** FISH analysis with a *PDGFRB* break-apart probe on interphase nuclei showing one normal intact fusion signal and one split signal (one red, one green) confirming *PDGFRB* gene rearrangement. **c** Metaphase FISH showing RP11-5644H16 to be split with signal on both the derivative 2 and the derivative 5, and RP11-378O10 translocated to the derivative chromosome 5. **d** Map of BAC probes relative to *SPTBN1* gene. Direction of *SPTBN1* transcription is towards the centromere on chromosome 2

Imatinib mesylate 200 mg daily was initiated. After 3 months of therapy, patient achieved complete hematological response and became transfusion independent. His dose of imatinib was tapered to 200 mg weekly in 1 year and patient has remained in hematological remission for more than 3 years. Although imatinib was originally designed as a specific inhibitor of the BCR-ABL tyrosine kinase, it has been shown to be effective toward PDGFRB-associated MPN [3, 4, 6, 7]. Prior study reported 10-year OS of 90% in patients with myeloid malignancies bearing *PDGFRB* fusion genes who were treated with imatinib [4]. Furthermore, achievement of rapid and durable complete cytogenetic and molecular responses on doses lower than 400 mg, suggests that patients with *PDGFRB* rearrangements may be more sensitive to imatinib [4]. Our case report highlights the exquisite sensitivity of *PDGFR* gene fusion rearrangement to imatinib in patients with myeloid malignancies and suggests lower weekly doses of imatinib can be considered in this patient group.

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