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CASE REPORT

# Myeloproliferative neoplasm with eosinophilia and coexisting *BCR::ABL1* and *PDGFRB* rearrangement: favorable and rapid response to imatinib

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**Abstract**

Here, we present a rare case of myeloproliferative neoplasms (MPN) with eosinophilia harboring both *BCR::ABL1* and *PDGFRB* rearrangements, posing a classification dilemma. The patient exhibited clinical and laboratory features suggestive of chronic myeloid leukemia (CML) and myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions (MLN-TK), highlighting the diagnostic challenges associated with overlapping phenotypes. Despite the complexity, imatinib treatment swiftly achieved deep molecular remission, underscoring the therapeutic efficacy of tyrosine kinase inhibitors in such scenarios. Furthermore, the rapid attainment of deep remission by this patient in response to imatinib closely resembles that observed in MLN-TK patients with *PDGFRB* rearrangements. Further research is warranted to elucidate the underlying mechanisms driving the coexistence of multiple oncogenic rearrangements in MPNs and to optimize therapeutic strategies for these complex cases.

**Keywords** BCR:ABL1 · CML · MLN-TK · PDGFRB · MPN

## Case presentation

A 20-year-old male patient presented with a two-week history of abdominal pain, accompanied by fever, abdominal distention, a significantly enlarged spleen (approximately 6.5 cm below the umbilicus), and tenderness in the left upper abdomen upon admission. The blood routine showed leukocytes at 379×10^9/L, eosinophils at 18.77×10^9/L, hemoglobin at 78 g/L, and platelets at 541×10^9/L. Upon further examination, reverse transcription-polymerase chain reaction (RT-PCR) identified positive results for *BCR::ABL1* (P210, IS quantification 86.34%), while the *JAK2-V617F* mutation tested negative. The results of bone marrow (BM) morphology revealed a remarkably active proliferation of nucleated cells, with a predominant population of myelocytes and metamyelocytes exhibiting intense proliferation and displaying normal morphology. Additionally, there was an observed increase in eosinophils and basophils. Furthermore, the evaluation of the peripheral blood smear displayed a significant elevation in white blood cells, primarily characterized by a left shift in the population of mature neutrophils. The BM biopsy morphology reveals an active proliferation of nucleated cells, with an increase in the granulocytic lineage (Fig. 1A). Chromosome results showed clonal chromosome abnormalities: 46, XY, t(5; 12) (q33; q24.1), t(9:22)(q34.1; q11.2)[20] (Fig. 1B). These results suggest the coexistence of *BCR::ABL1* and *GIT2::PDGFRB*. The patient was diagnosed with the chronic phase of chronic myelogenous leukemia (CML-CP) at a local hospital and was treated with 400 mg of imatinib orally daily.

His symptoms gradually improved and he was discharged to continue oral therapy with imatinib 400 mg daily. Four months later, a follow-up examination revealed a normal blood count, a karyotype of 46,XY [18]/46,XY, t(9:22)(q34.1;q11.2)[2] (Fig. 1C), and a decrease in BCR::ABL1^IS copies to 5.3% in the BM. The patient came to our hospital for reexamination 10 months after diagnosis, showing that the copies of *BCR::ABL1* had decreased to MMR

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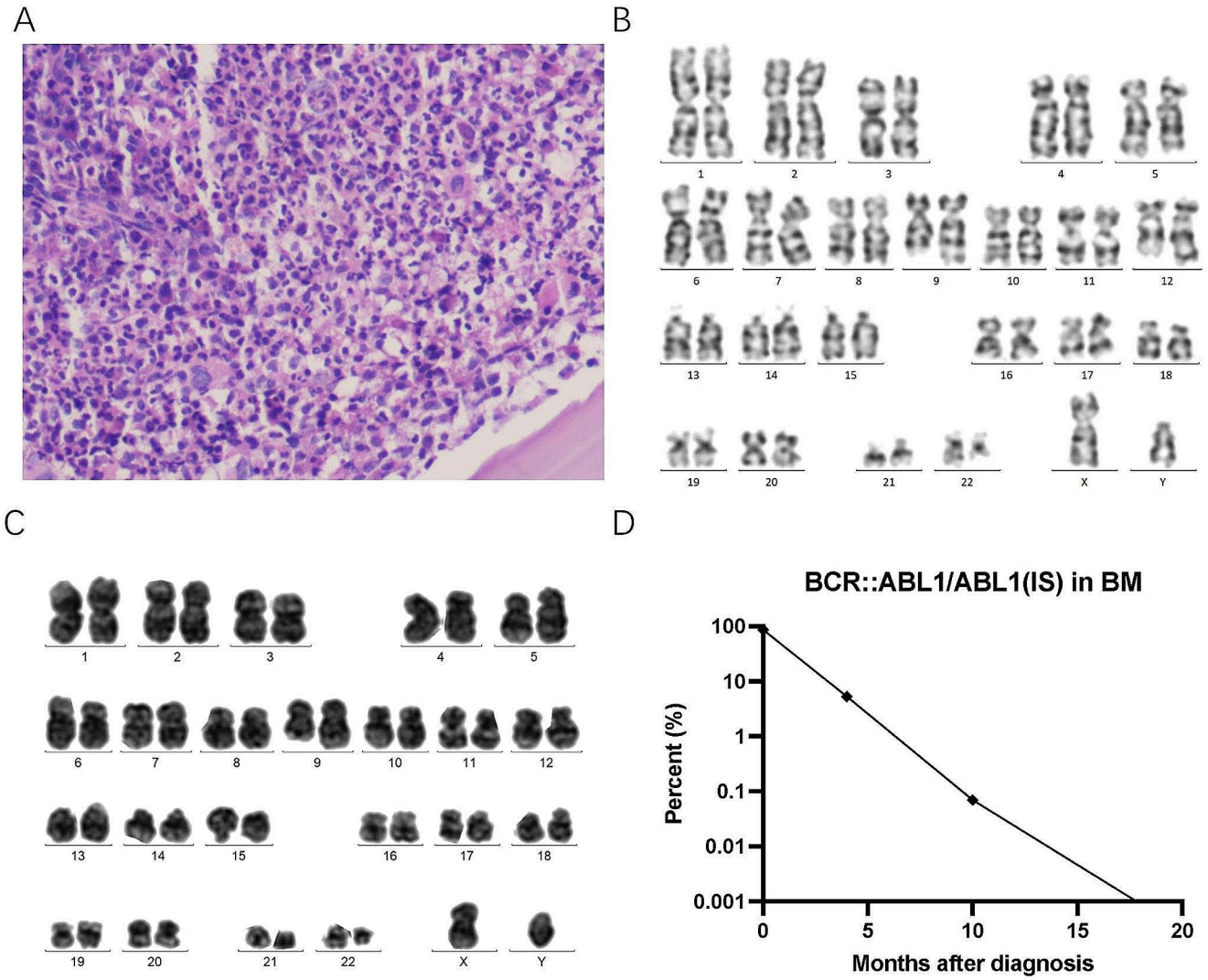


**Fig. 1** Morphologic, cytogenetic, and molecular findings in a patient with myeloid proliferative neoplasm with coexisting *BCR::ABL1* and *PDGFRB* rearrangement. (**A**) The bone marrow biopsy morphology reveals an active proliferation of nucleated cells, with an increase in the granulocytic lineage. The cells predominantly observed are in a more mature stage of development, with a sparse presence of less mature, immature cells. (**B**) G-banded bone marrow karyogram at diagnosis showing 46, XY, t(5; 12) (q33; q24.1), t(9:22)(q34.1; q11.2)[20]. (**C**) G-banded bone marrow karyogram at 4 months post-treatment showing 46,XY [18]/46,XY, t(9:22)(q34.1; q11.2)[2]. (**D**) Quantification of the BCR::ABL1 trend in bone marrow by reverse transcription-polymerase chain reaction

(*BCR::ABL1*^IS level of 0.0704%) and normal karyotype in the BM. He achieved *BCR::ABL1* MR5 (BCR::ABL1^IS level less than 0.001%) 18 months after diagnosis. The trend graph illustrating quantify of *BCR::ABL1* is presented in Fig. 1D.

## Discussion

This is a rare case in which *BCR::ABL1* and *PDGFRB* rearrangement coexist in a patient with MPN. Despite the identification of an additional chromosomal abnormalities (ACA), 5q33, in Philadelphia chromosome-positive cells at the initial diagnosis, the patient remains in the CML-CP, as the findings do not meet the diagnostic criteria for CML-AP [1]. A myeloid or lymphoid neoplasm, often with prominent eosinophilia and sometimes with neutrophilia or monocytosis, combined *PDGFRB* rearrangement should be diagnosed as myeloid/lymphoid neoplasms associated with rearrangement of *PDGFRB* [2]. The diagnosis was updated to myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions (MLN-TK) in the 5th edition of the WHO classification. MLN-TK may present as chronic myeloproliferative tumors, but the frequency of presentation as lymphoid tumors or acute myeloid leukemia varies [3]. For MLN-TK with *PDGFRB* rearrangement, usually there is t(5; 12)(q32; p13.2) with the formation of an *ETV6::PDGFRB* fusion gene. In uncommon variants,

other translocations with a 5q31-33 breakpoint led to the formation of other fusion genes, such as *GIT2::PDGFRB* [4]. In the setting of *PDGFRB*-related disease, the characteristics are more variable, which can manifest as chronic myelomonocytic leukemia, atypical chronic myeloid leukemia, or MPN, often accompanied by eosinophilia, or manifest as chronic eosinophilic leukemia [3]. So far, there have been no reports of CML associated with other clonal chromosomal abnormalities such as *PDGFRA*, *PDGFRB*, *FGFR1*, or *PCM1-JAK2* [5]. Meanwhile, no MLN-TK has manifested as *BCR::ABL1*-positive MPN.

For the first time, we present a case of an eosinophilia-associated MPN patient with coexisting *BCR::ABL1* and *PDGFRB* rearrangements, along with neutrophilia and splenomegaly, who exhibited an excellent response to daily imatinib at 400 mg. This patient meets the diagnostic criteria for both CML and MLN-TK, indicating the uniqueness of this case and warranting further investigation. It is believed that both CML and MLN-TK originate from abnormal pluripotent stem cells. In this particular case, the origins of the two genetic abnormality clones remain unknow. There are two possible explanations: the first involves CML associated with ACA, while the second entails a distinct entity characterized by concurrent *BCR::ABL1* and *PDGFRB* rearrangements.

We are inclined to believe that this patient represents a coexistence of *BCR::ABL1* and *PDGFRB* rearrangements. Firstly, at the initial diagnosis, all metaphases of the patient exhibited Philadelphia chromosome-positive cells combined with a translocation involving 5q33, which suggests a pre-existing condition rather than an acquired one post-treatment. Secondly, the patient's response to imatinib closely mirrors that of MLN-TK patients with *PDGFRB* rearrangements rather than CML. Notably, the patient achieved a profound molecular response (MR5) within just 18 months, a notably rapid progression. The 12-year incidences of achieving molecular responses MR4.5 and MR5 are reported as 72% and 54% in patients with CML, respectively [6]. Conversely, in patients with myeloid/lymphoid neoplasms with eosinophilia and *PDGFRB* rearrangements in the chronic phase receiving imatinib therapy, all patients achieved complete hematologic remission within a median of 2 months. Additionally, complete cytogenetic and/or molecular remissions were achieved in 92% and 86% of cases, respectively, over median durations of 10 and 19 months [7]. It is evident that compared to CML, patients with myeloid/lymphoid neoplasms with eosinophilia and *PDGFRB* rearrangements achieve a faster attainment of deep molecular remission when treated with imatinib. The patient's response pattern to imatinib closely resembles that of myeloid/lymphoid neoplasms featuring eosinophilia and *PDGFRB* rearrangements. Moreover, subsequent chromosomal metaphases during treatment showed disappearance of the 5q33 translocation preceding the Philadelphia chromosome, potentially indicating greater sensitivity of the *PDGFRB* rearrangement to imatinib.

Regrettably, the patient did not undergo testing for *PDGFRB* rearrangement via fluorescence in situ hybridization (FISH) or GIT2-*PDGFRB* by RT-PCR during the initial diagnosis at a regional hospital. This lack of diagnostic findings hindered our ability to provide direct evidence of *PDGFRB* fusion and left us with only a strong suspicion. However, considering the patient's rapid molecular response to imatinib, it lends support to the presence of a concomitant *PDGFRB* rearrangement.

In summary, our report underscores a rare and distinctive case of MPN with both *BCR::ABL1* and *PDGFRB* rearrangements, achieving rapid and profound remission following imatinib treatment. While further research is needed to confirm this, we lean towards considering it a unique subtype simultaneously harboring both *BCR::ABL1* and *PDGFRB* rearrangements, rather than classical CML with ACA.

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**Data availability** No datasets were generated or analysed during the current study.

## Declarations

**Competing interests** The authors declare no competing interests.

**Ethical approval** Written informed consent was obtained from the patient for the publication of any potentially identifiable data included in this article.

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