Successful treatment of a chronic myeloid leukemia patient with extreme thrombocytosis by a combination of imatinib and interferon-α: A case report

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Received September 22, 2024; Accepted January 2, 2025

DOI: 10.3892/etm.2025.12800

Abstract. Chronic myeloid leukemia with extreme thrombocytosis (CML-T), defined by a platelet count >1,000x10^9/l is a rare leukemia subtype. The present case report described a 66-year-old female CML-T patient presenting with a platelet count of 3,798x10^9/l, but a consistently normal spleen size. Following treatment with imatinib combined with interferon-α, the patient achieved hematological remission within 2 months, with a platelet count reduction to 311x10^9/l and complete cytogenetic remission after 10 months. The patient experienced myocardial infarction and liver injury during treatment, which was managed with supportive care. The present case suggested that imatinib combined with interferon-α may be a safe and effective treatment option for patients with CML-T and extreme thrombocytosis and suboptimal response to imatinib monotherapy.

Introduction

Chronic myeloid leukemia (CML), a clonal myeloproliferative neoplasm arising from pluripotent hematopoietic stem cells, is characterized by the Philadelphia chromosome and the resulting BCR-ABL1 fusion gene (1,2). This genetic abnormality leads to the production of a constitutively active tyrosine kinase, which drives the pathogenesis of CML (3,4). While CML typically follows a predictable course through chronic, accelerated and blast crisis phases, its clinical presentation may be heterogeneous. A subset of patients with CML present with marked thrombocytosis and when the platelet count reaches or exceeds 1,000x10^9/l, the condition is defined as CML with thrombocytosis (CML-T). This marked thrombocytosis significantly increases the risk of thromboembolic events, making CML-T a clinically challenging subtype of CML (5-7). Distinguishing CML-T from other myeloproliferative neoplasms, particularly essential thrombocythemia (ET), which is also characterized by elevated platelet counts (≥450x10^9/l), is paramount for accurate diagnosis and treatment (8). Although early clinical presentations can be similar, the underlying genetic abnormalities and therapeutic approaches differ. Management of ET primarily focuses on symptom control with agents like aspirin, hydroxyurea, anagrelide, or interferon-α (IFN-α), but these treatments are generally not curative (9). By contrast, CML-T, like other forms of CML, relies on tyrosine kinase inhibitors (TKIs), such as imatinib, to target the BCR-ABL1 fusion protein and control disease progression (10). Combining imatinib with IFN-α has shown synergistic potential in CML, potentially leading to improved outcomes (11,12). However, there is no established standard of care for CML-T, especially in cases with extreme thrombocytosis, and the optimal treatment strategy remains to be defined and warrants further study. The present report described a patient with CML-T presenting with an exceptionally high platelet count of 3,798x10^9/l and the unusual finding of normal spleen size, posing a significant diagnostic challenge. The patient's successful treatment with imatinib and interferon-α, resulting in complete hematological and cytogenetic remission, highlights the potential of this combination therapy in managing this rare and complex clinical entity. The present case underscored the need for further research into the efficacy and safety of combination therapy in CML-T, particularly in cases with extreme thrombocytosis.

Case presentation

Patient information. A 66-year-old female patient was admitted to Shandong Second Medical University (Weifang, China) in August 2023 with recurrent chest tightness and pain. The patient's medical history was notable for hypertension, diabetes mellitus and coronary artery disease for 20 years. The family history was noncontributory for thrombocytosis or other hematologic malignancies. The present case report was approved by the Medical Ethics Committee of the Affiliated

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Key words: chronic myeloid leukemia with thrombocytosis, imatinib, interferon-α, thrombocytosis

Hospital of Shandong Second Medical University (approval no. wyfy-2024-qt-051; date of approval: September 18, 2024; Weifang, China).

Diagnosis. On presentation, the patient's platelet count was markedly elevated at 3,798x10^9/l (normal range:150-450x10^9/l). Peripheral blood smear analysis revealed 5% blasts. Bone marrow aspiration and biopsy were performed as part of the diagnostic workup. Peripheral blood and bone marrow aspirate smears were collected before treatment and stained with Wright-Giemsa stain for 1 min at room temperature, followed by staining with a buffer solution for ~15 min at room temperature. The slides were then examined microscopically at 1,000x magnification. The bone marrow biopsy sample was fixed in 4% neutral buffered formalin at room temperature for at least 6 h, underwent gradient ethanol dehydration, xylene clearing and paraffin embedding following standard protocols, was sectioned at 3 μm thickness and stained with hematoxylin and eosin at room temperature for 3 min each. Microscopic evaluation was performed at x40 and x400 magnification. Results showed hypercellularity with myeloid predominance, marked megakaryocytic hyperplasia and prominent platelet aggregation (Fig. 1), as well as a markedly cellular marrow with an increased myeloid-to-erythroid ratio and a significant increase in predominantly small megakaryocytes on biopsy (Fig. 2). The cytogenetic analysis identified the Philadelphia chromosome t (9;22) (q34;q11.2; Fig. 3). Reverse transcription-quantitative PCR (RT-qPCR) was performed to detect the BCR-ABL1 p210 transcript, with an expression level of 70.78% on the International Scale (IS) (Fig. 4). RNA was extracted from 1x10^6 cells using the Lab-Aid 896 Blood Total RNA Extraction Kit (Xiamen Zeesan Biotech Co., Ltd.). RNA purity and concentration were assessed using a Thermo Scientific NanoDrop 2000 Spectrophotometer (Thermo Fisher Scientific, Inc.). cDNA synthesis was performed, and qPCR was carried out using TaqMan Gene Expression Master Mix (Applied Biosystems; Thermo Fisher Scientific, Inc.) in a 20 μl reaction volume. The forward primer sequences for BCR-ABL1 p210 were 5'-TCCGCTGACCATCAACAAGGA-3' and 5'-TCCGCTGACCATCAATAAGGA-3', and the reverse primer sequence was 5'-CACTCAGACCCTGAGGCTCAA-3'. ABL1 served as the reference gene with the following primer sequences: Forward 5'-TGGAGATAACACTCTAAGCATAACTAAAGGT-3' and reverse 5'-GATGTAGTTGCTTGGGACCCA-3'. PCR cycling conditions were: 50˚C for 20 min, 95˚C for 10 min, followed by 40 cycles of 95˚C for 15 sec and 60˚C for 60 sec. Quantification was performed using the standard curve method. Experiments were performed with three biological replicates, each in triplicate (technical replicates). To exclude ET, targeted sequencing was performed to screen for mutations within CALR (exon 9), JAK2 (exons 12,14, and 16), MPL (exon 10), and CSF3R (exons 14 and 17), which represent the most frequent mutational hotspots in myeloproliferative neoplasms, and no mutations were detected in this analysis.

Echocardiography demonstrated left ventricular hypertrophy and a reduced left ejection fraction, with an LVEF of 55% (normal range, 50-70%) and an electrocardiogram showed ST-T segment changes and T-wave inversion. All cardiac enzymes were within normal limits except for an elevated NT-proBNP level of 2,914.34 pg/ml (normal <125 pg/ml). Chest and abdominal computed tomography scans showed no evidence of pulmonary embolism or hepatosplenomegaly. Liver and kidney function tests and lipid profile were within normal limits. Based on these findings, the patient was diagnosed with extreme CML-T complicated by acute myocardial infarction.

Treatment and outcomes. At the initiation of treatment, the patient's platelet count was markedly elevated at 3,798x10^9/l, along with a white blood cell count of 38.75x10^9/l and a hemoglobin level of 117 g/l. Imatinib was initiated at 400 mg once daily. Imatinib therapy promptly normalized the leukocyte count; however, the reduction in platelet count was less pronounced. To mitigate the risk of thrombosis due to extreme thrombocytosis, the patient received seven sessions of therapeutic plateletpheresis. Despite these interventions, the platelet count remained at 1,356x10^9/l on day 10. After 10 days of imatinib monotherapy, the patient experienced episodes of chest tightness, shortness of breath and angina. Electrocardiography findings were consistent with acute subendocardial myocardial infarction. At the time of these cardiac events, the patient's platelet count was still markedly elevated at 1,356x10^9/l, suggesting a potential correlation between the extreme thrombocytosis and the myocardial infarction. Following treatment with aspirin, ticagrelor, isosorbide mononitrate and rosuvastatin, the patient's symptoms subsequently improved. Subsequent BCR-ABL1 kinase domain mutation analysis revealed no DNA or amino acid mutations, excluding imatinib resistance. Given the inadequate response of thrombocytosis to imatinib monotherapy, IFN-α was initiated on day 11 at a dose of 30 μg once daily via subcutaneous injection and this combination therapy led to a more rapid reduction in platelet count. After 20 days, the patient's clinical symptoms improved and discharge to home treatment followed. At discharge, the white blood cell count was 5.44 x10^9/l, hemoglobin was 106 g/l and platelet count was 752x10^9/l. which, although markedly reduced, remained above the threshold for complete remission. Notably, the patient experienced episodes of chest tightness, shortness of breath and angina during treatment. Electrocardiography findings were consistent with acute subendocardial myocardial infarction. These symptoms resolved following anticoagulant and antiplatelet therapy. The patient also experienced mild adverse events, including hypocalcemia, liver injury, fever and dizziness, all of which were managed with supportive care. Following discharge, the patient continued treatment with oral imatinib 400 mg once daily. The IFN-α regimen was adjusted to 30 μg twice weekly via subcutaneous injection. After one month of this adjusted combination therapy, a follow-up complete blood count revealed further hematologic improvement, with a white blood cell count of 5.21x10^9/l, hemoglobin of 112 g/l and platelet count of 311x10^9/l (Fig. 5). Complete hematological response (CHR) was confirmed by peripheral blood and bone marrow examination, with findings demonstrating normal white blood cell, platelet, and absolute neutrophil counts, absence of blasts and immature myeloid cells in peripheral blood, normocellular bone marrow with normal maturation, and <5% blasts. IFN-α was then discontinued and the patient continued on imatinib monotherapy

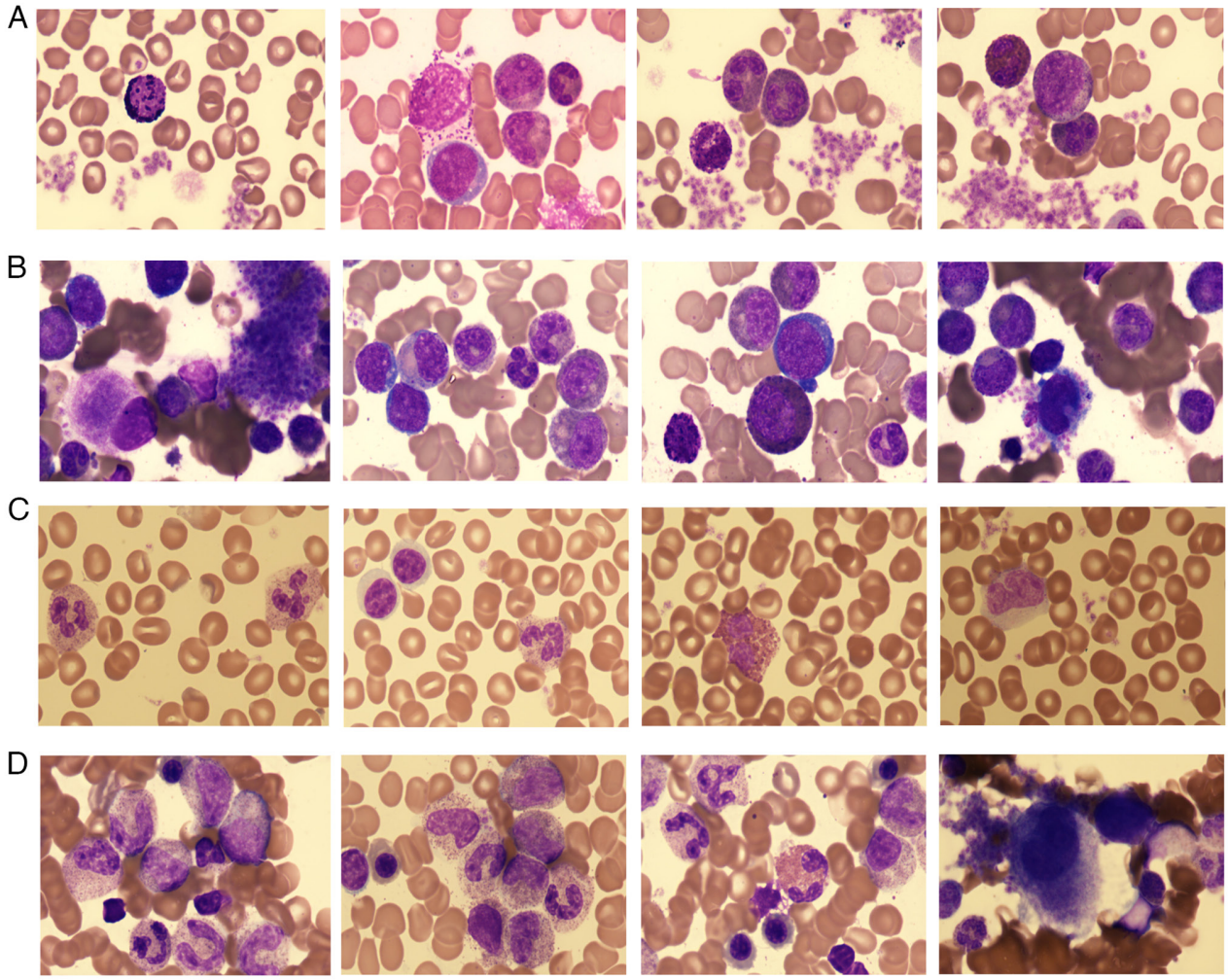

Figure 1. Peripheral blood and bone marrow smears. (A) Bone marrow aspirate before treatment: Hypercellular bone marrow with prominent granulocytic hyperplasia. Blasts and various stages of granulocytic maturation are observed. Eosinophils and basophils are readily identifiable. Megakaryocytes are significantly increased, with a predominance of small megakaryocytes. Platelets are seen in aggregates and sheets. (B) Peripheral blood smear before treatment: Leukocytosis is evident. Blasts and various stages of granulocytic maturation are observed. Eosinophils and basophils are readily identifiable. Platelet clumping is frequently observed. (C) Bone marrow aspirate after treatment: Cellular bone marrow with normal myeloid-to-erythroid ratios. Myelocytes and later stages of granulocytic maturation are observed. Megakaryocytes appear normal and platelets are dispersed with occasional small clusters. (D) Peripheral blood smear after treatment: White blood cell count is normal. Mature granulocytes, lymphocytes and monocytes are observed. Platelets are dispersed with occasional small clusters. (Magnification, x1,000, Wright-Giemsa stain).

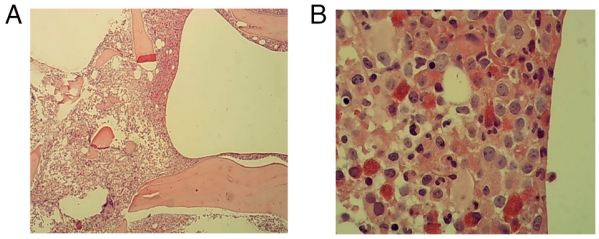

Figure 2. Bone marrow biopsy. (A) The bone marrow is markedly cellular with an increased myeloid-to-erythroid ratio. Myeloid cells are present at various stages of maturation, with a slight increase in immature forms. Eosinophils are readily observed. Erythroid precursors are predominantly late erythroblasts (magnification, x40; H&E stain). (B) Megakaryocytes are significantly increased, predominantly small megakaryocytes with fewer nuclear lobes. Scattered lymphocytes and plasma cells are observed (magnification, x400; H&E stain). H&E, hematoxylin and eosin.

400 mg once daily. After 10 months, cytogenetic analysis showed no detectable Philadelphia chromosome, indicating complete cytogenetic remission (CCyR). Since diagnosis in August 2023, the patient has received seven BCR-ABL1 fusion gene transcript level assessments, demonstrating a progressive reduction in transcript levels. The most recent evaluation in June 2024 revealed a BCR-ABL1 transcript level of 0.14% IS, approaching major molecular remission (MMR), defined as a BCR-ABL1 transcript level less than 0.1%. It is worth noting that imaging studies consistently showed a normal spleen size throughout the treatment course.

Follow-up and outcome. As of the most recent follow-up in September 2024, the patient remains on imatinib therapy and is stable, with no evidence of disease relapse. The patient's blood counts have remained within the normal range (Fig. 6).

Discussion

CML-T is a rare subtype of CML, defined by platelet counts that typically reach or exceed $1,000x10^9$/l. Although no

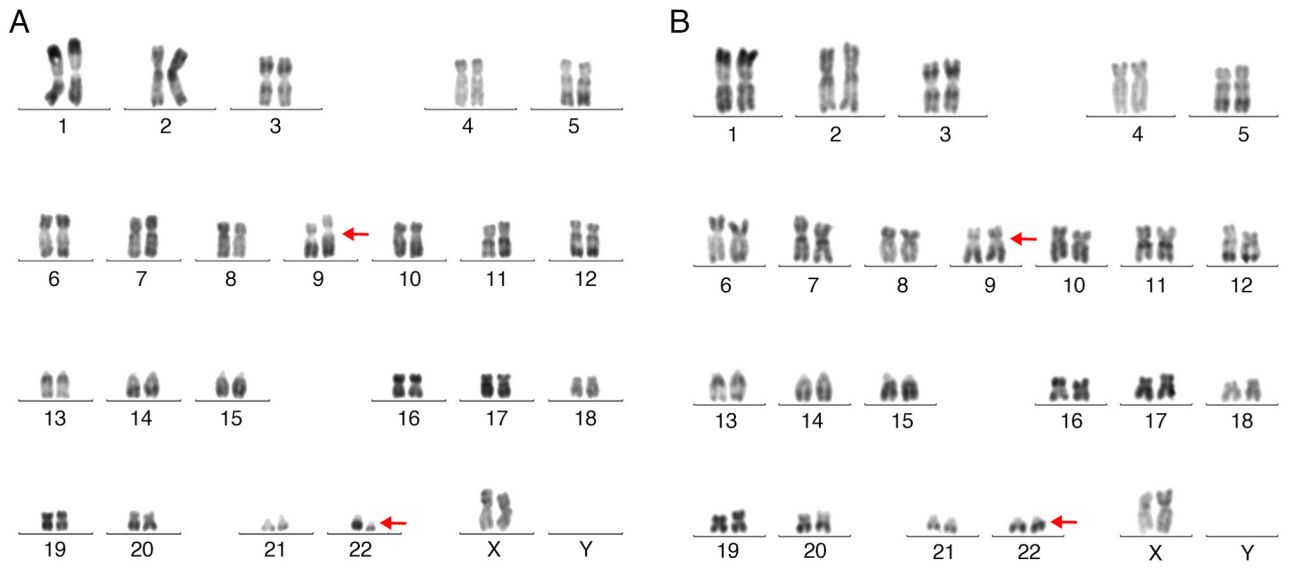

Figure 3. Cytogenetic analysis. (A) Pre-treatment karyotype showing the typical Ph+ translocation t(9;22) (q34.1;q11.2), with red arrows indicating chromosomes 9 and 22 involved in the translocation. (B) Post-treatment karyotype, no Philadelphia chromosome detected, achieving complete cytogenetic response, with red arrows indicating the normal chromosomes 9 and 22.

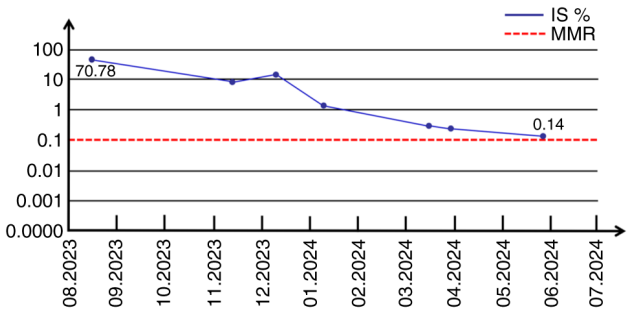

Figure 4. BCR-ABL1 fusion gene transcript level (IS%) trend. The patient received 7 BCR-ABL1 fusion gene transcript level tests, with an initial value of 70.78%. The transcript level gradually decreased with treatment, reaching 0.14% in June 2024, approaching the MMR criteria (IS% ≤0.1%). MMR, major molecular response; IS, International Scale.

standardized treatment for CML-T is currently available, previous studies have demonstrated a favorable response to imatinib therapy (10,13). Given the distinct therapeutic approaches required, differentiating CML-T from ET is crucial for treatment decision-making. The diagnosis of ET is primarily established by elevated platelet counts, increased bone marrow megakaryocytes and the presence of CALR, JAK2, MPL, or CSF3R mutations (14,15). By contrast, the presence of the Philadelphia chromosome or BCR-ABL rearrangement with isolated thrombocytosis should be diagnosed as CML, not ET, according to the World Health Organization diagnostic criteria (16). The patient presented with a platelet count of $3,798x10^9$/l, significantly higher than previously reported levels. This highlighted the rarity of CML-T and the challenges associated with its diagnosis, suggesting a potential unique mechanism underlying thrombocytosis in this patient. Notably, despite the extreme thrombocytosis, the patient's spleen size remained normal, adding to the diagnostic complexity. Although splenomegaly is a typical feature in most patients with CML, this patient consistently lacked splenomegaly throughout the disease course. Previous literature has documented cases of CML with concomitant myelofibrosis or thrombocytosis without splenomegaly (17,18). Additionally, research suggests that ~40% of patients with CML are asymptomatic in the early stages of the disease, with diagnosis often relying solely on laboratory abnormalities. Furthermore, the clinical presentation of CML can vary across different geographical regions (19,20). These findings highlight that factors such as the stage of CML and individual patient variability can influence the presence or absence of splenomegaly. The diagnosis and assessment of CML necessitate a comprehensive evaluation incorporating a multi-faceted approach rather than relying solely on spleen size.

Significant thrombocytosis, a hallmark of CML-T, is associated with increased blood viscosity, promoting thrombosis and elevating the risk of thromboembolic events (21). The patient experienced recurrent angina during treatment, potentially attributable to thrombosis secondary to extreme thrombocytosis. The mechanisms underlying the profound thrombocytosis observed in CML-T remain incompletely understood. The patient's extreme thrombocytosis and high BCR-ABL1 p210 fusion gene expression level (IS: 70.78%) suggested a potential role for BCR-ABL1 overexpression, and previous research has demonstrated a correlation between the BCR-ABL1 fusion gene and elevated platelet counts in CML (22). However, the precise mechanisms by which BCR-ABL1 directly influences megakaryocyte differentiation and platelet production remain unclear and warrant further investigation. BCR-ABL1 overexpression is hypothesized to disrupt normal megakaryocyte development, leading to excessive platelet production. Imatinib, a targeted BCR-ABL1 tyrosine kinase inhibitor, restores megakaryocyte function and reduces platelet counts in CML (23,24). BCR-ABL1p210, the most prevalent variant in CML, is associated with thrombocytosis, disease progression and adverse prognosis, as well as response to IFN-α and imatinib therapy (25-32). Other BCR-ABL1 variants, such as p185, p190 and p230, have also

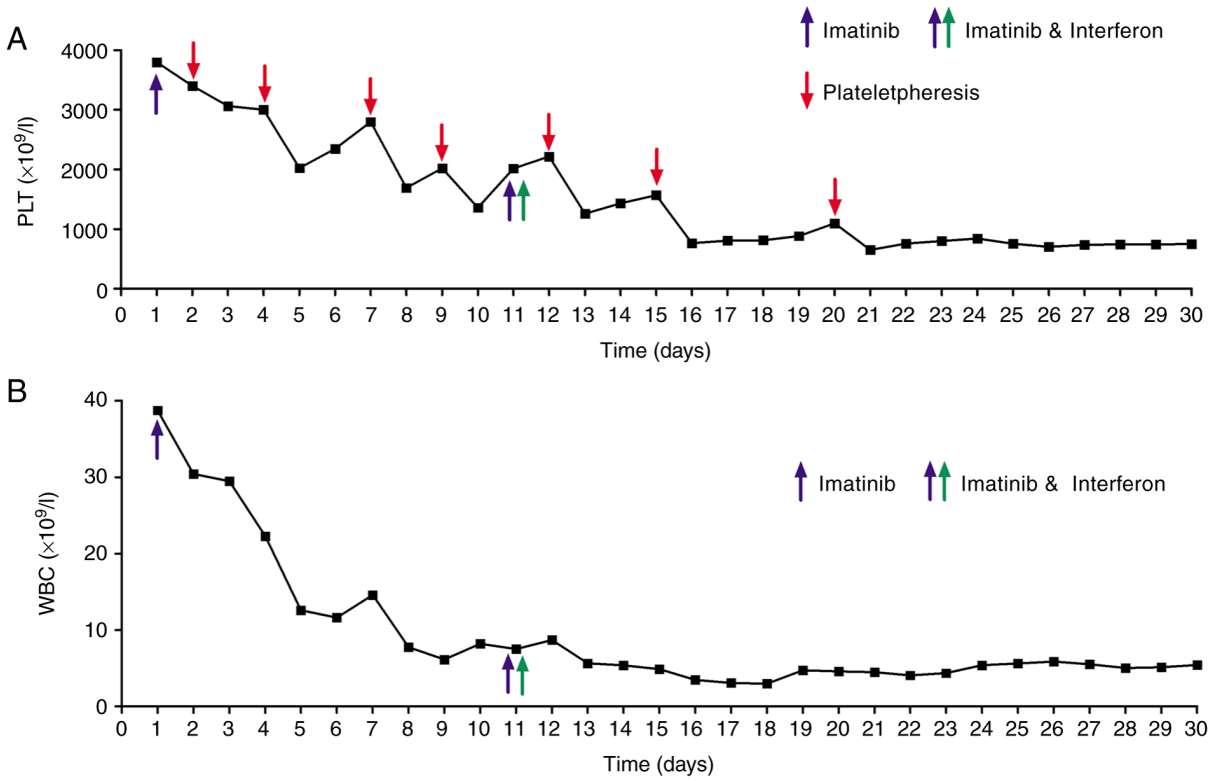

Figure 5. Changes of white blood cell and platelet count during the treatment. (A) Platelet count gradually decreased following imatinib therapy (blue arrow indicates the start of imatinib monotherapy), with plateletpheresis (red arrows indicate the time points of plateletpheresis) performed on days 2, 4, 7, 9, 12, 15 and 20. The addition of interferon-α (green arrow indicates the start of combined imatinib and interferon-α therapy) on day 11 further accelerated the decline. By day 30, platelet count had significantly decreased but remained elevated. (B) White blood cell count, initially elevated, rapidly decreased after imatinib therapy and remained within the normal range throughout treatment.

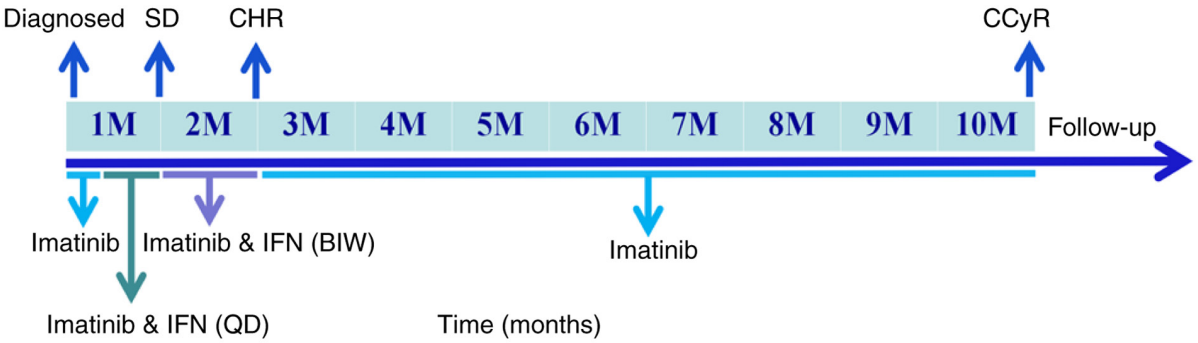

Figure 6. Clinical timeline. The patient received 10 days of imatinib monotherapy, followed by 20 days combined with daily IFN-α (QD) until symptom resolution and discharge. After discharge, treatment continued with imatinib combined with twice-weekly IFN-α (BIW) for one month, achieving a CHR. IFN-α was then discontinued and imatinib monotherapy was continued for 8 months, resulting in a CCyR. The final BCR-ABL1 level reached 0.14%, approaching MMR and the patient remains under follow-up. CHR, complete hematological response; CCyR, complete cytogenetic response; MMR, major molecular response; SD, stable disease.

been implicated in lymphoid progenitor cell transformation and thrombocytosis in CML. Furthermore, these variants also contribute to favorable outcomes, including complete remission and improved long-term survival, in patients with Philadelphia chromosome-positive acute lymphoblastic leukemia (33-40) (Table I). Furthermore, two major BCR-ABL1 mRNA transcript types exist, e14a2 and e13a2, with e14a2 associated with higher platelet counts and e13a2 with higher white blood cell counts (41). BCR-ABL1 transcript typing was not performed in this case and future research should explore the relationship between BCR-ABL1 transcript type and thrombocytosis in CML-T. Furthermore, the pathogenesis of thrombocytosis in CML-T may involve additional molecular mechanisms beyond BCR-ABL1. Mutations in genes such as MPL, THPO and JAK2, as well as dysregulated expression of thrombopoietin, IL-6 and other inflammatory mediators, have been implicated in driving platelet production in various thrombocytosis contexts, a finding that warrants further investigation (14,42-45).

Imatinib, the first-generation BCR-ABL1 TKI approved by the US Food and Drug Administration, significantly improves CML treatment by competitively binding to the BCR-ABL1

Table I. Roles of different BCR-ABL variants in leukemia.

First author, year	Cancer type	BCR-ABL variants	Clinical significance	(Refs.)
Ten Bosch *et al*, 1998	CML	BCR-ABLp210	Promotes thrombopoiesis through CrkL phosphorylation	(25)
Bennour *et al*, 2013	CML	BCR-ABLp210	Correlated with platelet counts in patients with CML	(26)
Arana-Trejo *et al*, 2002	CML	BCR-ABLp210/p 190/p230	Associated with platelet counts, splenomegaly and chromosomal abnormalities	(27)
Polampalli *et al*, 2008	CML	BCR-ABLp210	Associated with myeloid blast crisis in patients with CML	(28)
Al-Achkar *et al*, 2016	CML	BCR-ABLp210	Associated with prognosis in patients with CML	(29)
Pane *et al*, 1999	CML	BCR/ABLp 210	Affecting the responsiveness of patients with CML to IFN-α	(30)
Zhao *et al*, 2015	CML	BCR/ABLp 190/p210	Participation in imatinib resistance through ABL kinase domain mutations	(31)
Zhang *et al*, 2022	CML	BCR-ABLp210	Associated with thrombocytosis in patients with CML	(32)
Puil *et al*, 1994	CML	BCR-ABLp185/p 210	Participates in the occurrence of CML through Ras signaling pathway	(33)
Liu *et al*, 1999	CML	BCR-ABLp185	Activates megakaryocytes through JAK2/ STAT5 signaling	(34)
Verma *et al*, 2009	CML	BCR-ABLp190	Induce rapid transformation of lymphoid progenitor cells and poor prognosis	(35)
Melo *et al*, 1997	CML	BCR-ABLp230	Associated with thrombocytosis in patients with CML	(36)
Balatzenko *et al*, 2008	CML	BCR-ABLp190	Associated with extreme thrombocytosis in patients with CML	(37)
Adnan-Awad *et al*, 2008	CML	BCR-ABLp190/210	Upregulating interferon receptor expression through Src signaling	(38)
Gleissner *et al*, 2002	Ph(+) ALL	BCR-ABLp210	Associated with long-term survival of patient	(39)
Qiu *et al*, 2016	Ph(+) ALL	BCR-ABLp190/p 210	Associated with CR and long-term survival of patient	(40)

BCR, B cell receptor; ABL, Abelson murine leukemia viral oncogene homolog; CML, chronic myeloid leukaemia; ALL, acute lymphoblastic leukaemia; Ph, Philadelphia chromosome; IFN, interferon; CR, complete remission.

kinase domain, thereby inhibiting kinase activity, promoting apoptosis in leukemic cells and ultimately improving the prognosis of patients with CML (46,47). Previous reports suggest imatinib as a valuable treatment option for patients with CML presenting with the rare complication of thrombocytosis (48). Despite its efficacy in reducing platelet counts in CML, imatinib may increase bleeding risk potentially due to platelet apoptosis, aggregation inhibition, platelet derived growth factor receptor (PDGFR) downregulation and megakaryocyte apoptosis via PI3K/Akt pathway (49-51). Conversely, increased platelet activation after imatinib treatment in CML has also been reported (52). Close monitoring of platelet-related parameters during imatinib therapy is therefore warranted. Prolonged imatinib therapy may lead to drug resistance, potentially due to acquired BCR-ABL1 mutations, including point mutations, insertions and deletions, which compromise TKI therapy efficacy and potentially lead to treatment failure (53). While second- and third-generation TKIs show potential in overcoming resistance, they are associated with inherent cardiovascular risks, such as thrombotic vascular occlusion and heart failure. Consequently, caution is advised when prescribing these newer TKIs to patients with pre-existing cardiovascular conditions (3,54-58).

IFN-α demonstrates myelosuppressive activity, inhibiting the uncontrolled clonal proliferation of hematopoietic cells in MPNs, including CML and ET. Before the advent of TKIs, IFN-α was the standard first-line treatment for CML, particularly in patients ineligible for allogeneic hematopoietic stem cell transplantation (59-61). Additionally, IFN-α significantly reduces platelet counts in ET and other MPNs with thrombocytosis, probably through megakaryocyte normalization (62-64). Furthermore, its immunomodulatory effects enhance natural killer cell activity, leading to the destruction of CML cells (65). While imatinib has largely superseded IFN-α in CML treatment, it remains a valuable therapeutic option for patients intolerant to imatinib (66). Moreover, IFN-α can promote

monocyte differentiation into anti-tumor dendritic cells and activate CD8+ T cells, thus bolstering anti-tumor immunity in CML (67).

Combined IFN-α and imatinib therapy shows additive effects in chronic-phase CML, improving hematological responses, extending event-free survival and enhancing MMR rates (11,12,68). In the present case, initial imatinib monotherapy effectively controlled leukocyte counts but failed to adequately address persistently elevated platelet levels, thereby increasing the risk of thromboembolic events, as evidenced by recurrent angina. Therefore, IFN-α was added to the treatment regimen to further manage platelet counts and mitigate thrombotic risk. Although this combined therapy may offer benefits for patients with CML, particularly those with extreme thrombocytosis, including enhanced platelet reduction and the possibility of complete remission, as observed in this patient, it is crucial to acknowledge the increased risk of adverse events such as myelosuppression, hepatotoxicity and flu-like symptoms (69-72). This patient experienced neutropenia and liver injury during combined therapy, which were successfully managed with symptomatic treatment. Therefore, implementing IFN-α alongside imatinib necessitates carefully considering the risk-benefit profile and close clinical monitoring.

In conclusion, the present case report highlighted the successful treatment of a patient with CML-T and severe thrombocytosis using combined IFN-α and imatinib therapy, emphasizing the challenges in diagnosing and managing this rare condition. While imatinib monotherapy initially failed to control platelet counts adequately, the addition of IFN-α led to complete hematologic and cytogenetic remission, suggesting this combination may be a promising strategy for similar cases. However, as this is a single-center report with a limited sample size, larger prospective studies, ideally multicenter, randomized controlled trials, are crucial to validate these findings and establish optimal treatment regimens. Further research should investigate the long-term efficacy and safety of the combination therapy, refine patient selection criteria and explore alternative therapeutic approaches like novel TKIs. Additionally, elucidating the molecular mechanisms driving severe thrombocytosis in CML-T, including the role of BCR-ABL1 mutations, remains essential for developing targeted therapeutic interventions.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

MXJ was the primary investigator, leading the study design, data analysis and manuscript drafting. DLD conducted the literature review, revised the manuscript, prepared the figures and confirmed the authenticity of the raw data. ZZL contributed to data collection and experimental procedures. HYW independently verified the authenticity of all data cited in the manuscript, reviewed the manuscript and confirmed the treatment course. LC reviewed and edited the manuscript for final submission. DLD and HYW confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present case report was approved by the Medical Ethics Committee of the Affiliated Hospital of Shandong Second Medical University (grant no. wyfy-2024-qt-051; date of approval: September 18, 2024; Weifang, China).

Patient consent for publication

Written informed consent was obtained from the patient's family for the publication of this report and the accompanying images.

Competing interests

The authors declare that they have no competing interests.

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