DEKA IN MEDICINE

Case report

Extreme thrombocytosis as a rare initial manifestation of chronic myeloid leukemia: A case report

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ABSTRACT

BACKGROUND: Severe thrombocytosis is a rare presentation of chronic myeloid leukemia (CML), but can be associated with rapid advancement of the disease and severe consequences. The aim of this case report is to describe the management of CML with severe thrombocytosis simulating essential thrombocythemia (ET).

CASE: A 29-year-old male presented to emergency department with the symptoms of pain and swelling in left lower limb for four days. Swelling began in thigh and gradually spread to lower leg and was accompanied by pain on movement. Patient was diagnosed with CML in 2019 and on Imatinib 400 mg/day since then. Physical exam showed anemic conjunctiva, splenomegaly (Schuffner 1/8), and palpable mass of left gastrocnemius muscle. MRI revealed an intramuscular cystic mass suggestive of a lymphangioma. Laboratory results presented with severe anemia, leukocytosis, and spectacular thrombocytosis (6,143,000/µL). Bone marrow aspiration revealed elevated granulopoiesis and megakaryopoiesis, 10% myeloblasts, 5:1 myeloid-to-erythroid ratio, and positive platelet aggregation. Chronic-phase CML with transformation imitating ET was the diagnosis rendered. Treatment was with hydroxyurea, nilotinib, aspirin, intravenous fluids, and thrombocytapheresis. Two days after thrombocytapheresis, the patient complained of significant clinical improvement and was able to walk independently with minimal residual pain.

CONCLUSION: CML with massive thrombocytosis is noteworthy to present specifically as it may mimic ET and carry a risk of thrombotic complications. Therapy by multimodal approach using TKI, cytoreduction, and thrombocytapheresis may be highly effective.

KEYWORDS: Chronic myeloid leukemia; extreme thrombocytosis; essential thrombocythemia-like transformation; tyrosine kinase inhibitor; therapeutic thrombocytapheresis.

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INTRODUCTION

Treatment of chronic myeloid leukemia (CML) is a clinical issue, particularly in its association with atypical hematologic presentation.[1] CML is a type of chronic leukemia and accounts for 15–20% of all leukemia in adults, with a prevalence of 1–2 cases per 100,000 population in one year with tremendous mortality if left untreated.[2] The clinical course of CML is shaped by several factors, including disease phase, BCR-ABL mutation burden, response to therapy, and secondary hematologic responses. One of the uncommon but clinically relevant complications is severe thrombocytosis, which is either a part of disease evolution or transformation into other myeloproliferative neoplasms, i.e., essential thrombocythemia (ET).[1] Mechanistically, CML thrombocytosis may be secondary to megakaryocytic hyperproliferation due to constitutive BCR-ABL activation, and hematopoietic cytokine dysregulation. Although

not a feature of CML, thrombocytosis may aggravate the disease course and even considerably increase the risk for vascular complications.[3]

Extreme thrombocytosis is defined as a platelet count exceeding 1,000,000/μL and may occur in the context of either reactive thrombocytosis or as part of primary myeloproliferative neoplasms.[4] In CML, it is believed to result from JAK/STAT pathway activation and increased sensitivity of megakaryocytic precursors to growth factors, leading to massive platelet proliferation.[5] Some studies have reported that extreme thrombocytosis in CML is associated with a higher thrombotic risk, therapy resistance, and potential transformation to blast phase.[1,4] However, the frequency, exact mechanisms, and optimal management strategies for this condition remain unclear, as most literature focuses primarily on leukocytosis. Therefore, further documentation and evaluation of CML cases presenting with extreme thrombocytosis are needed to enrich the clinical understanding and inform management guidelines. This case report aims to describe the clinical presentation, diagnosis, and management of a patient with chronic-phase CML exhibiting extreme thrombocytosis mimicking transformation to ET. The findings are expected to enhance understanding of the clinical spectrum of CML and support the development of more tailored diagnostic and therapeutic approaches, especially in cases with atypical hematologic complications.

CASE PRESENTATION

A 29-year-old male presented to the Emergency Department of Dr. Saiful Anwar General Hospital with a complaint of swelling and pain in the left lower limb that had been present for four days. The swelling initially appeared in the left thigh and progressively extended to the lower leg, with pain worsening upon movement. The patient had been diagnosed with CML in 2019 based on bone marrow aspiration and molecular BCR-ABL testing. Since then, he had been regularly taking Imatinib 400 mg once daily. There was no relevant family history, and the patient denied fever, chest pain, hemoptysis, orthopnea, dyspnea, gum bleeding, or other bleeding symptoms.

On initial examination, the patient was afebrile and hemodynamically stable. Physical examination revealed anemic conjunctiva and splenomegaly (Schuffner 1/8). Palpation of the left leg identified a palpable mass in the gastrocnemius muscle. Other physical findings were within normal limits. The Karnofsky performance score was 90%. MRI of the left leg revealed an intramuscular cystic soft tissue mass involving the gastrocnemius and soleus muscles, suggestive of a lymphangioma with a differential diagnosis of intramuscular myxoma, without vascular involvement (Figure 1). Laboratory results showed severe anemia, neutrophil-dominant leukocytosis, and extreme thrombocytosis (platelet count: 6,143,000/μL). Bone marrow aspiration demonstrated increased granulopoiesis, 10% myeloblasts, elevated megakaryopoiesis with positive platelet aggregation, a myeloid-to-erythroid ratio of 5:1, and decreased erythropoiesis, suggesting chronic-phase CML with a transformation resembling ET (Figure 2). Quantitative BCR-ABL level was 3.74 × 10^6.

Given the extreme thrombocytosis and leukocytosis, a myeloproliferative neoplasm (MPN) was suspected. The most likely diagnosis was chronic-phase CML with ET-like transformation, with other causes considered less likely based on hematologic profile. The patient was treated with intravenous fluids (2000 mL/day), hydroxyurea (1000 mg twice daily), nilotinib (300 mg twice daily), and low-dose aspirin (80 mg once daily). Therapeutic thrombocytapheresis was planned to reduce the platelet burden. On day nine of hospitalization, two days post-thrombocytapheresis, the patient showed

significant clinical improvement and was able to ambulate independently, though mild pain on movement persisted.

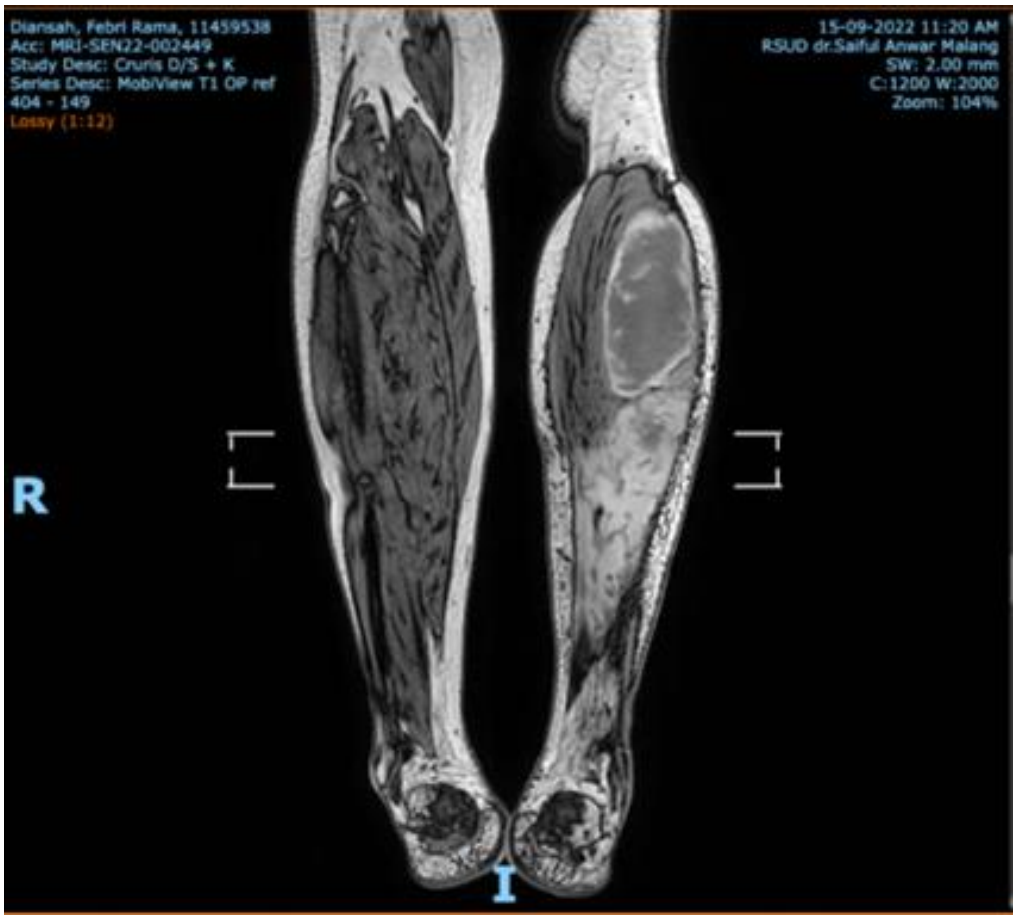

Figure 1. Magnetic resonance imaging (MRI) of the left lower leg revealed a well-defined cystic mass within the intramuscular region of the gastrocnemius and soleus muscles. The lesion appeared hypo- to slightly hyperintense on T1-weighted imaging (T1WI), and hyperintense on both T2-weighted imaging (T2WI) and proton density fat-saturated (PDFS) sequences. Diffusion-weighted imaging (DWI) demonstrated restricted diffusion. Post-contrast sequences showed heterogeneous enhancement. Associated bone marrow signal changes were observed in the adjacent left crural bone.

DISCUSSION

The patient in this case presented with a platelet count of 6,143,000/μL, which is clinically categorized as extreme thrombocytosis. This hematological abnormality is significant due to its potential to cause severe complications, including thrombosis, microcirculatory disorders, and organ failure if not properly managed. In most cases, thrombocytosis is reactive (reactive thrombocytosis, RT), occurring as a response to inflammation, infection, malignancy, or post-splenectomy status.[4] Thrombocytosis is defined as a platelet count exceeding 450 × 10^9/L, with approximately 90% of clinical cases classified as reactive. However, in patients with CML, thrombocytosis may represent a direct manifestation of the underlying myeloproliferative neoplasm rather than a reactive process.[6] Although thrombocytosis is not a common feature of CML, some patients may present with severe or even extreme thrombocytosis, as in this case. Severe thrombocytosis in CML is not only indicative of disease burden but has also been identified as a poor prognostic factor, associated with reduced survival and suboptimal therapeutic response. Extreme thrombocytosis may require adjunctive interventions such as thrombocytapheresis to rapidly lower platelet levels and prevent thrombotic complications.[7] Previous studies support these findings.[4,8,9] One study

reported that CML patients with extreme thrombocytosis exhibited delayed therapeutic response and a greater tendency to progress to the blast phase.[9] Another large cohort study found that significant thrombocytosis at diagnosis correlated with worse prognosis, especially when early molecular remission was not achieved.[4] Additionally, another report described severe thrombotic complications in CML patients with platelet counts exceeding 2 million/μL and emphasized the importance of aggressive management combining thrombocytapheresis and targeted therapy such as tyrosine kinase inhibitors (TKIs).[8] Therefore, the presence of extreme thrombocytosis in CML, as illustrated in this case, warrants special clinical attention and an integrated therapeutic strategy.

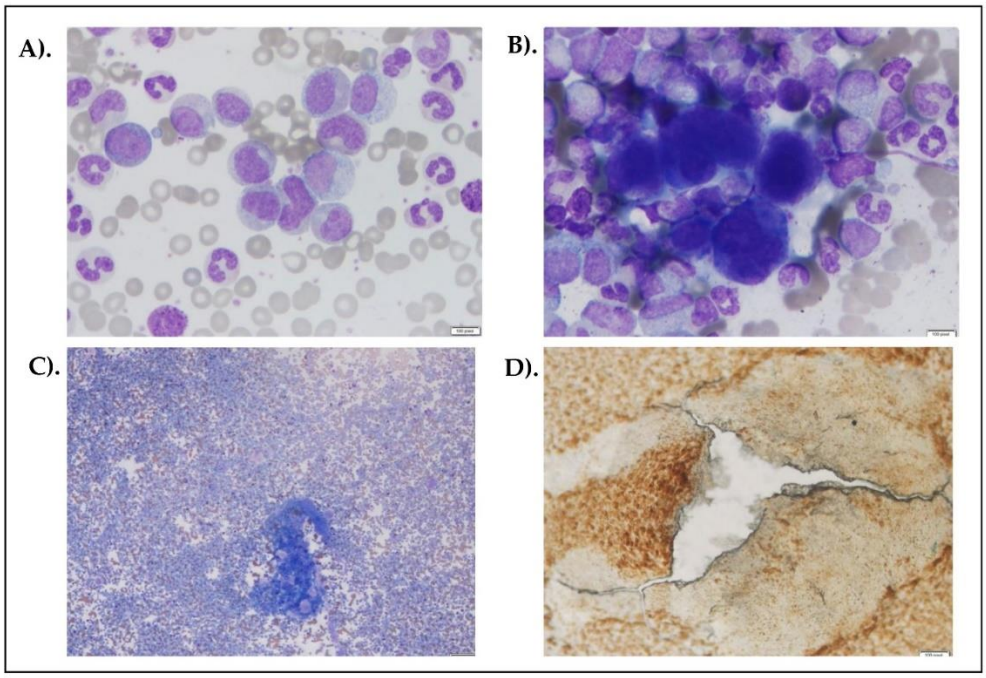

Figure 2. Bone marrow aspirate and biopsy findings. A). Peripheral blood smear showing increased polymorphonuclear (PMN) cells and marked thrombocytosis. B). Bone marrow aspirate reveals prominent megakaryocytic hyperplasia with clustering of enlarged, atypical megakaryocytes. C). Hypercellular marrow with reduced fat spaces, indicating increased hematopoietic activity. D). Perls' Prussian blue stain shows absence of iron storage, suggestive of negative marrow iron.

In this case, the patient was treated with a combination of hydroxyurea and imatinib to reduce platelet counts and prevent thrombotic events. Hydroxyurea is an antimetabolite that inhibits DNA synthesis in the S phase of the cell cycle and is predominantly utilized in the management of ET for its effectiveness in lowering platelet counts and thrombosis prevention.[10] Imatinib, however, has been the universal first-line treatment of chronic-phase CML for several decades. Imatinib is a BCR-ABL tyrosine kinase inhibitor, the primary oncogenic driver of CML.[11] The long-term efficacy of imatinib was demonstrated by Hochhaus et al., in which they concluded that nearly 11 years of treatment yielded sustained clinical responses with no unacceptable cumulative toxicity or long-term adverse effects. But in the case of inadequate response to imatinib in CML, second-generation TKIs such as nilotinib and dasatinib offer added potency and enhanced efficacy.[12] Several reports from literature reviews cite effective use of nilotinib and dasatinib in imatinib-resistant or imatinib-intolerant chronic-phase CML patients.[13,14] Therefore, TKI treatment should be individualized based on disease phase, prior therapeutic response, and potential long-

term toxicity. The use of cytoreduction with hydroxyurea and imatinib or nilotinib targeted therapy may be an effective treatment modality in cases of CML with extensive thrombocytosis, as in this patient.

In addition to pharmacologic therapy, the patient was also administered thrombocytapheresis as an adjunct treatment for speeding up platelet reduction. A case-series report of the management of hyperthrombocytosis by therapeutic thrombocytapheresis proposed that the procedure be seriously considered in such patients with a platelet count greater than 1,500 × 10^9/L, especially if there is significant clinical symptoms or risk of thrombosis.[15] Therapeutic thrombocytapheresis is beneficial in the rapid reduction of platelet counts in primary (e.g., MPNs) or secondary thrombocytosis patients to prevent or reduce clinical consequences such as thrombosis, microcirculatory impairment, or neurologic manifestations.[16] The American Society of Apheresis (ASFA) also recommends the process in the management of severe thrombocytosis, particularly in acute or symptomatic presentations.[17] In addition to platelet level reduction, thrombocytapheresis was reported to relieve symptoms of thrombocytosis.[16] In this case, one session of thrombocytapheresis was given to the patient, and clinical evaluation revealed a promising response with significant relief from pain and improved ambulation within a short duration after treatment. The procedural same was reported in a case study of a CML patient who had severe thrombocytosis and was discharged on hospital day 22 in stable condition. No recurrence of symptoms or rebound thrombocytosis occurred with 12-month follow-up by clinic visits and phone surveillance. The findings support thrombocytapheresis as an effective and safe short-term management approach for extreme thrombocytosis, particularly in high-risk CML patients who have severe hematologic manifestations.[7]

This case report has several clinical points and observations. First, chronic-phase CML patients could have extreme thrombocytosis—a rare but clinically important finding. This extends the knowledge that CML can mimic ET and manifest with leukocytosis only, rendering the diagnosis challenging. Second, the case underscores the requirement for diligent evaluation in CML patients presenting with new symptoms. The intramuscular mass and leg pain necessitated further imaging (MRI) and bone marrow aspiration to exclude CML presentations, secondary complications, or synchronous soft tissue tumors. Third, the case demonstrates that multimodal treatment with hydroxyurea, second-generation TKIs (nilotinib), and thrombocytapheresis can effectively treat severe thrombocytosis and avoid thrombotic danger in patients with CML. The multimodal therapy can serve as an example for future cases of this nature. Fourth, the case indicates that individualization of TKI treatment based on response to therapy is necessary. Whereas the patient had these days initially been managed with imatinib, escalation to nilotinib was indicated due to disease progression, it demonstrates that individualized management based on clinical and molecular response is crucial. Fifth, the case emphasizes the need for early detection of severe thrombocytosis and early intervention with thrombocytapheresis and early correction of clinical outcomes. It serves as a reminder to clinicians to remain vigilant for hematologic complications in CML and implement proper early management.

CONCLUSION

This case report illustrates an unusual clinical presentation of chronic-phase CML as severe thrombocytosis that imitates ET. Such a presentation is challenging from the diagnostic standpoint and needs multidisciplinary examination to exclude other myeloproliferative neoplasms. Diagnosis was established by comprehensive clinical

assessment, laboratory tests, imaging studies, and bone marrow aspiration. Management with a combination of hydroxyurea, second-generation tyrosine kinase inhibitor (nilotinib), and therapeutic thrombocytapheresis successfully reduced platelet counts and clinical symptoms. This case highlights the importance of early detection, extensive diagnostic evaluation, and individually adjusted therapeutic treatments for CML patients with severe hematologic complications to optimize clinical results.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The patient in this case report has provided informed consent for this publication.

CONFLICTS OF INTEREST

We have no conflict of interest

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AUTHOR CONTRIBUTION

Conceptualization: MRI, HPB; Data Curation: MRI, HPB; Formal Analysis: MRI, HPB; Investigation: MRI, HPB; Project Administration: MRI; Resources: MRI, HPB; Methodology: MRI, HPB; Software: MRI, HPB; Visualization: MRI; Supervision: HPB; Validation: HPB; Writing – Original Draft Preparation: HPB; Writing – Review & Editing: HPB. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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