Isolated Extreme Thrombocytosis as the Presenting Feature of Chronic Myeloid Leukemia—An Unusual Phenotype Treated With Plateletpheresis

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ABSTRACT

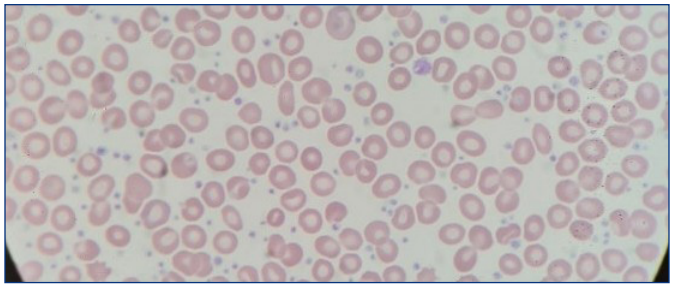
Chronic myeloid leukemia (CML) can rarely present with extreme thrombocytosis as the initial manifestation, a phenotype that can mimic essential thrombocythemia, leading to delayed diagnosis. We describe the case of a 54-year-old woman who was evaluated by outpatient hematology for isolated thrombocytosis with normal iron studies and leukocyte counts. Molecular testing confirmed BCR::ABL1 fusion, consistent with chronic phase CML. She was started on hydroxyurea, but her platelet count continued to rise, requiring hospitalization for close monitoring, where she was initiated on dasatinib, a tyrosine kinase inhibitor (TKI). As her platelets peaked above 4,000 × 10^9/L (Reference Range [RR]: 150–450 × 10^9/L), given the high risk of both thrombotic and bleeding complications, she underwent plateletpheresis, which effectively reduced counts before TKI therapy could achieve disease control. This case highlights the importance of considering the diagnosis of CML in patients with isolated thrombocytosis, particularly in women, and emphasizes the role of plateletpheresis as a potential preventive bridge until TKI therapy takes effect.

KEYWORDS: Chronic Myeloid Leukemia; Isolated Extreme Thrombocytosis; Plateletpheresis; Tyrosine Kinase Inhibitor

CASE PRESENTATION

A 54-year-old woman was referred to hematology clinic for persistent thrombocytosis. She had a long-standing history of fatigue, easy bruising, and intermittent pruritis involving her ears and anal area. One month prior, laboratory testing revealed a hemoglobin of 12.6 g/dl (RR: 11.5–16 g/dl), white blood cell (WBC) count of 9.7 x 10^9/L (RR: 4–10.8 x 10^9/L) with normal differential counts, and a platelet count of 2,707 x 10^9/L. Repeat testing demonstrated persistent and progressive thrombocytosis at 2,833 x 10^9/L, a mild leucocytosis of 11.4 x 10^9/L with neutrophilia of 8.8 x 10^9/L (RR: 1.5–7.7 x 10^9/L), eosinophilia of 0.7 x 10^9/L (RR: 0–0.5 x 10^9/L), and basophilia of 1 x 10^9/L (RR: 0–0.2 x 10^9/L). Iron studies were normal with ferritin of 101 ng/ml (RR: 30–252 ng/ml) and serum creatinine of 0.71 mg/dl (RR: 0.51–0.95 mg/dl). Overall, this was concerning for a myeloproliferative process rather than reactive thrombocytosis.

Figure 1. Peripheral blood smear on 100x showing numerous platelets with giant platelets.



Peripheral blood was sent for JAK2 V617F and calreticulin (CALR) mutation analysis, as well as for fluorescence in situ hybridization (FISH) testing of the BCR::ABL1 gene rearrangement. Work-up returned positive for the BCR/ABL fusion and she was diagnosed with chronic phase of CML. She was started on hydroxyurea 1000 mg daily for cytoreduction, and allopurinol 300 mg daily for prevention of tumor lysis syndrome (TLS). However, two days later, her platelets progressively rose to 3,073 x 10^9/L with elevated LDH of 362 U/L (RR: 120–246 U/L) and potassium of 6.3 mmol/L (RR: 3.5–5.1 mmol/L) for which she presented to the emergency department (ED) for further evaluation.

Fortunately, whole blood potassium in the ED was 3.8 mEq/L (RR: 3.2–4.7 mEq/L) which was consistent with pseudohyperkalemia in the setting of thrombocytosis. A peripheral smear revealed numerous platelets with giant platelets [**Figure 1**]. She was admitted for cytoreduction. A von Willebrand panel was sent to rule out acquired von Willebrand disease.

She was continued on hydroxyurea at 1000 mg daily, allopurinol 300 mg daily and started on tyrosine kinase inhibitor (TKI), dasatinib at 100 mg daily on day 2 of hospitalization, in addition to aspirin 81 mg daily after the von Willebrand panel returned normal (von Willebrand antigen 106% [RR: 42–176%]; Ristocetin cofactor 64% [RR: 40–163%]; Factor VIII activity 62.2% [RR: 50–150%]). Despite this, her platelets continued to climb, and hydroxyurea was increased to 1000 mg twice daily on day 3 of hospitalization. Her platelets went up to 4175 x 10^9/L on day 4 and given high risk for stroke and myocardial infarction from severe thrombocytosis, she

Table 1. Trend in laboratory values with treatment received during hospitalization

Day of hospitalization	Hemoglobin (g/dl)	Platelet count (x 10^9/L)	WBC count (x 10^9/L)	Treatment
1	11.4	3073	10	Received hydroxyurea 1000 mg daily
2	11.4	2819	9.8	Started dasatinib 100 mg daily and aspirin 81 mg daily
3	12.3	3439	11.5	Increased hydroxyurea to 1000 mg twice daily
4	12.7	4175	12.7	Received plateletpheresis
5	13.6	1033	13	Discharged home on dasatinib 100 mg daily, hydroxyurea 1000 mg twice daily, aspirin 81 mg daily

underwent plateletpheresis. Her platelet counts improved to 1033 x 10^9/L on day 5, when she was discharged home. See **Table 1** for trend in labs during hospitalization.

Due to anemia and leukopenia, hydroxyurea was stopped two weeks after discharge. The initial quantitative reverse transcriptase polymerase chain reaction (RT-PCR) testing for BCR/ABL1 returned positive for both p210 (34.5% of total ABL1) and p190 (0.01% of total ABL1) mRNA transcripts. She additionally developed thrombocytopenia one month later, for which dasatinib was briefly paused for a month, only to be resumed for uptrending platelet counts. Four months later, repeat quantitative RT-PCR testing for p210 was lower at 17.9% of total ABL1. The patient reported feeling better overall with resumption of her day-to-day activities.

DISCUSSION

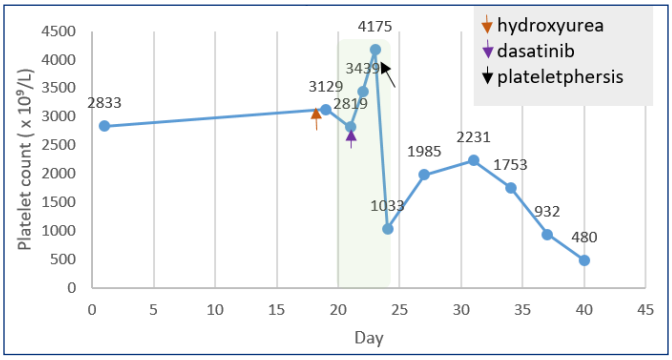
Myeloproliferative neoplasms (MPNs) are clonal hematologic malignancies marked by the increased production of terminally differentiated myeloid cells, including leukocytes, erythrocytes, and platelets.[1] They include the Philadelphia chromosome-positive chronic myeloid leukemia (CML), and the Philadelphia chromosome-negative MPNs, which include polycythemia vera (PV), essential thrombocythemia (ET), primary myelofibrosis (PMF) and a prefibrotic myelofibrosis (pre-PMF).[1] Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm with an estimated annual incidence of approximately two cases per 100,000 population.[2] The hallmark of CML is the Philadelphia chromosome, resulting from a balanced translocation that fuses Abelson murine leukemia (ABL1) gene on chromosome 9 with the breakpoint cluster region (BCR) gene on chromosome 22, producing the BCR::ABL1 oncoprotein.[2] This constitutively active tyrosine kinase drives the proliferation of mutated pluripotent hematopoietic stem cells (HSCs), with gradual displacement of the normal HSCs.[3]

Over 95% of CML cases present with the typical phenotype of leukocytosis dominated by granulocytes, myeloid immaturity with absent or few blasts, frequent basophilia, mild anemia, and normal to mildly increased platelet counts.[4] However, rare but striking phenotypes of BCR::ABL1-positive CML exist, one of which is BCR::ABL1-positive thrombocythemia.[4] BCR::ABL1-positive thrombocythemia is a phenotypic variant of CML, in which thrombocytosis can precede overt signs of CML,[4] and can mimic essential thrombocythemia (ET), which is a Philadelphia chromosome-negative MPN. Therefore, work-up for suspected ET should include testing for common driver mutations such as JAK2, CALR, and MPL, in addition to PCR analysis for BCR::ABL1, in order to distinguish ET from this phenotypic variant of CML, as it has different treatment implications. The National Comprehensive Cancer Network (NCCN) recommends FISH or RT-PCR testing of peripheral blood for BCR-ABL if available for all patients with suspected myeloproliferative neoplasms.[5] CML should be considered in females presenting with isolated thrombocytosis, as this phenotype has been reported to occur more frequently in women,[4] as in our patient.

The frontline management of BCR::ABL1-positive thrombocythemia currently follows the standard of care for CML, namely treatment with tyrosine kinase inhibitors (TKIs). In a systematic review by Findakly D et al, 20 cases of CML presenting with extreme thrombocytosis were identified up to the year of 2020, with mean age at diagnosis of 40.5 years and 65% of them being females.[6] Treatment often included hydroxyurea and TKI therapy. Five adult patients developed thrombotic complications including stroke, myocardial infarction, pulmonary embolism and/or miscarriages, and two of them underwent plateletpheresis.[6] More recently, Jia MX et al, in 2025, reported a patient presenting with chest pain who was started on imatinib and underwent seven sessions of plateletpheresis, yet platelet counts remained elevated and symptoms persisted. The condition ultimately resolved with the addition of interferon-α.[7]

We describe the case of a 54-year-old female with CML presenting as isolated and extreme thrombocytosis. This case highlights the importance of adhering to NCCN recommendations of BCR/ABL testing in all patients with suspected myelopriliferative neoplasms, despite the possibility of a low diagnostic yield, given the significant differences in treatment implications. She was initially sent to the ED for hyperkalemia out of an abundance of caution due to concern for tumor lysis syndrome, which in retrospect can be explained by pseudohyperkalemia in the setting of thrombocytosis. Her progressive thrombocytosis during hospitalization was concerning for potential thrombotic complications and hence received prophylactic plateletpheresis. She was also at risk of bleeding complications due

Figure 2. Trend in platelet count since presentation to hematology clinic. The brown arrow indicates initiation of hydroxyurea, and the purple arrow indicates initiation of dasatinib. The black arrow marks the timing of plateletpheresis. The shaded green area represents the duration of hospitalization. Hydroxyurea was stopped and dasatinib continued on day 40.



to the possibility of acquired von Willebrand disease as a consequence of thrombocytosis; however, the von Willebrand panel returned normal. To our knowledge, this is the first reported case in which plateletpheresis was performed as a preventive intervention prior to the development of thrombotic complications, serving as a bridge until a therapeutic response to tyrosine kinase inhibitor (TKI) therapy could be achieved (See **Figure 2** for trend in platelet counts with treatment). Currently, no well- established guidelines exist for the management of extreme thrombocytosis in CML.[7] Given its association with increased risk of thromboembolic events, management remains challenging.[7]

In conclusion, this case highlights the importance of including CML in the differential diagnosis for isolated thrombocytosis and the role of additional interventions when standard treatment fails to control counts. Isolated thrombocytosis in a female patient warrants testing for CML in addition to ET, PV, PMF as unusual phenotypes are known to be reported**.** Plateletpheresis maybe be used as an emergent bridge before response to TKI takes into effect to prevent thrombotic complications from extreme thrombocytosis**.** Further studies are needed to standardize treatment strategies, and elucidating the underlying molecular mechanisms can be helpful in guiding further therapeutic options.

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Disclosures

None

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