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Case Report

Atypical presentation of chronic myeloid leukemia as extreme thrombocytosis

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ABSTRACT

Chronic myeloid leukemia (CML) is a type of myeloproliferative neoplasm which typically presents with leukocytosis but rarely presents with extreme thrombocytosis with no/mild increase in leukocytes. Here, we describe a unique case of 42-year-old female with peripheral blood smear features that were favoring essential thrombocythemia (ET). However, further studies such as bone marrow and cytogenetic study were suggestive of CML in chronic phase. In some cases, CML mimics ET and cytogenetic study is the confirmatory test. ET and CML have different therapeutics and prognosis, and it is always necessary to consider CML as a differential diagnosis in cases of isolated thrombocytosis/extreme thrombocytosis cases.

Keywords: Chronic myeloid leukemia, Essential thrombocythemia, Extreme thrombocytosis, cytogenetics

INTRODUCTION

Chronic myeloid leukemia (CML) is myeloproliferative neoplasm that arises from abnormal pluripotent stem cells in the bone marrow.

The annual incidence of CML worldwide varies from 0.6 to 2.8/100,000.[1] According to a recent study, the annual incidence of CML in India ranged from 0.8 to 2.2/100,000 people and is the most frequent type of leukemia in India, accounting for 30–60% of all leukemia.[2]

Cytogenetically, it is characterized by the balanced reciprocal translocation of the chromosomes 9 and 22 - t(9;22)(q34.1; q11.2), resulting in the formation of Philadelphia chromosome, containing the BCR-ABL1 fusion gene.[3] This chimeric protein encodes for a protein with increased tyrosine kinase activity which has tumorigenic factor resulting in excessive production of granulocytes.[1]

50% of the newly diagnosed CML cases are asymptomatic at presentation and are diagnosed based on the abnormal white blood cell (WBC) count[3] with common findings at presentation such as anemia, weakness, fatigue, night sweats, and hepatosplenomegaly. Typically, CML presents as leukocytosis, with elevated immature granulocytes, basophilia, and eosinophilia in the peripheral blood.[4] Mild thrombocytosis is commonly seen in myeloproliferative neoplasm (MPN).

However, rarely, CML may present atypical features such as with isolated thrombocytosis/extreme thrombocytosis with/without increase in leukocyte count[4] leading to delayed diagnosis of CML or misdiagnosis as essential thrombocythemia (ET). Here, we present one such case of CML with extreme thrombocytosis.

CASE REPORT

A 40-year-old female presented with intermittent, moderate to high-grade fever, chest pain, dyspnea, and cough. Her vitals were stable at admission. Initial laboratory findings were hemoglobin - 9.3g/dL, WBC - 12.6 × (10) 9/L, with 76% neutrophils, 1% eosinophils, 3% basophils, and 2% atypical cells and platelet count of 2009 × (10) 9/L. The peripheral smear showed extreme thrombocytosis with few giant platelets [Figure 1]. Based on these findings, possibility of MPN, probably essential thrombocythemia (ET) was considered.

The ultrasonography revealed borderline splenomegaly. Echo showed large circumferential pericardial effusion with early signs of cardiac tamponade for which the patient underwent pericardiocentesis, and the fluid was negative for malignant cells.

Further bone marrow aspiration was normocellular marrow showing myeloid hyperplasia with basophilia, increase in blasts, and dysmegakaryopoiesis. Biopsy showed hypercellular marrow with marked megakaryocytic hyperplasia, hypolobated, dwarf, bulbous and a few stag horn megakaryocytes [Figure 2].

The molecular study for MPN showed positive for BCR-ABL1 fusion gene with no clinically relevant mutations in JAK2, CALR, and MPL.

Hence, with all these study findings, the final diagnosis of the case was concluded as chronic myeloid leukemia in the chronic phase.

The patient was started on low-dose aspirin, subsequently with tyrosine kinase inhibitors. The regular follow-up of the case showed a reduction in platelets.

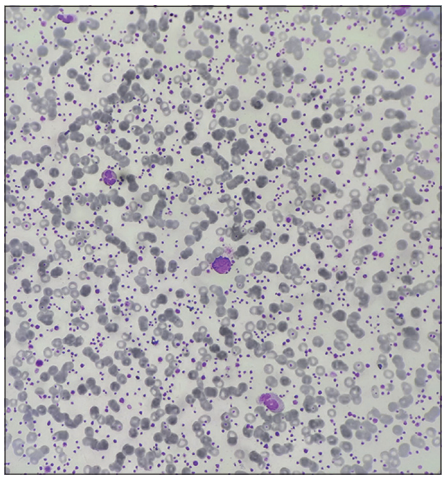

Figure 1: Peripheral smear showing extreme thrombocytosis.

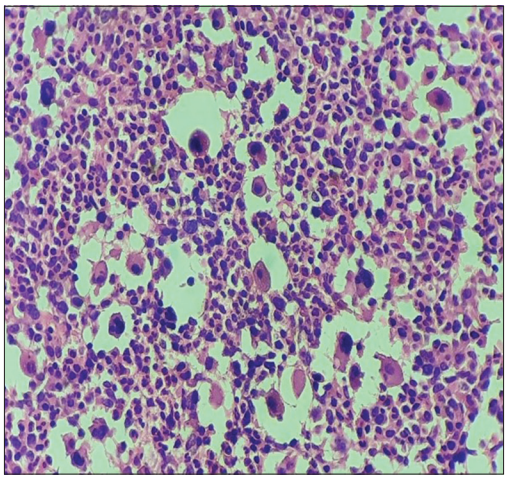

Figure 2: Bone marrow biopsy: Hypercellular marrow with megakaryocytic hyperplasia, dysmegakaryopoiesis and dwarf megakaryocytes.

DISCUSSION

Thrombocytosis is described as platelet count > 450 × (10)9/L and is a common feature in Myeloproliferative disorder (MPD). It could be reactive/paraneoplastic, where it is triggered by altered immunologic response to MPDs such as CML, ET, and polycythemia vera.[4]

Newly diagnosed cases of CML with a platelet count of >1000 × (10)9/L (extreme thrombocytosis) are exceptionally rare to find.[4] According to a study done by Sora *et al*. and Liu *et al*., extreme thrombocytosis is more commonly seen in female CML patients, as seen in our case.[5,6]

Symptomatic extreme thrombocytosis is very rare in CML. A few cases can present with digital ischemia, myocardial infarction, and neurological symptoms such as headache.[7]

Because of different therapeutic approaches and clinical outcomes, it is necessary to distinguish CML and ET, which might have similar initial clinical presentations. Hence, all cases of extreme thrombocytosis without leucocytosis, which often mimics ET, should be evaluated further.

If severe thrombocytosis and megakaryocytic hyperplasia is seen in the bone marrow without splenomegaly, it is difficult to differentiate between CML and ET without molecular and cytogenetic studies. However, in this case, along with splenomegaly, there was an increase in blasts and basophils in the marrow, so the diagnosis of CML was considered, which was later proved by the molecular study.

Cytogenetic analysis is an important tool in the diagnosis of CML and also in therapy. Bone marrow samples are superior to peripheral blood in detecting the BCR-ABL fusion gene.[4] Although the JAK2V617F mutation is found in 50% of cases of ET, it does not indicate a definitive diagnosis of ET, and ET is the diagnosis of exclusion.[8] Few CML cases with mild to moderate thrombocytosis can also have acquired JAK2V617F mutation.[9] Thus, detecting the BCR-ABL fusion gene is a significant diagnostic tool to differentiate CML and ET.

The other atypical presentation in our case was impending cardiac tamponade. CML with pericardial effusion and impending cardiac tamponade is a very rare occurrence. The proposed mechanism for pericardial effusion in CML is due to leukemic infiltration into the pericardium, extramedullary hematopoiesis, obstruction of vessels, increased permeability of vessels due to infiltration of interstitial tissue by leukemic cells. The patients may require urgent pericardiocentesis in hemodynamically unstable patients.[10]

CONCLUSION

From the above case, we conclude that in cases with extreme thrombocytosis with a normal/mild increase in the total count, CML should be the main differential diagnosis. These cases should be investigated for BCR-ABL translocation, which serves as a diagnostic and prognostic tool for CML.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent is not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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