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Unexpected high platelet counts in a potential platelet donor: A clue to essential thrombocythemia

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Abstract:

Essential thrombocythemia (ET) (primary thrombocythemia) is a nonreactive, chronic myeloproliferative clonal disorder in which sustained megakaryocyte proliferation leads to an increase in the number of circulating platelets. It is silent disorder and is diagnosed as high platelet counts with or without associated symptoms or as an accidental finding. We, hereby, report a case of ET as an incidental finding during screening of a potential platelet donor. Donors with high platelet count should be investigated properly to rule out ET. The role of transfusion medicine specialist is not only to recruit donors but also to identify such donors during screening and counsel them for detailed investigation and proper management.

Keywords:

Calreticulin mutation, essential thrombocythemia, peripheral smear, platelet donor screening, splenomegaly

Introduction

Essential thrombocythemia (ET), also known as essential thrombocytosis, is a myeloproliferative neoplasm (MPN) characterized by thrombocytosis (increase in the number of circulating platelets) with bone marrow megakaryocytic hyperplasia.^[1] MPN includes polycythemia vera, primary myelofibrosis (MF), and ET.^[2] The three heterogeneous disorders with clonal origin share different clinical, hematologic, and biological features. According to the World Health Organization, essential thrombocytosis is a disease that occurs when the platelet count is more than 450,000 with the presence of Janus kinase 2 (JAK2), calreticulin (CALR), or myeloproliferative leukemic virus oncogene (MPL) mutation and lacking clonal or reactive causes.^[3] Due to thrombocytosis, the risks of vascular

events such as thrombosis and hemorrhage are increased, and sometimes, there is conversion to a blast phase of MF.^[4] The primary cause of ET is the overproduction of hematopoietic cells due to the mutation of JAK2, CALR, or MPL gene. The presence of a mutation strengthens the diagnosis of all MPNs, as 97% of patients have some form of mutations, whether JAK2, CALR, or MPL. These genes are known as driver mutations due to the role they play in the development of a MPN. Approximately 55% of patients with essential thrombocytosis have the JAK2 mutation.^[5] It is a silent disorder and is diagnosed as high platelet counts with associated symptoms or as an incidental finding. We, hereby, report a case of ET as an incidental finding during the screening of potential platelet donor.

Case Report

A 31-year-old male presented for platelet donation. On preliminary testing, during the

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first visit, platelet counts were 1,586,000. Repeat testing on the same sample showed platelet counts to be 1,601,000 [Table 1]. ET was suspected. He had no history of thrombotic episodes such as headaches, digital pain, or any transient ischemic attacks. The donor was counseled about high platelet counts, and complete blood counts (CBC) tests were repeated at a referral center which showed high platelet counts of 1,354,000 and 1,314,000 on two occasions [Table 2]. Additional tests were advised by the hematologist, which included JAK2 mutation, chest X-ray for signs of pulmonary hypertension, ultrasonography of the abdomen for splenomegaly, electrocardiogram for signs of previous myocardial infarction, and urine examination for hematuria. All tests were normal except ultrasonography which showed splenomegaly, and peripheral smear showed markedly increased platelets. As JAK2 mutation was negative, CALR mutation was advised, which was positive [Table 3]. Reports confirmed the diagnosis of ET, and the patient was started on hydroxyurea, 500 mg once a day (OD). At the first follow-up in a month, platelet counts were 1,050,000. The dose of hydroxyurea was then increased to 500 mg twice a day (BD). The second follow-up indicated that platelet counts were 884,000. Anagrelide 0.5 mg OD was added to hydroxyurea, and platelet counts further dropped in subsequent months to normal levels [Figure 1]. The patient was advised to drink plenty of fluids, avoid any injury to the abdomen, and follow-up with hematologist regularly.

Table 1: Initial complete blood count results done in the department of transfusion medicine

Date	Hemoglobin (12.5-18 g/dl)	MCV (77-96 fL)	Platelet count (150-450 ×10 ⁹ per liter)
First time	15.0	98.0	1586
Repeat test	15.1	98.2	1601

MCV=Mean corpuscular volume

Table 2: Complete blood count results done at a referral center

Occasions	Hemoglobin (12.5-18 g/dl)	MCV (77-96 fL)	Platelet count (150-450 ×10 ⁹ per liter)
1	14.8	95.6	1354
2	15.3	94	1314

MCV=Mean corpuscular volume

Table 3: Additional tests for diagnosis of essential thrombocythemia

Tests	Results
Jak2 mutation	Negative
CALR mutation	Positive
Peripheral smear	Platelets increased
Ultrasonography of abdomen	Splenomegaly
Chest X-ray	Normal
ECG	Normal
Urine examination	Normal
C reactive protein	Normal

CALR=Calreticulin, ECG=Electrocardiogram

The patient was also counseled about therapeutic thrombocytapheresis in case if inadequate response to medications and/or if symptoms worsen.

Discussion

ET is a disorder of the myeloid stem cell that causes the expansion of the megakaryocytes in the bone marrow, with a persistent increase in the platelet count. ET patients could present with variable symptoms. In asymptomatic patients, thrombocytosis is usually an incidental finding on CBC which was observed in the present case. For symptomatic patients, the most common symptoms are migraines, headache, and dizziness.^[7] They can also present with various levels of thrombosis including hepatic vein thrombosis which is the hallmark of the disease, or they can present with symptoms such as transient ischemic attack, erythromelalgia, and easy bruising.^[6,7] The most common physical finding in essential thrombocytosis is splenomegaly, which is mild when compared to other MPNs. The evaluation of patients with essential thrombocytosis includes getting a CBC, a bone marrow biopsy, and genetic testing to evaluate for gene mutations. Platelet count should be more than 450,000. The bone marrow biopsy should show the evidence of increased proliferation of the megakaryocytic cell lines with increased numbers of enlarged, matured megakaryocytes. Because the symptoms of MPNs overlap, it is important to also rule out other causes of thrombocytosis, including clonal and reactive causes, before reaching a definite diagnosis of essential thrombocytosis.^[7] It is helpful to recognize which genetic mutation a patient has whether it is JAK2, CALR, or MPL because each of these mutations determines the clinical features, complications, and survival of MPN.^[8] Research shows that genetic testing will help to determine the phenotype and prognosis of essential thrombocytosis. For instance, a patient with CALR mutations of essential thrombocytosis has a better prognosis.^[9] Patients with ET are at high risk for thrombosis; hence, vigorous treatment is required for managing cardiovascular risk factors. Hence, a cardiovascular risk assessment is required and will direct the overall management of the patient. It is important

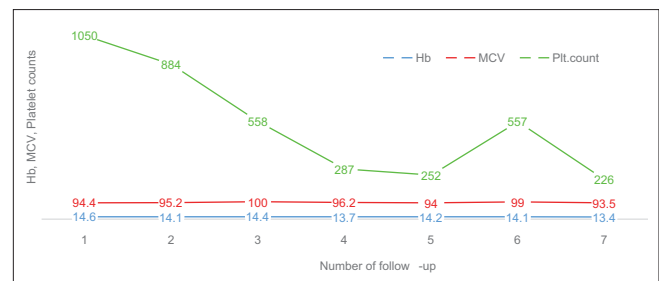


Figure 1: Hemoglobin, mean corpuscular volume, and platelet counts during the follow-up

to emphasize that before starting the therapy, patients should be evaluated for eventual progression to MF if they show symptomatic or progressive splenomegaly and other evidence of disease progression such as weight loss, night sweats, progressive leukocytosis, and/or thrombocytosis. The main treatment goals in ET include minimizing the risk for thrombosis and progression, normalizing peripheral blood counts, and reducing constitutional symptoms. Hydroxyurea is the best-documented therapy in ET and is recommended as first-line therapy in the majority of patients. Anagrelide may be used as the second-line treatment in patients resistant to or intolerant of hydroxyurea.^[10] Furthermore, improved diagnosis with rational treatment will help in achieving better treatment outcomes in these patients, who were previously left undiagnosed because of the insidious nature of the disease.^[8] Donors with high platelet count should be counseled and investigated properly to rule out ET. Cytoreductive therapy can be used to decrease the platelet count in high-risk patients. In emergencies, therapeutic plateletpheresis may be useful to achieve a rapid decrease in platelet counts in the setting of acute thrombosis and/or marked thrombocytosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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