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Case Report

JAK2 V617F negative essential thrombocythemia

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Introduction

Essential thrombocythemia (ET) is an acquired myeloproliferative disorder (MPD), characterized by persistent peripheral thrombocytosis and a tendency for thrombosis and hemorrhage.¹ Erythromelalgia is a kind of cutaneous manifestation, which appears as a thrombotic complication in patients with myeloproliferative disorders such as essential thrombocythemia and polycythemia vera.² In a retrospective study of 268 patients with essential thrombocythemia, related cutaneous manifestations were found in 58 (22%) and fifteen patients (26%) had erythromelalgia.³ We describe a case of Essential Thrombocythemia in a young lady who was diagnosed and managed at our hospital.

Case report

A 35 years old female patient presented in the outpatient department with chief complaint of pain and redness in the tip of the fingers and toes of two months duration associated with generalized weakness and occasional giddiness. No history of convulsion, arthralgia, fever, exacerbation in complaints with any food products/seasonal variation was elicited. On examination she had pallor and redness and tenderness of finger tips and toes (Fig. 1). There was no hepatosplenomegaly or lymphadenopathy.

Complete blood count and PBS examination revealed microcytic hypochromic anemia with thrombocytosis (platelet count: 15,00,000/cumm) (Fig. 2). No leukoerythroblastosis or dyspoietic cells were seen. Her biochemical examination was normal. ANA was negative and iron stores were normal.

Bone marrow examination revealed presence of clusters of megakaryocytes with deeply lobulated and hyperlobulated nuclei. Myeloid and erythroid series were normal. There was no increase in blast or dyspoietic cells, reticulin fibers or iron stores (Fig. 3).

Mutational studies were done and she was found to be negative for JAK 2 V 617 kinase mutation as well as for *Bcr-abl* gene mutation. Patient was put on tab Ecosprin 100 mg daily. Repeat CBC and PBS showed persistently raised platelet count though the absolute count had slightly decreased. Patient is on regular follow up and is improving.

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Fig. 1 – Erythromelalgia finger tips both hand.

Discussion

Essential thrombocytosis is an uncommon myeloproliferative disorder of unknown cause in which marked proliferation of the megakaryocytes in the bone marrow leads to elevation of platelet count. This increase in number of platelets is attributed to clonal expansion of multipotent stem cell which has differentiated into megakaryocytic lineage. The disease usually presents at a median age of 50–60 years with a second peak at around 30 years when it is more common in females. The reported annual incidence rates for ET range from 0.59 to 2.53/100,000 population. More than half of the cases are asymptomatic and are discovered accidentally on routine blood examination. Others may experience vasomotor (headaches, visual disturbances, lightheadedness, atypical chest pain, distal paresthesias, erythromelalgia), thrombotic, or hemorrhagic disturbances. Arterial and venous thromboses, as well as platelet-mediated transient

Fig. 2 – Peripheral blood smear showing thrombocytosis (400×).

Fig. 3 – Bone marrow biopsy showing large clusters of megakaryocytes with deeply lobulated and hyperlobulate nuclei. H&E stain (400×).

occlusions of the microcirculation and bleeding, represent the main risks for ET patients.⁴

The diagnosis of ET has always been a challenge as the disease shares phenotypic and pathologic similarities with other myeloproliferative neoplasms (MPNs), particularly polycythemia vera (PV) and primary myelofibrosis (PMF). The JAK2 V617F mutation clearly represents a new molecular marker for the Ph-negative patients. Initially described in PV patients, where it has been observed in 65–97% of the cases. It has also been detected in subsets of each of the other Ph-negative MPDs; in 23–57% of ET and 43–67% of IMF patients, as well as in some Ph-negative CML and MDS.⁵ Mutations in MPL are seen in approximately 4% of patients with ET and PMF, and mutations in TET2 have been observed in a variety of myeloid malignancies, including JAK2 V617F-positive and -negative ET. Hence we can see that due to the lack of a specific molecular marker and the non availability of MPL exon 10 and TET 2 mutation studies, the diagnosis of ET can only be settled after a step-by-step elimination of the other clinical situations associated with a protracted elevation of the platelet number. Both the WHO in 2008 and British Committee for Standards in Haematology (BCHS) in 2010 have laid out the criteria's for diagnosis of ET.^{6,7}

Few studies have been conducted on the effect of JAK2 V617F mutation on the overall disease process. It has been found that presence of the JAK2 mutation, especially if associated with leukocytosis, is a strong predictor of a subsequent thrombotic event and it does not have a protective role on haemorrhagic risk.⁸ The presence of an MPL mutation has a positive predictive value for higher rates of arterial thrombosis compared with JAK2/MPL-negative patients.

Our patient was JAK 2 and BCRABL1 negative. Diagnosis of ET was arrived at by a careful algorithmic approach in which

secondary causes of thrombocytosis was ruled out by assessment of inflammatory markers, peripheral blood smear, iron studies and bone marrow histology. The patient has been put on therapy with tab Ecospirin and is under regular follow up for occurrence of thrombotic and hemolytic complications.

Conflicts of interest

All authors have none to declare.

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