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A CASE OF ESSENTIAL THROMBOCYTOSIS (JAK 2+MTHFR GENE MUTATION +VE) WHO PRESENTED WITH VENOUS THROMBOSIS

Medicine

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ABSTRACT

Essential thrombocythemia (ET) is a myeloproliferative neoplasm (MPN) which generally follows a benign & indolent clinical course. Venous Thrombosis can be seen in the older age (>60 years) group , but is rare in the younger population. Here we present a case of a young female with ET & venous thrombosis (Superior mesenteric vein +portal vein +splenic vein thrombosis)

KEYWORDS

INTRODUCTION

Essential Thrombocythemia (ET) is a clonal hematopoietic stem cell disorder associated with the mutation JAK2(V617F), CALR & MPL & manifested by overproduction of platelets without any secondary cause.[3] ET has an incidence of 1-2/1,00,000 . There is a female preponderance. Reactive (secondary) thrombocytosis is a more common cause of elevated platelet counts & the common causes are infections, iron deficiency anemia, surgery, malignancy and trauma and these need to be excluded prior to considering the diagnosis of ET. ET may be complicated by thrombotic or hemorrhagic events. Microvascular thrombosis is common which can present as erythromelalgia, ocular migraine or transient ischaemic attack.[3] Venous thrombosis is the main cause of morbidity & mortality. There is a strong association of JAK2V627F mutation & development of thrombosis. We present a case report of ET (JAK 2 +VE) with Superior mesenteric vein, Portal vein & splenic vein thrombosis.

CASE REPORT

A 30 year old lady presented with upper epigastric pain associated with nausea since 11 days which was aggravated by food .The pain was characterized as acute, dull aching in nature not radiating to any side ,not associated with fever ,hematemesis, melena, chest pain, bowel abnormality or pedal edema .An abdominal examination revealed a large spleen upto the umbilicus .Other systems' examination was unremarkable .As a part of the evaluation of the abdominal pain, USG Abdomen was done which showed slightly altered echotexture of liver, splenomegaly, portal thrombosis with collaterals. For further workup CECT Abdomen was done which showed acute Superior mesenteric vein thrombosis, chronic portal & splenic vein thrombosis, portal cavernoma with peri gastric, peri splenic, peri pancreatic collaterals. On blood investigation HB was 12.9 gm/dl, WBC-7920/cumm and Platelet count was 7,16,000/cumm. In view of blood investigations & radiological evidence of a possible myeloproliferative disorder , further workup for thrombocytosis with thrombosis (after excluding secondary causes) was done and a JAK2(V667F) & MTHFR (C677T)mutation was asked for which turned out to be positive. UGI Scopy was done which showed four columns of grade 1 esophageal varices & pan portal hypertensive gastropathy with esophageal candidiasis. A Bone marrow Biopsy was done which showed a hypercellular marrow, increased megakaryocyte in clusters without any significant fibrosis & M:E Ratio which was normal . All these suggested a diagnosis of Essential thrombocythemia (JAK 2 + VE). She was subsequently treated with anticoagulation, hydroxyurea & single daily aspirin. After few weeks patient's platelet count normalized & she became asymptomatic.

DISCUSSION

We report a case of a young lady with ET presenting with venous thrombosis. Thrombosis is rarely seen in a younger patient with ET. Major risk factors for thrombosis in ET are advanced age, prior h/o thrombosis, hypercholesterolemia, smoking, diabetes and a JAK2 mutation.[6] Mechanisms behind thrombosis are hypothesised to be spontaneous aggregation of platelets, increased viscosity, displacement of circulating platelets toward the endothelium or an increased number of prothrombotic circulating endothelial cells seen among these patients.[6] JAK2V617F mutation has been found in these endothelial cells in some patients. Our patient had both JAK2V627F & MTHFR mutation. Both mutations are risk factors for thrombosis. As far as management of these patients is concerned,those who have thrombosis or age > 60 +JAK2V617 are included in the high risk category & they should be treated with anticoagulation +cytoreduction therapy +single daily aspirin therapy.[2] Our patient was treated with low molecular weight heparin followed by rivaroxaban +hydroxyurea, single daily aspirin & statins.

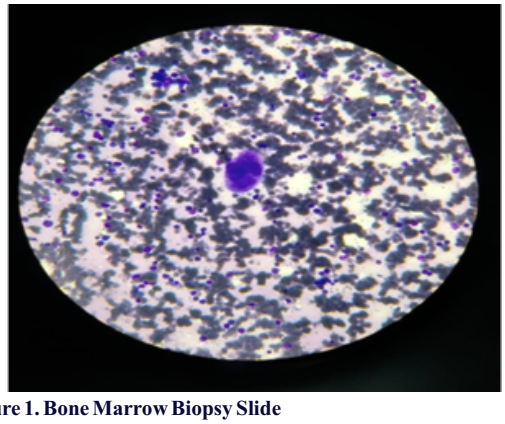

Figure 1. Bone Marrow Biopsy Slide

An elevated platelet count in an otherwise asymptomatic patient without cardiovascular risk factors requires no therapy. When the platelet count rises above 1 million/cumm, high molecular weight of von Willebrand multimers are removed from the circulation, resulting in an acquired von Willebrand disease.[3] Hydroxyurea & aspirin are more effective than anagrelide & aspirin because the risk of bleeding is higher when aspirin is combined with anagrelide.[3] Target Platelet count should be between 1,00,000 and 4,00,000/cumm.. Hydroxyurea is the 1st line cytoreductive therapy for ET. If target is not achieved & toxicity of hydroxyurea develops other cytoreductive therapy can be used e.g. pegylated interferon alpha 2a especially in younger patients & busulfan in older patients.in pregnancy pegylated interferon alpha 2a should be used.

According to the 2016 World Health Organization, the diagnosis of ET can be made if the following major criteria are met: (1) platelet count ≥ 450 ×109/L; (2) increased numbers of enlarged and hyperlobated mature megakaryocytes in the bone marrow without left shift and no

more than grade 1 reticulin fibrosis; (3) not meeting criteria for other myeloproliferative neoplasms, myelodysplastic syndrome, leukemia, or other myeloid disorders; (4) presence of JAK2, CALR, or MPL mutation. Alternatively, ET may be diagnosed if the first three major criteria are met, and another clonal marker is identified or reactive thrombocytosis is excluded [1].

In a retrospective study by Rose at al. involving 801 adult patients with thrombocytosis, primary thrombocytosis (myeloproliferative neoplasm) was observed in 5.2% of cases; other (secondary) causes included infection in 47.9%, trauma or postsurgical state in 24.5%, other cancer in 10.7% & and iron-deficiency anaemia in 7.4%. Extreme thrombocytosis (platelet count ≥1 million per cubic millimetre) is infrequent, occurring in less than 2% of patients [5][7] In another retrospective study by Girodon at al. involving 1076 patients with essential thrombocythemia conducted by the Mayo Clinic, the median age at diagnosis was 58 years (range, 18 to 96), 67% were women, palpable splenomegaly was present in 17%, and the median platelet count was 876,000 per cubic millimetre (range, 451,000 to 3,460,000)& thrombosis was present in 21%[4][7]

CONCLUSION

Thrombosis is rarely seen in young patients of ET. We report here a case of a young lady with ET presenting with a venous thrombosis. Pharmacological therapy alone is appropriate in patients without any surgical intervention but needs to be continued lifelong.

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