Case Report

Severe Thrombocytosis in Chronic Liver Disease Secondary to Iron Deficiency Anemia: A Case Report

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Abstract

Thrombocytopenia is the commonest haematological abnormality seen in chronic liver disease. Thrombocytosis is of two types: Primary and secondary. In secondary form of thrombocytosis usually there is mild to moderate elevation of platelet count. Here, we present a case of 60 year old patient, a known case of chronic liver disease who presented with severe thrombocytosis secondary to iron deficiency anaemia. Thrombocytosis normalized with treatment of iron deficiency anaemia with parenteral iron.

Keywords: Severe thrombocytosis, Iron deficiency anaemia, Chronic liver disease

Introduction

Thrombocytopenia is the most common haematological abnormality seen in a patient with chronic liver disease. Normal platelet count is 1.5-4.5 lacs/mm^3. Platelet count exceeding the level of 10 lacs/mm^3 is mainly due to chronic meyeloproliferative disease. Reactive thrombocytosis secondary to iron deficiency anaemia will rarely exceed the level of 7 lacs/mm^3.[1] Here, we present a case of reactive (secondary) thrombocytosis secondary to iron deficiency anaemia in a patient with chronic liver disease.

Case Presentation

A 60-year old male, chronic alcoholic, presented to medical emergency with complaints of progressive abdominal distension and pedal edema for one month. There was no history of fever, orthopnea, palpitations, abdominal pain and decreased urine output.

On examination, he was conscious, oriented with pulse rate of 82 beats/min, respiratory rate of 18/min and blood pressure of 120/80 mmHg. Pallor and pedal edema were present. There was no jaundice, jugular venous pressure was not raised. Systemic examination revealed moderate ascites and splenomegaly. Rest of the systemic examination was unremarkable.

On investigation, he had haemoglobin of 6.2 g/dl, total leukocyte count of 10,300/mm^3 with 90% neutrophils and 10% lymphocytes and platelet count of 16.7 lacs/mm^3. His KFT/ serum electrolytes, LFT were normal except for hypoalbuminemia (serum albumin-2.6 g/dl). Thyroid profile was normal. His coagulation profile was normal. Stool for occult blood was negative thrice. CXR was normal. USG abdomen showed nodular liver with heterogenous echotexture and splenomegaly. CECT abdomen was suggestive of liver cirrhosis with portal hypertension with multiple portosystemic

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collaterals and ascites. There was evidence of portal vein thrombosis also. His iron studies showed serum iron of 0.5 µmol/L (normal range 8-26 µmol/L) and serum ferritin in nonmeasurable range. Fundus examination revealed pale disc. Bone marrow aspiration showed microcytic hypochromic anemia with pencil cells, tear drop cells, target cells and anisopoikilocytosis. Platelet count was increased with few giant platelets. Bone marrow biopsy was suggestive of iron deficiency anemia with thrombocytosis. Serologies for HIV, hepatitis B and hepatitis C were negative. UGI endoscopy showed grade 1 esophageal varices. However, there was no history of bleeding from any site.

Besides symptomatic treatment for portal hypertension, patient was given parenteral iron and then oral iron therapy was continued. There was dramatic response in platelet count which reduced to the normal range in a week's time (16.7 L to 3.92 lakhs/mm^3).

Discussion

Thrombocytopenia is considered as the most common haematological abnormality in patients of chronic liver disease (CLD) which is seen in around 76% of cases.[2] It is also regarded as poor prognostic marker in patients of CLD.[3] Multiple factors lead to the development of thrombocytopenia in cirrhosis patient which can broadly be divided into factors leading to decreased production, splenic sequestration and increased destruction of platelets. Decreased platelet production can be due to depressed thrombopoetin (TPO) levels or direct bone marrow suppression by alcohol, viruses, iron overload, and medication. Increased platelet destruction occurs through increased shear stress which leads to increased platelet aggregation, increased fibrinolysis, immunologic destruction, bacterial translocation and bacterial infection.[4]

Thrombocytosis can be primary or secondary. Secondary thrombocytosis is more common than the primary one in the ratio of approximately 8:1 (87.7% Vs 12.3%).[5] Essential thrombocytosis is the most common cause of primary thrombocytosis. Short-lived form of secondary thrombocytosis is seen with acute bleeding, major surgical procedures, trauma or after severe physical exertion. However, thrombocytosis caused by chronic infection, malignancy, iron deficiency, and chronic inflammatory diseases lasts longer. Infections account for sizeable number of cases of secondary thrombocytosis and non infectious causes include tissue damage, malignancy, and iron deficiency anemia.[5] Our patient presented with secondary type of thrombocytosis due to iron deficiency.

The mechanisms responsible for association of iron deficiency anaemia and reactive thrombocytosis is still not clear. Serum erythropoietin levels increase in response to anaemia or arterial hypoxemia. Some degree of amino acid sequence homology occurs between thrombopoetin and erythropoietin (EPO). Increased erythropoietin level in patients with iron deficiency anaemia may cause thrombocytosis as a result of cross-reactivity at the level of thrombopoetin receptor c-mpl because of the existing homology between erythropoietin and thrombopoetin.[6] Also, erythropoietin and thrombopoetin can stimulate megakaryocytic proliferation synergistically at the level of bipotent erythroid/ megakaryocyte progenitor cells. However, the mechanism of thrombocytosis in iron deficiency anemia is not so simple as not all the cases of iron deficiency anemia and increased erythropoietin results into thrombocytosis. So, there could be some additional factor responsible for thrombocytosis in patients with increased erythropoietin level. The pathogenesis behind the reactive (secondary) thrombocytosis may include elevated endogenous level of thrombopoietin, interleukin-6, other cytokines, or catecholamines that may be produced in inflammatory, infectious or neoplastic conditions or in situations of stress.[5] Other causes of thrombocytosis are clonal proliferation and it becomes a diagnostic challenge for the physician to distinguish it from the reactive thrombocytosis. Clonal thrombocytosis is a type of chronic meyeloproliferative disorder also known as essential thrombocytosis. There are no specific laboratory tests to distinguish between primary and secondary form of thrombocytosis. Abnormalities in simple tests like ESR and CRP may suggest secondary form of thrombocytosis however, if no cause is apparent bone marrow biopsy or keeping a watch over platelet count for a longer period may be required. In our case the bone marrow smear and biopsy did not provide any clue for the diagnosis of any meyeloproliferative disease which ruled out the clonal proliferation of platelet to the best of our knowledge.

In our patient we found that platelet counts returned to normal level after iron therapy which further supported the finding that reactive thrombocytosis was due to iron-deficiency anaemia in this patient of chronic liver disease. There is usually mild to moderate elevation in platelet count in patients with reactive throbocytosis but in our case there was severe thrombocytosis (16.7 lakhs/mm^3) which normalized after administration of parenteral iron. Thrombocytosis of such an extent was present in our case in response to iron deficiency anaemia despite various factors responsible for development of thrombocytopenia being present in the setting of chronic liver disease.

To conclude, thrombocytosis in the setting of chronic liver disease does not always indicate towards a malignant cause. The secondary form of thrombocytosis is much more common than primary one. Clinicians must be aware of iron deficiency anaemia as a cause of reactive thrombocytosis which normalizes with treatment of anaemia.

Conflict of Interest: None

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