Case Study

Recurrent thrombocytopenia in a patient with severe iron deficiency anemia

Abstract

Iron deficiency anemia is commonly associated to thrombocytosis, but cases of thrombocytopenia have been reported. Recurrent cases of iron deficiency with thrombocytopenia are even more unusual; therefore, we present a patient with recurrent thrombocytopenia in the setting of intermittent iron deficiency anemia. The mechanism of platelet count variation in response to iron remains poorly understood. There are multiple possible explanations, including but not limited to the diphasic response of platelets to erythropoietin and the dual function of iron in platelet production. This case highlights the importance of an iron replacement trial for the individuals with documented iron deficiency and thrombocytopenia. An iron treatment trial could spare the patients with iron responsive thrombocytopenia from more invasive diagnostic modalities looking for primary bone marrow disorders.

Keywords: thrombocytopenia, iron deficiency anemia, menorrhagia

Introduction

In most cases of iron deficiency anemia, the platelet count reactively increases or remains within the normal range [1, 2]. Only a few cases in the literature report the association between severe iron deficiency anemia and thrombocytopenia [3-11]. The exact mechanism of thrombocytopenia in this setting is not well understood. Herein, we present the case of a 30-year-old female with recurrent episodes of thrombocytopenia induced by severe iron deficiency anemia that had a complete response to iron replenishment.

Case Presentation

A 30-year-old African American woman presented to the emergency department with generalized weakness, fatigue, pagophagia, and shortness of breath associated with heavy menstrual bleeding. She reported a 1-year history of uterine fibroids associated with menorrhagia, confirmed by pelvic ultrasonography and treated with oral contraceptives that had failed to control the heavy menstrual periods. She denied any other sources of bleeding.

On physical examination, the patient was afebrile and her vital signs were normal, however, she did have significant pallor. She did not have jaundice, petechia, ecchymosis or purpura. The cardiopulmonary exam was normal. There was no hepatomegaly, splenomegaly, or lymphadenopathy. Her complete blood count showed a red blood cell count of 2.27 x 10^6/uL (normal range: 3.86 – 5.17), an hemoglobin of 4.9 g/dl (normal range: 12.1-15.8), a hematocrit of 16.4% (normal range: 35.8 - 46.5), a mean corpuscular volume of 72.4 fl (normal range: 85 – 99), a red cell distribution width of 33.2 % (11.7 – 15.2%), a platelet count of 77 x 10^3/uL (normal range: 154 - 393), a white blood cell count of 3.6 x 10^3/uL (normal range: 4 – 10.5), an absolute neutrophil count of 1.2 K/uL (normal range: 2 - 7.3) and a corrected reticulocyte index 0.67 indicating a hypoproliferative anemia. The results of the iron studies were consistent with profound iron deficiency anemia as the patient had a ferritin level of 1.8 ng/mL (normal range: 8 - 252) and a TIBC of 478 ug/dL (normal range: 250 – 450). There was no laboratory evidence of hemolysis. The peripheral blood smear revealed microcytosis and hypochromasia with decreased but large platelets. She was then admitted to the inpatient unit and treated with 2 units of packed red blood cells and intravenous iron. Work up for autoimmune diseases, infectious causes and hemoglobinopathies returned negative. Her vitamin B_{12} and folate levels were within the normal limits and a CT scan confirmed the absence of hepatosplenomegaly. A review of the patient's records revealed that 12 months before, she presented with another episode of iron deficiency anemia associated with thrombocytopenia caused by menorrhagia. At that time, she underwent an upper endoscopy with biopsy which was negative for celiac disease and did not show other sources of bleeding. She did not agree to undergo a colonoscopy. In this previous hospitalization, she was given a blood transfusion and intravenous iron which caused the patient’s platelet to recover from 43 x 10^3/uL to 1017 x 10^3/uL and her severe anemia to resolve. Ultimately, her platelet counts stabilized to 258 x 10^3/uL.

Although the presence of both severe anemia and thrombocytopenia raised the question of a bone marrow disorder, based on the previous history the patient had with low platelets and iron deficiency anemia that responded to iron replenishment, we decided not to perform a bone marrow biopsy. After discharge patient continued to receive intravenous iron replacement in an outpatient setting. Menorrhagia was controlled with Depo-Provera and the patient returned to have normal menstrual periods. On a follow up visit approximately 2 months after discharge, the patient experienced complete recovery of all of her cytopenias and severe anemia. As the patient remained asymptomatic, intravenous iron replacement was

discontinued but she continues to be monitored with complete blood counts, iron panels, and physical exams.

Discussion

Iron deficiency anemia has been typically associated with thrombocytosis, but some cases of thrombocytopenia have been reported [3-11], especially in the pediatric literature [10,11]. Recurrent cases of this uncommon association are even fewer with only one case reported of a male with recurrent iron deficiency anemia and thrombocytopenia [12].

The exact mechanism of platelet count variation in respect to iron remains unknown, it was hypothesized that the amino acid sequence similarity between erythropoietin (EPO) and thrombopoietin (TPO) could explain the more common presentation of reactive thrombosis [13], but this would fail to explain the presence of thrombocytopenia with iron deficiency anemia and the lack of cross competition between these two cytokines in cells altered to express functional forms of both the Mp1 receptor and the EPO receptor [14]. A more plausible explanation for EPO induced platelet count variation is that thrombopoiesis may have a diphasic response to EPO, as models with moderate Epo stimulation obtained by the standard doses of recombinant human EPO cause a moderate elevation of platelet counts but intense EPO stimulation causes some degree of thrombocytopenia [15]. It has also been hypothesized that there is a two-compartment iron system in which iron can inhibit the rise in platelet count above steady-state levels via some inhibitory mechanism against thrombopoietin but at the same time, iron is required for the production of an integral portion of the platelet [16]. This model is further supported by the fact that iron is required for platelet protein synthesis [17] and is part of the elemental composition of platelets[18]. Iron deficiency stimulates thrombopoiesis, but only to the extent when sufficient iron is available for the synthesis of essential platelet components. In the present case, the course of the platelet count in relationship to iron replacement supports this compartmental model as shown in figure 1, as when in severe iron deficiency the platelet count is diminished but when iron is available it overcorrects up to 1 million platelets and then returns to baseline.

Conclusion

Although iron deficiency with thrombocytopenia presents uncommonly, this association has been reported in the literature. Clinicians should consider iron deficiency induced thrombocytopenia as a differential diagnosis when more common causes of thrombocytopenia have been ruled out. This case highlights the importance of an iron replenishment trial for the individuals with recurrent thrombocytopenia. Iron replenishment

trial could spare the patients with iron responsive thrombocytopenia from more invasive diagnostic modalities.

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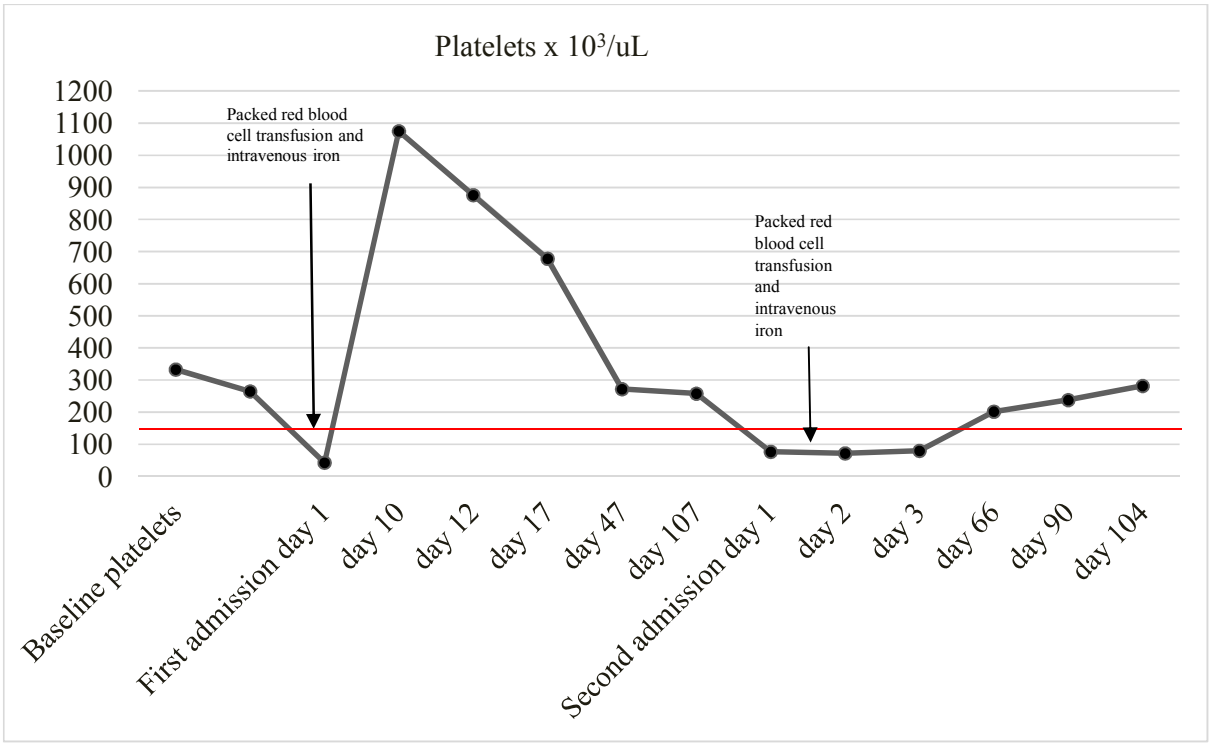

Figure 1. Platelet production in response to iron replenishment