Case Report:

Iron deficiency anemia with thrombocytosis: a diagnostic challenge

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Abstract:
Thrombocytosis, a common hematologic finding can present as incidental finding and pose a great diagnostic challenge. Thrombocytosis can be due to reactive process or due to clonal disorder. Platelet count more than 1,000x10^3/mm^3 is usually caused by clonal disorder. Reactive causes like Iron deficiency anemia rarely lead to platelet counts more than 700x10^3/mm^3. Here we report a case of a young woman presenting with iron deficiency anemia associated with thrombocytosis with platelet count 1,308x10^3/mm^3.

Keywords: Thrombocytosis, Iron deficiency anemia

Introduction
Thrombocytosis is commonly encountered in clinical setting with majority of cases discovered incidentally. Thrombocytosis can be attributed to autonomous (neoplastic) overproduction or as a reactive overproduction secondary to infections, iron deficiency anemia, malignancies. Iron deficiency anemia usually results in mild to moderate degree of reactive thrombocytosis. The mechanism leading to secondary or reactive thrombocytosis is not completely understood. The accelerated megakaryopoiesis may result due to elevated megakaryocytic growth factors such as thrombopoietin, Interleukin (IL)-6 or IL-11. But despite many efforts exact cause behind enhanced megakaryopoiesis is vaguely known and further investigation is required.

Case Report
A 23 year old female presented with pain abdomen, fatigue and shortness of breath since 1 month. She had history of heavy menstrual bleeding since 6 months. There was no history of bleeding from other sites. On examination pallor was present, no icterus, petechiae, ecchymosis or purpuric lesions were noted. Her haemoglobin was 7.4g/dl (Normal range 12-15g/dl), platelet count was 1,308x10^3/mm^3(normal range 150-450x10^3/mm^3). Total leucocyte count and differential leucocyte count were within normal range. Total leucocyte count- 6700 (Normal 4-11x10^3/mm^3, differential leucocyte count-neutrophils 65%, lymphocyte 30%, monocyte 3%, eosinophil 2%, basophil 0%. Mean corpuscular volume was 62.8 fl (Normal range 80-100 fl), Mean corpuscular haemoglobin was 16.3pg (Normal range 27-32 pg), Mean corpuscular haemoglobin concentration was
25.9 g/dl (Normal range 32-37 g/dl), Red cell distribution width (RDW) was 27.2% (Normal range 11%-15%). Iron studies revealed serum iron 20 µg/dl (Normal range 50-170 µg/dl), serum ferritin was 5.56 ng/dl (Normal range 12-150 ng/dl), serum transferring binding capacity was 416.8 mg/dl (Normal range 204-360 mg/dl), percent saturation was 6% (Normal range 16-45%). Results of iron studies were consistent with iron deficiency anemia. The peripheral blood smear showed microcytic hypochromic cells with increased number of platelets. Bone marrow aspiration study revealed erythroid hyperplasia with micronormoblastic erythropoiesis and megakaryocytic hyperplasia. Overall bone marrow picture does not support diagnosis of Essential thrombocytopenia. Megakaryocytes were normal in morphology, giant megakaryocytes were absent and megakaryocytes donot show clustering. Prussian blue stain revealed decreased storage iron. Ultrasound of pelvis showed anteverted uterus with heterogenous thickening of endometrium with thickness of 14 mm. Histological examination of endometrial biopsy revealed irregularly cystically dilated glands with minimal atypia consistent with diagnosis of simple endometrial hyperplasia without atypia. Her coagulation parameters were normal. Patient was administered one unit of packed red cells and was advised to take oral iron supplements along with progesterone therapy. 5 weeks after iron supplementation her haemoglobin was increased to 11.2 g/dl and platelet count decreased to 480x10^3/mm^3.

**Discussion**

Platelets (thrombocytes) are produced by mature megakaryocytes. Adult humans produce about 100 billion thrombocytes per day. The major pathophysiologic cases of thrombocytosis i.e. an elevated platelet count are 1) clonal including essential (or primary) thrombocytosis and other myeloproliferative disorders like polycythaemia vera, chronic myelogenous leukemia, idiopathic myelofibrosis, myelodysplastic syndrome with 5q abnormality 2) reactive in which thrombocytosis occurs secondary to variety of acute and chronic clinical conditions like acute infection, Iron deficiency anemia, malignancies, inflammatory bowel disease. Studies had shown that reactive thrombocytosis is more common than primary or clonal thrombocytosis. Iron deficiency anemia is shown to be associated with reactive thrombocytosis but platelet count rarely exceeds 700x10^3/mm^3 as was depicted by Sanchez and Ewton. Platelet counts exceeding 1000x10^3/mm^3 was observed in few reports only. In our patient keeping in view of severe thrombocytosis haematological malignancy was suspected initially. However bone marrow smear examination did not support the diagnosis of Essential thrombocytosis or other myeloproliferative disorders and iron studies further establishes the diagnosis of iron deficiency anemia. Moreover normalisation of platelet counts after correction of iron status of the patient rules out the diagnosis of essential thrombocytosis. The mechanisms behind secondary thrombocytosis are not well defined and seems to be complex and diverse. Thrombopoietin is the key hormone which regulates megakaryocyte differentiation and proliferation in association with various cytokines like IL-1, IL-6, IL-11. It has been shown that there is an amino acid sequence homology between thrombopoietin and erythropoietin. In iron deficiency anemia erythropoietin level gets increased which explains thrombocytosis in Iron deficiency.

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anemia. However few reports suggested that reactive thrombocytosis and iron deficiency relationship is more complex as few patients with iron deficiency anemia and elevated erythropoietin levels do not present with thrombocytosis, pointing towards the possibility of involvement of some additional factor present in some iron deficient patients which support the stimulatory potential of erythropoietin on thrombopoiesis. Tefferi A et al reported elevated IL-6 levels in patients with reactive thrombocytosis or clonal thrombocytosis with reactive thrombocytosis thereby supporting the possible pathogenic role of elevated IL-6 levels in reactive thrombocytosis. But contrasting findings were reported by Akan et al whereby none of these cytokines had any effect on reactive thrombocytosis in iron deficiency anemia. So to establish the etiology of thrombocytosis in iron deficiency anemia further investigations needs to be performed. In our case bone marrow smears showed megakaryocytic hyperplasia. Till now only few reports mentioned the elevated megakaryocyte counts in iron deficiency anemia thereby resulting in increased platelet production. In general reactive thrombocytosis even when extremely high does not cause thrombotic or bleeding complications and hence does not require treatment. Thrombotic complications were occasionally reported in iron deficiency anemia.

**Conclusion**

This case establishes the association of an extreme thrombocytosis secondary to iron deficiency anemia. The fact to be stressed is that even in the presence of an extremely high platelet count possibility of reactive thrombocytosis should be considered and underlying cause should be investigated because in secondary thrombocytosis treatment of an underlying cause normalises the platelet count.

**References**

4) Kulnigg-Dabsch S, Evstatiev R, Dejaco C, Gasche C. Effect of Iron Therapy on Platelet Counts in Patients with Inflammatory Bowel Disease-

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