Clinical Medicine Insights: Blood Disorders

CASE REPORT

Idiopathic Thrombocytopenia with Iron Deficiency Anemia

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Abstract: We report a rare case of anemia and thrombocytopenia as a result of uterine fibroid and adenomyosis, complicated by immune thrombocytopenic purpura (ITP). Symptoms were presented as menorrhagia and metrorrhagia in a 34-year-old African American woman, who was later treated with blood and platelet transfusion and iron therapy with steroids. Uterine fibroids are commonly found to cause hematologic disturbances such as anemia and reactive thrombocytosis and, less commonly, thrombocytopenia. Moreover, such hematologic disturbances are secondary to heavy and irregular uterine bleeding, which is typically presented. A previous uterine fibroid diagnosis was made and reconfirmed by pelvic and transvaginal ultrasound to exclude other locoregional pathologies. ITP was suggested by Coombs test and several other serologies, leading to confirmation via bone marrow biopsy. In a previous case study, we reported positive responses in hemotecrit and platelet count after the introduction of iron therapy to an iron-depleted middle-aged female presenting severe anemia and thrombocytopenia.[1]

Keywords: thrombocytopenia, anemia, fibroid

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Introduction

Iron deficiency anemia was present in 1% to 2% of adults who according to the Third National Health and Nutrition Examination Survey (NHANES III).[2] Iron deficiency occurs in 11% of women, most often premenopausal, as well occurring in up to 4% of men. Iron deficiency anemia is one of the common anemias and is usually associated with reactive thrombocytosis.[3] Thrombocytosis, when presented with iron deficiency anemia, is suggested to be due to the stimulation of platelet production. Platelet production is induced by erythropoietin, whose levels are typically increased in patients with iron-deficiency anemia. Augmented levels of iron deficiency leads to normalization and an eventual decline in platelet numbers. The decline in platelets may be related to the variation in the activity of iron-dependent enzymes in megakaryocytosis and thromboiesis.[4] The pathogenesis of ITP is presumed to be related to increased platelet destruction along with inhibition of platelet production via the production of specific autoantibodies.[5]

Chronic heavy or prolonged uterine bleeding is a common gynecologic problem and can be classified further as ovulatory or anovulatory. Chronic heavy or prolonged uterine bleeding can result in severe anemia, where severe bleeding may lead to the necessity of immediate medical evaluation and treatment. Furthermore, uterine leiomyomas, arising from the smooth muscle cells of myometrium, are the most commonly presented pelvic tumor in female patients.[6]

We report a rare case of anaemia and immune thrombocytopenia in a 34-year-old African American woman who presented with menorrhagia and metrorrhagia secondary to multiple uterine fibroids. Her conditions were resolved with the introduction of packed red blood transfusion, platelets support, steroids, and iron therapy. Few documented cases of thrombocytopenia associated with bleeding secondary to uterine fibroids have been reported previously. Our case also establishes that thrombocytopenia can occur with anemia in a patient with menorrhagia and metrorrhagia. Moreover, in similar cases, patients do respond to iron therapy and etiology treatments with positive results.

Case Summary

A 34-year-old African American female patient was admitted to a medical intensive care unit (MICU) presenting with symptoms of menorrhagia and metrorrhagia as a result of multiple uterine fibroids. Testing and evaluation led to the diagnosis of iron deficiency anemia and immune thrombocytopenia. The patient presented with little past medical history except chronic iron-deficiency anemia diagnosed in 1994 during oral surgery workup. The patient's anemia was attributed to heavy menses as a result of adenomyosis uteri and multiple uterine fibroids. She presented with a heavy vaginal bleed of 5-months duration along with lightheadedness palpitations, severe weakness, and fatigue. Her physical exam was unremarkable and showed no sign of icterus, ecchymosis, and petechiae; however, the patient had marked pallor. At the time of evaluation, the patient was hemodynamically stable with blood pressure of 120/70 mmHg, pulse of 110 beat per minute, temperature of 98.6 °F and a respiratory rate of 19 breaths per minute.

As part of a routine examination, a complete blood count was analyzed, which presented negative for any further medical complications. An ultrasound of the pelvis obtained as part of the evaluation

Table 1. Admission blood values of 34-year-old female patient presenting iron deficiency anemia and thrombocytopenia, CBC, and blood chemistry results.

Variant	Initial value
Leukocyte count	$4.2 \times 10^3/mm^3$
Hemoglobin	5.6 g/dL
Hematocrit	19.6%
Platelet count	$16 \times 10^3/mm^3$
MCV	46.6 μm^3
Serum iron	10.1 µg/dL
Serum ferritin	3.85 ng/mL
Serum transferrin	331.12 mg/dL
Serum vitamin B_{12}	695 pg/mL
Serum folate	18.6 ng/mL
Iron binding capacity	413.9
Homocysteine	7.1 µmol/L
Methylmalonyl acid	18 µg/dL
ANA	Negative
PT	12 seconds
PTT	32 seconds
INR	0.9
Direct Coombs	Positive
Rheumatoid factor	Negative
Hepatitis B	Negative
Hepatitis C	Negative
CRP	$<$0.5 mg/dL
Reticulocyte count	1.3%

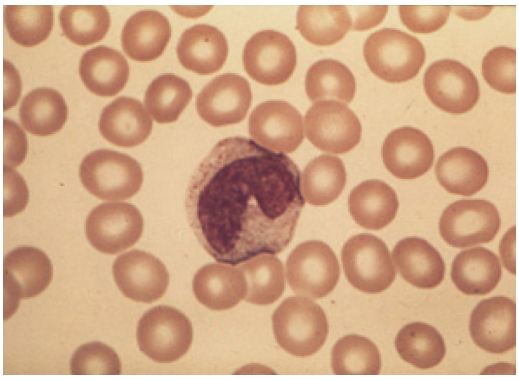

Figure 1. Peripheral blood smear showing erythrocytes, a huge neutrophil, and lack of platelets in our case of a 34-year-old female presenting severe anemia and immune thrombocytopenia.

for a heavy vaginal bleed revealed an anteverted uterus with heterogenous parenchyma, calcified anterior myoma, and a 0.54 cm ecchodense wall thickness exhibiting adenomyosis. Laboratory studies on admission revealed the following values: white blood cell (WBC), 4200/mm^3; hemoglobin, 5.6 g/dL; hematocrit, 19.6%; and platelet count, 16,000/mm^3. The differential counts were as follows: reticulocyte count, 0.031%; polymorphnucleocytes (PNL), 62%; lymphocytes, 28%; and mono, 7%. Moreover, iron deficiency anemia suggested as follows: ferritin, 3.85 ng/dL; transferrin, 331.12 mg/dL; B12, 695 pg/dL; folate, 18.6; methylmalonolic acid, 18; and homocysteine, 7.1. Coagulation parameter values were within a normal range exhibiting a prothrombin time (PT) of 12 seconds, a partial thromboplastin ime (PTT) of 32 seconds, and international normalized ratio (INR) of 0.9. A peripheral blood smear from the patient with ITP illustrates a decreased number of platelets, as well a normal appearing neutrophil and several erythrocytes. The absence of other findings from the peripheral smear was important in the diagnosis of ITP more so than the observed findings. Moreover, this smear demonstrateed an absence of immature leukocytes, as presented in leukemia and fragmented erythrocytes as typically exhibited in thrombotic thrombocytopenic purpura. Furthermore, the peripheral blood smear did not indicate pseudothrombocytopenia, which is typically distinguish by clumps of platelets.

The patient was given total of 3 units of packed red blood cells each with a volume of 350 mL, as well a high dose progesterone in the form of northindrone given 10 mg orally three times a day. Iron therapy treatments consisted of intravenous iron in the form of ferrilicit 125 mg for 2 doses on 2 consecutive days followed by 325 mg of iron sulphate given three times a day orally preceeding intravenous therapy. In addition, 500 mg daily of vitamin C and 1 mg daily of folate were given orally. After the first transfusion of blood, the patient dropped platelets count to 13,000/mm^3. She then received decadrone for four days based on a positive Coombs test. The patient continued to drop platelets to 9000/mm^3 and received another unit of platelets, and then the platelet count gradually started to rise. The patient's complete blood count (CBC) was followed serially, and the last CBC on discharge showed resolution of anemia with hemoglobin 9.7 g/dL and platelets of 60,000/mm^3. In the meantime, a bone marrow biopsy was done, which confirmed immune thrombocytopenia. Two months after the initial presentation, the patient had a hemoglobin of 12.2 g/dL and platelet count of 86,000/mm^3 (Fig. 3 and Table 2).

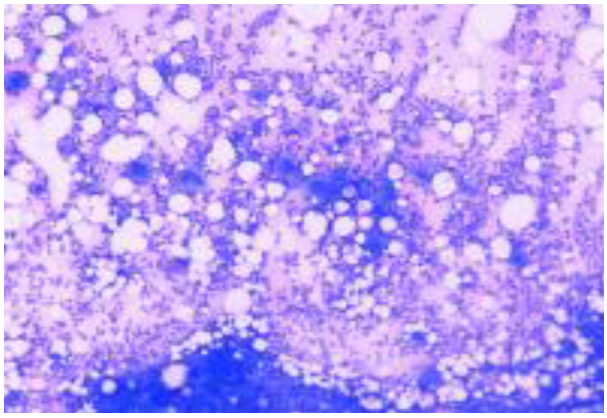

Figure 2. Bone marrow tissue section taken from a biopsy in our case of a 34-year-old female presenting severe anemia and Immune thrombocytopenia.

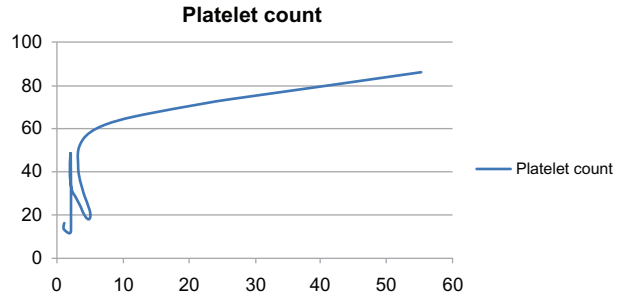

Figure 3. Platelets count in 34-year-old female patient against time.
Notes: The x-axis shows time in days, the y-axis shows count in thousand/mL.

Table 2. Serial blood test results for case patient day (g/dL) (%) (cells/mm^3) (cells/mm^3) (μm^3) (% of erythrocytes).

Day and time	Hemoglobin (x/g/dL)	Hematocrit (%)	Platelet count 1000x/mm^3	Leukocyte count 1000x/mm^3	MCV μm^3	Reticulocyte count %
1	5.6	19.6	16	4.2	56.6	N/A
1	2.95.3	18.1	13	4.2	57.4	1.3
2	6.2	20.4	12	4.8	74.1	N/A
2	7.3	23.7	48	7.9	73.9	N/A
2	7.3	27.4	34	7.9	75.3	N/A
3	7.6	24.4	27	4.7	76.3	N/A
5	7.5	24.4	19	5.5	76.5	N/A
6	9.1	28.8	60	10.1	78	2.8
55	12.2	36.2	86	4.7	92	N/A

Note: Day 1 is the day of admission to the hospital.
Abbreviations: MCV, mean corpuscular volume; N/A, data not available.

Discussion

In this report, we noted that blood transfusion and iron therapy coincided with steroids is the cornerstone treatment in patients who present with iron deficiency anemia and immune thrombocytopenia. This case further illustrates that thrombocytopenia can present transiently with severe iron deficiency anemia; however, this observation has rarely been reported.

The exact mechanism of thrombocytopenia occurring with severe anemia in menorrhagic patients is not fully understood. However, it is suggested that thrombocytopenia may be related to the alteration in the activity of iron-dependent enzymes in thrombopoiesis. Moreover, it is known that iron has both synthetic and regulatory roles in thrombopoeisis.[7] Low platelet counts are connected with decreased production and increased degradation, similarly noted in the red blood cell system. Two additional mechanisms for low platelet count include dilutional or distributional thrombocytopenia as well as spurious or pseudothrombocytopenia. Also, it may be noted that low platelet count may arise in immune thromcytopenia disorders. Laboratory examination should start with CBC and a peripheral smear prepared from a freshly shed sample of nonanticoagulated blood. These laboratory procedures allow for estimation of platelet numbers, morphology, condition of platelet clumping, and any associated blood cell changes that may be exhibited. CBC and peripheral blood smear helped confirm the presence or absence of thrombotic thrombocytopenic purpura and acute leukemia as expeditiously as possible, since delay in these diagnoses and initiating therapy may be fatal.[8]

Uterine leimyomas and adenomyosis are benign tumors that are mostly asymptomatic, yet can cause significant problems such as heavy uterine bleeding. This was evident in our case and was confirmed by pelvic and transvaginal ultrasound. Furthermore, symptoms atypically presented relate to the number, size, and location of fibroid. There is unclear bleeding etiology with possibilities including both microscopic and macroscopic abnormalities of the uterine vasculature, impaired endometrial hemostasis, or molecular dysregulation of angiogenic factors.[9]

In our case of heavy uterine bleeding with severe iron deficiency anemia and thrombocytopenia, we had gradual normalization of platelet count and hemoglobin concentration after introduction of iron and supportive therapy. This platelet response to iron therapy suggests that there is a complex and potentially subtle mechanisms behind this process, which may be due to "resetting" of the erythrocyte and platelet-producing systems in the bone marrow coinciding with iron repletion.[10]

Morris et al presented similar cases of four pediatric patients with iron deficiency anemia and severe thrombocytopenia at initial presentation. All four patients' hemoglobin concentrations and platelet counts normalized within 1 to 3 weeks of initiating iron supplementation, similar to our results. However, these patients compared to our case had a platelet "overshoot" phenomenon during iron therapy regimens. Furthermore, in our case, the patient had a component of immune mediated thrombocytopenia, which is noted and confirmed by serology including Coombs test. Moreover, an initial drop of platelet count occurred despite blood transfusion and iron therapy regimens.[11]

Perlman et al described six children with iron deficiency and thrombocytopenia. When treated with iron therapy, a response of significant thromocytosis had occurred within the first 24 hours of treatment. This was a phenomenon that was explained by the theory of Bilic and Bilicgthat suggests iron therapy in anemia-thrombocytopenia may result in normalization up to an overcorrection of platelet count due to erythropoietin and thrombopoietin homology.[12,13]

Ganti et al, treated a 39-year-old female Jehovah's Witness with several months' history of heavy irregular menses and severe iron deficiency. As blood transfusion was not possible, intravenous iron replacement therapy was given, which led to a transient leucopenia and thrombocytopenia. Both leucopenia and thrombocytopenia had recovered upon continuing iron supplementation, while our case, which had a drop in platelet count after iron therapy and transfusion, was most likely due to immune thrombocytopenia. The pathogenesis of ITP is presumed to be related to increased platelet destruction along with inhibition of platelet production via the production of specific autoantibodies which explains our disease course. Furthermore, our case demonstrates of the vital role of iron therapy in restoration of red blood cell and platelet cell count in iron depleted individuals.[14]

Conclusion

Due to the commonly encountered cases of severe anemia and thrombocytopenia with underlying gynecologic causes in females during there reproductive period, more research input must be geared towards exploring various associated etiologies. Furthermore, an establishment of solid management guidelines must be proposed, especially if a concomitant pathogenesis such as immune thrombocytopenia is presented.

Author Contributions

RI made the initial evaluation of the patient in emergency department, wrote the draft of the manuscript and supervised editing. JAA and JG took over care when the patient was moved to MICU, and contributed to writing of the manuscript. ID made the tables and curves, and presented the figures. TC did the editing. AG revised and assisted in reformatting the manuscript and conclusions. MZ was the main mentor who set the treatment plan, finalized the paper and made critical revisions. All authors reviewed and approved of the final manuscript.

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Competing Interests

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