Title: Pancytopenia, as a Presentation of Iron Deficiency: Report of Two Cases and Review of the Literature

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ABSTRACT

Introduction: One of the most common nutritional deficiencies worldwide is iron deficiency. Fatigue, pallor, vertigo, dyspnea, cold intolerance, lethargy, palpitation, headache and pallor of the mucous membranes or nail beds are the most common symptoms and signs of iron deficiency. Thrombocytosis is commonly seen in iron deficiency anemia, and it seems that erythropoietin plays the main role in this finding. At the other hand, thrombocytopenia and even leukopenia have been reported in iron deficiency, but pancytopenia is a very rare condition.

Case Presentation: In this report, we present two unusual cases of pancytopenia due to severe iron deficiency that improved after treatment with oral iron supplements.

Conclusion: Iron deficiency anemia, if sufficiently severe, may be associated with reduced platelet and leukocyte counts and should be considered as a differential diagnosis in all patients with pancytopenia.

Keywords: Pancytopenia, Iron deficiency, Anemia
1-Introduction

Iron deficiency is the cause of about half cases of anemia in worldwide population (1, 2). In addition to anemia, thrombocytosis is also seen in patients with iron deficiency; the cause of thrombocytosis is stimulation of platelet precursors due to moderately increased erythropoietin (3). Thrombocytopenia rarely can be a part of iron deficiency presentations (4). Also, leukopenia has been found in patients with iron deficiency anemia (5), but pancytopenia is very rare presentation of iron deficiency (4, 6).

2-Case presentation

Case 1

A 16-year-old boy was admitted with a 20-days history of weakness, lethargy and fatigue. Physical examination revealed a normal vital sign with severe pallor, and there were no hepatosplenomegaly and lymphadenopathy.

Complete blood count (CBC) showed: white blood cell (WBC) count 2.0×10^3, neutrophils 32.2 %, lymphocytes 58.8 %, monocytes 7%, eosinophil 2%, platelet count 75×10^3/μL, red blood cell (RBC) count 3.0×10^6, hemoglobin 6 g/dL, mean corpuscular volume (MCV) 58.7 fl, mean corpuscular hemoglobin (MCH) 16.4 pg, retic count 1%. Direct agglutination test, stool exam and stool occult blood test were negative and serum lactate dehydrogenase (LDH) was 176 U/L. Chest X-ray (CXR) and abdominopelvic sonography did not show abnormal findings.

Peripheral blood smear showed severe hypochromic microcytic anemia, thin and elongated red blood cells and marked decrease in other cells (Figure 1). Bone marrow aspiration showed hypercellular marrow with increase in megakaryocytes and no blasts. The patient’s serum ferritin level was severely decreased (0.9 ng/ml). Hemoglobin electrophoresis was consisted of A1 98.1%, A2 1.9 % and F 0.5%.

Treatment was started with oral iron supplement. One-week later ferritin level raised to 7.1 ng/ml and pancytopenia resolved. New laboratory data showed: WBC 6.8 x 10^3/μL, lymphocytes 20%, neutrophils 66%, monocytes 10%, eosinophils 4%, hemoglobin 8.8 g/dL and platelet 564 x 10^3/μL. One month later, serum ferritin increased to 58 ng/ml and hemoglobin level reached to 14.0 g/dL.
Case 2

A 14-year-old boy presented with fatigue and pallor for 2 months. There was no history of bleeding. Physical examination showed no abnormal findings but pallor.

Laboratory data showed: WBC 2.1 x 10^3 /uL, lymphocytes 36%, neutrophils 56%, monocytes 6%, Eosinophils 2%, hemoglobin 4 g/dL, RBC count 3.26x10^6, MCV 55.2 fl, MCH 12.3 pg, retic count 1%, platelet 345 x 10^3 /uL. LDH was 313 U/L and direct agglutination test and stool occult blood test were negative. In peripheral blood smear there were hypochromic microcytic RBCs with some tear drop cells and ovalocytes. Bone Marrow aspiration showed cellular marrow with no blasts. Hemoglobin electrophoresis was normal but patients’ serum ferritin was decreased to 2 ng/ml.

Iron treatment started immediately. Two weeks later, hemoglobin level increased to 11.8 g/dL, but the platelet count was decreased to 146 x 10^3 /uL This decrease in platelet count was transient and one month later the platelet count reached 250 x 10^3 /uL.

3-Discussion and Review of the Literature

Iron deficiency is an important public health problem all over the world and iron deficiency anemia is the most nutritional deficiency especially in children (7).

Fatigue, pallor, weakness, vertigo, dyspnea, cold intolerance, lethargy, palpitation, headache and pallor of mucous membranes or nail beds are most common symptoms and signs of iron deficiency (3, 7, 8).

In addition to the anemia clinical symptoms and signs, hypochromia and microcytosis are seen in peripheral blood smear of patients with iron deficiency anemia; but before this change become appear, alterations in the red cell distribution width (RDW) and the hemoglobin distribution width (RDW) could be seen (8). As iron stores fall, Serum iron and Serum ferritin levels decrease and TIBC increases; but a transferrin saturation of less than 10% may observe as “gold standard” against other tests. Pencil cells or Cigar cells (Figure 1), very thin and elongated red blood cells, are characteristic of iron deficiency in peripheral blood smear (9).

Thrombocytosis is a usual finding in iron deficiency anemia and it seems that stimulation of thrombopoietin receptors on megakaryocytes by high level erythropoietin is main cause (3, 7); but this hypothesis has not been proved experimentally (9).

Thrombocytopenia rarely seen in iron deficiency anemia (4, 6, 10), the mechanism behind this is not exactly clear, but may be related to direct stimulation of the erythropoietin receptor on megakaryocytes or shunting hematopoiesis into the erythroid precursors pathway Instead of megakaryopoiesis(7, 11). Another mechanism is change in iron-dependent enzymes in megakaryocytes (6, 12).
Leukopenia is other sign which may see in iron deficiency anemia and research’s report incidence about 17% in anemic patients; This incidence seems to be higher in patients with hemoglobin level under 8 g/dL (5). The reason of leukopenia in iron deficiency anemia is also unclear. High level of erythropoietin in animal experiments and human in vitro studies caused down-regulation in neutrophil production; this phenomenon may occur in patients with severe anemia (13, 14).

As we said previously, co-occurrence of leukopenia and thrombocytopenia, in iron deficiency anemia is very rare and pancytopenia may suggest other diagnoses such as bone marrow failure or malignancy. In our cases, which presented with pancytopenia, bone marrow aspiration showed no evidence of malignancy or bone marrow failure.

Iron treatment should be started immediately after diagnosis, especially in symptomatic patients (2). There are inexpensive and effective oral iron preparations like ferrous sulfate, gluconate, and fumarate. Iron is administrated at a dose of 4-6 mg/kg/day divided into three-times-a-day dose or single-daily dose on an empty stomach (2, 9, 15).

Reticulocytosis starts on day 3 and reaches peak at 5-7 days (16). Due to the rarity of pancytopenia in the context of iron deficiency, there is no clear evidence in literatures to determine time to recovery of leukopenia and thrombocytopenia (4-6), and even there are reports of transient exacerbation of cytopenia after iron treatment (4, 17); Just like transient thrombocytopenia in our second patient.

As we mentioned above, in our patient’s pancytopenia resolved during one week after treatment with oral iron supplements. This finding was another reason to prove that iron deficiency was the main cause of pancytopenia in these patients.

4-Conclusion:

Severe iron deficiency anemia may be associated with pancytopenia and should be added to the list of conditions leading to pancytopenia.
Figure 1. Peripheral Blood Smear: hypochromic microcytic anemia and Pencil cells (Cigar cells)
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Footnotes

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