

Case Report:

Pancytopenia as a Presentation of Iron Deficiency: A Case Report



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ABSTRACT

One of the most common nutritional deficiencies worldwide is iron deficiency. Fatigue, pallor, vertigo, dyspnea, cold intolerance, lethargy, palpitation, headache, and the pallor of the mucous membranes or nail beds are the most frequent symptoms and signs of iron deficiency. Thrombocytosis is commonly observed in iron deficiency anemia; it seems that erythropoietin plays the main role in this respect. Furthermore, thrombocytopenia and even leukopenia have been reported in iron deficiency; however, pancytopenia is a very rare condition. In this report, we presented two unusual cases of pancytopenia due to severe iron deficiency that improved after treatment with oral iron supplements. Iron deficiency anemia, if sufficiently severe, may be associated with reduced platelet and leukocyte counts. Accordingly, this condition should be considered as a differential diagnosis in all patients with pancytopenia.

1. Context

Iron deficiency is the cause of about half of the cases of anemia worldwide (1, 2). In addition to anemia, thrombocytosis is detected in patients with iron deficiency; the cause of thrombocytosis is the stimulation of platelet precursors due to moderately increased erythropoietin (3). Thrombocytopenia can rarely be a part of iron deficiency presentations (4). Besides, leukopenia was found in patients

with iron deficiency anemia (5); however, pancytopenia is a very rare presentation of iron deficiency (4, 6).

2. Case Presentation

Case 1

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

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Complete Blood Count (CBC) revealed the following: White Blood Cell (WBC) count: 2.0×10^3 , neutrophils: 32.2%, lymphocytes: 58.8%, monocytes: 7%, eosinophil: 2%, platelet count: $75 \times 10^3/\mu\text{L}$, 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, and retic count: 1%. Direct agglutination test, stool exam, and stool occult blood test was negative and Serum Lactate Dehydrogenase (LDH) was equal to 176 U/L. Chest X-Ray (CXR) and abdominopelvic sonography presented no abnormal findings.

Peripheral blood smear demonstrated severe hypochromic microcytic anemia, thin and elongated red blood cells, as well as a marked decrease in other cells (Figure 1). Bone marrow aspiration illustrated hypercellular marrow with increased 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 initiated with an oral iron supplement. A week later, the ferritin level raised to 7.1 ng/mL, and pancytopenia was resolved. New laboratory data were as follows: WBC: $6.8 \times 10^3/\mu\text{L}$, lymphocytes: 20%, neutrophils: 66%, monocytes: 10%, eosinophils: 4%, hemoglobin: 8.8 g/dL, and platelet: $564 \times 10^3/\mu\text{L}$. One month later, serum ferritin increased to 58 ng/mL and hemoglobin level reached 14.0 g/dL in the patient.

Case 2

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

Laboratory data were as follows: WBC: $2.1 \times 10^3/\mu\text{L}$, lymphocytes: 36%, neutrophils: 56%, monocytes: 6%, eosinophils: 2%, hemoglobin: 4 g/dL, RBC count: 3.26×10^6 , MCV: 55.2 fl, MCH: 12.3 pg, retic count: 1%, and platelet: $345 \times 10^3/\mu\text{L}$. LDH was equal to 313 U/L and the direct agglutination test and stool occult blood test results were negative. In peripheral blood smear, there were hypochromic microcytic RBCs with some teardrop cells and ovalocytes. Bone Marrow aspiration demonstrated cellular marrow with no blasts. Hemoglobin electrophoresis was normal; however, the patients' serum ferritin was decreased to 2 ng/mL.

Iron treatment was started immediately. Two weeks later, hemoglobin level increased to 11.8 g/dL; however, the platelet count was decreased to $146 \times 10^3/\mu\text{L}$. This decrease in platelet count was transient and one month later, the platelet count reached $250 \times 10^3/\mu\text{L}$.

3. Discussion

Iron deficiency is an essential public health problem globally; iron deficiency anemia is the most prevalent nutritional deficiency, especially in children (7).

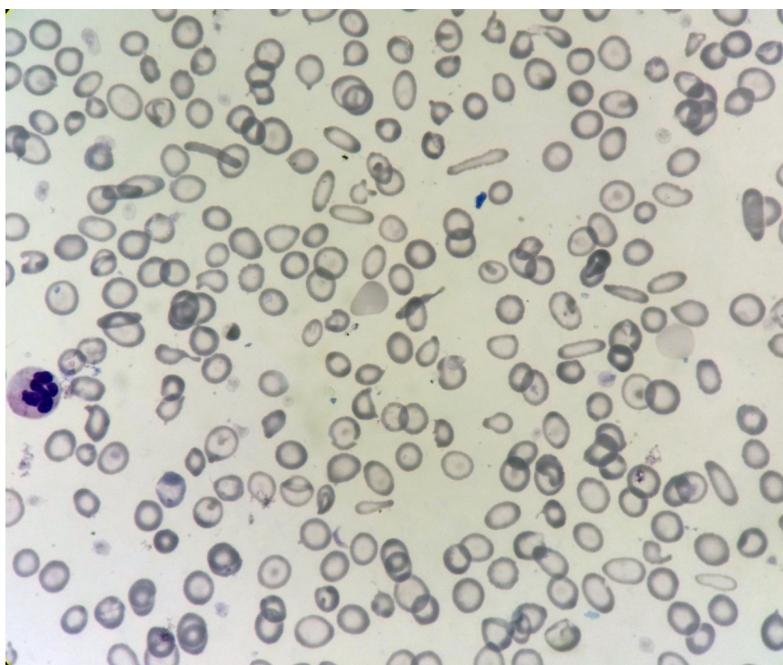


Figure 1. Peripheral blood smear: Hypochromic microcytic anemia and Pencil cells (Cigar cells)

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

In addition to the anemia's clinical symptoms and signs, hypochromia and microcytosis are observed in the peripheral blood smear of patients with iron deficiency anemia; however, before this change become apparent, alterations in the Red Cell Distribution Width (RDW) and the Hemoglobin Distribution Width (HDW) could be detected (8). As iron stores fall, serum iron and serum ferritin levels decrease and TIBC increases; however, transferrin saturation of <10% may be observed as "gold standard" against other tests. Pencil cells or Cigar cells (Figure 1), as well as very thin and elongated red blood cells, are characteristics of iron deficiency in peripheral blood smears (9).

Thrombocytosis is a usual finding in iron deficiency anemia; the stimulation of thrombopoietin receptors on megakaryocytes by high-level erythropoietin seems to be the main cause (3, 7). However, this hypothesis has not been experimentally proved (9). Thrombocytopenia is rarely observed in iron deficiency anemia (4, 6, 10). The mechanism behind this remains unclear; however, it may be related to the direct stimulation of the erythropoietin receptor on megakaryocytes or shunting hematopoiesis into the erythroid precursors' pathway instead of megakaryopoiesis (7, 11). Another mechanism is the change in iron-dependent enzymes in megakaryocytes (6, 12).

Leukopenia is another sign which may be observed in iron deficiency anemia. Evidence suggests its incidence to be about 17% in patients with anemia. This incidence seems to be higher in patients with hemoglobin levels <8 g/dL (5). The reason for leukopenia in iron deficiency anemia also remains undiscovered. High levels 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 mentioned earlier, the co-occurrence of leukopenia and thrombocytopenia in iron deficiency anemia is very rare; pancytopenia may suggest other diagnoses, such as bone marrow failure or malignancy. In our cases that presented with pancytopenia, bone marrow aspiration revealed no evidence of malignancy or bone marrow failure.

Iron treatment should be initiated immediately after the diagnosis, especially in symptomatic patients (2).

There are inexpensive and effective oral iron preparations, such as ferrous sulfate, gluconate, and fumarate. Iron is administered 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 a peak in 5-7 days (16). Due to the rarity of pancytopenia in the context of iron deficiency, there is no clear evidence in the literature to determine the time to recovery of leukopenia and thrombocytopenia (4-6). Besides, there are even reports of the transient exacerbation of cytopenia after iron treatment (4, 17); just like transient thrombocytopenia in our second reported patient.

As mentioned, our patient's pancytopenia resolved one week after the treatment with oral iron supplements. This finding was another reason to support 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.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles were considered in this article. The study participants were informed about the purpose of the research and its implementation stages. Written informed consent was obtained from the patients' parents for the publication of this case report.

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Authors contributions

All authors equally contributed to preparing this article.

Conflicts of interest

The authors declared no conflict of interest.

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