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Hematology Quiz – Case 45

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2016, 33(1):126–128

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A 41-year-old man was admitted to our Department because of severe anemia. He had complained about weakness, fatigue, headache, and dyspeptic symptoms for the four months. His past medical and family history was unremarkable.

On admission, the physical examination revealed pallor, a sensitivity in the upper abdomen while patient's temperature, blood pressure and pulse rate were within normal limits. The nails were fragile tending to thinning and flattening. There was a mild atrophy of the lingual papillae and an angular stomatitis. The spleen was slightly enlarged (only the tip was felt); no hepatomegaly or lymphadenopathy was observed. The neurological examination revealed no abnormalities.

His hematological profile was as follows: WBC 6.8×10^9/L (differential count: neutrophils 56%, lymphocytes 35%, monocytes 6% and eosinophils 4%), Hb 7.0 g/dL, Ht 22.2%, MCV 70.3 fL, MCH 23.0 pg, MCHC 29.6 g/dL, RDW 17.6% and platelet count 304×10^9/L. The reticulocyte count was 4.6% and the ESR was 50 mm/1h. The examination of the peripheral blood smears revealed hypochromia, microcytosis, anisopoikilocytosis and mild elleiptocytosis (fig. 1). The morphology of granulocytes and platelets was normal. Serum biochemistry was within normal limits except of the following: iron concentration 45 μg/dL, ferritin levels 20 ng/mL and TIBC 316 μg/dL. Bone marrow aspiration is shown in figure 2. The thyroid function tests, the X-rays of the chest and the electrocardiographic evaluation were revealed no abnormalities. The ultrasonography of the abdomen was normal while the endoscopy of the upper gastrointestinal system revealed a moderate esophageal hiatal hernia with the presence of ulceration to the gastric mucosa at the neck of the hernial sac.

The diagnosis was established and the administration of the

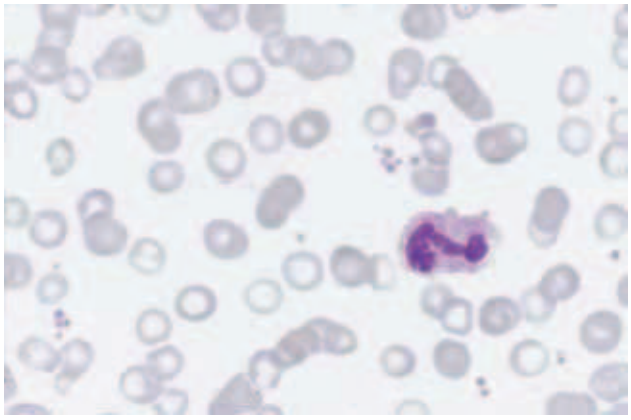

Figure 1

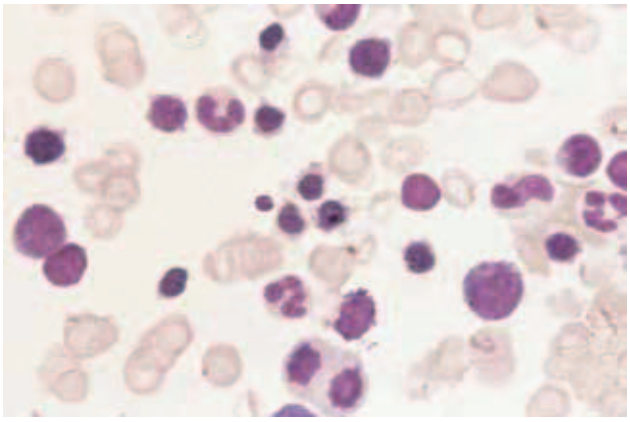

Figure 2

appropriate medication was started. One month after treatment initiation the hemoglobin level was 10.6 g/dL and the hematocrit 32%. The reticulocyte count was 7.8% and the peripheral blood smears image is shown in figure 3. Three months of treatment resulted in the correction of blood parameters, the normalization of the tongue and nails appearance and the absolute relief of the dyspeptic symptoms.

Comment

In iron deficiency anemia, initially the bone marrow iron stores begin to decrease (primary ferritin increase) and after that there is a decrease of hemosiderin. The decrease of ferritin values is an earlier finding in iron deficiency. Following that the bone marrow iron stores are reactively activated and there is an increase of transferring values (resulting thus in an increase of total iron binding capacity [TIBC]); as a result, the serum iron levels are decreased and therefore there is a decrease of siderophyllin saturation index. In bone marrow smear after Perls staining there is a disappearance of sideroblasts (absence of intracellular and extracellular iron). After a long term iron deficiency, anemia is present (initially microcytic and later hypochromic). The presence of these characteristics of anemia are due to decrease of hemoglobin synthesis (ferrum is the main heme component).

The decrease of hemoglobin synthesis results in mitosis increase of the erythroid series cells, which is dependent on cellular hemoglobin content, resulting in microcytic red cell production as compared to normal (initially, only the presence of isolated microcytosis without anemia). Later there is anemia, which is a hypoproductive central etiology anemia because of quantitative bone marrow erythroid series insufficiency.

If blood loss continues, even after bone marrow iron stores exhaustion, there are insufficient amounts of available iron for the preservation of normal erythrocytic mass and thus the hemoglobin erythrocytic content falls. Following that, progressive change of peripheral blood values appears. Initially the hemoglobin concentration in red cells falls, down to normal individual limits, while the red cells become progressively hypochromic and microcytic. When anemia ensues the concentration of hemoglobin falls below normal and there is a synchronous microcytic transformation of red cells (MCV and MCH decreased values). With these alterations there is no initial change of MCHC values and the red cells become normochromic. The MCHC value decreases only in the late stages of anemia when the red cells become hypochromic (20–80% of patients with iron deficiency anemia have a normal MCHC value and the value is decreased only if the hemoglobin concentration falls lower than 7 g/dL for women and 9 g/dL for men).

Anemia of different severity (microcytic, MCV less than 80 fL, hypochromic, MCH less than 27 pg, without reticulocytes increase). In the peripheral blood smear there is microcytosis, hypochromia, anisocytosis, poikilocytosis or target cells. The number of leukocytes –and neutrophils– is in normal limits, while the platelet number is often increased (reactive thrombocythemia).

Bone marrow aspiration is not very helpful for the correct diagnosis. An erythroblastic hyperplasia with mature normoblast predominance (shift to the right of the erythroid series) is present with a hypochromic appearance (retardation of hemoglobinization), while in Prussian blue staining a disappearance of extracellular and intracellular iron is present (absence of normal sideroblasts).

Hypochromic anemia is accompanying some chronic disorders. It represents the most frequent etiology of hospitalized patients and is accompanied by chronic disorders such as infections, malignant diseases, connective tissue diseases, renal insufficiency and other rare diseases.

The characteristic findings are:

- Mild anemia, without morphological alterations of red cells, while more infrequently a relative degree of hypochromia is present and sometimes hypochromia and microcytosis.
- Low serum iron values, low TIBC and low transferrin saturation are present, while the bone marrow iron stores are initially normal. The development of anemia usually needs about two months from the beginning of the disease and it is usually stabilized on a personal hemoglobin level. Anemia accompanying the chronic diseases must be differentiated from iron deficiency anemia because there is not any response to ferrum supplementation treatment. The only manner of differential diagnosis is to show the presence or absence of bone marrow iron stores, but this way is not the most practical manner for such frequent anemia. The simplest and more useful examination is the determination of serum ferritin levels which is representative of iron stores levels. The TIBC determination may often be helpful because it is frequently lower in anemia of chronic diseases and commonly higher in iron deficiency anemia.

Frequent cause of errors: The association of iron and vitamin B_{12} or follic acid deficiency can result in normocytic anemia (iron deficiency is masked after B_{12} or follic acid treatment, full reconstitution of anemia after iron replacement therapy).

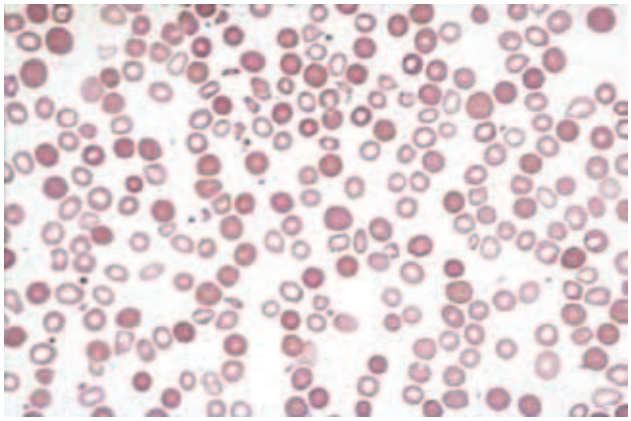

Figure 3

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