MODERN APPROACHES TO THE DIAGNOSIS AND TREATMENT OF VITAMIN B12 DEFICIENCY ANEMIA

Juraeva N.T., Radjabova S.O.

EMU University

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Abstract. Vitamin B12 deficiency anemia (Addison–Biermer anemia, pernicious anemia, hyperchromic anemia) is a hematological disorder caused by impaired hematopoiesis due to a deficiency of vitamin B12 or impaired absorption ***of this vitamin. Vitamin B12 deficiency Avgust result from inadequate nutrition, strict*** dieting, or prolonged fasting. However, vitamin B12 deficiency can sometimes ***occur despite sufficient dietary intake. This Avgust be associated with a deficiency of*** intrinsic factor (Castle's factor), which is essential for vitamin B12 absorption in the intestine. Insufficient production of intrinsic factor may be caused by congenital abnormalities, the formation of antibodies against the gastric parietal cells responsible for its production, or structural changes in the stomach following surgery or inflammation. Vitamin B12 deficiency may also be associated with liver and kidney disorders, malignant tumors, and intestinal parasites. The clinical manifestations of vitamin B12 deficiency can be divided into three main groups: gastrointestinal, neurological, and hematological. The most common manifestation is anemia, which is usually accompanied by gastrointestinal disturbances. ***Neurological symptoms are variable, tend to develop later, and Avgust occur even in*** the absence of anemia. Pernicious anemia (also known as Addison–Biermer anemia) is a human-specific disorder caused by vitamin B12 (cobalamin) deficiency resulting from malabsorption [1].

Materials and Methods

The diagnosis of vitamin B12 deficiency anemia is based primarily on the patient's medical history and laboratory findings. Peripheral blood analysis in patients with vitamin B12 deficiency anemia reveals the following changes: the mean corpuscular volume (MCV) increases to 95–110 fL in mild to moderate anemia and to 110–150 fL in more severe cases. In most patients, MCV gradually increases over several months, even in the absence of anemia and other clinical symptoms. An increase in MCV by 5 fL from the baseline level should raise suspicion of megaloblastic anemia and prompt further investigation. An MCV >120 fL is generally associated with megaloblastic anemia and helps exclude other causes of macrocytosis. However, MCV may remain within the normal range when vitamin B12 deficiency is accompanied by iron deficiency anemia, thalassemia, or anemia of chronic disease.

The red blood cell count may be markedly reduced. The severity of anemia does not correlate with the severity of neurological manifestations, which often precede hematological abnormalities. The red cell distribution width (RDW) is usually significantly increased. Mean corpuscular hemoglobin (MCH) is elevated, reaching 33–38 pg in moderate anemia and up to 56 pg in severe anemia, whereas mean corpuscular hemoglobin concentration (MCHC) generally remains within the normal range. The reticulocyte count is decreased, usually below 0.5%. Thrombocytopenia and leukopenia may also occur. Peripheral blood smears demonstrate marked anisocytosis and poikilocytosis, with characteristic macro-ovalocytes, schistocytes, polychromatophilia, Cabot rings, Howell–Jolly bodies, and normoblasts. Macro-ovalocytes are typically associated with megaloblastic anemia and, less commonly, with myelodysplastic syndromes.

An early sign of megaloblastic hematopoiesis is neutrophil hypersegmentation. The presence of more than 5% of neutrophils with five segments or any number of neutrophils with six or more segments supports the diagnosis.

Bone marrow examination reveals erythroid hyperplasia with megaloblastic changes. Abnormalities may be present in all hematopoietic cell lines, accompanied by signs of ineffective erythropoiesis. In cases of concomitant iron deficiency, megaloblastic changes in the erythroid lineage may be masked; however, abnormalities in the granulocytic lineage persist.

Biochemical blood analysis typically demonstrates a marked increase in lactate dehydrogenase (LDH), predominantly in fractions I and II, as well as a decrease in alkaline phosphatase activity. Due to intramedullary hemolysis, the level of indirect bilirubin is increased. Serum iron and ferritin levels, as well as bone marrow iron stores, are almost always elevated [3,4].

Results and Discussion

In vitamin B12 deficiency anemia, the serum vitamin B12 level is decreased. The reference range is 100–250 pg/mL. Elevated levels of methylmalonic acid (reference range: 70–279 nmol/L) and homocysteine (reference range: 5–15 μmol/L) are also characteristic of vitamin B12 deficiency. A positive therapeutic response is demonstrated by improvement in the patient's general condition, as well as normalization of hematological and biochemical parameters during treatment.

The differential diagnosis should include disorders associated with megaloblastic hematopoiesis or macrocytosis:

1. Folate deficiency anemia.
2. Anemias characterized by megaloblastic hematopoiesis: congenital orotic aciduria, Lesch–Nyhan syndrome, thiamine-responsive megaloblastic anemia, congenital dyserythropoietic anemia, refractory megaloblastic anemia, and erythroleukemia.

3. Disorders associated with macrocytosis without signs of megaloblastic hematopoiesis: aplastic anemia, autoimmune hemolytic anemia, liver disease, hypothyroidism, and sideroblastic anemia.

Treatment and Secondary Prevention of Vitamin B12 Deficiency Anemia

Vitamin B12 is administered at a dose of 5 mg/kg per day in children younger than one year, 100–200 μg per day in children older than one year, and 200–400 μg per day in adolescents. The treatment course lasts 4 weeks. Maintenance therapy consists of weekly administration of the same dose for 2 months, followed by administration twice a month for the subsequent 6 months.

If the underlying cause of anemia cannot be eliminated, annual preventive courses of vitamin B12 therapy are recommended, with 10–15 injections per course. In general, patients do not require red blood cell transfusions. Indications for red blood cell transfusion include a hemoglobin level below 50 g/L, severe infections, and cardiovascular complications.

In some patients, iron deficiency may become apparent during vitamin B12 treatment due to increased erythropoiesis. This may prevent complete normalization of hematological parameters and requires standard treatment with iron preparations.

Conclusion

Vitamin B12, also known as cobalamin, is a water-soluble vitamin essential for the normal functioning of the brain and nervous system, as well as for hematopoiesis. It is one of the eight B vitamins and functions primarily as a cofactor in numerous metabolic processes in the human body, particularly DNA synthesis and regulation, fatty acid synthesis, and energy production.

Vitamin B12 deficiency leads to a characteristic form of anemia and may cause neurological and gastrointestinal disorders. Severe vitamin B12 deficiency is

associated with subacute combined degeneration of the spinal cord, which involves demyelination of the posterior and lateral columns. Clinical manifestations may include memory and cognitive impairment, sensory loss, motor disturbances, impaired posterior column function, and disturbances of proprioception.

In advanced stages of vitamin B12 deficiency, psychosis, paranoia, and severe depression may occur. If left untreated, neurological complications can result in permanent disability. Studies have demonstrated that neurological symptoms may resolve rapidly following vitamin B12 replacement therapy, highlighting the importance of early diagnosis and timely treatment to prevent or reverse neurological complications.

References

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