VITAMIN B_{12} DEFICIENCY ANEMIA CLINICAL-LABORATORY DIAGNOSTICS AND TREATMENT METHODS

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Vitamin B12 deficiency is a disease that develops based on the disruption of DNA synthesis and is primarily caused by a deficiency of B12 intake.

Vitamin B12 deficiency is present in 0.1% of the general population, and its frequency is 1% among children.

The main reasons for the development of B12 deficiency are as follows:

- Impaired nutrition (strict vegetarianism, excessive alcohol consumption);
- Insufficient intake (lack of intrinsic factor, gastrectomy, competition for absorption in Diphyllobothriasis);
- Improper utilization (enzyme deficiency, liver diseases, poor quality diet);
- Increased demand (hyperthyroidism, pregnancy, parasitic infections, thalassemia);
- Increased excretion (insufficient binding of cobalamin to transcobalamin in the ileum, liver disease, kidney disease).

The coenzyme of vitamin B12, methyl cobalamin, participates in DNA synthesis by catalyzing the transition of folic acid to its active form (5-10 methylene tetrahydrofolate). In turn, the active form of folic acid helps in the formation of thymidine from uridine monophosphate, which participates in DNA synthesis. If DNA synthesis is disrupted, the maturation process of the cell becomes active before cell division. This leads to impaired cell division, development, and maturation. As a result, red blood cells, as well as leukocytes and platelets, become larger in size. This characteristic condition in the bone marrow is called megaloblastic hematopoiesis.

The second coenzyme of vitamin B12, deoxyadenosyl cobalamin, is involved in the breakdown and synthesis of fatty acids. Impaired breakdown of fatty acids leads to the accumulation of toxic propionic and methylmalonic acids in the nervous system, which causes damage to the posterior and lateral columns.

According to the rules, patients with a significant decrease in hemoglobin level and a noticeable decrease in the number of red blood cells should seek medical help. Clinical manifestations are characterized by disturbances in the gastrointestinal tract, hematopoietic system, and nervous system. Patients complain of general weakness, fatigue, dizziness, shortness of breath, and dyspeptic symptoms. Some patients lose their appetite and develop aversion to meat and other food types. At different stages of the disease, there may be a burning sensation and pain in the tongue, especially when using acidic products. Patients may experience disturbed sleep, tingling sensations in

the distal extremities, and a feeling of "cotton feet". Neurological disorders in vitamin B12 deficiency are called subacute combined degeneration of the spinal cord, and its most common symptoms are paresthesia and ataxic gait. Neurological disorders can manifest as depression, mental confusion, memory impairment, and even psychosis. Approximately 25% of patients with cobalamin deficiency experience neurological diseases with normal or nearly normal hematological indicators. The patient's skin color is pale lemon yellow, and the sclera becomes icteric.

Manifestations of vitamin B12 deficiency in the bone marrow:

1. Decreased vitamin B12 in the blood.

2.Peripheral blood:

- Decreased erythrocytes and hemoglobin;
- Erythrocyte macrocytosis (9-12 μm), megalocytosis (larger than 12 μm);
- Erythrocyte hyperchromia - loss of color;
- Erythrocyte poikilocytosis - change in shape;
- Jolly bodies (nuclear remnants);
- Cabot rings (nuclear membrane);
- Hyper segmentation of segmented neutrophils - increase in the number of segments to 5 or more;
- Decreased reticulocytes.
- Presence of basophilic granules in the cytoplasm of erythrocytes;
- Reticulocytotic occurs 5-7 days after administration of cyanocobalamin.
- Treatment with cyanocobalamin (Vitamin B12) leads to an increase in erythrocytes and hemoglobin.

In severe cases of anemia:

- Development of megaloblasts;
- Decreased platelets, increased macro platelets;
- Leukopenia without septic syndrome;
- Polychromatophilia - appearance of polychromatophilic erythrocytes;
- Appearance of myelocytes and metamyelocytes;
- Increased reticulocytes due to hemolysis in the splenic sinuses with increased megakaryocytes.

2. Megaloblastic type of hematopoiesis and erythroid hyperplasia are observed in the bone marrow.

Diagnostic algorithm for vitamin B12 deficiency in peripheral blood:

- Mandatory assortment of medical services:
- Initial examination by a general practitioner (examination, consultation);
- Cytological analysis of bone marrow aspirate (myelogram calculation);
- Study of platelets and reticulocytes in the general blood test;
- Obtaining a cytological preparation of bone marrow aspirate through puncture.
- Additional assortment of medical services used for insufficient mandatory assortment or inadequate effectiveness of treatment:

- Radioactive determination of vitamin B12;
- Histological examination of bone marrow aspirate (trepan biopsy);
- Determination of folate acid level in blood plasma;
- Determination of folate acid level in red blood cells.

Additional tests are performed at specialized hematology clinics. Some tests from the additional assortment may not be covered by mandatory medical insurance.

Example of a complete blood count in vitamin B12 deficiency: hemoglobin - 61 g/l; erythrocytes - 1.4x1012/l, hematocrit - 18%, MCV - 129 fl, MCH - 36.4 PG, leukocytes - 1.9 x 109/l. Leukocyte differential count: neutrophils - 50%, lymphocytes - 45%, monocytes - 5%, platelets - 70 x109/l, reticulocytes - 0.2%, ESR - 25 mm/hour. Anisocytosis++, macrocytosis+++, hyper chromia, and polisegmentation of neutrophil nuclei are noted.

Differential diagnosis involves distinguishing vitamin B12 deficiency from diseases associated with macrocytic anemia syndrome. This includes chronic erythromyeloid, myelodysplastic syndromes, large spleen and liver, liver cirrhosis, some hemolytic anemias, parasitic infections (diphyllobothriasis), malabsorption due to small intestinal or enteritis atrophy, and folate deficiency.

Food and food products are processed differently depending on the functional state of the digestive and cardiovascular systems. However, in any case, the daily diet should include at least 130-150g of protein (mainly from animals, poultry, fish, dairy products, cottage cheese, and others). To prevent the deposition of fat in the liver, the consumption of fat should be reduced to 70g per day. The amount of carbohydrates should not exceed 400g. Vitamin B12 is mainly found in meat, liver, heart muscles, and egg yolks. It is less common in milk and dairy products. Patients with vitamin B12 deficiency are treated with injections of cyanocobalamin (vitamin B12) into the muscle or vein (Table 8.3). The usual initial daily dose of the drug is 500-1000 mcg. With an increase in the level of hemoglobin, the dose can be reduced to 200-400 mcg per day. The effectiveness and efficiency of therapy are determined by the reticulocyte crisis, which is characterized by a maximum increase in the number of reticulocytes in 4-10 days after the start of treatment with cyanocobalamin (vitamin B12). Normalization of peripheral blood parameters and replenishment of its reserves in the liver (filling its depots with vitamin B12 to a normal level of 3000-10000 mcg) depend on the etiology and initial severity of the deficiency. If it is not possible to eliminate the pathophysiological mechanisms that contribute to its development, treatment with cyanocobalamin is carried out every month at a dose of 500 mkg.

Patients with vitamin B12 deficiency should undergo regular blood tests every 3 months under dispensary supervision, and once a month during stable remission.

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