HEREDITARY SPHEROCYTIC ANEMIA CLINICAL-LABORATORY DIAGNOSTICS AND TREATMENT METHODS

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Hereditary spherocytic anemia is a pathological subgroup of hemolytic anemias characterized by splenomegaly and the presence of spherocytic red blood cells in the peripheral blood.

The disease is widely spread in various European countries (1:2500). It is less common in Japan and African countries.

The disease has a familial characteristic and is predominantly inherited in a dominant pattern, resulting from mutations in genes encoding membrane cytoskeletal proteins of erythrocytes.

Anomalies in the erythrocyte cytoskeletal proteins can vary: spectrin and ankyrin anomalies are frequently observed, while other cytoskeletal anomalies such as 4.1. are less common. The severity of spectrin deficiency is present in all affected patients and its severity correlates directly with the severity of hemolysis. Modified erythrocytes contain potassium salts, adenosine triphosphate, and several enzymes. The ability to change shape and volume in the smallest toroidal system of the erythrocytes is lost. These rigid cells are sequestered and destroyed in the spleen. Splenomegaly develops in patients. The lifespan of erythrocytes decreases from 120 to 12-14 days. This requires increased compensatory erythropoiesis in the bone marrow.

The main manifestations of hereditary spherocytic anemia are jaundice, splenomegaly, and anemia. Commonly, skin and sclera become yellowish, hypothermia, pallor, increased physical activity, and sensitivity to stressful factors are observed. Hemolysis often occurs.

In young patients, there may be a delay in physical development. The compensatory capabilities of hematopoiesis decrease, leading to the development of anemia syndrome and the appearance of relevant complaints and symptoms in patients.

Splenomegaly develops due to the increased destruction of red blood cells in the red pulp. In hereditary spherocytosis, the liver is significantly enlarged. Aplastic crisis can develop in some patients with hereditary spherocytic anemia.

Hereditary spherocytic anemia is characterized by micro spherocytosis in the blood smear, presence of reticulocytotic, and decreased osmotic resistance of erythrocytes.

The onset of minimal hemolysis, also known as fragility, occurs at a sodium chloride concentration of 0.60-0.70 (0.48 normal), and its end (maximum hemolysis) occurs at 0.40 (0.32 normal). During hemolytic crisis, reticulocytotic occurs, sometimes exceeding 50%, and an increased number of normoblasts appear in the peripheral blood. Neutrophil leukocytosis may develop during this period. In cases of aplastic crisis, a sharp decrease in hemoglobin and erythrocyte levels is observed, along with reticulocytopenia.

Characteristics of hereditary spherocytic anemia include:

- Presence of micro spherocytes in the peripheral blood;
- Family history of the disease and the presence of the disease in close relatives;
- Decreased osmotic resistance of erythrocytes;
- Hemolytic anemia occurring within the cell.

Laboratory indicators specific to hereditary spherocytic anemia include:

1. Peripheral blood:

- Decreased red blood cells and hemoglobin;
- Increased hypochromia of erythrocytes;
- Decreased diameter of erythrocytes;
- Increased reticulocytes;
- In micro spherocytosis, small 5-6 μm hyperchromic erythrocytes appear;
- Increased unconjugated bilirubin in the blood;
- Increased iron levels in the blood.

Hemolytic crisis in hereditary spherocytic anemia is characterized by the following:

- The appearance of a large number of immature red blood cells called normoblasts;
- Reticulocyte count exceeding 30%.

Diagnostic protocol for patients with hereditary spherocytic anemia.

List of mandatory medical services:

- Initial consultation with a general surgeon (examination, consultation);
- Complete blood count, including examination of platelets and reticulocytes;
- Determination of total bilirubin level in the blood;
- Determination of unconjugated and conjugated bilirubin levels in the blood;
- Examination of erythrocyte sedimentation rate;
- Direct antiglobulin test (Comb's test);
- Indirect antiglobulin test (indirect Comb's test).

Additional types of medical services may be used if necessary, such as:

- Cytological examination of red blood cell morphology (calculation of red blood cell formulas);
- Hypoxic test to identify osmotic fragility of red blood cells;
- Determination of free hemoglobin levels in plasma;

- Determination of glucose-6-phosphate dehydrogenase levels in erythrocyte hemolysate;
- Determination of AST levels in the blood;
- Determination of ALT levels in the blood;
- Determination of γ-glutamyl transferase levels in the blood;
- Determination of alkaline phosphatase levels in the blood;
- Examination of osmotic fragility of erythrocytes;
- Examination of acid resistance of erythrocytes;
- Determination of ABO blood groups (A, B, O);
- Determination of Rh factor;
- Genetic testing for hereditary hemoglobin disorders (HbS, HbC, etc.);
- Agglutination test for red blood cell aggregation;
- Determination of thermal hemolysins in the blood;
- Determination of cold agglutinins in the blood;
- Determination of biphasic hemolysins in the blood.

An example of a complete blood count in hereditary spherocytic anemia: hemoglobin - 81 g/L, red blood cells - 2.7 × 1012/L, hematocrit index - 32%, MCV - 89 fl, MCH - 28.4 pg, white blood cells - 17.9 × 109/L. White blood cell differential: neutrophils - 75%, lymphocytes - 23%, monocytes - 2%, platelets - 170 × 109/L, reticulocytes - 32%, ESR - 25 mm/hour. Anisocytosis ++. Micro spherocytosis is noted.

Osmotic resistance of erythrocytes (ORE) refers to the ability of erythrocytes to withstand various agents (osmotic, chemical, mechanical) that cause their fragmentation. In clinical practice, ORE is often determined by measuring the resistance of erythrocytes to hypotonic solutions. In hypotonic solutions, erythrocytes change in diameter (swell), and a hypotonic solution with a concentration of 0.85% sodium chloride (NaCl) is used for erythrocytes. The minimal osmotic resistance of erythrocytes is determined in the most concentrated hypotonic solution, i.e., when erythrocytes begin to swell. In normal conditions, the minimal osmotic resistance is equal to 0.55-0.46% sodium chloride. The maximal osmotic resistance is observed at the lowest hypoosmolar concentration of sodium chloride and represents the maximum swelling of all erythrocytes. In adults, it is equal to 0.34-0.28%.

In hereditary micro spherocytic anemia, erythrocytes show a significant decrease in osmotic fragility. An increase in ORE is observed in hemolytic diseases, toxicosis, bronchopneumonia, malaria, lymphoma, leukemia, and liver cirrhosis. An increase in ORE is also observed in sickle cell anemia and mechanical jaundice.

Determine the osmotic resistance of erythrocytes.

To do this, 12 probes are numbered and placed in the state, and reduced concentration solutions of NACI are prepared.

Probe Numbers	1	2	3	4	5	6	7	8	9	10	11	12
0.9% NaCI, ml	8,3	7,8	7,2	6,7	6,1	5,6	5,0	4,5	4,0	3,8	3,6	3,4
Distilled water, ml	1,7	2,2	2,8	3,3	3,9	4,4	5,0	5,5	6,0	6,2	6,4	6,6

Concentration of the solution %	0,75	0,70	0,65	0,60	0,55	0,50	0,45	0,40	0,36	0,34	0,32	0,30

Each sample is collected with 40 μl of blood and mixed, then left in a centrifuge at 3000 revolutions per minute for one hour or 5 minutes. The result is determined based on the color of the sediment and the appearance of agglutinated red blood cells.

Differential diagnosis is performed between anemia syndrome and liver cirrhosis syndrome, which is associated with hemolytic jaundice. Differential diagnosis with the development of hemolytic jaundice is carried out with other hemolytic anemias, congenital and acquired, mostly autoimmune - primary and symptomatic; with the toxic effect of chemical substances (arsenic, sulfonamides); with PTG; with infections (glandular fever).

In cases where the clinical manifestations of hemolysis and anemia are compensated, symptomatic therapy is usually sufficient. Patients with mild hemolysis are advised to take folic acid at a dose of 3-6 mg per day (Table 8.4). In cases of severe anemic syndrome, as well as in aplastic crises, blood transfusion is performed to replenish red blood cells with low hemoglobin levels.

One of the main methods of treating patients with hereditary spherocytic anemia is splenectomy. Surgical treatment is indicated for patients with moderate and severe anemia, especially in the presence of cholelithiasis, especially in young patients. Splenectomy is performed in children with caution due to the higher risk of postoperative complications.

Patients with hereditary spherocytic anemia should eliminate fatty foods, legumes, lentils, boiled meat, and products containing vinegar from their diet.

Hospitalization is necessary for patients with signs of cardiac insufficiency, severe hemolytic crisis, aplastic crisis, and the need for splenectomy.

Regular follow-up examinations are conducted until splenectomy is performed (once every 3 months, with a stable course of the disease - once every 6 months). Individual treatment regimens are available for patients with hereditary spherocytic anemia, as unsupervised treatment can lead to a hemolytic crisis. After a long-term remission of at least 2 years following splenectomy, patients are discharged from registration and are no longer under the supervision of a hematologist.

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