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HEMOLYTIC DISEASE IN THE FETUS AND NEWBORNS

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Abstract:

Hemolytic disease of the newborn is a congenital disease of the fetus and the newborn due to isoimmunological incompatibility of fetal and maternal blood for erythrocyte antigens. The disease remains one of the more frequent causes of jaundice and anemia in newborns. The incidence of GBN ranges from 3-6%. Lethality from this disease is currently 2.5%.

Keywords: Jaundice, Edema Syndrome, Fetal Dropsy, Liver

INTRODUCTION.

More than 14 major erythrocyte antigenic - systems are known and more than 100 erythrocyte antigens have been identified, which can sensitize the body and lead to the formation of antibodies. In most cases, hemolytic disease in the fetus and newborn develops due to incompatibility between the blood of the mother and fetus by the Rh factor and its subtypes, the ABO system, and less frequently by other red blood cell antigens - the Kell, Duffy, Kid, etc. The rhesus factor was discovered in 1940 by Winner. The rhesus factor is an antigenic system consisting of 6 major antigens. For their designation use Fisher terminology Cc, Dd, Ee, or Winner rh¢ hr¢, Rh0 Hr0, rh¢¢¢ hr¢¢.It is conventionally accepted that it is D-antigen (lipoprotein) determines the belonging of blood to the rhesus-positive and has a pronounced isoantigenic activity. The rhesus antigen itself is located on the inner surface of the red blood cell membrane. It is not found in other organs and tissues, and has no natural antibodies to itself. Differentiation of the D-antigen in the fetus begins at 5-6 weeks of fetal development, and by 5-6 months of fetal development its antigenic activity becomes very high. It is encoded by 6 genes, linked by 3 on the same chromosome. Rh factor inheritance is by genocomplexes consisting of 3 antigens. Rhesus system genes can be in the homozygous DD and heterozygous Dd state. In the heterozygous variant, the D gene does not show signs of dominance relative to the d gene. Inheritance of the rhesus factor, like other group traits, obeys Mendel's law. A rhesus-positive man in a marriage with a rhesus-negative woman can be homozygous or heterozygous. In the first case, all children will be Rh-positive; in the second case, 75% of children will be Rh-positive and 25% will be Rh-negative. Various antigens of the rhesus system have different frequencies: D - 85%, C - 70%, E - 30%. hemostasis system, proteases, complement (C3,C5), changes the entire spectrum of cytokines, which significantly affects the pathogenesis of GBN. Exacerbates the disease - fetal and neonatal hypoxia, SBP, acidosis, hypoglycemia, hypoalbuminemia, immaturity of the liver conjugation system.

FATHER'S WATER.

Patogenesis: This form of IBD develops with prolonged exposure of the immature fetus to large amounts of antibodies at 20-29 weeks' gestation in the case of rhesus conflict and rarely in the case of group incompatibility. The action of rhesus antibodies on red blood cells, leads to their intravascular hemolysis with the development of hemolytic anemia and hyperbilirubinemia. Indirect bilirubin (IB) formed as a result of hemolysis of erythrocytes is removed through the placenta, which determines the absence of jaundice in the newborn baby at birth. As a result of hemolytic anemia develops: first - hemic hypoxia, which leads to metabolic disorders, disruption of glucose metabolism, the predominance of catabolic processes with increased formation of creatinine, urea, uric acid, and secondly - activated extramedullary hematopoiesis in the liver and spleen, leading to their increase and release into the fetal bloodstream immature forms of red blood cells: reticulocytes and normoblasts. As a result of the activation of phagocytosis (neutrophils and macrophages) and the impact of immune complexes on the vascular wall, its damage occurs with the release of immune complexes from the bloodstream, with their subsequent deposition on organs (liver, kidneys, heart, spleen) and fetal tissues, which leads to their damage.
The development of edema syndrome is caused by:
- hypoalbuminemia - 45-40 g/l (due to reduced albumin synthesis in the liver), which leads to a decrease in oncotic pressure in the vascular channel, transudation of the liquid part of blood with the development of hypovolemia and edema;
- decreased drainage function of the lymphatic system;
- Decrease of filtration function of kidneys with the development of oliguria,

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anuria;
- development of aldosteronism with activation of ADH;
- Increased permeability of the vascular wall and release of fluid into the interstitium;
-development of heart failure.
The development of hemorrhagic disorders in this form of GBN is due to the low level of procoagulants synthesized in the liver.
CLINIC: At birth, there is a sharp pallor of the skin, marked general edema with a significantly enlarged abdomen (ascites, hepatosplenomegaly), expansion of the boundaries of relative heart dullness with a manifestation of acute heart failure. Respiratory disorders in these patients are due to hypoplasia of the lungs, which were intrauterine compressed by the enlarged liver or due to the development of GBM. CNS side is dominated by cerebral depression syndrome. Acute renal failure develops very often. Hemorrhagic syndrome is characteristic.
Fetal and neonatal hemolytic disease develops after the 29th week of intrauterine development due to the supply of antibodies to the fetus antenatally and/or at the time of delivery. Depending on when and in what quantity the antibodies have reached the fetus or child, the timing and form of the disease will depend:
Congenital or postnatal, jaundice, anemic, edema.
YELLOW form is one of the most frequent clinical forms of GBN (90%). It is caused by erythrocyte hemolysis and accumulation of indirect bilirubin (IB), which has an affinity for lipids, which can lead to lesions of brain cell nuclei, has cytotoxic effect on a number of organs and systems (kidneys, heart, adrenal glands, immune system). The cytotoxic effect of NB is manifested by changes in the structure of cell membranes and disruption of their function. NB is a water-soluble substance and is eliminated from the body with the help of the liver. In high concentrations NB has a pyrogenic effect, inactivates surfactant, reduces pancreatic insulin production, which leads to hyperglycemia. In the congenital form of jaundice appears since birth, with postnatal jaundice in the first hours or days of life. The earlier jaundice appears, the more severe the disease. Jaundice reaches its maximum intensity on days 2-4 of life. There is also a moderate increase in the liver and spleen.
ANEMICAL form occurs in 10-20% of cases of the disease. It is manifested by pallor of the skin and mucous membranes, moderate hepatosplenomegaly, and a systolic murmur may be heard. Jaundice may be absent or subtle. As the level of NB in the bloodstream increases, children become lethargic, adynamic, and their physiological reflexes decrease. With massive penetration of antibodies into the fetus in the antenatal period after 29 weeks of intrauterine development, newborns may present with the OTC form of GBN.
The severity of hemolytic disease in newborns is determined by the level of hemoglobin, bilirubin and the type of edema.

INDEXES OF SEVERITY
Light moderate severe
Hemoglobin (g/l) 140-120 110-90 80-70
Bilirubin(μmol/l) 51(61)-85.6 85.7-136.8 over 136.8
Edema edematous syndrome ascites anasarca
The clinic of nuclear jaundice is characterized by its stages: Stage 1 - apneic or asphyxial (decreased reflexes, muscle tone, hypodynamia, regurgitation, apneic attacks, cyanotic attacks, pathological yawning); Stage 2 - spastic or manifest clinical manifestations (restlessness, stiffness, hypertonicity, head tilted back, swollen fontanelle, seizures, episthotonus, wide-open eye slits, floating eyeballs, "setting sun" syndrome, Grefe symptom, hyperthermic syndrome, heart rhythm disorder); Stage 3 - imaginary well-being, which may last up to 3-4 weeks (the pathological neurological symptoms disappear); Stage 4 - residual effects (deafness, cerebral palsy, delayed psychomotor and speech development, paresis, dysarthria, etc.). д.).
Peculiarities of clinical manifestations of GBN according to the ABO system
1. Most often develops when the blood group of the mother is 0(I) and the child is A(II).
2. The development of the disease is possible in the first pregnancy without sensitization of the woman's body.
3. 3. ABO-associated GBN is milder than any other conflict.
4.Jaundice appears later, by the end of 2-3 days of life.
5. 5. Congenital jaundice, edema and fetal hydrops are virtually non-existent in this conflict.
5. Congenital jaundice, edema and fetal hydrops are virtually non-existent in this conflict.
6. Hepatolienal syndrome is uncommon.
Hemolytic disease in newborns leads to the development of
secondary immunodeficiency due to:
Damage to immune system cells by immune complexes and indirect bilirubin,
- decreased levels of complement, due to its binding by antibodies,
- blockage of the macrophage system by immune complexes,
- decreased titers of protective antibodies (IgG) from the mother to the fetus.
DIAGNOSIS OF GBP
PRENATAL:
- obstetric history

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- amniocentesis (study of amniotic fluid): increased optical density (N 0.35-0.5), increased bilirubin, glucose (over 1.5 mmol/l), protein (over 3g/l) and decreased estrogen levels,
- Immunological monitoring - determination of IgM titer by hemagglutination test (diagnostic titer for a and b-antibodies is 1:512 or more; rhesus antibodies in the first half of pregnancy is 1:32, in the second half - 1:128 or more; "jumping titer"; positive indirect Coombs reaction in the mother, indicating the presence of IgG,
- Gel test,
- Ultrasound of fetus and placenta - placenta thickened, hepatosplenomegaly,
ascites, Buddha pose,
- fetal hypoxia on CTG,
POSTNATAL:
1.Identification of newborns at risk of developing GBN.
2.Clinical manifestations: jaundice and pallor of the skin, edema, neurological symptoms, hepatolienal syndrome, etc.
3.Laboratory diagnosis:
- Determination of blood group and Rh factor in newborns born to mothers with O (I) group and Rh-negative blood,
- determination of the bilirubin level in umbilical cord blood at birth (over 51-61 μmol/l),
- dynamics of bilirubin level by its fractions (Polacek or Kingstone scales),
- Determination of the hourly increase in bilirubin (more than 5-6 μmol/L)
Br2 - Br1
T2 - T1- General blood count: Hb, Er, Tr - reduced, reticulocytes - more than 7%0 , normoblasts - more than 50%, moderate leukocytosis,
- Immunological: direct Coombs reaction, reveals the presence of AG-AT complexes, the test material is erythrocytes of the newborn, to which is added antiglobulin serum, which contributes to the agglutination of the existing complexes. In case of group incompatibility this reaction is positive in the first 2-3 days, Rh-conflict - positive from birth; indirect Coombs reaction indicates the presence of free blocking antibodies - IgG, for this purpose the serum of a sick child is used, where red blood cells of known antigenic structure (group and Rh identity) are added, then after a certain interval the red blood cells are washed with subsequent addition of the antiglobulin serum. The reaction is positive on day 1-2.
- Determination of immunoglobulins in the blood serum of newborns - increase in IgM, IgA and decrease in IgG.
- Antibody-dependent cell-mediated cytotoxicity test (AZCC) for ABO conflict (to donor serum monocytes of the baby).
- Determination of allohemagglutinin titer in the mother's blood and milk, in protein and saline media, to distinguish natural agglutinins from immune ones in ABO conflict (when there are immune antibodies, allohemagglutinin titer in protein media is 2 times higher than in salt media).
- In the case of a conflict between mother and child for other rare erythrocyte antigens, an individual compatibility test is performed (erythrocytes of the child, blood serum of the mother, hemagglutination is noted).

TREATMENT OF HEMOLYTIC DISEASE IN NEWBORNS

I. Conservative.
II. Surgical.

I. CONSERVATIVE:

- stabilization of cell membranes (vit. E, A, ATP, 5% glucose)
- Atyhemorrhagic therapy (decinone, adroxone, etamsilate)
- activation of the liver conjugation system (phenobarbital, zixorin, benzonal 5-10 mg/kg/day)
- choleretic drugs - allochol, 12.5% magnesia sulfate, cholesteromine, electrophoresis of the liver area with 2% and 6% magnesia sulfate for a course of 5 days,
- sorbents - agar-agar 0.4-0.5 g, carbolene 0.25 three times a day,
- detoxification therapy with 5%, 7.5%, 10% glucose, with hypoproteinemia - 5-10% albumin. In critical figures of bilirubin, colloidal preparations in infusion therapy are contraindicated. The volume of fluid for infusion is calculated on the basis of LP and LPPT for phototherapy (20ml/kg) or from the volume on the 1st day of life 60-70 ml/kg; 2nd - 80-90 ml/kg ; 3rd day - 100-110ml/kg,
- prescription of metalloparferine (promotes heme resistance to the enzyme hemoxygenase),
- Phototherapy with lamps of blue, blue, green light, halagen, tungsten with a wavelength of 450-470 nm, at a distance of at least 0.5 meters from the child, which leads to the transformation of toxic isomer of bilirubin Z-Z in the skin into non-toxic isomer Y-Y, which is water-soluble, nontoxic and excreted by the kidneys. The course dose is 60-70(90) hours. Treatment is continuous (12-24h) and intermittent. With anemia and infectious diseases with an elevated PB fraction, phototherapy is not carried out.
- Purifying enemas in the first hours of life to remove bilirubin from the intestine, which in high concentrations is contained in the meconium.

II. OPERATIVE:
a) Replacement blood transfusion.
b) Plasmapheresis.
c) Hemosorption.

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Indications:
1. Bilirubin level.
In umbilical blood more than 68-70 μmol/l
1st day 170 μmol/l
24 hours 256 μmol/l
Day 3 over 340-400 (430-450) μmol/l
2. Hourly increase in bilirubin, more than 6-8 (10-11) μmol/l/h.
Anemia II - III degree, Hb less than 100 g/l.
4. Positive Coombs test.
5. Severe course of WBC with OPC in previous children, increasing signs of bilirubin intoxication.

SELECTION OF BLOOD FOR ZPK OPERATION

ZPC surgery is performed at 2 or 3 times the circulating blood volume (CBC), which in neonates is 85-90 ml and is calculated according to the formula: 85-90 ml) x 2(3) x body weight (kg) or at the rate of 180ml/kg, 240ml/kg for preterm infants and 150-170ml/kg for premature infants.
For the operation, "fresh" blood is used, with a preparation period of no more than three days.
The components of transfused blood depend on the type of conflict:
- for Rh-incompatibility, single-group rhesus-negative Er mass and plasma (or AB IV) or whole, single-group, rhesus-negative baby blood;
- in case of ABO-incompatibility - O(I) group red blood mass (washed red blood cells), rhesus-negative child's blood and AB(IV) plasma in the ratio of 2:1. If AB(IV) plasma is not available, plasma of the child's group identity can be used;
- in case of a double conflict, group O(I) red blood cell mass, rhesus-negative and AB(IV) plasma in a 2:1 ratio is transfused. The operation is performed under sterile conditions. The umbilical vein is catheterized, tests for group (cold and heat) and biological compatibility (3-fold injection of transfused blood by 3 ml in 3 min) are performed, after which the blood is injected and removed alternately by 5-10 ml. The duration of the operation depends on the volume of transfused blood and averages 2 to 2.5 hours. After each 100 ml of transfused blood, a 10% solution of gluconate Ca 1ml/kg is injected into the umbilical vein. During the operation, the volume of blood withdrawn should match the volume of blood injected.
After the completion of OPC, the first 3 hours hourly thermometry, monitor diuresis, red blood counts, glucose, electrolytes, bilirubin.

CONCLUSIONS:

To prevent the birth of children with hemolytic disease, all pregnant women in antenatal clinics are tested for blood rhesus factor and blood group is determined. Pregnant women with Rh-negative blood are registered. They find out whether they have not had a blood transfusion before, whether the children were born with hemolytic disease, and identify cases of stillbirths and abortions. Blood tests for Rh antibodies are conducted regularly. Women with Rh-negative blood are not recommended to have an abortion in their first pregnancy

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