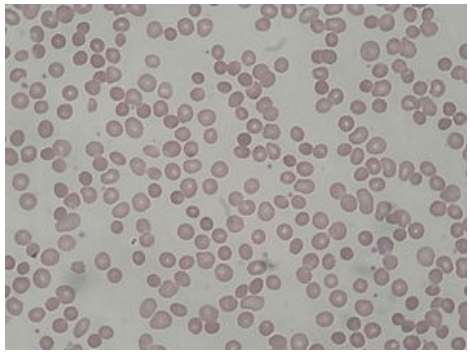
Corpuscular hemolytic anemia

Hereditary spherocytosis

Hereditary spherocytosis is a **genetic disease** (AD , it can also be acquired) conditioned by **a gene defect for structural proteins of the cytoskeleton and membrane of erythrocytes** (spectrin, ankyrin, protein III, protein IV.1). The lipid bilayer is insufficiently anchored to the spectrin layer and parts of it separate when passing through the splenic sinuses. The surface of the erythrocyte decreases relative to its internal volume, which **leads to a change in shape** from biconcave to spherical or ellipsoidal. **The deformability** of erythrocytes and **resistance** to repeated passages through capillaries, especially splenic sinuses , is reduced (splenectomy has a therapeutic effect). It is one of the most common types hemolytic anemia in Northern Europe. [1]


Hereditary Spherocytosis (smear)

The incidence is reported to be in the range of 1:3000, but is probably higher due to unrecognized mild forms.

Clinical picture

- Anemia (hemolysis in crises, among them only mild anemia);
- splenomegaly ;
- increased incidence of reticulocytes in the blood;
- hemolytic icterus , event. gallstones ;
- in the blood smear, small spherocytes (missing central clearing) with slightly changed MCV ;
- in the liver hemosiderosis and fibrosis;
- bone marrow hyperplasia and osteoporosis .

Enzymatic defects of erythrocytes

- They affect the glucose metabolism of erythrocytes , they are manifested by paroxysmal or chronic hemolysis, they tend to be AR (half the amount of enzyme is usually enough to maintain metabolism).
- Eg: Glucose-6-phosphate dehydrogenase deficiency or pyruvate kinase deficiency[2].

Hemoglobinopathies

- Disorders of hemoglobin synthesis causing hemolytic anemia or reducing the ability of hemoglobin to carry oxygen.

Paroxysmal nocturnal hemoglobinuria

This is a disease that is classified as anemia from increased loss of erythrocytes. Specifically, the survival of erythrocytes is shortened. It is an acquired disease.

Mechanism of formation

The cause of the disease is a **mutation in the PIG-A gene** in the stem cell of the bone marrow. It is a gene that codes for an enzyme to create a **phosphatidyl-inositol-glycosyl anchor (GPI anchor)** . This anchor attaches certain proteins to the cell membrane. These proteins are responsible for the inactivation of some complement components. Thanks to their influence, the C6-C9 lytic complex is not formed, thus protecting blood cells from hemolysis. Carriers of a mutation in the PIG-A gene lack these proteins. Thus, the cell is not protected against lysis by complement. The disease is called nocturnal hemoglobinuria for the reason that complement is also activated by an acidic environment and slight acidification of the organism occurs during sleep. Thus, **attacks of hemolysis** occur at night , which are manifested by hemoglobinuria in the morning.

The PIG-A gene is located on the X chromosome, in patients with PNH the mutation of 1 base is most often present, or deletion or insertion of several bases may also occur. In the pathogenesis of the disease, the mutation of the gene for the protein **DAF** and **MIRL** is applied . These two proteins are also named after the monoclonal antibodies they react with, such as CD55 and CD59. Pathological clones of erythrocytes have a shortened survival time.

- Protein (antigen) CD55 (=DAF) inhibits activation of C3 and C5 components of complement.
- Protein (antigen) CD59 (=MIRL) inhibits the activity of the terminal complement complex (C5b+C6+C8+C9).

According to the deficiency of GPI-bound proteins, several classes of erythrocytes are distinguished:

- PNH III. erythrocytes – complete deficiency of GPI-bound proteins;
- PNH II. erythrocytes – synthesis of GPI proteins is partially preserved;

- PNH I. erythrocytes – residual normal erythrocytes.

Bone marrow failure can also contribute to the pathogenesis of the disease. This process is caused by immune mechanisms. Under the influence of a certain nox, cytotoxic T-lymphocytes will be activated. This is followed by the induction of apoptosis of normal hematopoietic stem cells. Other GPI-bound proteins, such as TRAIL-3, are used in apoptosis. Another factor leading to apoptosis can be the reduction of telomere length.

In addition to the pathological clone of erythrocytes, there are also defects in platelets and granulocytes. Both pathological cell clones and normal cells can be found in the blood.

Classification

The first classification divides PNH into hemolytic and hypoplastic forms.

- **In the hemolytic form**, a large number of PNH III erythrocytes are present in the blood. Episodes of intravascular hemolysis occur.
- **The hypoplastic form** in the blood is less PNH III erythrocytes, more PNH II. Small signs of hemolysis, there is cytopenia in the blood.

The second classification divides PNH into the classic form, PNH accompanying another specific bone marrow disorder, and the subclinical form.

- **The classic form** is characterized by intravascular hemolysis, a high risk of thrombosis
- **PNH accompanying another specific bone marrow disorder** occurs together with aplastic anemia, myelodysplastic syndrome, hemolysis is milder in this form, and significant pancytopenia is present.
- **The subclinical form** can also occur with other diseases.

Main speeches

- **morning hemoglobinuria** (in 25% of patients, hemolysis is chronic in the rest) caused by acidosis at night (increase in pCO 2 activates complement);
- significant **hemosiderosis of the kidneys** with hemosiderinuria (losses of iron in the urine);
- **anemia ;**
- **bleeding manifestations**
- **hemolytic jaundice**
- **GIT symptoms**
- **iron deficiency**
- **thrombosis or embolism**
- **infection**
- **neurological symptoms**

Complication

The most common complication is the formation of thrombosis. Unusual localization of thromboses (abdominal landscape, CNS, lungs) is typical for PNH. Damage to the surface of platelets by complement is used in the pathogenesis. Renal insufficiency is very common. Free Hb causes lipid peroxidative damage and NO consumption, which leads to vasoconstriction.

Links

related articles

- Anemia
- Hemolytic anemia extracorpuscular

Source

- PASTOR, Jan. *Langenbeck's medical web page* [online]. [cit. 12.4.2010]. <http://langenbeck.webs.com>.

Reference

1. POSPÍŠILOVÁ, D. *Anémie u dětí* [online]. The last revision 2007-08-22, [cit. 2011-07-20]. <www.ocol.cz/_data/1188998010_00.ppt>.
2. SOUČEK, Miroslav, Jindřich ŠPINAR a Petr SVAČINA. *Vnitřní lékařství pro stomatology*. 1. vyd. Praha: Grada, 2005, 380 s.