Paroxysmal nocturnal hemoglobinuria

Template:Working

PNH:

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.

Etiopathogenesis

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 insult, 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 symptoms

- **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**

Complications

The most common complication is the formation of thrombosis. Unusual localization of thromboses (abdominal cavity, 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.

Diagnosis and treatment

Sources

Related Articles

- Anemia
  - Hemolytic corpuscular anemias

Sources

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