E12. **PAROXYSMAL NOCTURNAL HEMOGLOBINURIA.**

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Paroxysmal nocturnal hemoglobinuria (PNH) is a condition characterized by a defect in the receptor glycosylphosphatidyl-inositol (GPI), due to a defect in the PIG-A gene, causing a partial or complete absence of GPI-linked proteins, particularly CD59 (membrane inhibitor of reactive lysis, or protectin) and CD55 (decay accelerating factor), resulting in increased sensitivity of erythrocytes to the hemolytic action of complement.

The disease has a mean age of onset at 32 years, and a slight predominance of females (53.2%), with the predominant clinical manifestations of damage hematopoietic function: aplastic or hypoplastic anemia (44%), myelodysplastic syndrome (5.8%), myelofibrosis (0.4%), and acute myeloid leukemia (0.4%).

Common symptoms are: fatigue (80%), dyspnea (64%), headache (63%), and hemoglobinuria (62%). In men, erectile dysfunction is described in 38% of men with this condition.

Other common complications are: history of thrombotic events in 15.5%, impaired renal function in 13.9%, 31.1% in anticoagulant therapy.

Survival is closely related to the severity of complications, of which the most common are: pancytopenia (15%), thrombosis (28%) and myelodysplastic syndrome (5%). It described a considerable mortality in PNH, with a median survival of 14.6 years and a risk of death by 35% in five years.

Diagnosis is difficult because the polymorphic clinical picture and should be suspected in the following situations: evidence of non-immune acquired hemolytic anemia with evidence of intravascular hemolysis, cytopenias, venous thrombosis, aplastic anemia, myelodysplasia and episodic dysphagia or abdominal pain.

Confirmation of diagnosis is based on identification of PNH clone. In the past, was indirectly diagnosed by showing sensitivity of erythrocytes to lysis by complement or by the sucrose lysis test and the Ham acid hemolysis test.

Currently, the identification of PNH clone by flowcytometry is a direct method for identifying defects in the granulocyte membrane receptors (CD24, CD16, flyers, CD157), monocytes (CD14, flyers) and erythrocytes (CD59, CD55) and quantification clone sensitivity of 0.01%.

Identification of PNH clone in other hematopoietic failure disease has important prognostic and response to treatment in aplastic anemia indicating a good prognosis immunosuppressive therapy. In patients with PNH clone periodic monitoring PNH every 6-12 months is indicated.

PNH treatment was based (in the absence of a specific treatment) on supportive therapy: recovery of iron and folate, red blood cell transfusions, immunosuppression and stimulation of hematopoiesis.

Treatment with monoclonal antibodies (eculizumab) brings a dramatic improvement in response to treatment, and significantly reduces the stem-cell transplant indication.

Allogeneic stem cell transplantation is the only curative treatment option, but there was described a survival advantage of PNH clone in transplanted patients.

In future, it is expected the possibility of gene therapy.