Congenital glycosylation disorders

Congenital disorders of glycosylation (CDG) are diseases caused by defects in the enzymes involved in the synthesis of glycoprotein oligosaccharide chains. Glycoproteins are proteins that have oligosaccharide (glycan) chains covalently attached to the central protein chain. The binding of these chains is called glycosylation and takes place on the endoplasmic reticulum and in the Golgi apparatus. It is a post-translational modification of proteins. According to the type of binding by which carbohydrates are bound to proteins, we divide glycoproteins into N-glycoproteins, O-glycoproteins (and now also C-glycoproteins and phosphoglycoproteins).

These diseases include diseases with N-glycosylation disorders, O-glycosylation, combined N- and O-glycosylation disorders, as well as lipid glycosylation disorders. The most common cause of CDG is defective N-glycan synthesis. To date, 21 enzymes in N-glycan synthesis are known to be defective. The term N-glycan is used for both N-linked oligosaccharides and polysaccharides.

The inheritance of the glycosylation disorders described so far is autosomal recessive. CDG syndrome is one of several rare inherited metabolic disorders in which the glycosylation of various tissue proteins and / or fats is insufficient or defective. This disease often causes serious, sometimes fatal, failure of several different organ systems. Although the number of patients with CDG is not high as it is a rare disease, there are still about 50 different subtypes of CDG that have been identified to date.

In total, about 1,000 cases are known in the world, of which about 800 with the most common type of CDG - PMM2-CDG (CDG-Ia), which is caused by a mutation in the PMM2 gene. Iron

Types of diseases

So far, over twenty types of congenital glycosylation disorders have been discovered. Most CDGs are expected to be discovered. Congenital glycosylation disorders are divided into two groups - I and II, according to the biochemical pathway defect. Each of these two groups also contains a subgroup, according to the defective enzyme.

- Type I CDG - assembly disorder, including dolichol phosphate production disorders
- Type II CDG - transport disorder (processing)

Symptoms

CDG affects many organs and the symptoms vary from type to disease. Some symptoms tend to be more pronounced at different ages. Most types of CDG are associated with neurological disorders, facial dysmorphia, growth retardation, blood clotting disorders, liver and digestive tract diseases.

Clinically, CDG syndrome usually manifests as early as neonatal or infant.

- **CDG symptoms in children:**
  - hypotension
  - failure to thrive
  - delayed development
  - hepatopathy
  - coagulopathy
  - esotropia
  - cerebellar hypoplasia
- **CDG symptoms in adolescents and adults:**
  - ataxia
  - dysarthria
  - retinitis pigmentosa
  - progressive scoliosis

Diagnostics

Prenatal diagnosis in pregnancies at risk of CDG is possible by DNA analysis, the test is performed in the 15th-19th week of pregnancy.

Congenital glycosylation disorders are an autosomal recessive disease, but studies have shown that if parents give birth to a child with CDG, the risk of their next child having CDG is 1: 3, not 1: 4, as would be expected in AR disease. At a later age in CDG patients, the diagnosis can be made by a simple test analyzing serum transferrin glycosylation.

Prognosis and treatment

The most common form of CDG is CDG Ia, there are about 700 patients with this type in the world. There are about 20 patients with CDG Ib type and about 30 patients with CDG Ic. Other types have been described in a small number of individuals. Some children with CDG have serious, life-threatening health problems.

There is still no specific drug for the treatment of CDG, with the exception of type CDG Ib and some patients with CDG IIc. CDG Ib type (phosphomannoisomerase defect) is characterized by enteropathy, in which proteins are lost, coagulopathy and liver involvement, but without neurological disorders.

Effective therapy is oral administration of mannose. Fucose supplement is administered in patients with CDG type IIc (defective GDP-fucose transmission). As a result, infections will stop and health will improve. Unfortunately, delayed development will not improve. All types of CDG (except CDG Ib) need increased calorie intake.

Links

related articles

- Glycoproteins
- Glycosylation

External links

- defects Congenital Disorders of Glycosylation Overview (NCBI) (https://www.ncbi.nlm.nih.xn--jov-dma/)
- cdgs.com (http://www.cdgs.com)

References

- FERNANDES, John. Diagnosis and treatment of hereditary metabolic disorders. 1st edition. Prague: Triton, 2008. pp. 576-580. ISBN 978-80-7387-096-6.