Congenital disorders of glycosylation

Congenital disorders of glycosylation (CDG, *congenital disorders of glycosylation*) are diseases whose cause lies in **defects of enzymes involved in the synthesis of oligosaccharide chains of glycoproteins**. Glycoproteins are proteins that have chains of oligosaccharides (glycans) covalently attached to the central protein chain. The attachment of these chains is referred to as glycosylation and takes place on the endoplasmic reticulum and in the Golgi apparatus. It is a post-translational modification of proteins. Glycoproteins are divided into N-glycoproteins, O-glycoproteins (and now also C-glycoproteins and phosphoglycoproteins) according to the type of bond with which carbohydrates are attached to proteins.

These diseases include diseases with disorders of N-glycosylation, O-glycosylation, combined disorders of Na-O-glycosylation as well as disorders of lipid glycosylation. The most common cause of CDG is defective N-glycan synthesis. So far, 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 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 deficient or defective. This disease often causes severe, sometimes fatal, failure of several different organ systems. Although the number of patients with CDG is not high because it is a rare disease, there are still about 50 different subtypes of CDG that have been identified so far.

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

Types of disease

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

- **Type I CDG – assembly** disorder including disorders of dolichol phosphate formation
- **Type II CDG – transport** (processing) disorder

Symptoms

CDG affects many organs and symptoms vary from disease to disease. Some symptoms tend to be more obvious 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 already in the newborn or infant age.

- **CDG symptoms in children:**
  - hypotonia
  - not thriving
  - delayed development
  - hepathopathy
  - coagulopathy
  - esotropia (convergent squint)
  - cerebellar hypoplasia
- ***with* CDG symptoms in adolescents and adults:**
  - ataxia
  - dysarthria
  - retinitis pigmentosa
  - progressive scoliosis

Diagnosis

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

Congenital glycosylation disorders are **autosomal recessive diseases**, but studies have shown that if parents have a child with CDG, the risk that their next child will have CDG is 1:3, not 1:4, as would be expected for AR disease. At a later age, CDG patients can be diagnosed with a simple test analyzing **the glycosylation of serum transferrin**.

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 type **CDG Ib**, 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**, except for CDG type Ib and some patients with CDG IIc. CDG Ib type (phosphomannoisomerase defect) is characterized by protein-losing enteropathy, coagulopathy and liver involvement, but without neurological disorders.

Oral administration of mannose is an effective **therapy**. A fucose supplement is given to patients with type CDG IIc (defective GDP-fucose transfer). Thanks to this, infections will stop and the state of health will improve. Unfortunately, delayed development will not improve. All types of CDG (except CDG Ib) need increased caloric intake.

Links

Related articles

- Glycoproteins
- Glycosylation

External Links

- Defects Congenital Disorders of Glycosylation Overview (NCBI) (https://www.ncbi.nlm.nih.jové)
- 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 .