Glycogenosis

Glycogenosis storage diseases (GSDs) are **inherited metabolic disorders with a deficiency in enzyme or transport protein activity that results in either abnormal glycogen structure or abnormal tissue content** .Inheritance of all types of GSD is **autosomal recessive** , with the exception of only two subtypes of GSD IX, in which inheritance is linked to the X chromosome.

Etiopathogenesis

The cause of these diseases is zero or insufficient synthesis of functional proteins (enzymes and transporters) that are involved in either glycogenolysis or glycogenesis. Depending on the enzyme, glycogenoses can be divided into several types, which differ in clinical course as well as biochemical finding and prognosis.

Biochemical image

The following symptoms most often dominate in the laboratory examination:

- hypoglycemia
- hyperlactatemia
- metabolic acidosis
- hyperlipidemia
- hyperuricemia

Laboratory finding	**Glycogenosis (type)**		
	I	III	VI
Hypoglycemia	+++	++	+
Hyperlactacidemia	++	-	-
Metabolic acidosis	+	-	-
Hyperlipidemia	++	+/-	+/-
Hyperuricemia	+	+/-	-

Division

A summary of the divisions and basic characteristics can be found on the subpage Classification and basic characteristics of glycogenoses.

Depending on the type of storage

- with accumulation **in the cytosol** - all GSDs except II
- with accumulation **in lysosomes** - GSD II

According to organ disability

- **generalized**: II, IV
- **liver**: Ia, Ib, III, VI, IX, 0
- **muscle**: V, VII; muscle involvement may be part of type II, III, IX
- with **myocardial infarction**: II, III, one of subtypes IX
- with **kidney disability** : Ia, Ib
- **brain:** disease with polyglucosan bodies in adults - branching enzyme deficiency (glucan 1-6 transferase), Lafor's disease

Muscle glycogenosis

- **symptoms:** muscle weakness and weakness, fatigue, increased muscle pain and attacks of myolysis (possibly also hemolysis)
- They usually show up after the age of 20
- **laboratory finding:** elevated level CK-MM, AST, ALT, LDH; in urine myoglobinuria; because muscle tissue does not affect glucose homeostasis, in type V, VII (exclusively muscle GSD) there is no hyperlactacidemia and dyslipidemia in the blood test results
- **treatment:** symptomatic; demonstrated beneficial effect of increased protein intake

Hepatic glycogenosis

- **Symptoms:** hepatomegaly, smaller stature
- **laboratory findings:** hyperlactacidemia, dyslipidemia, ketotic hypoglycemia, hyperuricemia

Glycogenosis type 0 (aglycogenosis) == Lack of the enzyme **glycogen synthetase** in liver (not missing in muscles, leukocytes and enterocytes). Hepatic glycogen is reduced below 2% of normal. **Clinical picture** Conditions of severe hypoglycemia with convulsions - lead to brain damage and mental retardation. They occur mainly in the morning, after a night of fasting, they are accompanied by ketonemia. After glucose administration, prolonged hyperglycemia is observed (since glucose cannot be stored in the form of glycogen) and an increase in serum lactate (the liver does not form glycogen, glucose is metabolized to lactate).

- Urgent diagnosis is essential for a child's survival.
- Hypoglycaemic episodes can be prevented by frequent administration of protein-rich foods.

Glycogenosis type Ia (von Gierk 's disease, hepatorenal) == Disorder of glucose-6-phosphatase activity (converts glucose-6-β into glucose, which is released from the liver into the blood if necessary). AR hereditary disease, gene is at 17. chromosome u. Clinical picture It starts in infant's age progressive hepatomegaly (liver function is normal, cirrhosis does not develop) and fasting hypoglycemic convulsions.

- During febrile conditions, hypoglycaemia is more common and is accompanied by lactic acidosis (hyperlactacidemia is due to an excess of glucose-6-phosphate, which is further metabolized by glycolysis, the products of which are lactate and pyruvate) with [[Kussmaul respiration]. Kussmaul breathing]].
- Characteristic facies: "doll face".
- The body adapts to hypoglycemia - the secretion of insulin decreases, it activates lipase in adipose tissue → hyperlipoproteinemia occurs → their increased breakdown produces ketone bodies, which together with lactate contribute to acidosis.
- Administration of glucagon does not increase glucose but lactate.
- Galactose, fructose and glycerol also require hepatic G-6-Pase for conversion to glucose → administration of sucrose and lactose leads to hyperlactacidemia with only a small increase in blood glucose levels.
- Growth slows down and puberty is delayed.
- Xanthoma y, nephromegaly and related renal disorders with hypertension, gout, adenoma y in the liver may occur in adulthood.

Laboratory

- fasting hypoglycaemia (common only in infants and toddlers)
- hyperlipidemia and hyperlactacidemia, which blocks the excretion of uric acid and conditions hyperuricemia

Diagnostics

- **UZ**: hepatomegaly and nephromegaly, there may be adenomas in the liver
- **Biopsy liver**: steatosis and glycogen proliferation

Therapy

The goal is to prevent severe hypoglycemia and MAC

- diet therapy - frequent administration of nutrition with reduced animal fats, lactose, sucrose and fructose
  - Caloric needs are mainly covered by maltodextrins and starches.
- From toddler age we serve cornstarch after each meal.
- At night, continuous feeding with a nasogastric tube is suitable so that we give 30% of the daily intake at night.
- In acute metabolic breakdown with lactic acidosis during infections, we must administer i.v. glucose.
- **Supportive pharmacotherapy**: administration of a xanthine oxidase inhibitor (allopurinol) to prevent gout and urate nephropathy (however, because uric acid is a strong antioxidant, it is an effort to keep its blood levels at the upper limit of the normal range); in severe hypertriacylglycerolemia - nicotinic acid and fibrates (to reduce the risk of cholelithiasis and pancreatitis).

Complication

Hepatic adenomas, osteopenia, anemia, polycystic ovaries, pulmonary hypertension, depression (comprehensive treatment).

Prognosis

It is good in childhood, in adulthood there is a risk of developing liver, renal and cardiovascular complications.

Glycogenosis type I non a

Glc-6-β translocase defect (glucose-6-phosphate transporter across the ER membrane). Clinical picture It is indistinguishable from Ia.

- Other symptoms include - neutropenia with neutrophil dysfunction → frequent infections of the respiratory tract, urinary tract and skin.
- Most patients have symptoms of non-specific intestinal inflammation (prolonged diarrhea).

Pharmacotherapy

Protrimoxazole prophylaxis; administration of GCSF (granulocyte colony-stimulating factor) → in the long run, however, leads to hypersplenism, kidney cancer, AML.

Type II glycogenosis (generalized, Pompe disease)

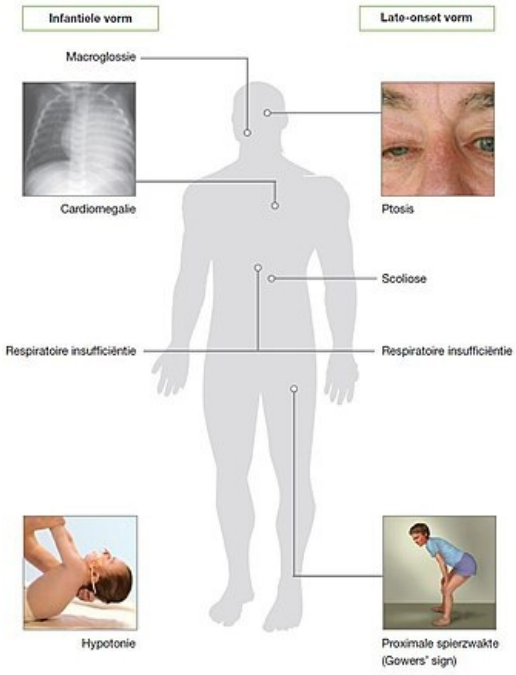
In 1932, the Dutch pathologist Dr. J. C. Pompe[1]. It is a AR inherited disease caused by a mutation in the lysosomal acid gene **α-1,4-glucosidase** (GAA).

- The gene for GAA was located on the long arm of chromosome 17 (17q23) [1].

As a result of deficiency or insufficient activity of the GAA enzyme, lysosomal glycogen accumulates in many tissues, especially in skeletal muscle and in the infant and in the myocardium, to a lesser extent in the endothelium of the vascular system, in the CNS (especially in astrocytes), in liver and kidneys[1].

- Incidence: 1:40 000, 4 patients are currently diagnosed in the Czech Republic (however, considerable underdiagnosis of this disease is expected due to insufficient neonatal screening)[1].

Prenatal diagnosis it is possible - finding abnormal lysosomes in amniocytes.



Clinical picture in Pompe disease

Clinical picture

Classical infantile form (IIa)

- Affects infants (enzymopathy) - always lethal.
- Within weeks and months, the child becomes completely hypotonic - weakly sucks (→ failing), breathing superficially (→ susceptibility to respiratory infections and sleep apnea).
- Distinct **cardiomegaly**, on ECG high P, shortened PQ and transmission disorders.
- Liver slightly enlarged, macroglossia also described.
- Consciousness is not violated, neither is the intellect.
- Common aspiration pneumonia with atelectasis mi
- Death around 2 years of respiratory failure.

Laboratory finding: Increased level of liver and muscle enzymes in the blood (ALT, AST, LDH, CK). The presence of oligosaccharides in the urine.

Late type - juvenile and adult form (IIb)

- Affects older children and adults (enzymopenia)
- Clinically "heterogeneous" (due to the number of different mutations that may occur in the GAA gene; over 200 have been described) → severity is determined by the residual activity of the enzymes.
- cardiomegaly is smaller, ECG normal, often arrhythmia.
- Death usually around the age of 30 to 40 (depending on the age of the manifestation). Sometimes it does not have to shorten life, it allows a sedentary job.

Symptoms

Muscle involvement (muscle weakness, hypotension) of the pelvic girdle (difficult to get up) and pharynx (problems with food intake) dominates, respiratory muscles are also affected (apnea pauses in sleep, shortness of breath) → the most common cause of death is respiratory failure; however, the myocardium is not affected.

Diagnostics

- Clinical examination.
- Laboratory finding of decreased GAA activity in leukocytes or fibroblasts.
- Molecular-biological mutation of the gene for a given enzyme.
- Demonstration of glycogen deposits in the biopsy sample (muscle).
- Skin biopsy - an abnormality of lysosomes detectable by electron microscopy.

Therapy

It only slows down progression; enzyme replacement therapy (ERT) with Myozyme® (infusion form), contains the precursor GAA α-glucosidase, which is converted to the active enzyme by an acidic environment in lysosomes; symptomatic therapy (rehabilitation, supportive medication, balneotherapy). Type III glycogenosis (Cori 's disease, Forbes' disease) Rare AR hereditary disease. It is a disorder of glycogen branching degrading enzymes (**1,6-glucosidase** and **1,4-glucantransferases** debrancher). It evokes a similar picture to GSD I, but has a milder course.

Glycogenosis type IV (Andersen's disease)

Rare AR hereditary disease, about 10 cases described so far. The defective enzyme is **glucan-1-6-transferase** (branching enzyme) → polysaccharide accumulation without branching points.

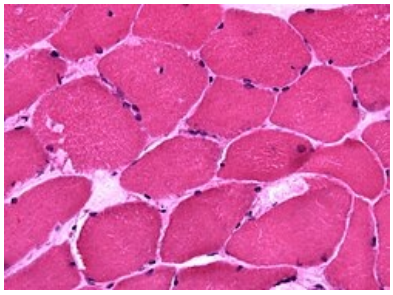
Infantile type

Speeches Severe hepatic impairment (cirrhosis, hepatosplenomegaly, portal hypertension) and heart, ascites; rapidly progressing, with infaust prognosis (death usually occurs as a result of heart or liver failure in the 2nd year of life)

Juvenile, adult form

Atypical, the manifestation is generalized.

Glycogenosis type V (McArdler's syndrome)



Skeletal muscle biopsy, McArdler's syndrome: vacuolar myopathy in muscles.

Myophosphorylase deficiency → muscles have an increased glycogen content, which forms vacuoles (up to 4%). Speeches Decreased exercise tolerance, muscle weakness, atrophy and convulsions

The first symptoms usually appear around the age of 30. − 40. year of life, but they can even earlier

When myolysis occurs, the patient is at risk of renal failure due to myoglobinuria.

Glycogenosis type VI (Hers' disease)

Hepatic phosphorylase deficiency.

Symptoms similar to type Ia glycogenosis, but milder

Hepatomegaly and morning hypoglycemia are typical

Glycogenosis type VII (Tarui 's disease)

Phosphofructokinase deficiency in muscles and erythrocytes. Speeches Similar to type 5 glycogenosis There is also a reduced tolerance of exercise, increased glycogen content in the muscles. Hemolytic anemia may also occur.

Glycogenosis type IX

- Phosphorylase kinase deficiency.
- has seven subtypes
- X bound disease
- glycogen accumulates in the liver and / or muscles and in one subtype even in the myocardium (type 6 with infaust prognosis)

Clinical signs

- Hepatic impairment is the same as for glycogenosis I, but very mild with good prognosis and low risk of decompensation.
- As with type 5 glycogenosis, the muscle damage is mild

Laboratory findings

Hepatic are the same as for glycogenosis I and muscle as for glycogenosis 5, but both are milder.

Links

Related Articles

- Hereditary disorders of sugar metabolism

Template:Pathobiochemistry of metabolic pathways (Masopust)

External links

[1] (http://www.agsdus.org/) [2] (http://www.solen.sk/index.php?page=pdf_view&pdf_id=3744&magazine_id=3) [3] (http://www.solen.cz/pdfs/neu/2009/01/10.pdf) [4] (http://www.sdruzenimeta.cz/pompeho_choroba) [5] (http://www.sekk.cz/ELM_ukonceni.pdfencyklopedie/A/AJEJM.htm)

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1. SLOUKOVÁ, Eva – OŠLEJŠKOVÁ, Hana – VOHÁŇKA, Stanislav. Pompeho choroba. *Pediatrie pro praxi* [online]. 2009, y. 10, p. 156–158, Available from <http://www.solen.cz/pdfs/ped/2009/03/04.pdf>. ISSN 1803-5264.