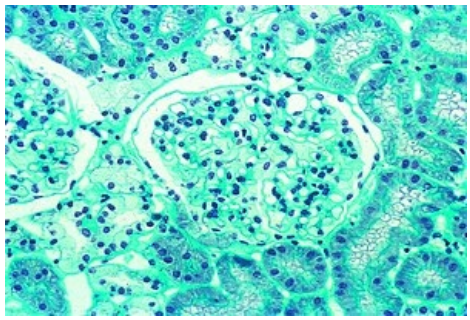
Fabry Disease

Fabry disease or **sphingolipidosis** is characterized as a metabolic lysosomal disease with a frequency of 1:40,000. It is a gene mutation on the long arm of the sex chromosome X encoding the lysosomal enzyme *alpha-galactosidase* (alpha-GAL). This results in reduced or absent activity of **alpha-GAL**, resulting in deposits of *globotriasylceramide* (CL-3) in the endothelium and visceral tissues. The process leads to multisystem damage to the kidneys, heart and CNS. It was first described in 1898 by W. Anderson and J. Fabry as *angiokeratoma corporis diffusum universale*, *morbus Fabry* or *Anderson-Fabry disease*.

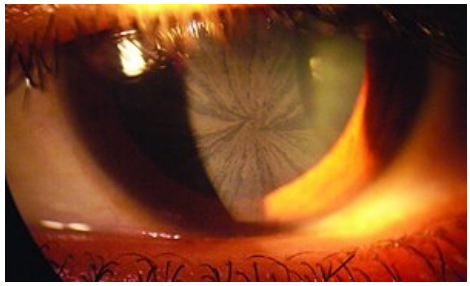


Fabry disease - kidney biopsy

Inheritance

Today we already know 200 mutations. Males (XY) are affected by the fully developed form of the disease. The daughters of these men get a defective X chromosome. The sons of these men are healthy because they get a Y chromosome from the father. Affected women (XX) can pass on either a healthy or a defective X chromosome, in the event that the woman does not have two defective X chromosomes.

Clinical picture



A patient with *cornea verticillata*

As the first symptoms, appearing in childhood, are **acroparesthesia** - burning pain, tingling, tingling in the limbs. **Digestive distress** causes deposition of glycosphingolipids in autonomic ganglia of intestine and mesenteric vessels. There is diarrhea, abdominal pain, especially after eating, bloating, nausea and vomiting, which can lead to loss of appetite and weight loss (anorexia). Reduced or absent ability to sweat (**hypohidrosis, anhidrosis**) is caused by damage to sweat gland cells and the autonomic nervous system. **Skin manifestations** - angiokeratomas (wart-like skin formations that arise from the growth of the keratinized part of the skin and the weakening of the vascular wall) - occurring on the buttocks, perigenital, in the navel area, thighs and in some cases also on the mucous membranes (in the mouth). Weakening of the vessel wall results in the formation of **angiectasia** - small, slightly raised, purple-red dilated blood vessels on the skin. The number and size of these lesions gradually increases with age. Furthermore, there are changes on the cornea − a typical change that can be observed by slit-lamp examination is *cornea verticillata*. Whitish spiral stripes form in the cornea. The severe clinical course includes: **ACMP, progressive renal insufficiency, cardiovascular diseases**, which are the most common cause of death of patients with Fabry disease. However, the course of Fabry disease is more severe in men.

Diagnostics

Genetic testing, molecular diagnostics and biopsy are essential in the diagnosis.

Treatment

The standard is **enzyme replacement therapy**. Two preparations are available, namely *α-agalsidase* and *agalsidase β.*

Symptomatic treatment includes treatment of pain and acroparesthesia - Phenytoin, Carbamazepine, Gabapentin, analgesics to opiates.

Furthermore, *nephroprotective treatment* − ACE inhibitors and angiotensin receptor blockers.

Treatment of digestive problems - pancreolipase, metoclopramide, H_2 blockers, loperamide hydrochloride, change in eating habits.

Cardiac treatment - antiarrhythmics, implantation of a cardiac pacemaker, treatment of angina pectoris - ACE inhibitors, angiotensin receptor blockers, diuretics, possibly beta-blockers, anopyrine, warfarin (for atrial fibrillation), implantation of a cardioverter defibrillator (malignant arrhythmia, permanent ventricular tachycardia),

or heart transplantation.

Summary video

Links

Related articles

- Lysosomal diseases

External links

- Fabryho choroba – popis onemocnění prof. MUDr. Jan Bultas, CSc., II. interní klinika 1.LF UK v Praze (https://int2.lf1.cuni.cz/fabryho-choroba)

Source

- SOLÍK, P – GONCALVESOVÁ, E. "Infiltratívne kardiomyopatie". *"Lekárske listy".* 2011, vol. 2, p. 19, ISSN 1335-4477.