Fabry disease

Fabry disease (FD) (Sphingolipidose) is metabolic disorder which underlaying cause is incorrect lysosomal storage due to deficiency of specific enzyme- in this case Alpha-galactosidase. frequency 1:40 000. As other lysosomal storage diseases is Fabry disease inherited. Affected gene coding alpha-galactosidase is located on q-arm of X chromosome. Result of mutation of Alpha-GAL gene is reduced or none activity, which leads to accumulation of ceamide trihexoside (also known as globotrialosylceramide) in endothelium and visceral tissues. This whole procces leads to multisystem damage of heart, kidneys and CNS. In 1898 W. Andersonom a J. Fabrym described this disease as *angiokeratoma corporis diffusum universale*, *morbus Fabry*, or *Anderson-Fabry disease.*

Prevalence of Fabry disease is 1:40 000- 80 000 in the world. After Gaucher disease is FD the most common lysosomal storage disease.

Heredity

Over 200 mutations are known today causing Fabry disease.

Men (XY) are mainly affected by fully developed form. Daughters these men have have one defective X chromosome from father but sons are healthy, because fathers pass only Y chromosome to their sons. Affected women can pass defective or healthy X chromosome. náhled|250px|Pacient s *cornea verticillata*

Clinical features

Fabry disease manifests in 2 forms

→ **1. Classical form** with multiorgan damage

→ **2. Atypical form**- affecting only some organ systems

1.Classical form

Early symptoms as typical tetrad:

- Acroparesthesia- burning pain, discomfort, itching due to small fiber neuropathy mainly in palms and feet
- Gastrointestinal symptoms- caused by storage of glykosphingolipides into autonomic ganglia and mesenterial vessels - diarrhoea, abdominal pain, flatulance, nausea, vomiting → anorexia
- Hypohidrosis or anhidrosis - diminished or absent sweating, due to damage of cells of sweat glands and autonomic nervous system.
- Angiokeratomas - a hyperkeratic, benign, wart-like lessions made up of capillaries, often red, blue or black. - located on glutes inguinal region, thighs, sometimes also in mouth

Other early symptoms includes

- corneal clouding- *cornea verticillata* (centrally located gray-brown deposits of corneal epithelium),
- cataract

In early adulthood disease progress and manifests by heart and renal complications

- Heart complications- Hypertrophic cardiomyopathy, heart rhythm disorders,
- Renal complications- Chronic renal failure leading to terminal renal failure.

Diagnosis

In diagnostics is essential genetic testing, molecular diagnostics and biopsy, but it is good to know- Fabry disease is progressive life shortening disease, for pacients is crucial to start treatment as soon as possible, because up to 25 % pacients with FD are treated for different diagnosis. Clinical suspicion comes from detailed anamnesis focused on known symptoms of the disease, same apply to physical examination. For definitive diagnosis in men is possible to assess activity of α- GAL in plasma, leucocytes or fibroblasts.

Therapy

Therapy fo FD in specific and non-specific.

Specific therapy

- ERT (enzyme replacement therapy), 2 preparations are available- agalsidase-α and agalsidase-β. Drug

administration is intravenously, taking 120-180 min. once in 14 days.

- Oral therapy (migalastat)= pharmacologic chaperone that can bind to, stabilize, and enhance the residual activity of certain missense mutations.

Non-specific treatment

- Symptomatic treatment of pain and acroparesthesis- phenytoin, carbamazepin, gabapentin, analgetics up to opioids.
- Nephroprotective treatment- ACE inhibitors and calcium channel blockers.
- GIT symptoms treatment- pancreolipase, metoclopramide, H_2- blockers, loperamide- hydrocholoride, change in eatings habits.
- Cardiological treatment- antiarrythmics, pacemaker implantation, ACE inhibitors, angiotensin receptors blockers, diuretics, beta blockers, anopyrin, warfarin, heart transplantation, cardioverter defibrillator implantation- in case of malign arrythmia, sustained ventricular tachykardia

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