FABRY DISEASE

WHAT IS FABRY DISEASE?

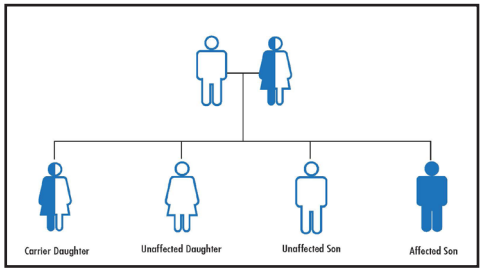
Fabry disease is classified as a lysosomal storage disorder (LSD). Lysosomes are cell organelles that digest and recycle various molecules. Disorders that result in the accumulation of molecules within the lysosomes, including Fabry disease, are identified as LSDs.

THE CAUSE

Fabry disease is caused by mutations in the GLA gene. The purpose of this gene is to code for the production of an enzyme called alpha-galactosidase A. This enzyme is found in the lysosomes and is responsible for breaking down a fatty material called globotriaosylceramide. Mutations in the gene alter the structure and function of the enzyme. Globotriaosylceramide builds up in cells lining the skin, blood vessels, kidneys, heart and nervous system.

INHERITANCE PATTERN

Fabry disease is inherited as an X-linked condition. Most affected individuals are males. Because males have only one X chromosome, one mutation is sufficient to cause the disorder. Female carriers, having two X chromosomes, will show milder symptoms or none at all.



If a mother is a carrier of Fabry disease, whether she has symptoms or not, and the father does not have a mutation in the GLA gene, the risk to each child depends on whether the child is male or female.

- Each son has a 50% chance to be unaffected and a 50% chance to be affected
- Each daughter has a 50% chance to be unaffected, and a 50% chance to be a carrier

If a father has Fabry disease and the mother is not a carrier, all of their sons will be unaffected, and all daughters will be carriers.

Fabry disease affects 1 in 40,000 to 60,000 males.

PATIENT CARE

DIAGNOSIS

1. Enzymatic testing to measure alpha-galactosidase A activity levels in plasma, leukocytes, and/or cultured cells
2. DNA mutation analysis of the GLA gene

MANAGEMENT

- Medications for relief of pain
- ACE inhibitors or ARBs for renal protection
- Supportive care from cardiology, genetics, nephrology, neurology, ophthalmology, dermatology, and audiology

TREATMENT

Enzyme replacement therapy:

- Agalsidase alfa (Brand name: Fabrazyme) - Manufactured by Sanofi Genzyme to reduce globotriaosylceramide deposition in capillary endothelium of the kidney and certain other cell types.
- Migalastat hydrochloride (Brand name: Galafold) - Manufactured by Amicus Therapeutics to treat adults with milder symptoms.

WHAT ARE THE SYMPTOMS?

Symptoms of Fabry disease depend upon the level of alpha-galactosidase A activity present.

For males with <1% activity, (classical form), symptoms appear in childhood or adolescence as acroparesthesia, angiokeratomas, hypohidrosis, corneal opacities, and proteinuria.

Males with >1% enzyme activity may have

1) a renal variant with symptoms associated with end-stage renal disease, but without skin lesions or pain;

2) a cardiac variant usually presenting in the sixth-eighth decade of life with left ventricular hypertrophy, cardiomyopathy, and arrhythmia, and with proteinuria without end-stage renal disease; or

3) stoke or transient ischemic attack in the presence of cardiovascular disease.

RESOURCES

Gene Reviews: FABRY
ncbi.nlm.nih.gov/books/NBK1292/#fabry

Genetics Home Reference
ghr.nlm.nih.gov/condition/fabry

Genetic and Rare Diseases
rarediseases.info.nih.gov

Greenwood Genetic Center
Where Compassion Inspires Progress

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