Fabry disease

Fabry disease is an inherited disorder that results from the buildup of a particular type of fat, called globotriaosylceramide, in the body's cells. Beginning in childhood, this buildup causes signs and symptoms that affect many parts of the body. Characteristic features of Fabry disease include episodes of pain, particularly in the hands and feet (acroparesthesias); clusters of small, dark red spots on the skin called angiokeratomas; a decreased ability to sweat (hypohidrosis); cloudiness or streaks in the front part of the eye (corneal opacity or corneal verticillata); problems with the gastrointestinal system; ringing in the ears (tinnitus); and hearing loss. Fabry disease also involves potentially life-threatening complications such as progressive kidney damage, heart attack, and stroke. Some affected individuals have milder forms of the disorder that appear later in life and affect only the heart or kidneys.

Frequency

Fabry disease affects an estimated 1 in 40,000 to 60,000 males. This disorder also occurs in females, although the prevalence is unknown. Milder, late-onset forms of the disorder are probably more common than the classic, severe form.

Causes

Fabry disease is caused by mutations in the GLA gene. This gene provides instructions for making an enzyme called alpha-galactosidase A. This enzyme is active in lysosomes, which are structures that serve as recycling centers within cells. Alpha-galactosidase A normally breaks down a fatty substance called globotriaosylceramide. Mutations in the GLA gene alter the structure and function of the enzyme, preventing it from breaking down this substance effectively. As a result, globotriaosylceramide builds up in cells throughout the body, particularly cells lining blood vessels in the skin and cells in the kidneys, heart, and nervous system. The progressive accumulation of this substance damages cells, leading to the varied signs and symptoms of Fabry disease.

GLA gene mutations that result in an absence of alpha-galactosidase A activity lead to the classic, severe form of Fabry disease. Mutations that decrease but do not eliminate the enzyme’s activity usually cause the milder, late-onset forms of Fabry disease that typically affect only the heart or kidneys.

Inheritance Pattern

This condition is inherited in an X-linked pattern. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes in each cell. In males (who have only one X chromosome), one altered copy of the GLA gene in each cell is sufficient to cause the condition. Because
females have two copies of the X chromosome, one altered copy of the gene in each cell usually leads to less severe symptoms in females than in males, or rarely may cause no symptoms at all.

Unlike other X-linked disorders, Fabry disease causes significant medical problems in many females who have one altered copy of the GLA gene. These women may experience many of the classic features of the disorder, including nervous system abnormalities, kidney problems, chronic pain, and fatigue. They also have an increased risk of developing high blood pressure, heart disease, stroke, and kidney failure. The signs and symptoms of Fabry disease usually begin later in life and are milder in females than in their affected male relatives.

A small percentage of females who carry a mutation in one copy of the GLA gene never develop signs and symptoms of Fabry disease.

Other Names for This Condition

- alpha-galactosidase A deficiency
- Anderson-Fabry disease
- angiokeratoma corporis diffusum
- angiokeratoma diffuse
- ceramide trihexosidase deficiency
- Fabry's disease
- GLA deficiency
- hereditary dystopic lipidosis

Diagnosis & Management

Genetic Testing Information

- What is genetic testing? /primer/testing/genetictesting
- Genetic Testing Registry: Fabry disease https://www.ncbi.nlm.nih.gov/gtr/conditions/C0002986/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov https://clinicaltrials.gov/ct2/results?cond=%22Fabry+disease%22
Other Diagnosis and Management Resources

- Baby's First Test
  https://www.babysfirsttest.org/newborn-screening/conditions/fabry
- GeneReview: Fabry Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1292

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/ geneticbraindisorders.html
- Health Topic: Lipid Metabolism Disorders
  https://medlineplus.gov/ lipidmetabolismdisorders.html

Genetic and Rare Diseases Information Center

- Fabry disease
  https://rarediseases.info.nih.gov/diseases/6400/fabry-disease

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Fabry Disease Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Fabry-Disease-Information-Page
- National Institute of Neurological Disorders and Stroke: Lipid Storage Diseases Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Lipid-storage-diseases-Information-Page

Educational Resources

- Emory University School of Medicine
  http://genetics.emory.edu/documents/resources/factsheet44.pdf
- International Center for Fabry Disease, Mount Sinai School of Medicine
  https://icahn.mssm.edu/research/fabry
- MalaCards: fabry disease
  https://www.malacards.org/card/fabry_disease
- Merck Manual Consumer Version: Overview of Cholesterol and Lipid Disorders
  https://www.merckmanuals.com/home/hormonal-and-metabolic-disorders/cholesterol-disorders/overview-of-cholesterol-and-lipid-disorders
• National Kidney Foundation  
https://www.kidney.org/atoz/content/fabry

• Orphanet: Fabry disease  
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=324

Patient Support and Advocacy Resources
• Fabry International Network  
http://www.fabrynetwork.org/
• Fabry Support & Information Group  
https://fabry.org/
• Metabolic Support UK  
https://www.metabolicsupportuk.org/
• National Fabry Disease Foundation  
https://www.fabrydisease.org/
• National Organization for Rare Disorders (NORD)  
https://rarediseases.org/rare-diseases/fabry-disease/
• National Tay-Sachs & Allied Diseases Association, Inc.  
https://www.ntsad.org/

Clinical Information from GeneReviews
• Fabry Disease  
https://www.ncbi.nlm.nih.gov/books/NBK1292

Scientific Articles on PubMed
• PubMed  
https://www.ncbi.nlm.nih.gov/pubmed?term=%28Fabry+Disease%5BMAJR%5D%29+AND+%28Fabry+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22+AND+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
• FABRY DISEASE  
http://omim.org/entry/301500
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