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My46 Trait Profile

Fabry disease

Other Names: Anderson-Fabry Disease, Alpha-Galactosidase A Deficiency

Fabry disease is a genetic condition characterized by the body's inability to break down a certain fatty substance called globotriacylceramide. It is caused by mutations in the GLA gene that makes the alpha galactosidase A protein.

Characteristics of Fabry disease

Individuals with Fabry disease cannot properly breakdown a certain fatty substance called globotriacylceramide (GL-3). GL-3 cannot be broken down because the enzyme, alpha galactosidase A (AGA), is not working properly. Without enough AGA, GL-3 builds up in various tissues and blood vessels of the body. This build-up of GL-3 over time causes problems with the skin, kidneys, stomach, intestines, heart, brain, and nerves. Although symptoms can vary from one person to another, disease symptoms almost always become debilitating and life threatening.

Common symptoms in childhood include: a purplish-pink skin rash (i.e., angiokeratomas), decreased sweating (i.e., hypohidrosis), fatigue, diarrhea, headaches, frequent overheating, protein in the urine, and burning or tingling pain in their hands or feet (i.e., acroparesthesia). Children can also have episodes of severe pain which are usually triggered by illness, overheating, or stressful situations. As people with Fabry disease move into the teenage and adult years without treatment, the GL-3 continues to build up, causing increased health problems including: hearing loss, leaky heart valves (i.e., mitral valve prolapse), enlargement of the lower heart chambers (i.e., left ventricular hypertrophy), heart attacks, stroke, kidney disease, and depression. Both men and women can be affected by Fabry disease.

In addition to the classic type described above, there are two atypical forms of Fabry disease – the cardiac variant type and the renal variant type. Both forms present later in life, and usually do not have the angiokeratomas, acroparesthesias or hypohidrosis seen in the classic form of Fabry disease.

Diagnosis/Testing

A diagnosis of Fabry disease can be made by measuring the AGA enzyme activity from a blood sample. A person with Fabry disease often has deficient (low) enzyme activity. A diagnosis of Fabry disease can also be done by genetic testing for a change or mutation in the GLA gene. This gene makes the AGA enzyme that is responsible for breaking down the fatty substance GL-3. Most individuals with Fabry disease have a mutation in the GLA gene. Mutations in this gene prevent the AGA enzyme from working properly, resulting in a build-up of GL-3 in various organs of the body.

Management/Surveillance

Enzyme replacement therapy (ERT) is a medical treatment available for Fabry disease. ERT provides the AGA enzyme that is missing in individuals with Fabry disease through regular intravenous (IV) infusions. ERT is a lifelong treatment for Fabry disease and is not a cure.

Supportive care for Fabry disease focuses on managing symptoms. Medications can be used to decrease pain, as well to decrease the amount of protein in the urine. Affected individuals with damaged kidneys may need kidney transplants. Regular care and follow up with cardiology, nephrology, neurology, gastroenterology, pulmonology and other specialists as needed is recommended to detect and manage symptoms.

Mode of inheritance

Fabry disease is inherited in an X-linked recessive manner. This means that in females, both copies of the GLA gene (i.e., one on each X chromosome) must have a change or mutation, whereas in males, only one copy of the GLA gene must have a mutation to be affected. A female with a mutation in one copy of the GLA gene is said to be a "carrier" of Fabry disease, and is typically not affected.

Risk to family members

If a father is affected with Fabry disease, his daughters will be carriers of Fabry disease and his sons will be unaffected. If a mother is a carrier of Fabry disease, each daughter has a 1 in 2 chance (i.e., 50%) of being a carrier and each son has a 1 in 2 chance (i.e., 50%) of being affected with Fabry disease.

Special considerations

In the past, it was believed that carriers of Fabry disease would not have Fabry-related health problems because they had a normal second copy of the gene. However, women can and do have Fabry-related health problems. In many cases, woman can have health problems to the same degree as their male counterparts.

Resources

Fabry Support and Information Group
http://www.fabry.org
The National Fabry Disease Foundation
http://www.fabrydisease.org/
Genetics Home Reference: Fabry disease
http://ghr.nlm.nih.gov/condition/fabry-disease

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