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My46 Trait Profile

Glycogen Storage Disease type 1

Other Names: von Gierke's disease

Glycogen storage disease type I is a metabolic disorder characterized by the body's inability to break down a large sugar molecule called glycogen. It is caused by mutations in the G6PC and SLC37A4 genes, each of which makes a protein involved in breaking down glycogen.

Characteristics of Glycogen Storage Disease type 1

Glucose, a sugar present in food, is the body's main source of energy. Energy is required by all organs of the body, including the brain, heart, and liver, for normal function. When a person eats, they use some glucose for immediate energy needs, and the extra glucose is stored in the liver in the form of glycogen for later use. Individuals with glycogen storage disease type I (GSDI) are not able to use this stored glucose for energy. Because of this, they are at risk for having episodes of low blood sugar (i.e. hypoglycemia), which can cause seizures and coma. Children with GSDI have large livers (caused by accumulation of glycogen), which often cause the abdomen to protrude. This is sometimes the first sign that a child has GSDI. Over time, the liver typically decreases in size, but is at risk for developing tumors (i.e. hepatoadenomas), which are usually non-cancerous. Children with GSDI are typically shorter than other children their age. This is because their bodies do not receive the energy that they need to grow at a typical rate. Ongoing symptoms may include kidney disease, osteoporosis, and high blood pressure. Additionally, most people with GSDI develop gout, which is a type of arthritis that is caused by a buildup of uric acid in the joints. GSDI also causes an accumulation of fats and cholesterol in the blood. Some individuals may have dark spots called xanthomas, which are areas where cholesterol collects under the skin.

Diagnosis/Testing

There are two main subtypes of GSD1: GSD type Ia, and GSD type 1b. GSD1a is caused by changes or mutations in the G6PC gene which makes the glucose-6-phosphatase protein. GSD1b is caused by mutations in the SLC37A4 gene which makes the glucose-6-phosphate translocase protein. These two proteins work together to break down glycogen to glucose when the body needs glucose for energy. Mutations in either of these genes interfere with this process.

A diagnosis of GSD1 can also be made by testing the level of glucose-6-phosphatase and glycogen present in a person's liver. This requires a liver biopsy, which is a procedure performed by a doctor where a very small part of the liver is removed with a needle for testing. Low glucose-6-phosphatase and high glycogen levels confirm the diagnosis of GSDIa.

Management/Surveillance

In order to have enough energy for the body to work properly, people with GSDI must eat frequently, so that they always have a fresh supply of glucose. Most children and adults with GSDI eat uncooked cornstarch every 4-6 hours. Cornstarch is used because it is digested slowly and thus releases glucose slowly. Individuals with GSDI are often recommended to eat a diet that is high in complex sugars (i.e. complex carbohydrates), and avoid foods with simple sugars such as table sugar (sucrose), sugar from fruits (fructose), and sugar from milk (lactose and galactose). Following a careful diet improves growth in childhood, and helps to prevent or improve liver tumors and kidney problems.

Gout, high blood pressure, and osteoporosis are treated the same as they would be in people without GSDI. Periodic ultrasounds of the abdomen may be recommended to check for presence or progression of liver tumors. Blood monitoring for cholesterol, fat, and uric acid levels may be performed regularly.

Liver transplantation is a cure for GSDI. This is a serious surgery that has its own risks, and therefore transplantation is only offered to people with very severe disease.

Mode of inheritance

GSDI is inherited in an autosomal recessive pattern. This means that an individual has to inherit two mutations (i.e., one from each parent) to be affected with GSD1. If both parents are carriers of a mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with GSD1.

Risk to family members

Parents of a child with GSD1 are carriers of GSD1. If a sibling of a child with GSD1 is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of GSD1.

Special considerations

None

Resources

Association for Glycogen Storage Disease
http://www.agsdus.org/
Genetics Home Reference: Glycogen storage disease type I
http://ghr.nlm.nih.gov/condition/glycogen-storage-disease-type-i
American Liver Foundation: Type I Glycogen Storage Disease
http://www.liverfoundation.org/abouttheliver/info/gsdi/

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