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My46 Trait Profile

Glycogen Storage Disease type IX

Other Names: Phosphorylase kinase deficiency, PhK deficiency, Liver phosphorylase kinase deficiency

Glycogen storage disease type IX is a rare condition characterized by the body's inability to fully break down stored glucose called glycogen. It is caused by mutations in in the genes PHKA2, PHKB, and PHKG2, each of which makes a subunit of the phosphorylase b kinase enzyme.

Characteristics of Glycogen Storage Disease type IX

Glycogen storage disease type IX (GSD IX) is caused by a deficiency of an enzyme called phosphorylase b kinase (PhK). PhK helps to break down glycogen, the storage form of glucose, into glucose. Glucose is a sugar that the body uses for energy. In people with GSD IX, glycogen builds up in the liver causing it to be enlarged (hepatomegaly). This is usually seen in the first year or two of life. In some affected children, the accumulation of glycogen damages the liver and causes scarring (fibrosis). More severe liver damage (cirrhosis) can occur in some children, but is not as common. People with GSD IX may have low glucose levels (hypoglycemia) and increased amounts of byproducts from the breakdown of fats (ketones) in their blood if they do not eat regularly. Finding ketones in the blood is a sign that the body is using fat for energy because the blood glucose level is low. Some people with GSD IX have mild muscle weakness and get tired easily. Children with GSD IX tend to be small for their age and may go through puberty at a later age than their peers. Catch up growth usually occurs and most adults are within the normal range for height.

The symptoms of GSD IX are mild in some people while in others, they are more severe. However, in general, the symptoms tend to improve with age. Based on our current knowledge, most adults do not show any symptoms of the condition.

Diagnosis/Testing

GSD IX is caused by a lack of the PhK enzyme. How well the PhK enzyme works (i.e. its activity) can be measured in a blood sample, liver biopsy or muscle biopsy sample. In some people with GSD IX, the PhK activity is normal in laboratory tests. Therefore, a normal result does not rule out the diagnosis. If a liver biopsy sample is available, the amount of glycogen can be measured and will typically be elevated in people with GSD IX.

Genetic testing is also available. Individuals with GSD IX may have changes or mutations in the PHKA2, PHKB or PHKG2 genes. These genes make parts or subunits of the PhK enzyme. Mutations in any of these genes may result in the enzyme not working properly.

Management/Surveillance

Management of GSD IX often involves regular evaluations by a doctor and nutritionist familiar with glycogen storage diseases. Blood glucose and ketone levels should be monitored regularly, especially if an affected child is not eating well during illness, after changes in diet, or at times of intense or sustained physical activity.

Hypoglycemia can be prevented by small, frequent meals, uncooked cornstarch and a high protein diet. Given the liver complications in GSD IX, it is often recommended that imaging of the liver be done every 1-2 years.

Mode of inheritance

GSD IX may be inherited in one of two patterns of inheritance: X-linked recessive and autosomal recessive. They are explained below.

X-linked recessive inheritance (PHKA2 gene):

GSD IX is most often inherited in an X-linked recessive pattern. The gene mutations causing this type of inheritance are found on the X chromosome. An X-linked recessive pattern means that in females, both copies of the gene (i.e., one on each X chromosome) must have a change or mutation, whereas in males, only one copy of the gene must have a mutation to be affected. A female with a mutation in one copy of the PHKA2 gene on the X chromosome is said to be a carrier of GSD IX.

Autosomal recessive inheritance (PHKB gene, PHKG2 gene):

Autosomal recessive inheritance means that an individual has to inherit two mutations (i.e., one from each parent) to be affected. If both parents are carriers of a mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with the condition.

Risk to family members

The risk to family members depends on the pattern of inheritance.

X-linked recessive inheritance (PHKA2 gene):

If a father is affected with GSD IX, his daughters will be carriers of GSD IX and his sons will be unaffected. If a mother is a carrier of GSD IX, each daughter has a 1 in 2 chance (50%) of being a carrier and each son has a 1 in 2 chance (50%) of being affected with GSD IX. Some carrier females have symptoms of GSD IX although they are usually milder than the symptoms seen in males.

Autosomal recessive inheritance (PHKB gene, PHKG2 gene):

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

Resources

Association for Glycogen Storage Disease
http://www.agsdus.org/

Genetics Home Reference: Glycogen storage disease type IX
http://ghr.nlm.nih.gov/condition/glycogen-storage-disease-type-ix

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