Glucose phosphate isomerase deficiency

Description

Glucose phosphate isomerase (GPI) deficiency is an inherited disorder that affects red blood cells, which carry oxygen to the body's tissues. People with this disorder have a condition known as chronic hemolytic anemia, in which red blood cells are broken down (undergo hemolysis) prematurely, resulting in a shortage of red blood cells (anemia). Chronic hemolytic anemia can lead to unusually pale skin (pallor), yellowing of the eyes and skin (jaundice), extreme tiredness (fatigue), shortness of breath (dyspnea), and a rapid heart rate (tachycardia). An enlarged spleen (splenomegaly), an excess of iron in the blood, and small pebble-like deposits in the gallbladder or bile ducts (gallstones) may also occur in this disorder.

Hemolytic anemia in GPI deficiency can range from mild to severe. In the most severe cases, affected individuals do not survive to birth. Individuals with milder disease can survive into adulthood. People with any level of severity of the disorder can have episodes of more severe hemolysis, called hemolytic crises, which can be triggered by bacterial or viral infections.

A small percentage of individuals with GPI deficiency also have neurological problems, including intellectual disability and difficulty with coordinating movements (ataxia).

Frequency

GPI deficiency is a rare cause of hemolytic anemia; its prevalence is unknown. About 50 cases have been described in the medical literature.

Causes

GPI deficiency is caused by mutations in the *GPI* gene, which provides instructions for making an enzyme called glucose phosphate isomerase (GPI). This enzyme has two distinct functions based on its structure. When two GPI molecules form a complex (a homodimer), the enzyme plays a role in a critical energy-producing process known as glycolysis, also called the glycolytic pathway. During glycolysis, the simple sugar glucose is broken down to produce energy. Specifically, GPI is involved in the second step of the glycolytic pathway; in this step, a molecule called glucose-6-phosphate is converted to another molecule called fructose-6-phosphate.

When GPI remains a single molecule (a monomer) it is involved in the development and

maintenance of nerve cells (neurons). In this context, it is often known as neuroleukin (NLK).

Some *GPI* gene mutations may result in a less stable homodimer, impairing the activity of the enzyme in the glycolytic pathway. The resulting imbalance of molecules involved in the glycolytic pathway eventually impairs the ability of red blood cells to maintain their structure, leading to hemolysis.

Other *GPI* gene mutations may cause the monomer to break down more easily, thereby interfering with its function in nerve cells. In addition, the shortage of monomers hinders homodimer formation, which impairs the glycolytic pathway. These mutations have been identified in individuals with GPI deficiency who have both hemolytic anemia and neurological problems.

Learn more about the gene associated with Glucose phosphate isomerase deficiency

- GPI

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Glucose-6-phosphate isomerase deficiency
- Glucosephosphate isomerase deficiency
- GPI deficiency
- Nonspherocytic hemolytic anemia due to glucose phosphate isomerase deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Hemolytic anemia due to glucophosphate isomerase deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0272064/)

Genetic and Rare Diseases Information Center

- Glucosephosphate isomerase deficiency (https://rarediseases.info.nih.gov/diseases/2502/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- ANEMIA, CONGENITAL, NONSPHEROCYTIC HEMOLYTIC, 4; CNSHA4 (https://omim.org/entry/613470)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28glucose+phosphate+isomerase+deficiency%5BTIAB%5D%29+OR+%28glucosephosphate+isomerase+deficiency%5BTIAB%5D%29+OR+%28glucose-6-phosphate+isomerase+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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