Phosphoglycerate Kinase Deficiency

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Phosphoglycerate kinase deficiency is a genetic disorder that affects the body's ability to break down the simple sugar glucose, which is the primary energy source for most cells. Researchers have described two major forms of the condition.

Keywords: genetic conditions

1. Introduction

The most common form is sometimes called the hemolytic form. It is characterized by a condition known as chronic hemolytic anemia, in which red blood cells are broken down (undergo hemolysis) prematurely. Chronic hemolytic anemia can lead to unusually pale skin (pallor), yellowing of the eyes and skin (jaundice), fatigue, shortness of breath, and a rapid heart rate. Some people with the hemolytic form also have symptoms related to abnormal brain function, including intellectual disability, seizures, and stroke.

The other form of phosphoglycerate kinase deficiency is often called the myopathic form. It primarily affects muscles, causing progressive weakness, pain, and cramping, particularly with exercise. During exercise, muscle tissue can be broken down, releasing a protein called myoglobin. This protein is processed by the kidneys and released in the urine (myoglobinuria). If untreated, myoglobinuria can lead to kidney failure.

Most people with phosphoglycerate kinase deficiency have either the hemolytic form or the myopathic form. However, other combinations of signs and symptoms (such as muscle weakness with neurologic symptoms) have also been reported.

2. Frequency

Phosphoglycerate kinase deficiency appears to be a rare disorder. About 30 families with affected members have been reported in the scientific literature.

3. Causes

Phosphoglycerate kinase deficiency is caused by mutations in the *PGK1* gene. This gene provides instructions for making an enzyme called phosphoglycerate kinase, which is involved in a critical energy-producing process in cells known as glycolysis. During glycolysis, the simple sugar glucose is broken down to produce energy.

Mutations in the *PGK1* gene reduce the activity of phosphoglycerate kinase, which disrupts energy production and leads to cell damage or cell death. It is unclear why this abnormality preferentially affects red blood cells and brain cells in some people and muscle cells in others. Researchers speculate that different *PGK1* gene mutations may have varying effects on the activity of phosphoglycerate kinase in different types of cells.

The Gene Associated with Phosphoglycerate Kinase Deficiency

- PGK1

4. Inheritance

This condition is inherited in an X-linked recessive pattern. The *PGK1* gene is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both

copies of the gene to cause the disorder. Females with one altered *PGK1* gene, however, may have some features of phosphoglycerate kinase deficiency, such as anemia. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

5. Other Names for This Condition

- PGK deficiency
- PGK1 deficiency
- phosphoglycerate kinase 1 deficiency

References

1. Aasly J, van Diggelen OP, Boer AM, Brønstad G. Phosphoglycerate kinasedeficiency in two brothers with McArdle-like clinical symptoms. Eur J Neurol.2000 Jan;7(1):111-3.
2. Beutler E. PGK deficiency. Br J Haematol. 2007 Jan;136(1):3-11. Review.
3. Flanagan JM, Rhodes M, Wilson M, Beutler E. The identification of a recurrent phosphoglycerate kinase mutation associated with chronic haemolytic anaemia andneurological dysfunction in a family from USA. Br J Haematol. 2006Jul;134(2):233-7.
4. Noel N, Flanagan JM, Ramirez Bajo MJ, Kalko SG, Mañú Mdel M, Garcia Fuster JL,Perez de la Ossa P, Carreras J, Beutler E, Vives Corrons JL. Two newphosphoglycerate kinase mutations associated with chronic haemolytic anaemia and neurological dysfunction in two patients from Spain. Br J Haematol. 2006Feb;132(4):523-9. Erratum in: Br J Haematol. 2006 May;133(4):451. Flanagan, John [corrected to Flanagan, Jonathan M]; Perez de la Ossa, Pablo [added]; Carreras,Josep [added].
5. Sotiriou E, Greene P, Krishna S, Hirano M, DiMauro S. Myopathy andparkinsonism in phosphoglycerate kinase deficiency. Muscle Nerve. 2010May;41(5):707-10. doi: 10.1002/mus.21612.
6. Spiegel R, Gomez EA, Akman HO, Krishna S, Horovitz Y, DiMauro S. Myopathicform of phosphoglycerate kinase (PGK) deficiency: a new case and pathogenicconsiderations. Neuromuscul Disord. 2009 Mar;19(3):207-11. doi:10.1016/j.nmd.2008.12.004.
7. Svaasand EK, Aasly J, Landsem VM, Klungland H. Altered expression of PGK1 in afamily with phosphoglycerate kinase deficiency. Muscle Nerve. 2007Nov;36(5):679-84.