Deoxyguanosine kinase deficiency

Description

Deoxyguanosine kinase deficiency is an inherited disorder that can disrupt the normal function of the liver, brain, and muscles. Researchers have described different forms of this disorder. Approximately 75 percent of affected individuals have the hepatocerebral form, which causes serious problems in the liver (hepato-) and brain (cerebral). Approximately 20 percent of people with deoxyguanosine kinase deficiency have the isolated hepatic form, which causes liver disease without serious neurological problems. The myopathic form is the least common form; it affects approximately 5 percent of people with deoxyguanosine kinase deficiency. The myopathic form causes problems with the skeletal muscles, which are the muscles used for movement. The signs and symptoms of deoxyguanosine kinase deficiency can vary, even among members of the same family.

Infants with the hepatocerebral form of deoxyguanosine kinase deficiency typically have low blood glucose levels (hypoglycemia) and a buildup of lactic acid in the body (lactic acidosis) soon after birth. Within the first few weeks of life, these infants typically begin to show signs of liver disease and brain dysfunction. Neurological signs and symptoms may include weak muscle tone (hypotonia), abnormal involuntary eye movements (nystagmus), developmental delays, and, rarely, seizures. Early signs of liver disease may include an enlarged liver (hepatomegaly) and yellowing of the skin and the whites of the eyes (jaundice). Liver disease usually progresses to liver failure.

Signs and symptoms of the isolated hepatic form of deoxyguanosine kinase deficiency may appear soon after birth or during childhood. Like those with the hepatocerebral form, people with the hepatic form often have liver disease that worsens over time and may progress to liver failure. Some affected individuals have additional signs and symptoms that indicate the involvement of other body systems, such as the kidneys and the heart.

Signs and symptoms of the myopathic form often appear in adulthood, although they sometimes appear earlier in life. In addition to problems with the skeletal muscles, people with the myopathic form of deoxyguanosine kinase deficiency can have heart problems, brain abnormalities, or weakness of the eye muscles. People with the myopathic form typically do not have liver disease.

Without intervention, most individuals with deoxyguanosine kinase deficiency have a shortened life expectancy. Those with liver disease typically do not survive past early

childhood, while those with the myopathic form may survive into middle or late adulthood.

Frequency

More than 200 individuals with deoxyguanosine kinase deficiency have been reported in the medical literature. The prevalence in the general population is estimated to be approximately 1 in 114,000 individuals.

Causes

The *DGUOK* gene provides instructions for making the enzyme deoxyguanosine kinase. This enzyme plays an important role in mitochondria, which are the energy-producing centers inside the cell. Mitochondria each contain their own DNA, known as mitochondrial DNA or mtDNA, that is essential for their normal function. Deoxyguanosine kinase is involved in producing and maintaining the building blocks (nucleosides) that make up mtDNA.

The variants (also called mutations) in the *DGUOK* gene that cause deoxyguanosine kinase deficiency reduce or eliminate the activity of the deoxyguanosine kinase enzyme. Reduced enzyme activity leads to problems with the production and maintenance of mtDNA. A decrease in the amount of mtDNA (known as mitochondrial DNA depletion) impairs mitochondrial function in many of the body's cells and tissues. These problems lead to the brain, liver, and muscle dysfunction associated with deoxyguanosine kinase deficiency.

Learn more about the gene associated with Deoxyguanosine kinase deficiency

- DGUOK

Inheritance

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

Other Names for This Condition

- DGUOK deficiency
- DGUOK-related mitochondrial DNA depletion syndrome, hepatocerebral form
- Mitochondrial DNA depletion syndrome 3 (hepatocerebral type)
- Mitochondrial DNA depletion syndrome, hepatocerebral form due to DGUOK deficiency
- MTDPS3

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Mitochondrial DNA depletion syndrome 3 (hepatocerebral type) (https://www.ncbi.nlm.nih.gov/gtr/conditions/C5191055/)

Genetic and Rare Diseases Information Center

- Mitochondrial DNA depletion syndrome (https://rarediseases.info.nih.gov/diseases/13643/index)
- Mitochondrial DNA depletion syndrome, hepatocerebral form due to DGUOK deficiency (https://rarediseases.info.nih.gov/diseases/13644/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- MITOCHONDRIAL DNA DEPLETION SYNDROME 3 (HEPATOCEREBRAL TYPE); MTDPS3 (https://omim.org/entry/251880)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28deoxyguanosine+kinase+deficiency%5BTIAB%5D%29+OR+%28mitochondrial+DNA+depletion+syndrome%29%29+AND+%28dguok%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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