Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency

Description

Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency is a rare condition that prevents the body from converting certain fats to energy, particularly during periods without food (fasting).

Signs and symptoms of LCHAD deficiency typically appear during infancy or early childhood. Many affected infants have feeding difficulties, such as an extreme dislike of certain foods or of eating at all (food or feeding aversion), nausea, and vomiting. Other signs and symptoms include lack of energy (lethargy), low blood glucose (hypoglycemia) , weak muscle tone (hypotonia), delayed development of milestones, liver problems, and abnormalities in the light-sensitive tissue at the back of the eye (retina). Affected individuals can have impaired vision or difficulty seeing things far away (myopia) or in low light (night blindness). These vision problems worsen over time. Later in childhood, people with this condition may experience muscle pain, breakdown of muscle tissue (rhabdomyolysis), and a loss of sensation in their arms and legs (peripheral neuropathy). Infants and children with LCHAD deficiency are also at risk of serious heart problems, such as a weakened heart (cardiomyopathy) and heart failure; breathing difficulties; coma; and sudden death.

Problems related to LCHAD deficiency can be triggered when the body is under stress, for example during periods of fasting, illnesses such as viral infections, or weather extremes. This disorder is sometimes mistaken for Reye syndrome, a severe disorder that may develop in children while they appear to be recovering from viral infections such as chicken pox or flu. Most cases of Reye syndrome are associated with the use of aspirin during these viral infections.

Frequency

The incidence of LCHAD deficiency is unknown. One estimate, based on a Finnish population, indicates that 1 in 62,000 pregnancies is affected by this disorder. In the United States, the incidence is probably much lower.

Causes

Variants (also known as mutations) in the *HADHA* gene cause LCHAD deficiency. The *HADHA* gene provides instructions for making part of an enzyme complex called

mitochondrial trifunctional protein. This enzyme complex functions in mitochondria, the energy-producing centers within cells. As the name suggests, mitochondrial trifunctional protein contains three enzymes that each perform a different function. This enzyme complex is required to break down (metabolize) a group of fats called long-chain fatty acids. Long-chain fatty acids are found in foods such as milk and certain oils. These fatty acids are stored in the body's fat tissues. Fatty acids are a major source of energy for the heart and muscles. During periods of fasting, fatty acids are also an important energy source for the liver and other tissues.

Variants in the *HADHA* gene that cause LCHAD deficiency disrupt one of the functions of this enzyme complex. These variants prevent the normal processing of long-chain fatty acids from food and body fat. As a result, these fatty acids are not converted to energy, which can lead to some features of this disorder, such as lethargy and hypoglycemia. Long-chain fatty acids or partially metabolized fatty acids may also build up and damage the liver, heart, muscles, and retina. This abnormal buildup causes the other signs and symptoms of LCHAD deficiency.

Learn more about the gene associated with Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency

- HADHA

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have variants. 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

- 3-hydroxyacyl-CoA dehydrogenase, long chain, deficiency
- LCHAD deficiency
- Long-chain 3-hydroxy acyl CoA dehydrogenase deficiency
- Long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency
- Long-chain 3-OH acyl-CoA dehydrogenase deficiency
- Trifunctional protein deficiency, type 1

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3711645/)

Genetic and Rare Diseases Information Center

- Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency (https://rarediseases.info.nih.gov/diseases/6867/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency%22)

Catalog of Genes and Diseases from OMIM

- LONG-CHAIN 3-HYDROXYACYL-CoA DEHYDROGENASE DEFICIENCY (https://omim.org/entry/609016)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28long-chain+3-hydroxyacyl-CoA+dehydrogenase+deficiency%5BTIAB%5D%29+OR+%28LCHAD%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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