Published on *My46* (https://www.my46.org) 01/23/2022

My46 Trait Profile

Holocarboxylase synthetase deficiency

Holocarboxylase synthetase deficiency is a genetic condition characterized by the body's inability to use biotin. It is caused by mutations in the HLCS gene that make an enzyme called holocarboxylase synthetase.

Characteristics of Holocarboxylase synthetase deficiency

Holocarboxylase synthetase deficiency (HLCSD) is a condition characterized by an inability to use biotin in the body. Biotin is an important vitamin that helps the body function (grow and develop) properly. By attaching to enzymes that help build and break down proteins, fats, and carbohydrates in the body, biotin is a "helper" vitamin essential for these processes to occur. Holocarboxylase synthetase is an enzyme that is very important in this process because it helps biotin "attach" to these enzymes. When there are problems with holocarboxylase synthetase, biotin cannot attach properly and normal body functions are disrupted.

Individuals with HLCSD can have a range of signs and symptoms that can be life-threatening if untreated. These can include vomiting, tachypnea (rapid breathing), irritability, lethargy (lack of energy, sluggish), skin problems, and seizures that may progress to coma. Individuals with HLCSD typically show symptoms very soon after birth, from the first few hours to first weeks of age. Infants who do not get treatment can have serious long-term symptoms such as cerebal edema (fluids in the brain) and coma, and can develop growth and developmental delays later on in childhood.

Diagnosis/Testing

Individuals with HLCSD have changes or mutations in a gene called HLCS. This gene makes the holocarboxylase synthetase enzyme. This enzyme is responsible for attaching biotin to help important enzymes function properly. Mutations in the HLCS gene can cause this enzyme not to work properly, and therefore it is unable to attach biotin in the right places at the right times.

Some babies with HLCSD are diagnosed early in life through newborn screening (NBS) because they have abnormal buildup of acids that can be detected by laboratory testing. NBS tests a spot of blood from the baby's heel and looks for many disorders. While it does not generally screen specifically for HLCSD, it can sometimes be picked up this way when looking for other disorders that share similar biochemical characteristics (i.e. biotinidase deficiency).

Ultimately, diagnosis is based on clinical symptoms and specific buildup of acids that suggest HLCSD. It can be confirmed by demonstrating deficient holocarboxylase synthetase enzyme activity in leukocytes (white blood cells) or fibroblasts (connective tissue cells), or by genetic testing.

Management/Surveillance

It is recommended that these individuals be treated with a special biotin supplement called "unbound" biotin or "free" biotin to meet the body's needs.

This is usually the primary treatment, although additional treatment may be necessary depending on the symptoms of the individual. Treatment should be started as soon as possible after diagnosis and must be continued lifelong. In general, individuals with HLCSD who are started on treatment earlier have a better clinical outcome and may avoid symptoms all together. However, each individual can be affected differently. Affected individuals should be managed routinely and monitored for later-onset complications.

Individuals with HLCSD are usually followed by a doctor and dietician specializing in metabolic diseases. They typically also see other doctors to be screened for development of other symptoms.

Mode of inheritance

HLCSD is inherited in an autosomal recessive pattern. This means that an individual has to inherit two HLCS mutations (i.e., one from each parent) to be affected with HLCSD. If both parents are carriers of a HLCS mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with HLCSD.

Risk to family members

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

Special considerations

None

Resources

Genetics Home Reference: Holocarboxylase synthetase deficiency
http://ghr.nlm.nih.gov/condition/holocarboxylase-synthetase-deficiency
Organic Acidemia Association
http://www.oaanews.org

References

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Wolf B. Disorders of biotin metabolism. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. The Metabolic Basis of Inherited Disease. New York, NY: McGraw-Hill; 1992:2083-103. Print.

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