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My46 Trait Profile

Long chain 3-Hydroxyacyl-CoA dehydrogenase deficiency

Other Names: Long-chain acyl-CoA dehydrogenase deficiency

Long Chain 3-Hydroxyacyl-CoA dehydrogenase deficiency is a genetic condition in which the body cannot break down long chain fats for energy. It is caused by mutations in the HADHA gene that makes an enzyme called long chain 3-hydroxyacyl-CoA dehydrogenase.

Characteristics of Long chain 3-Hydroxyacyl-CoA dehydrogenase deficiency

Long chain 3-Hydroxyacyl-CoA dehydrogenase deficiency (LCHADD) is a genetic condition in which the body cannot break down long chain fatty acids for energy. As a result, these fatty acids (called long chain 3-hydroxy fatty acids) build up in the body. The accumulation of long-chain fatty acids can be harmful to the body and cause health problems. An individual with LCHADD lacks an important energy source, as fatty acids are usually broken down to produce energy for the body.

Symptoms of LCHADD generally present in the first year of life and may be mild or severe. The most common symptoms of LCHADD include low blood sugar (hypoglycemia) without production of ketones (byproducts from the breakdown of fats) and liver dysfunction. Hypoglycemic crises (caused by low blood sugar and lack of ketones) are most often triggered by infection and/or going too long without eating (fasting). Other symptoms include low muscle tone (hypotonia), enlarged heart and/or liver, tiredness and lack of energy (lethargy), and poor feeding. Other symptoms may also develop during childhood even with treatment. These include retinal abnormalities (retinitis pigmentosa), peripheral neuropathy (damage to the nerves carrying information back and forth to the brain), and/or the breakdown of muscle tissue.

There are three main classes of severity in LCHADD. The severe cardiomyopathic form occurs when infants present in early infancy with low blood sugar and heart/multi-organ failure. The infant-onset hepatic form occurs when infants present in the first year of life with low blood sugar and liver dysfunction. The third class, late-onset neuromyopathic form, presents later with muscle damage and peripheral neuropathy that worsens over time.

Pregnant women carrying a baby affected with LCHADD may also have symptoms of the condition. It is common for the mother of a child with LCHADD to experience maternal liver disease during the third trimester of pregnancy. These conditions are dangerous for the mother and baby and, in some cases, may lead to maternal death and/or premature delivery of the baby.

Diagnosis/Testing

Most individuals with LCHADD have changes or mutations in the HADHA gene. This gene makes the long-chain 3-hydroxyacyl-CoA dehydrogenase enzyme that is responsible for breaking down long chain fatty acids. Mutations in this gene that cause the enzyme to not be made or not be made properly, results in many of the health problems seen in individuals with LCHADD.

Many babies with LCHADD are diagnosed early in life through newborn screening (NBS). NBS tests a spot of blood from the baby’s heel and looks to see if there is a buildup of long chain fatty acids in the body, which suggests the

LCHAD enzyme is working properly. NBS test results are confirmed with additional blood or urine chemical tests and usually testing of the HADHA gene.

Management/Surveillance

Management of LCHADD focuses on decreasing the buildup of long-chain fatty acids and providing another source of energy for the body. Long-chain fatty acids come from food, standard infant formula, and breast milk. Individuals with LCHADD are placed on strict low fat diets as they cannot break down the fats from food. Some long chain fats are essential – this means that bodies need them to function properly. Oftentimes individuals with LCHADD have to take essential fatty acid supplements. Blood tests are done regularly to test the amount of long chain fatty acids and essential fatty acids in the body. Individuals with LCHADD also supplement with medium chain triglycerides (MCT), which bypass the missing or dysfunctional LCHAD enzyme and can be broken down for energy. Medium-chain fats are found in special infant formulas, supplemental oil, emulsion, and/or powder.

It is important for individuals with LCHADD to not go too long without eating (fasting). The body likes to use stored fatty acids as an energy source during periods of fasting. This is especially true during illness. Illness increases the body's energy demands and often decreases an individual's appetite. Individuals with LCHADD cannot use the fatty acids stored in the body for energy. Therefore, without a source of energy from food, they are at risk of low blood sugar and even coma or death. These individuals, especially children, often have to go to the emergency room to receive intravenous (IV) dextrose (sugar) during illness. Individuals should be given an emergency protocol letter which details the treatment that should be started.

Individuals with LCHADD are usually followed by a doctor and dietitian specializing in metabolic diseases. They typically also see other doctors to be screened for the development of other symptoms (heart and retinal abnormalities). There are no clear ways to prevent retinal abnormalities in LCHADD; however, some research suggests a link between the amount of long-chain fatty acid buildup and the progression of these problems.

Mode of inheritance

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

Risk to family members

Parents of a child with LCHADD are carriers of LCHADD. Carriers of LCHADD do not show any signs of the condition. If a sibling of a child with LCHADD is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of LCHADD.

Special considerations

None

Resources

Genetics Home Reference: Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency
http://ghr.nlm.nih.gov/condition/long-chain-3-hydroxyacyl-coa-dehydrogenase-deficiency
Medical Home Portal
http://www.medicalhomeportal.org/diagnoses-and-conditions/lchadd-tfp-deficiency/description
Fatty Oxidation Disorders Family Support Group
http://www.fodsupport.org/lchad.htm

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