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My46 Trait Profile

Lysosomal acid lipase deficiency

Other Names: Cholesteryl Ester Storage Disease, Wolman disease

Lysosomal Acid Lipase Deficiency is a rare condition characterized by a problem processing cholesterol which leads to liver disease, atherosclerosis and early death. It is caused by mutations in a gene called LIPA that makes the lysosomal acid lipase enzyme.

Characteristics of Lysosomal acid lipase deficiency

Lysosomal acid lipase deficiency (LALD) is a rare, inherited condition that results in problems with cholesterol processing in the liver and in other cells of the body. Children and adults with LALD typically have high LDL cholesterol (bad cholesterol) and low HDL cholesterol (good cholesterol), and are at high risk to develop liver disease and liver failure.

Signs and symptoms in LALD can vary, and may begin in infancy, early childhood or adulthood. The most severe end of the LALD spectrum, often called Wolman disease, has infantile onset and babies do not survive past the first year of life if untreated. Cholesteryl ester storage disease describes individuals with LALD who make sufficient LAL enzyme to survive beyond the first year of life. Symptoms may include diarrhea, abdominal pain, growth delay, fatigue and an enlarged liver and spleen. Some individuals with LALD may not experience any symptoms, and a doctor may not suspect LALD until blood tests reveal unexplained high LDL cholesterol, low HDL cholesterol and high liver enzymes, or physical examination reveals an enlarged liver.

Diagnosis/Testing

The diagnosis of LALD is made by a blood test that measures lysosomal acid lipase (LAL) enzyme activity. This enzyme is responsible for processing cholesterol. Children and adults with LALD have very low LAL enzyme activity, so this enzyme does not work properly. LALD can also be diagnosed by genetic testing for changes or mutations in a gene called LIPA. The LIPA gene instructs the body to make the LAL enzyme. Mutations in the LIPA gene can result in LAL enzyme that does not function properly.

It is also possible to diagnose LALD by looking at a liver biopsy sample under a powerful microscope called electron microscopy. Characteristic crystals called birefringent cholesteryl ester crystals are present, and microvesicular steatosis, which is an uncommon form of fatty liver, micronodular cirrhosis and fibrosis, are also indicative of LALD. However, a liver biopsy is not necessary to diagnose LALD, since the blood test is reliable and less invasive.

Management/Surveillance

People with LALD should see a metabolic genetics specialist and receive genetic counseling. The cholesterol problems in LALD can cause heart and vascular diseases, so evaluation by a cardiovascular specialist is recommended. A liver disease doctor (hepatologist) or doctor specializing in diseases of the digestive system (gastroenterologist) should monitor the liver disease, and an endoscopy may be required to look at the digestive tract. Blood tests to measure cholesterol, triglycerides, liver enzymes, coagulation time, hemoglobin and platelets should be done at least once each year.

There is no approved treatment for LALD at this time. However, clinical trials (see http://www.clinicaltrials.gov) are now underway for a promising treatment called enzyme replacement therapy for both sub-types of LALD,

cholesteryl ester storage disease and Wolman disease.

Mode of inheritance

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

Risk to family members

Parents of a child with LALD are carriers of LALD. If a sibling of a child with lysosomal acid lipase deficiency is known to be unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of a LIPA gene mutation. Siblings of affected individuals may benefit from testing since they may be unaware of having a progressive disease.

Special considerations

An extremely severe, infantile form of the LALD spectrum, commonly called Wolman disease, is caused by LIPA gene mutations that produce essentially no enzyme activity, and is fatal in the first year of life if untreated. Wolman disease presents in the first months after birth with a huge belly from the very enlarged liver and spleen, vomiting, diarrhea (often yellow in color), growth failure and anemia. Imaging studies including X-rays, ultrasound or MRI may show spots on the adrenal glands (above the kidneys) called adrenal calcifications, which are present in many but not all individuals with infantile-onset LALD. This form of LALD is more common in people of Iranian Jewish ancestry, with a carrier frequency of about 1 in 32 individuals.

Resources

LAL SOLACE: Support Organization for Lysosomal Acid Lipase Deficiency – Advocacy, Care and Expertise)
http://www.lalsolace.org
Genetics Home Reference: Cholesteryl ester storage disease
http://ghr.nlm.nih.gov/condition/cholesteryl-ester-storage-disease
LAL Deficiency Source
http://www.laldeficiencysource.com

References

Bernstein, DL. et al. (2013)."Cholesteryl ester storage disease: review of the findings in 135 reported patients with an underdiagnosed disease." Journal of Hepatology 58(6): 1230-1243.

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