Lysosomal Acid Lipase Deficiency/ Cholesterol Ester Storage Disease

Lysosomal Acid Lipase (LAL) deficiency is an inherited, genetic disorder. To understand the implications of this it is useful to know a little about this enzymes normal activity. The human body contains many different types of cells.

A basic cell has many components as you can see from the diagram below, including the nucleus which contains chromosomes. Within the cell there is a small compartment called the lysosome - this contains all the enzymes the cell needs to manage its recycling of waste products.

The LAL enzyme breaks down fatty material (cholesteryl esters and triglycerides) within the cell. When this process is ineffective there is a resulting build-up of these materials in the liver, the gut or other important organs including the walls of blood vessels.

Inheritance
LAL deficiency is an inherited genetic disorder described medically as an ‘autosomal recessive disease’. Each person has 23 pairs of chromosomes which contain genes – they receive 1 set from each parent. Genes contain the necessary information to allow our body to be formed and to function. It is estimated that every human being has 8-10 genes that have changes within them (called mutations) however only some can cause disease. A person with LAL Deficiency has inherited one faulty copy of the gene from the mother and one faulty copy of the gene from the father. Having only one copy of the faulty gene does not usually lead to the disease, although the person with one copy of the faulty gene becomes a carrier of the disease and can pass on the faulty copy to their children. When both parents are carriers, there is a 25% (one in four) chance with each pregnancy that their child will have LAL Deficiency. If you would like further information about the inheritance pattern in your personal circumstances or to know whether it is likely that any other members of your family are affected please discuss this with your physician or specialist nurse.

Symptoms

There are 2 main types:

Early onset – sometimes called Wolman Disease. This affects 1-2 babies for every million births and is usually fatal in the first year.

Late onset – sometimes called Cholesteryl Ester Storage Disease (CESD), affects 25 individuals per million births and may lead to liver fibrosis, cirrhosis, liver failure and death. Also, there may be an increased risk of strokes because of potential build-up of lipid in the walls of major arteries (atherosclerosis). This can affect both children and adults.

Features include:

- A high cholesterol and high triglyceride level: A high 'bad' cholesterol (LDL), A very low 'good' cholesterol (HDL)
- A larger than normal liver due to fat accumulation - hepatomegaly
- Increases in liver enzymes (transaminases: AST and ALT)
- Unexplained chronic liver disease
- LAL deficiency can be diagnosed by a blood test measuring enzyme levels or genetic mutation analysis.

**Treatment**

LAL Deficiency is a serious and life-threatening disease, and there are currently no approved treatments.

**Supportive treatment**

A variety of supportive therapies are used to try and slow the progress of the disease, including special diets and drugs for disease complications, but there is no evidence that these measures improve or even stay the progress of the disease. On an experimental basis, bone marrow transplantation has been recommended for early onset LAL Deficiency (Wolman disease), but its high death rate is influenced by the aggressive course of the disease, the poor health of the patient and liver damage that increases the toxicity of pre-transplant medical conditioning.

For children and adults with late onset LAL Deficiency (CESD), the physician may prescribe cholesterol-lowering drugs (‘statins’ and/or ezetimide) because of the high levels of cholesterol and other fats in the blood (high ‘bad’ cholesterol (LDL)). Although these drugs can reduce cholesterol levels to some extent, they have not been shown to improve the underlying disease and the often severe liver manifestations. Liver transplantation has been performed in some severe cases although there is limited information available to date on long term outcomes.

Advances in medicine mean that there are new treatments under investigation in clinical trials for LAL-D. Further information can be found on the clinicaltrials.gov website and on our research page for any trials currently available at Addenbrooke’s.