Tyrosinemia

What is tyrosinemia?

Hereditary tyrosinemia type 1, also called hepatorenal tyrosinemia, is a genetic disorder that affects the breakdown of an amino acid called tyrosine. It is associated with the development of severe liver disease in infants and also linked to the development of kidney disease and nerve problems in children.

The disease is inherited in an autosomal recessive fashion which means that in order to have the disease, a child must receive two defective genes, one from each parent. In families where both parents are carriers of the gene for the disease, there is a one in four risk that a child will have tyrosinemia.

About one person in 100,000 is affected with tyrosinemia globally. However, the disease is particularly common in specific region of Quebec where one person in 20 is a carrier of the defective gene, and one person in 1,846 is affected with the actual disease.

What causes tyrosinemia?

Tyrosine is an amino acid which is found in most animal and plant proteins. Amino acids are the building blocks of proteins and are required by the body for proper functioning. Tyrosine is needed for the creation of certain hormones and melanin, the chemical that gives skin, hair, and eyes colour. The major site for metabolism of tyrosine in humans is in the liver.

Tyrosinemia is caused by an absence of the enzyme, fumarylacetoacetate hydrolase (FAH), which is essential in the metabolism of tyrosine. The absence of FAH leads to a buildup of toxic products, such as succinylacetone, in various body tissues, which in turn results in progressive damage to the liver and kidneys, and may affect nerve function.

What are the symptoms of tyrosinemia?

The symptoms of the disease vary and can be distinguished between, acute and chronic.

In the acute form of the disease, problems appear in the first month of life. Babies may show poor weight gain, a large liver and spleen, a distended belly, swelling of the legs, and an increased tendency for bleeding (such as nose bleeds). Yellowing of the skin and eyes, which is called jaundice, may or may not occur. Even with therapy, death from liver failure often occurs between three and nine months of age unless a liver transplant is performed.

Some children have a chronic form of tyrosinemia which means that they will experience a more gradual onset and less severe symptoms. Children with chronic disease usually experience enlargement of the liver and spleen, distended bellies with fluid, poor weight gain, vomiting, and diarrhea. Affected children usually develop scarring and hardening of the liver, known as cirrhosis, and liver failure. These children also require liver transplantation.

Children with chronic tyrosinemia may develop weak bone due to damage to the kidneys and are at an increased risk of developing liver cancer because they are exposed to the toxic products from tyrosine metabolism for a longer period of time.

Nerves may be affected in children with poorly controlled tyrosinemia. If this happens, children may experience episodes of pain, muscle stiffness or weakness, vomiting, injury from teeth grinding or jaw clenching, and in severe cases, trouble breathing. Between these episodes, children often return to normal functioning.

How is tyrosinemia diagnosed?

The diagnosis of tyrosinemia is based on blood and urine tests. In both the acute and chronic forms of the disease, blood tests that look at liver function are often abnormal and tests that indicate liver damage may be elevated. The toxic product, succinylacetone, can be measured in the urine which confirms the diagnosis. Prenatal diagnosis is possible and can be performed by measuring succinylacetone or FAH levels in the fluid surrounding the baby in the womb.

How is tyrosinemia treated?

It is customary to place infants and children with tyrosinemia on diets that are low in the amino acids phenylalanine, methionine and tyrosine. These amino acids are found in foods that are high in protein such as meats, dairy products, nuts and beans, and therefore these foods should be limited in the diet. Strict attention to nutrition and adequate vitamin and mineral intake does not cure tyrosinemia, but helps to control the complications of poor tyrosine metabolism and support normal development and growth.

In addition to dietary modification, treatment with a medication called nitisinone (also known as NTBC, an abbreviation of its full chemical name) has been shown to be beneficial. It works by stopping the breakdown of tyrosine into succinylacetone and other toxic products. Nitisinone helps to treat and prevent episodes of nerve problems, and prolong kidney and liver function. However, the risk of developing liver cancer still remains high and some children still develop liver failure later in life. It appears that starting nitisinone early after birth lowers the risk of developing liver failure and cancer later in life. For this reason frequent monitoring is still required in children who receive modified diets and nitisinone to ensure the development of liver problems is caught early. Despite treatment, some children may still need to undergo a liver transplant.

At the present time, liver transplantation remains the only way of establishing normal tyrosine metabolism and treating the disease once it has reached the more advanced stages.

This information is current for February 2015.