
Citrullinemia – Amino Acid Disorder

What are amino acid disorders?

The amino acid disorders are a class of inherited metabolic conditions that occur when certain amino acids either cannot be broken down or cannot be produced by the body, resulting in the toxic accumulation of some substances and the deficiency of other substances.

What is citrullinemia?

Citrullinemia is a urea cycle defect. The urea cycle is the body's system for getting rid of waste nitrogen and for synthesizing arginine and urea. Hyperammonemia, a toxic build-up of ammonia in the blood, results when one of the enzymes in the urea cycle is not functioning well.

What is its incidence?

Citrullinemia affects about 1 in every 60,000 babies born in Ontario.

What causes the disease?

Mutations in the gene for argininosuccinic acid synthetase, one of the six enzymes in the urea cycle, results in enzyme that is not working well or is deficient.

What are the clinical features of the disease?

Although babies with citrullinemia may appear normal at birth, without treatment they may soon start to have symptoms of hyperammonemia, which can lead to coma and death. Symptoms of hyperammonemia can include lethargy, vomiting, poor appetite, seizures, hypotonia and muscle weakness, and breathing problems. Episodes of hyperammonemia may occur after prolonged periods without food, such as during an illness, because the body begins to break down the protein found in muscle tissue, or after a high-protein or large meal.

There is also a milder form of citrullinemia with a later age of onset; the presentation is variable.

How is the diagnosis confirmed?

The diagnosis is confirmed by measuring amino acid levels in blood and urine. Citrulline levels will be elevated in the blood while arginine levels will be low. Orotic acid levels will be elevated in the urine. Enzyme studies may also be helpful in confirming the diagnosis. Diagnostic testing is arranged by specialists at your regional treatment centre.

What is the treatment of the disease?

A low protein diet and a special medical formula are often recommended in children with citrullinemia. Dietary supplementation with arginine is also recommended. A medication called sodium phenylbutyrate may be considered. Children with citrullinemia should also avoid going long periods without food. This special diet can prevent hyperammonemic episodes and their sequelae. In an acute symptomatic episode, IV glucose and fluids can be given, along with other medications that can help the body to get rid of harmful substances and to decrease the level of ammonia in the blood. Specialists at your regional treatment centre will coordinate treatment.

What is the outcome of treatment?

Babies who have a prolonged period of hyperammonemia may suffer from brain damage. Children who begin treatment before any symptoms of the disease occur may develop normally, however, some children may have some neurological impairment despite treatment.

Can a family have more than one child with citrullinemia?

Citrullinemia is inherited as an autosomal recessive disease. Parents of a child with citrullinemia are assumed to be carriers for the disease and have a 1 in 4 (25%) chance, in each pregnancy, of having another child with this condition. Prenatal testing for citrullinemia can be done as early as 10-12 weeks of pregnancy. Genetic counselling to discuss the benefits of prenatal testing options in more detail is recommended.

Resources

<http://www.newbornscreening.info/Parents/aminoaciddisorders/ASAS.html>

<http://www.nucdf.org/>