Argininosuccinic Aciduria

Argininosuccinic Acid Lyase Deficiency

What is Argininosuccinic aciduria?

It is one of the urea cycle defects due to deficiency of one of the enzymes that is involved in the urea cycle. As a result of this deficiency of this enzyme, hyperammonemia occur which leads to irreversible brain damage.

What causes the disease?

Mutations in the *ASL* genes are a potential cause of the argininosuccinate lyase enzyme deficiency. This enzyme is one of the six enzymes that are involved in the urea cycle.

What are the clinical features of the disease?

The most common and most severe form is characterized by hyperammonemia within the first few days after birth. Newborns typically appear healthy for the first 24 hours but within the next few days, they develop vomiting, lethargy, and hypothermia and refuse to accept feeding. Tachypnea and respiratory alkalosis are early findings. If untreated, leads to worsening lethargy, seizures, coma, and eventually death. Other clinical findings includes: hepatomegaly and trichorrhexis nodosa (coarse and friable hair. There is a late onset form: ranges from episodic hyperammonemia (triggered by acute infection or stress or by non-compliance with dietary restrictions and/or medication) to cognitive impairment, behavioral abnormalities, and/or learning disabilities in the absence of any documented episodes of hyperammonemia.

How is the diagnosis confirmed?

The diagnosis is confirmed by measuring amino acid levels in blood and urine. Argininosuccinic acid and orotic acid levels will be elevated in the urine. Citrulline levels will be elevated in the blood while arginine levels will be low. DNA molecular testing of ASL gene as well as enzymatic studies may also be helpful in confirming the diagnosis.

What is the treatment of the disease?

A low protein diet and a special medical formula are often recommended in children with this disorder. Dietary supplementation with arginine is also recommended. A medication called sodium phenylbutyrate may be considered. Children should not be kept without food for extended periods of time. This special diet can prevent hyperammonemic episodes and their sequelae. In an acute symptomatic episode, IV D10% 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.

A Biochemical genetics specialist and a Metabolic Genetics dietitian should coordinate the treatment.