Ornithine Transcarbamylase Deficiency (OTCD) Overview

Washington State Department of Health Newborn Screening Technical Advisory Committee
June 16, 2021

ABOUT THE CONDITION

The urea cycle is the body's way to get rid of ammonia, a toxic byproduct of our normal body processes. Ornithine transcarbamylase deficiency (OTCD) is an inherited urea cycle disorder in which the body cannot remove the ammonia waste. It is the most common of all urea cycle disorders.

Ammonia is formed when the body breaks down proteins from food. Ornithine transcarbamylase is one of the enzymes needed in this process. Normally, ammonia is excreted through the urine. When a baby cannot make any or enough of that enzyme, it can lead to a toxic build-up of ammonia in the body called hyperammonemia.

Levels of severity and onset of the disorder vary. Being an X-linked recessive condition, males are more affected than females (prevalence is about 1:56,000 boys). Affected males often develop severe early-onset symptoms and can die in the first week of life. Females are less likely to be affected and can be considered carriers of the disorder, although carriers can present mild symptoms of OTCD.

SYMPTOMS

Excess ammonia is toxic to the brain and nervous system. It can result in neurodevelopmental delay, intellectual disability, and death. The severity of OTCD is dependent on enzymatic compromise and the degree of hyperammonemia.

Early-onset symptoms can include lethargy, failure to thrive during the first week of life, and hyperammonemic coma with sepsis-like symptoms. Developmental delay and hyperammonemia crises can be experienced by survivors.

Males and females with late-onset OTCD can have high elevations of ammonia later in life. Symptoms can include confusion, lethargy, migraine, abdominal pain, vomiting, failure to thrive, psychiatric symptoms, and autism-like symptoms. Some patients can experience hyperammonemic crisis and death.

DIAGNOSIS

OTCD can be diagnosed through the testing of blood for amino acids and urine for organic acids. Genetic testing can be used to confirm diagnosis. There is good genotype/phenotype correlation, meaning the severity of outcomes relates to the specific genetic variant in the baby. The absence of hyperammonemia rules out urea cycle disorders.

TREATMENT

The goal of treatment is to prevent excess ammonia in order to avoid hyperammonemic episodes. Treatment can include a low protein diet, amino acid support, vitamin and mineral supplementation and medication, such as nitrogen scavengers, to improve the excretion of nitrogen waste. Dialysis is effective in decreasing ammonia levels if there is resistance to first line medication. Liver transplants can cure OTCD and normalize ammonia levels, though there are risks with surgery, post-operative complications and the patient requires life-long use of immunosuppressants.