Published on *My46* (https://www.my46.org) 10/16/2021

My46 Trait Profile

Citrullinemia type 1

Other Names: Classic citrullinemia, Argininosuccinate synthetase deficiency

Citrullinemia type 1 is a genetic condition characterized by the body's inability to remove waste nitrogen from the body's bloodstream. It is caused by mutations in a gene called ASS1 that makes the protein argininosuccinate synthase (ASS).

Characteristics of Citrullinemia type 1

Individuals with citrullinemia type 1 cannot properly remove nitrogen from the body's bloodstream. Citrullinemia type 1 belongs to a group of metabolic disorders called urea cycle disorders. The urea cycle is responsible for removing nitrogen, a waste product of protein metabolism, from the blood and converting it to urea. Urea is then eliminated from the body in urine. In urea cycle disorders, the waste nitrogen does not get converted to urea, and instead accumulates in the form of ammonia. The body is unable to tolerate large amounts of ammonia. Although the severity of citrullinemia type 1 varies, symptoms of the condition usually appear within the first few days of life. Affected infants usually seem normal at birth, but as large quantities of ammonia build up in the body, lack of energy (lethargy), poor feeding, vomiting, seizures, loss of consciousness, and increased pressure in the skull are common. These medical problems can be life-threatening.

Other forms of citrullinemia type 1 can present later in childhood or adulthood. Sometimes, women with citrullinemia type 1 have severe symptoms only during pregnancy or shortly after the birth of their baby. Some people never have symptoms of the disorder.

Diagnosis/Testing

Most infants with citrullinemia type 1 are diagnosed within the first few days or weeks of life through newborn screening (NBS). NBS tests a spot of blood from the baby's heel to see if the ASS enzyme is working properly. NBS test results are confirmed with additional blood and urine chemical tests, as well as with genetic testing of the ASS1 gene. This gene makes the argininosuccinate synthase (ASS) enzyme. This enzyme is involved in the urea cycle which is responsible for breaking down or processing ammonia. It is the buildup of ammonia and other products (i.e. citrulline) that cause symptoms of citrullinemia type 1. Most individuals with citrullinemia type 1 have changes or mutations in the ASS1 gene.

Management/Surveillance

Management of citrullinemia type 1 depends on early diagnosis, control of ammonia levels, and control of pressure in the skull (intracranial pressure). Medications and dialysis can help control ammonia levels in the blood. Liver transplantation has been found to be effective in some cases. It is important that individuals with citrullinemia type 1 avoid excess protein intake, and be followed by a metabolic nutritionist. It is important that individuals with citrullinemia type 1 contact their doctor if they have any symptoms of high ammonia levels. These symptoms can include, but are not limited to, mood changes, disorientation, headaches, low energy, vomiting, and refusal to eat.

Mode of inheritance

Citrullinemia type 1 is inherited in an autosomal recessive pattern. This means that an individual has to inherit two ASS1 mutations (i.e., one from each parent) to be affected with citrullinemia type 1. If both parents are carriers of a ASS1 mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with citrullinemia type 1. Babies born in the United States are screened for citrullinemia type 1 by newborn screening.

Risk to family members

Parents of a child with citrullinemia type 1 are carriers of the condition. If a sibling of a child with citrullinemia type 1 is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of citrullinemia type 1.

Special considerations

None

Resources

Genetics Home Reference: Citrullinemia
http://ghr.nlm.nih.gov/condition/citrullinemia
Medical Home Portal: Citrullinemia
http://www.medicalhomeportal.org/newborn/citrullinemia
Save Babies Through Screening Foundation, Inc.
http://www.savebabies.org/
National Urea Cycle Disorders Foundation
http://www.nucdf.org
Urea Cycle Disorders Consortium
http://rarediseasesnetwork.epi.usf.edu/ucdc/

References

Engel, K. et al. (2009)."Mutations and polymorphisms in the human argininosuccinate synthetase (ASS1) gene." Human Mutation 30(3): 300-307.
Thoene JG. (Updated 11 August 2011). Citrullinemia Type I. In: GeneReviews at GeneTests Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1997-2013. Available at http://www.ncbi.nlm.nih.gov/books/NBK1458/. Accessed [11/08/2013].

Created: 11/2013 **Created by:** Jaclyn Foster, MS, Samuel Yang, MD
Updated: mm/yyyy **Edited by:** Seema Jamal, MSc, LCGC