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My46 Trait Profile

Citrullinemia type 2

Other Names: Citrin deficiency, Adult-onset citrullinemia, Neonatal intrahepatic cholestasis caused by citrin deficiency

Citrullinemia type 2 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 SLC25A13 that makes the citrin protein.

Characteristics of Citrullinemia type 2

Individuals with citrullinemia type 2 cannot properly remove nitrogen from the body's bloodstream. Citrullinemia type 2 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.

Citrullinemia type 2 has two forms: neonatal onset and adult onset. The neonatal onset form has symptoms that begin in the newborn period. It is typically characterized by poor growth and liver disease. With treatment (e.g., certain vitamins and lactose-free formulas), most affected individuals improve by 1 year of age. However, some infants do not improve and develop liver failure. The adult onset form mostly affects the central nervous system. Common features include, but are not limited to, high ammonia levels in the blood (hyperammonemia), sudden onset of abnormal behaviors (i.e. aggression, irritability, hyperactivity), disorientation, seizures, and coma. These symptoms can be life-threatening. Certain medications, infections, alcohol, sugar, surgery, and/or a previous liver disorder (neonatal cholestasis) can trigger these symptoms. Interestingly, individuals with citrullinemia type 2 tend to avoid carbohydrates and crave protein. Citrullinemia type 2 is found most commonly in the Japanese population.

Diagnosis/Testing

Citrullinemia type 2 is caused by changes or mutations in the SLC25A13 gene. This gene makes a protein called citrin. Citrin plays an important role in the urea cycle. Since the urea cycle is responsible for getting rid of waste nitrogen in the body, when the citrin protein is not working properly, the urea cycle is disrupted. This causes nitrogen to not be effectively processed and leads to ammonia accumulation in the body. The buildup of ammonia causes the symptoms seen in citrullinemia type 2.

Management/Surveillance

Management of citrullinemia type 2 requires dietary intervention and medications. Liver transplantation has been effective in some cases, and is the most effective treatment for the adult-onset form. It is important that individuals with citrullinemia type 2 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. It is recommended that individuals with citrullinemia type 2 follow a high fat and protein diet that is low in carbohydrates.

Mode of inheritance

Citrullinemia type 2 is inherited in an autosomal recessive pattern. This means that an individual has to inherit two SLC25A13 mutations (i.e., one from each parent) to be affected with citrullinemia type 2. If both parents are carriers of

a SLC25A13 mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with citrullinemia type 2.

Risk to family members

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

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

Dimmock, D. et al. (2009)."Citrin deficiency, a perplexing global disorder." Molecular Genetics & Metabolism 96(1): 44-49.
Ikeda, S. et al. (2001)."Type II (adult onset) citrullinaemia: clinical pictures and the therapeutic effect of liver transplantation." Journal of Neurology, Neurosurgery, and Psychiatry. 71(5): 663-670.
Kobayashi K, Saheki T, Song YZ. (Updated 5 January 2012). Citrin Deficiency. 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/NBK1181/. Accessed [11/08/2013].
Saheki, T. et al. (2010)."Citrin deficiency and current treatment concepts." Molecular Genetics & Metabolism 100 Suppl 1: S59-64.
Song, YZ. et al. (2011)."Genotypic and phenotypic features of citrin deficiency: five-year experience in a Chinese pediatric center." International Journal of Molecular Medicine 28(1): 33-40.

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