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My46 Trait Profile

Tyrosinemia type 1

Other Names: Hepatorenal tyrosinemia, Fumarylacetoacetate hydrolase deficiency

Tyrosinemia type 1 is a metabolic disorder characterized by the body's inability to fully break down an amino acid called tyrosine. It is caused by mutations in the FAH gene that makes fumarylacetoacetase.

Characteristics of Tyrosinemia type 1

Tyrosinemia type 1 is a rare genetic condition in which the body cannot break down an amino acid called tyrosine. Amino acids are the building blocks of protein. Tyrosine is found in many of the foods we eat, including breast milk and infant formula. If an individual with tyrosinemia type 1 is given foods that contain tyrosine, harmful substances (i.e., succinylacetone) build up in the body and damage the liver, brain, and bones. Early signs of tyrosinemia type 1 can include feeding problems, liver disease, low blood sugar, extreme sleepiness and poor weight gain. If untreated, this build up can lead to serious and permanent health problems or death. When tyrosinemia type 1 is diagnosed and treated early, liver, kidney and neurological problems can be prevented and growth and intelligence can be normal.

Diagnosis/Testing

Most infants with tyrosinemia 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 FAH enzyme is working properly. NBS test results are confirmed with additional blood and urine chemical tests, and possibly with genetic testing of the FAH gene. This gene makes the fumarylacetoacetase enzyme that is responsible for breaking down or processing tyrosine. Most individuals with tyrosinemia type 1 have changes or mutations in the FAH gene. If a pregnancy is known to be at risk for tyrosinemia type 1, amniocentesis can be used for prenatal diagnosis. There are two other types of tyrosinemia; each type has distinctive symptoms and is caused by a deficiency in a different enzyme.

Management/Surveillance

Children with tyrosinemia type 1 are treated by a team of health care specialists. This team monitors their tyrosine and succinylacetone levels, development and other health issues associated with tyrosinemia. Since the amino acid tyrosine is found in most foods we eat, including breast milk and infant formula, it is very important that individuals with tyrosinemia type 1 follow a special low protein (low tyrosine, low phenylalanine) diet. This diet includes a medical formula designed to provide all amino acids except for tyrosine and phenylalanine to ensure good nutrition. A specific medication called nitisinone is also prescribed which decreases the production of harmful succinylacteone. Some children who do not respond to the above therapies may require liver transplant. It is recommended that an emergency treatment plan is made to ensure that during times of illness, a child with tyrosinemia type 1 will be assessed for signs and symptoms of a metabolic crisis (e.g., poor feeding, vomiting, lethargy, excessive sleepiness, irritability) and treated appropriately.

Mode of inheritance

Tyrosinemia type 1 is inherited in an autosomal recessive pattern. This means that an individual has to inherit two FAH mutations (i.e., one from each parent) to be affected. If both parents are carriers of a FAH mutation, they have a 1

in 4 (25%) chance with each pregnancy of having a child with tyrosinemia type 1. Babies born in the United States are screened for tyrosinemia type 1 by newborn screening.

Risk to family members

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

Special considerations

None

Resources

Genetics Home Reference: Tyrosinemia
http://ghr.nlm.nih.gov/condition=tyrosinemia
Medical Home Portal: Tyrosinemia type 1
http://www.medicalhomeportal.org/newborn/tyrosinemia-type-1
About Tyrosinemia: New Parent's Guide
http://depts.washington.edu/tyros/abouttyr.htm

References

de Laet, C. et al. (2013)."Recommendations for the management of tyrosinaemia type 1." Orphanet Journal of Rare Diseases. 8:8.
Sniderman King L. et al. (Updated 25 August 2011). Tyrosinemia Type 1. 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/NBK1515/. Accessed [1/13/2014].

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