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Argininemia

Background

Argininemia is a rare Urea Cycle defect caused by deficiency of Arginase in liver and erythrocytes. Arginase is the final enzyme in the Urea Cycle that catalyzes the breakdown of arginine to ornithine and urea, which is the major metabolite carrying waste nitrogen destined for urinary excretion. Patients with Arginase deficiency have elevated levels arginine in blood. The deficient Arginase gene is located on chromosome 6.

Clinical

Patients with Argininemia may present from two months to four years of age. Symptoms are progressive spastic paraplegia, failure to thrive, delayed milestones, hyperactivity and irritability, with episodic vomiting, hyperammonemia and seizures. Mental retardation is a result of cerebral atrophy which leads to microcephaly. Hepatomegaly may be present.

Testing

Argininemia may be detected by newborn screening using tandem mass spectrometry of a dried blood spot. Affected patients have elevations in arginine ranging from 5- to 10-fold, while other amino acids are usually in the normal range. Arginase enzyme activity can also be eluted and measured from the dried blood spot. Hyperammonemia is moderately severe. The patient's urine contains elevated levels of orotic acid, along with increased levels of the diamino acids: arginine, lysine, cystine and ornithine. The deficient Arginase activity is tissue specific for the liver and erythrocyte. Heterozygous carrier individuals have partially reduced enzyme activity, but are clinically unaffected. Several mutations have been reported in the gene. Identification of the mutations allows prenatal diagnosis and genetic testing for other family members.

Treatment

Argininemia is a rare disorder and few patients have been treated from an early age, prior to onset of disabling symptoms. Dietary restriction of protein is the basic treatment, with supporting therapy to prevent and control the hyperammonemia.

Because the diagnosis and therapy of argininemia is complex, the pediatrician is advised to manage the patient in close collaboration with a consulting pediatric metabolic disease specialist. It is recommended that parents travel with a letter of treatment guidelines from the patient's physician.

Inheritance

This disorder most often follows an autosomal recessive inheritance pattern. With recessive disorders affected patients usually have two copies of a disease gene (or mutation) in order to show symptoms. People with only one copy of the disease gene (called carriers) generally do not show signs or symptoms of the condition but can pass the disease gene to their children. When both parents are carriers of the disease gene for a particular disorder, there is a 25% chance with each pregnancy that they will have a child affected with the disorder.

References

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www.perkinelmergenomics.com | Genomics@perkinelmer.com | 1-866-354-2910