Malonic Aciduria

Background

Malonic Aciduria is a rare disorder caused by deficiency of Malonyl-CoA Decarboxylase (MCD). MCD is an enzyme that catalyzes the degradation of malonyl-CoA. Malonyl-CoA is a substrate for fatty acid synthesis and it also regulates oxidation of fatty acids by controlling their uptake into mitochondria. MCD may therefore regulate fatty acid synthesis and oxidation by affecting intracellular malonyl-CoA levels, but its function is not completely known. The gene for MCD, located on chromosome 16, has been cloned and mutations identified in patients with MCD deficiency.

Clinical

The presentation of malonic aciduria due to MCD deficiency is variable, ranging from an acute neonatal onset to later in childhood. Patients have symptoms of developmental delay, seizures, hypotonia, diarrhea, vomiting, metabolic acidosis, hypoglycemia, and ketosis. Hypertrophic cardiomyopathy can be seen.

Testing

Newborn screening of a dried blood spot using tandem mass spectrometry reveals elevation of malonyl-carnitine, which is characteristic of the disorder. Confirmatory studies include urine organic acids, which show elevations in malonic acid, methylmalonic acid, and possibly other organic acids. Studies on cultured fibroblasts confirm a decrease in MCD activity. Identification of mutations in the MCD gene may be useful for genetic counseling.

Treatment

There is limited experience in managing this rare disorder. Dietary modification to increase the amount of calories from carbohydrate relative to fat has been effective in improving metabolic abnormalities. Extended fasting should be avoided. Carnitine supplementation has been beneficial in some patients.

Because the diagnosis and therapy of Malonic Aciduria 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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