

2-Methylbutyryl-CoA Dehydrogenase Deficiency

Background

Deficiency of 2-Methylbutyryl-CoA Dehydrogenase (also called Short/Branched-Chain Acyl-CoA Dehydrogenase or SBCAD) results from a defect in the metabolism of the branched-chain amino acid Isoleucine. The disorder was described in 2000 and only a few patients have been identified. The gene (SBCAD), located on chromosome 10, has been cloned and mutations identified in several patients.

Clinical

SBCAD Deficiency can have a highly variable presentation, ranging from poor feeding, lethargy, hypoglycemia, and metabolic acidosis at a few days of age to completely “asymptomatic” individuals. Those patients with symptoms have tended to display developmental delay, seizure disorder, or progressive muscle weakness in infancy and childhood. Long-term clinical follow-up, however, is lacking and the true clinical spectrum of the disease is yet to be determined. It is possible that some patients may have escaped onset of symptoms because they were not subjected to a metabolic stress.

Testing

Newborns can be screened for SBCAD Deficiency using tandem mass spectrometry analysis of a dried blood spot. The finding of elevated five-carbon acylcarnitine (C5) indicates either SBCAD Deficiency or Isovaleryl-CoA Dehydrogenase deficiency. To differentiate and make a diagnosis, further testing is required. Urine organic acid analysis from a patient suspected of SBCAD Deficiency will reveal elevation of 2-methylbutyryl-glycine with lesser increases of 2-methylbutyrylcarnitine and 2-methylbutyric acid. Plasma free carnitine levels are low to normal. Identification of mutations in the SBCAD gene may permit prenatal diagnosis.

Treatment

Treatment of patients with SBCAD Deficiency involves a low protein diet, particularly reduction of the amino acid Isoleucine, and carnitine supplementation. During an acute episode, aggressive use of glucose and electrolytes will be necessary. Carnitine is indicated during acute episodes, and perhaps chronically in some patients.

Because the diagnosis and therapy of SBCAD Deficiency 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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