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GENOMICS

Short Chain Hydroxy Acyl-CoA Dehydrogenase Deficiency (SCHAD)

Background

Short-chain-3-hydroxyacyl-CoA dehydrogenase (SCHAD) deficiency is a disorder of mitochondrial fatty acid β-oxidation. SCHAD is one of two enzymes that carry out the third step (of four) in the β-oxidation of fatty acids – the other enzyme being long-chain hydroxyacyl-CoA dehydrogenase (LCHAD), which acts on longer-chain substrates. SCHAD deficiency impairs oxidation of fatty acids of short-chain length (4 carbons and shorter). The gene for SCHAD has been cloned and mutations identified in several patients.

Clinical

SCHAD deficiency has been reported in only a few patients and the true spectrum of the disease remains to be defined. Most patients have hypoglycemia as the major symptom with seizures, neurologic sequela or even death as the outcome. Several patients have presented in the first days or months of life with hypoglycemic seizures secondary to hyperinsulinism. Other patients have presented after one year of age with acute onset of vomiting, lethargy and hyponatremic seizures. One patient has presented at 16 years of age with recurrent episodes of hypoketotic hypoglycemia, myoglobinuria, encepha-lopathy and cardiomyopathy.

Testing

Newborn screening for SCHAD deficiency using tandem mass spectrometry of a dried blood spot identifies elevated levels of hydroxybutyryl-carnitine (C4-OH). Urine organic acid analysis may reveal the presence of 3-hydroxyglutaric acid in some patients. Plasma insulin measurement should be obtained at the time a child presents with hypoglycemia to rule out hyperinsulinism. Measurement of SCHAD activity in fibroblasts allows the diagnosis of affected individuals. Identification of mutations in the SCHAD gene raises the possibility of prenatal diagnosis.

Treatment

Although the most effective therapy for SCHAD deficiency is not established, prevention of hypoglycemia with frequent feedings seems appropriate. Fasting should be avoided, particularly during times of illness. Dietary supplementation with uncooked food-grade cornstarch after the first year or two of life should be considered, because it may permit longer periods of normoglycemia. Those patients with documented hyperinsulinism have responded to treatment with diazoxide. High carbohydrate intake should be encouraged during illness, with initiation of intravenous glucose supplementation if the child is unsuccessful in keeping down fluids, or unable to take adequate oral feedings. It is recommended that parents have written instructions in their possession at all times to present to emergency personnel should the child become symptomatic.

Because the diagnosis and therapy of SCHAD 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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