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Short Chain L-3-Hydroxyacyl-CoA Dehydrogenase Deficiency

Medium/short chain L-3-hydroxyacyl-CoA dehydrogenase (M/SCHAD) is a complicated inherited disorder of fat metabolism. When the body has used up its stores of available sugars for energy, it must turn to fats. In each cell in the body, this breakdown of fats takes place very efficiently in special membrane defined bodies called mitochondria, by a four-step process known as β -oxidation. M/SCHAD is a member of a protein family that performs the third step, with each member designed to work on fats of different lengths. In addition, M/SCHAD has a second completely different role inside the mitochondria where it is a component in the regulation of insulin secretion. Without M/SCHAD, too much insulin goes into the blood, making the sugar levels in the blood too low. Loss of that insulin control is the most dangerous aspect of the M/SCHAD defect (306). Because of the expanded newborn screening program, today many potential M/SCHAD patients are identified right after birth, before they can show symptoms.

Signs and symptoms

The symptoms of M/SCHAD deficiency include extreme sleepiness, irritability, poor appetite, and mood changes. If they do not get treated medically, they can have fever, diarrhea, vomiting, and low blood sugar which can progress to seizures and coma. These symptoms usually appear the first time the child gets an illness where they stop eating regularly. Without regular feedings, SCHAD deficient infants develop a type of low blood sugar called hypoketotic hypoglycemia. It occurs because SCHAD patients secrete too much insulin into the blood. The insulin causes the blood levels of glucose to drop, leaving too little glucose to provide energy in even minor stresses like an ear infection or diarrhea. In addition, while most people can save their blood glucose by switching to fats for energy during illnesses or other stresses, these infants cannot make this switch normally. This combination of dysfunctions leaves the patients with blocks in two different means to provide energy from glucose (303-305). Infants with M/SCHAD may also have liver disease (MJ Bennett).

Diagnosis

[M/SCHAD deficiency](#) is very rare and difficult to diagnose. Most patients have symptoms in early infancy. Today, the first suspicion of M/SCHAD defects is usually the detection of high levels of the fat products 3-hydroxy-C4-carnitine and 3-hydroxy-C6-carnitine in blood spots during expanded newborn screening (Stanley C 2011). After the newborn screen results are validated, infants will be sent to their physician to look for the combination of low blood sugar with high levels of insulin (hyperinsulinemic hypoglycemia), and their urine will be taken to

search for elevation of another fat product, 3-hydroxyglutarate (stanley). ([303-305](#)). Skin cells from infants with the defect may have reduced M/SCHAD activity. The final diagnosis depends on the identification of mutations in the gene for M/SCHAD. Gene mutations have only been found in patients who have abnormal fats as described above and excess insulin. In several patients, abnormal metabolites or enzymatic studies suggestive of M/SCHAD deficiency with a normal M/SCHAD gene sequence have been reported. In these cases, the underlying disorder remains unclear.

Genetics

Everyone has two genes that make the M/SCHAD protein and, to make it confusing, this same gene has two names (*HADHSC* or *HADH*). In children with M/SCHAD, both genes contain mistakes (mutations) that result in either no protein or protein that does not work well. The disorder is inherited in an autosomal recessive manner with one mutated gene for M/SCHAD coming from each parent. Parents of children with M/SCHAD only occasionally carry two mutant genes. Rather, each parent usually carries a single bad gene, while the other gene is normal. For them, the one good HADHSC gene makes enough protein to keep the parents healthy. When both parents carry a mutation (are carriers), there is a 25% chance in each pregnancy for the child to have M/SCHAD. There is a 50% chance for the child to be a carrier, just like the parents, and, there is a 25% chance for the child to inherit two healthy genes.

Treatment

The goal of treating SCHAD deficiency is to avoid low blood sugar (hypoglycemia). Because SCHAD defects can lower blood sugar by two different mechanisms, it is treated with two different approaches. First, to reduce the circulating insulin levels, the drug diazoxide is given ([306](#)). Second, since SCHAD patients have limited abilities to use fats, avoid excessively relying on fat for energy by avoiding fasting and making certain that plenty of carbohydrates and sugars are given. If the SCHAD patient is sick and will not take in sugars by eating or drinking them, they may need to be given intravenous (IV) fluids with glucose solutions to prevent the blood sugar level from dropping.