Carnitine Palmitoyltransferase II Deficiency

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Carnitine palmitoyltransferase II (CPT II) deficiency is a condition that prevents the body from using certain fats for energy, particularly during periods without food (fasting). There are three main types of CPT II deficiency: a lethal neonatal form, a severe infantile hepatocardiomuscular form, and a myopathic form.

genetic conditions

1. Introduction

The lethal neonatal form of CPT II deficiency becomes apparent soon after birth. Infants with this form of the disorder develop respiratory failure, seizures, liver failure, a weakened heart muscle (cardiomyopathy), and an irregular heart beat (arrhythmia). Affected individuals also have low blood sugar (hypoglycemia) and a low level of ketones, which are produced during the breakdown of fats and used for energy. Together these signs are called hypoketotic hypoglycemia. In many cases, the brain and kidneys are also structurally abnormal. Infants with the lethal neonatal form of CPT II deficiency usually live for a few days to a few months.

The severe infantile hepatocardiomuscular form of CPT II deficiency affects the liver, heart, and muscles. Signs and symptoms usually appear within the first year of life. This form involves recurring episodes of hypoketotic hypoglycemia, seizures, an enlarged liver (hepatomegaly), cardiomyopathy, and arrhythmia. Problems related to this form of CPT II deficiency can be triggered by periods of fasting or by illnesses such as viral infections. Individuals with the severe infantile hepatocardiomuscular form of CPT II deficiency are at risk for liver failure, nervous system damage, coma, and sudden death.

The myopathic form is the least severe type of CPT II deficiency. This form is characterized by recurrent episodes of muscle pain (myalgia) and weakness and is associated with the breakdown of muscle tissue (rhabdomyolysis). The destruction of muscle tissue releases a protein called myoglobin, which is processed by the kidneys and released in the urine (myoglobinuria). Myoglobin causes the urine to be red or brown. This protein can also damage the kidneys, in some cases leading to life-threatening kidney failure. Episodes of myalgia and rhabdomyolysis may be triggered by exercise, stress, exposure to extreme temperatures, infections, or fasting. The first episode usually occurs during childhood or adolescence. Most people with the myopathic form of CPT II deficiency have no signs or symptoms of the disorder between episodes.

2. Frequency

CPT II deficiency is a rare disorder. The lethal neonatal form has been described in at least 18 families, while the severe infantile hepatocardiomuscular form has been identified in approximately 30 families. The myopathic form occurs most frequently, with more than 300 reported cases.

3. Causes

Mutations in the *CPT2* gene cause CPT II deficiency. This gene provides instructions for making an enzyme called carnitine palmitoyltransferase 2. This enzyme is essential for fatty acid oxidation, which is the multistep process that breaks down (metabolizes) fats and converts them into energy. Fatty acid oxidation takes place within mitochondria, which are the energy-producing centers in cells. A group of fats called long-chain fatty acids must be attached to a substance known as carnitine to enter mitochondria. Once these fatty acids are inside mitochondria, carnitine palmitoyltransferase 2 removes the carnitine and prepares them for fatty acid oxidation. Fatty acids are a major source of energy for the heart and muscles. During periods of fasting, fatty acids are also an important energy source for the liver and other tissues.

Mutations in the *CPT2* gene reduce the activity of carnitine palmitoyltransferase 2. Without enough of this enzyme, carnitine is not removed from long-chain fatty acids. As a result, these fatty acids cannot be metabolized to produce energy. Reduced energy production can lead to some of the features of CPT II deficiency, such as hypoketotic hypoglycemia, myalgia, and weakness. Fatty acids and long-chain acylcarnitines (fatty acids still attached to carnitine) may also build up in cells and damage the liver, heart, and muscles. This abnormal buildup causes the other signs and symptoms of the disorder.

3.1. The Gene Associated with Carnitine Palmitoyltransferase II Deficiency

- CPT2

4. Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- carnitine palmitoyltransferase 2 deficiency
- CPT II deficiency
- CPT2 deficiency

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