



State of CT Genetics Newborn Screening Program Health Care Provider Fact Sheet

Carnitine / Acylcarnitine Translocase Deficiency (CACT OR CAT)

Carnitine-acylcarnitine translocase (CAT) deficiency is an autosomal recessive disorder of long chain fatty acid oxidation. There are two phenotypes for this disorder: severe neonatal onset with cardiomyopathy (no survivors) and a milder phenotype with hypoglycemia but no cardiomyopathy. The carnitine-acylcarnitine carrier is an inner mitochondrial membrane protein that catalyzes the mole-to-mole exchange between internal carnitine and external acylcarnitines. CAT deficiency is a severe disease that can cause neonatal or infantile sudden death. About twenty cases of this disorder have been reported. In most patients the presenting features were neonatal neurological distress (lethargy, poor feeding), cardiac rhythm disorders and Hypoketotic hypoglycemia with hyperammonemia. Hepatomegaly, hypertrophic cardiomyopathy, muscle weakness and multi-organ failure may develop secondarily. Urine organic acids are more or less informative for the biological diagnosis. Determination of the blood acylcarnitine profile and in vitro fatty acid oxidation studies in lymphocytes or fibroblasts are the two main ways to establish the diagnosis. As soon as a fatty acid oxidation disorder is suspected, the most important goal is to provide sufficient glucose to prevent adipose tissue lipolysis. Delay may result in sudden death, cardiac arrhythmia, collapse or permanent brain damage.

Clinical Features

- Hypoketotic hypoglycemia
- Hepatomegaly
- Cardiomyopathy with ventricular arrhythmia
- Hypothermia
- Neurological deterioration
- Hyperammonemia
- Muscle weakness
- Convulsions
- Apnea
- SIDS

Diagnosis

Newborn screening—Tandem mass spectrometry C16, C18, C18:1

Low plasma free carnitine, elevated esterified carnitine in blood and urine, long-chain acylcarnitine fraction elevated in plasma

Confirmation—a second sample may be requested or follow up testing will be done at the Metabolic Treatment Center at Yale or UCONN Genetics

Situations that risk metabolic decompensation

Metabolic decompensation can be triggered by the catabolic processes that occur in the course of an infection, after an immunization or with a prolonged period of fasting. Infants may be more subject to sudden death than older children.

Monitoring

Clinical observation is the most important tool for monitoring patients with CAT. They should be observed for recurrent vomiting, refusal to eat, increased lethargy, apnea or seizures. In these situations, immediate evaluation in the emergency room is necessary. In situations of metabolic decompensation hypoglycemia can develop, but a normal blood glucose does not rule out metabolic instability and should never be a reason to delay therapy. It is also important for the primary care provider and the Metabolic Treatment Center to develop an on-going collaborative relationship in caring for these patients.

Treatment

Treatment mainly involves the blockade of lipolysis and avoiding fasting by glucose infusion or frequent meals and nocturnal nasogastric feeding with a high-carbohydrate / low-fat diet. Carnitine supplementation is also considered helpful. Medium-chain triglycerides intake must be restricted, since they are only partially utilized in these patients. Prenatal diagnosis is available.

Carnitine therapy is mandatory to counter the defects of long chain fatty acid entry into the mitochondria. Carnitine therapy has long remained controversial because of a theoretical risk of acute accumulation of long-chain acylcarnitines, which were found to be arrhythmogenic in experimental situations. However, it is very well tolerated. Carnitine probably acts by lowering the accumulation of acylCoA and restoring the CoA pool in mitochondria.

- Avoid fasting.
- Feed at regular intervals during the day and limit overnight fasting
- Should not go without food intake longer than 4 hours for the first 4 months of life; 6 hours for ages 4-8 months; and no longer than 8 hours thereafter
- The Metabolic Treatment Center will set a patient's diet prescription that determines the optimum percentage of fat, carbohydrate, and protein.
- Increased carbohydrate intake and cornstarch therapy is necessary during acute illness. The use of cornstarch therapy is an ongoing treatment and is even more necessary during acute illness
- If the child is vomiting or refuses to eat, (s)he needs to be taken to an emergency room for IV administration of 10% dextrose.
- The parents usually have an emergency protocol with them. This protocol, provided by the Metabolic Treatment Center, contains basic information about the disorder, necessary diagnostic investigations and guidelines for treatment.
- Infants and children with CAT should have regularly scheduled visits at the Metabolic Treatment Center.

Illness

- Any illness can potentially lead to metabolic decompensation
- Prevention and/or early intervention is of particular importance
- Provide high-carbohydrate feedings including cornstarch
- Avoid dehydration
- Closely monitor blood glucose and intake; even if blood glucose is normal, metabolic decompensation can occur.
- Consult with the Metabolic Treatment Center within 24 hours of the onset of the illness

Immunization

- Immunizations must be kept current.
- All children with CAT should have a yearly vaccine for influenza.
- There is no contraindication to any immunization because of CAT.
- Parents and physicians should be alerted to the need for immediate evaluation if high fever, lethargy or vomiting occurs in the first 24 hours.
- After an immunization without any other clinical symptoms, administration of acetaminophen or ibuprofen is warranted.

Surgical/surgical procedures

- Discuss any plans for surgical and dental procedures with the Metabolic Treatment Center
- Infants and children with CAT can undergo necessary anesthetic/surgical procedures.
- Any surgical procedure constitutes a potentially catabolic situation.
- Any surgery should include hospitalization pre- and postoperatively.

- Preoperative fasting should be avoided with 10% dextrose being started preoperatively and continuing postoperatively until the child is eating and drinking well.
- If complicated surgery, or a postoperative period, as an inpatient is required, the procedure should be done at a hospital with a metabolic service.

Growth and development

- It is crucial to closely monitor all growth parameters on a regular basis.
- In cases with neurological deficits, the child should be referred to an early intervention program and developmental progress closely monitored by both the metabolic team and the primary care provider.



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