



# Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)

## Background

Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD) is a disorder of  $\beta$ -oxidation of fatty acids. The enzymatic deficiency is one of four mitochondrial acyl-CoA dehydrogenases that carries out the initial dehydrogenation step in the  $\beta$ -oxidation of fatty acids. VLCAD deficiency impairs oxidation of dietary and endogenous fatty acids of long chain length (16 carbons and longer). The buildup of the long chain fatty acid acyl-CoA intermediates results in toxic effects to normal metabolism. The gene is on chromosome 17 and encodes a protein that functions on the inner mitochondrial membrane.

## Clinical

Two general presentations have been reported with VLCAD deficiency, although both can vary considerably. Infants can present with severe, sepsis-like symptoms resembling a Reye-like syndrome, which is often lethal. The patient may be hypoglycemic with fasting and have metabolic acidosis, elevated liver enzymes with hepatomegaly (due to steatosis), cholestasis, hypertrophic cardiomyopathy, proteinuria, and hematuria.

A second presentation has later onset and exhibits lethargy and coma with fasting. These patients have hypoketotic hypoglycemia, hepatomegaly, recurrent "infections", and easy fatigue resulting in recurrent sore muscles. Some present with exercise-induced rhabdomyolysis.

## Testing

Newborn screening using tandem mass spectrometry detects increased levels of C14:1, C16, and C12 acylcarnitines indicating a probable case of VLCAD deficiency. Clinical testing may reveal hypoglycemia with elevations of lactate, pyruvate, ammonia, and CK. Elevated dicarboxylic acids, both saturated and unsaturated, are often seen on urine organic acid analysis when the patient is ill. Enzyme studies performed on cultured fibroblasts can also be used to indirectly detect VLCAD activity using a labeled probe for  $\beta$ -oxidation.

## Treatment

VLCAD deficiency patients are treated with carnitine supplementation and strict avoidance of fasting. Maintaining glucose homeostasis is accomplished with frequent feedings, restricting dietary fat and increasing carbohydrates, using medium-chain triglycerides (MCT) oil supplementation and possibly cornstarch if necessary to prevent hypoglycemia. Workup of a suspected VLCAD deficient patient should rule out Medium Chain Acyl-CoA Dehydrogenase deficiency (MCAD) or Glutaric Aciduria Type II (GA-II), because MCT oil supplementation is contra-indicated for these disorders. For individuals with VLCAD, it is imperative that the lethargic patient receives parenteral glucose to avoid hypoglycemia.

Because the diagnosis and therapy of VLCAD 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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