Disease Name	**Very Long-Chain Acyl-CoA Dehydrogenase Deficiency**
Alternate name(s)	N/A
Acronym	VLCAD
Disease Classification	Fatty Acid Oxidation Disorder
Variants	Yes
Variant name	With and without cardiomyopathy
Symptom onset	Primarily neonatal but some variability.
Symptoms	Hypoketotic hypoglycemia, hepatomegaly, myopathy, cardiomyopathy, adult-onset myopathy.
Natural history without treatment	Sudden infant death due to cardiac abnormalities is common.
Natural history with treatment	Diagnosis and treatment seem to decrease risk for sudden death.
Treatment	Avoidance of fasting, high carbohydrate, low-fat diet supplemented with MCT oil, IV glucose during illness, cornstarch supplementation, avoidance of long chain fatty acids, possible carnitine supplementation.
Other	May have history of a sibling dying of SIDS.
Physical phenotype	No particular dysmorphisms. Cardiomyopathy in infants.
Inheritance	Autosomal recessive
General population incidence	Rare – exact incidence not known
Ethnic differences	None reported
Population	N/A
Ethnic incidence	N/A
Enzyme location	Mitochondrial matrix, heart, liver
Enzyme Function	Long chain fatty acid beta-oxidation
Missing Enzyme	Very long-chain acyl-CoA dehydrogenase
Metabolite changes	Dicarboxylic aciduria, decreased urinary carnitine at times of illness, plasma free carnitine - normal to low, increased plasma long-chain acylcarnitines mildly increased ammonia, lactate and creatine kinase.
Prenatal testing	Enzyme and protein analysis. If a mutation in a proband is detected, DNA prenatal diagnosis via CVS or amniocytes is possible.
MS/MS Profile	Elevated C16:1, C14:2, C14:1, C18:1
OMIM Link	http://www.ncbi.nlm.nih.gov/omim/201475
Genetests Link	www.genetests.org
Support Group	FOD Family Support Group http://www.fodsupport.org Save Babies through Screening Foundation http://www.savebabies.org Genetic Alliance http://www.geneticalliance.org

Newborn Screening ACT Sheet
[Elevated C14:1 +/- other long-chain Acylcarnitines]
Very Long-Chain Acyl-CoA Dehydrogenase (VLCAD) Deficiency

Differential Diagnosis: Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency.

Condition Description: VLCAD deficiency is a fatty acid oxidation (FAO) disorder. Fatty acid oxidation occurs during prolonged fasting and/or periods of increased energy demands (fever, stress), when energy production relies increasingly on fat metabolism. In a FAO disorder, fatty acids and potentially toxic derivatives accumulate because of a deficiency in one of the mitochondrial FAO enzymes.

YOU SHOULD TAKE THE FOLLOWING ACTIONS:

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy).
- Consult with pediatric metabolic specialist.
- Evaluate the newborn (poor feeding, lethargy, hypotonia, hepatomegaly, arrhythmia, evidence of cardiac decompensation). If signs are present or infant is ill, initiate emergency treatment with IV glucose and oxygen. Transport to hospital for further treatment in consultation with metabolic specialist. If infant is normal initiate timely confirmatory/diagnostic testing, as recommended by specialist.
- Educate family about need for infant to avoid fasting. If the infant becomes even mildly ill (poor feeding, vomiting, or lethargy), immediate treatment with IV glucose is needed.
- Report findings to newborn screening program.

Diagnostic Evaluation: Plasma acylcarnitine profile may show increased C14:1 acylcarnitine (and lesser elevations of other long chain acylcarnitines). Diagnosis is confirmed in consultation with the metabolic specialist by mutation analysis of the VLCAD gene and additional biochemical genetic tests.

Clinical Considerations: VLCAD deficiency may present acutely in the neonate and is associated with high mortality unless treated promptly; milder variants exist. Features of severe VLCAD deficiency in infancy include hepatomegaly, cardiomyopathy and arrhythmias, lethargy, hypoketotic hypoglycemia, and failure to thrive. Treatment is available.

Additional Information:

New England Consortium of Metabolic Programs
Genetics Home Reference

Referral (local, state, regional and national):

Testing
Clinical Services