**Disease Name:** VERY LONG-CHAIN ACYL-CoA DEHYDROGENASE DEFICIENCY (VLCAD DEFICIENCY)

**Classification:** Fatty acid oxidation disorder

**Genetic Information:**
- **Inheritance:** Autosomal recessive
- **Population Incidence:** Unknown
- **Ethnic Incidence:** No known population at increased risk
- **Gene & Location:** ACADVL, VLCAD - 17p11.2-p11.1
- **Common Mutation:** No common mutations seen.

**Disease Information:**
- **OMIM #** 201475
- **Symptom Onset:** Variable, depending on the phenotype, ranging from neonatal to adult onset.

**Symptoms:** Approximately 50% present as infants with nonketotic hypoglycemia, hepatic dysfunction and cardiomyopathy, and this has been generally lethal.

33% present in late infancy or childhood with episodes of nonketotic hypoglycemia and hepatic dysfunction, but no cardiac involvement. There is generally a mildly increased ammonemia, lactate, and creatine kinase.

Approximately 20% present as adolescents or adults with symptoms limited to muscle fatigue, rhabdomyolysis and myoglobinuria triggered by exercise or fasting. There is no hypoglycemia or cardiac involvement.

**Physical Findings:** No particular dysmorphisms. Cardiomyopathy in infants.

**Treatment:** The mainstay of treatment is a high carbohydrate; low fat diet supplemented with MCT oil and strict avoidance of fasting and prolonged exercise. Aggressive support with calories and fluid is needed for intercurrent illnesses. Carnitine use is controversial.

**Natural History without treatment:** Patients with the infantile form of the disease usually die in the first year of life. The late infantile hepatic presentation children will die without treatment. The adult form can progress to renal failure if the myoglobinuria is not addressed.
The infantile form is generally fatal, although there are now reports of survivors and complete resolution of cardiomyopathy with early diagnosis and treatment. The later onset patients can survive if treated appropriately. In general the outcome is believed to be good for patients who are identified presymptomatically.

Defect in palmitoyl-CoA dehydrogenase. Responsible for reducing acyl-CoA’s of chain lengths C14-C20. This is the first and rate-limiting step in the beta-oxidation of fatty acids by the mitochondria for energy metabolism.

C14:1 (tetradecenoyl carnitine)- elevated
C14:1/C12:1 ratio >3

Prenatal diagnosis is possible in families with a previously affected child.

In the mouse model, there have been arrhythmias and death even in older mice. Confirmatory and diagnostic metabolic testing may be normal even in patients with a known VLCAD mutation.

Prepared for the NW Regional Newborn Screening Program by Sara Copeland MD, Judith Tuerck RN MS and Lorinda Paradise at OHSU in Portland, OR.

References:


28. OMIM- Online Mendelian Inheritance in Man; ACYL-CoA DEHYDROGENASE, VERY LONG-CHAIN, DEFICIENCY OF- *201475*


60. Yoon HR, Strauss AW, Yoo HW. “Sudden death in a Korean infant with very long-chain acyl-CoA dehydrogenase deficiency”, J Inherit Metab Dis 2001; 24: 407-408.