

Disease Name:

BETA KETOTHIOLASE DEFICIENCY

(ALPHA-METHYLACETOACETIC ACIDURIA; 2-METHYL-3-HYDROXYBUTYRIC ACIDEMIA; MITOCHONDRIAL ACETOACETYL-CoA THIOLASE DEFICIENCY; MAAT DEFICIENCY; T2 DEFICIENCY; 3-OXOTHIOLASE DEFICIENCY; 3-KETOTHIOLASE DEFICIENCY; 3-KTD DEFICIENCY)

Classification: Organic aciduria and disorder of ketone body metabolism

Genetic Information:

Inheritance: Autosomal recessive

Population Incidence: Unknown

Ethnic Incidence: No known population at increased risk

Gene & Location: ACAT1 gene on 11q22.3-q23.1

Common Mutation: None, in 19 patients identified 24 mutations have been found

OMIM # #203750

Disease Information:

Symptom Onset: Mean age at presentation is 15 months (range 3 days to 48 months). There are documented cases of asymptomatic patients with enzyme deficiency. Frequency of decompensation attacks falls with age and is uncommon after the age of 10.

Symptoms: Symptoms include intermittent episodes of severe metabolic acidosis and ketosis accompanied by vomiting (often hematemesis), diarrhea and coma that may progress to death. There is great clinical heterogeneity between patients. Infancy is the period of highest risk for decompensation. Death or neurologic complications can occur. Neurologic damage includes striatal necrosis of the basal ganglia, dystonia and/or mental retardation. Other symptoms include cardiomyopathy, prolonged QT interval, neutropenia, thrombocytopenia, poor weight gain, renal failure and short stature. If neurologically intact, patients are normal between episodes.

Physical Findings: No particular dysmorphisms.

Treatment: Acute management of the ketoacidosis is supportive with IV glucose and bicarbonate. Bicarbonate therapy is often required long term. While protein restriction is not usually necessary, protein rich diets and ketogenic diets should be avoided. Carnitine supplementation can be used. The family should monitor urinary ketones to be alert for impending metabolic crisis.

Natural History without treatment:	Clinical outcome varies widely with a few patients suffering severe psychomotor retardation or death as a result of their initial attack and others with normal development and no episodes of acidosis. Despite severe recurrent attacks, appropriate supportive care can result in normal development.
Natural History with treatment:	With early diagnosis and treatment apparently normal development occurs.
<u>Metabolic Information:</u>	Missing Enzyme & Location: Mitochondrial acetoacetyl-CoA thiolase enzyme- Normally interconverts 2-methylacetoacetyl-CoA to propionyl-CoA plus acetyl-CoA
	MS/MS profile: C5:1 (tiglyl or 3-methylcrotonyl carnitine)- elevated C5-OH (3-hydroxy-2-methylbutyryl carnitine) – elevated
	Prenatal testing: Enzyme analysis on amniocytes or CVS is possible. If mutation is known, can perform mutation analysis.

Miscellaneous Information:

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

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