Genetic Fact Sheets for Professionals

Organic Acid Disorders

Screening, Technology, and Research in Genetics is a multi-state project to improve information about the financial, ethical, legal, and social issues surrounding expanded newborn screening and genetic testing – http:// www.newbornscreening.info

Disease name	**Maple syrup urine disease**
Alternate name(s)	Branched chain ketoaciduria, Branched chain alpha-keto dehydrogenase deficiency
Acronym	MSUD type 1A, BCKD deficiency
Disease classification	Organic Acid Disorder
Variants	Yes
Variant name	MSUD type 1B, MSUD Type II, Intermittent branched-chain ketoaciduria, Intermediate branched-chain ketoaciduria, Thiamine responsive MSUD
Symptom onset	Neonatal with some variability
Symptoms	Lethargy progressive to coma and possible death, vomiting, difficulty feeding, opisthotonic posturing, hypoglycemia, possible high pitched cry.
Natural history without treatment	Neurologic abnormalities and profound mental retardation.
Natural history with treatment	Normal IQ and development may be expected if treatment is initiated before first crisis, but development is delayed in the severest cases.
Treatment	Dietary restriction of the branched chain amino acids and supplementation with medical formula. Thiamine supplementation in thiamine responsive patients.
Other	“Maple syrup”-like odor to urine (usually present during crisis)
Physical phenotype	None
Inheritance	Autosomal recessive
General population incidence	1:200,000

Ethnic differences	Yes
Population	Mennonites, French-Canadians
Ethnic incidence	1/760 (Mennonites)
Enzyme location	Inner mitochondrial membrane; liver, kidney, leukocytes and fibroblasts.
Enzyme function	Catalyzes the decarboxylation of oxoacids.
Missing enzyme	Branched-chain ketoacid dehydrogenase (BCKAD). This enzyme is a multienzyme complex with 3 components – E1, E2 and E3.
Metabolite changes	Increased leucine, isoleucine and valine in plasma and urine, increased organic acids in urine.
Gene	Four genes are involved in formation of multicomplex enzyme.
Gene location	E1alpha = 19q13.1-13.2 E1beta = 6p21-22 E2 = 1p31 E3=7q31-32
DNA testing available	Yes
DNA testing detail	Common mutation present in Mennonites (Y393N-alpha) and comprehensive DNA mutation analysis.
Prenatal testing	Enzyme testing by CVS or amnio. If mutation is known, DNA testing may be available.
MS/MS profile	Leucine elevated, leucine to alanine ratio elevated.
OMIM link	www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?248600
Genetests link	www.genetests.org/servlet/access?prg=j&db=genestar&site=&fcn=d&id=12600&qry=22186&res=nous&res=nointl&key=hp5d0Ly2h80eI&show_flag=c
Support group	The MSUD Family Support Group www.msud-support.org Children Living with Inherited Metabolic Diseases www.climb.org.uk National Coalition for PKU and Allied Disorders www.pku-allieddisorders.org

Document Info

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