Beta-ketothiolase deficiency

Beta-ketothiolase deficiency is an inherited disorder in which the body cannot effectively process a protein building block (amino acid) called isoleucine. This disorder also impairs the body's ability to process ketones, which are molecules produced during the breakdown of fats.

The signs and symptoms of beta-ketothiolase deficiency typically appear between the ages of 6 months and 24 months. Affected children experience episodes of vomiting, dehydration, difficulty breathing, extreme tiredness (lethargy), and, occasionally, seizures. These episodes, which are called ketoacidotic attacks, sometimes lead to coma. Ketoacidotic attacks are frequently triggered by infections, periods without food (fasting), or increased intake of protein-rich foods.

Frequency

Beta-ketothiolase deficiency appears to be very rare. It is estimated to affect fewer than 1 in 1 million newborns.

Causes

Mutations in the *ACAT1* gene cause beta-ketothiolase deficiency. This gene provides instructions for making an enzyme that is found in the energy-producing centers within cells (mitochondria). This enzyme plays an essential role in breaking down proteins and fats from the diet. Specifically, the ACAT1 enzyme helps process isoleucine, which is a building block of many proteins, and ketones, which are produced during the breakdown of fats.

Mutations in the *ACAT1* gene reduce or eliminate the activity of the ACAT1 enzyme. A shortage of this enzyme prevents the body from processing proteins and fats properly. As a result, related compounds can build up to toxic levels in the blood. These substances cause the blood to become too acidic (ketoacidosis), which can damage the body's tissues and organs, particularly in the nervous system.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- 2-alpha-methyl-3-hydroxybutyricacidemia
- 3-alpha-ketothiolase deficiency
- 3-alpha-ktd deficiency
- 3-alpha-oxothiolase deficiency
- 3-Ketothiolase deficiency
- 3-Methylhydroxybutyric acidemia
- alpha-Methylacetoacetic aciduria
- BKT
- MAT deficiency
- Mitochondrial 2-methylacetoacetyl-CoA thiolase deficiency - potassium stimulated
- Mitochondrial acetoacetyl-CoA thiolase deficiency
- T2 deficiency
- β-ketothiolase deficiency

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Elevated C5-OH Acylcarnitine
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C5-OH.pdf

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Deficiency of acetyl-CoA acetyltransferase
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1536500/

Other Diagnosis and Management Resources

- Baby's First Test
  https://www.babysfirsttest.org/newborn-screening/conditions/beta-ketothiolase-deficiency

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Amino Acid Metabolism Disorders
  https://medlineplus.gov/aminoacidmetabolismdisorders.html
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Beta ketothiolase deficiency
  https://rarediseases.info.nih.gov/diseases/872/beta-ketothiolase-deficiency

Educational Resources

- Orphanet: Beta-ketothiolase deficiency
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=134
- Screening, Technology And Research in Genetics
  http://www.newbornscreening.info/Parents/organicaciddisorders/BKD.html
- Virginia Department of Health
  http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_BKT_English.pdf

Patient Support and Advocacy Resources

- Metabolic Support UK
  https://www.metabolicsupportuk.org/
- Organic Acidemia Association
  https://www.oaanews.org/bkt.html

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28beta-ketothiolase+deficiency%5BTIAB%5D%29+OR+%283-ketothiolase+deficiency%5BTIAB%5D%29+OR+%28alpha-methylacetoacetic+aciduria%5BTIAB%5D%29+OR+%28peroxisomal+thiolase+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- ALPHA-METHYLACETOACETIC ACIDURIA
  http://omim.org/entry/203750

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