HSD10 disease

HSD10 disease is a disorder that affects the nervous system, vision, and heart. It is typically more severe in males than in females. Most affected males have a form of HSD10 disease in which early development seems normal, followed by a stage in which affected individuals rapidly lose skills they have acquired. This developmental regression often occurs between the ages of 1 and 2 and results in severe intellectual disability and loss of communication skills and motor skills such as sitting, standing, and walking. This form of the disorder is referred to as the infantile type. Less commonly, affected males have severe neurological problems from birth and never develop motor skills. This form is called the neonatal type. Males with the infantile or neonatal type frequently have weak muscle tone (hypotonia), recurrent seizures (epilepsy), and vision loss that gradually gets worse. Weakening of the heart muscle (cardiomyopathy) also occurs and is a common cause of death in males with severe HSD10 disease. Many affected males do not survive beyond early childhood.

Females with HSD10 disease may have developmental delay, learning problems, or intellectual disability, but they do not experience developmental regression. Some affected females have additional features of this condition, such as epilepsy, movement problems, and hearing loss. Affected females appear to have a normal life expectancy.

Frequency

HSD10 disease is a very rare disorder. Its prevalence is less than 1 in 1 million people.

Causes

HSD10 disease is caused by mutations in the *HSD17B10* gene, which provides instructions for making the HSD10 protein. This protein is located within mitochondria, the energy-producing centers inside cells, where it is involved in the production (synthesis) of proteins. While most protein synthesis occurs in the fluid surrounding the nucleus (cytoplasm), a few proteins are synthesized in the mitochondria.

During protein synthesis, in either the mitochondria or the cytoplasm, molecules called transfer RNAs (tRNAs) help assemble protein building blocks (amino acids) into chains that form proteins. The HSD10 protein is part of a group of proteins (a complex) that is involved in making functional mitochondrial tRNA molecules, which aid in the synthesis of mitochondrial proteins. Normal mitochondrial protein production is essential for the formation of the groups of proteins that convert the energy from food into a form cells can use.

The *HSD17B10* gene mutations that cause HSD10 disease reduce the amount of HSD10 protein in cells, impair their structure or function, or both, which leads to a deficiency of the functional complex in which it plays a part. This deficiency impairs

the production of mitochondrial tRNAs. Without enough tRNAs, the mitochondrial synthesis of proteins involved in cellular energy production is reduced. A shortage of these proteins results in insufficient energy production in cells of the brain, eyes, and heart, leading to the characteristic features of HSD10 disease.

Inheritance Pattern

This condition is inherited in an X-linked pattern. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes in each cell. In males, who have only one X chromosome, a mutation in the only copy of the gene in each cell is sufficient to cause the condition. In females, who have two copies of the X chromosome, one altered copy of the gene in each cell can lead to less severe features of the condition or may cause no signs or symptoms at all. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- 2-methyl-3-hydroxybutyric aciduria
- 2-methyl-3-hydroxybutyryl-CoA dehydrogenase deficiency
- 2M3HBA
- 3-hydroxy-2-methylbutyryl-CoA dehydrogenase deficiency
- 3H2MBD deficiency
- 17β-hydroxysteroid dehydrogenase type 10 deficiency
- HSD10 deficiency
- hydroxyacyl-CoA dehydrogenase II deficiency
- MHBD 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: HSD10 disease
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3266731/

Other Diagnosis and Management Resources

- Baby's First Test
  https://www.babysfirsttest.org/newborn-screening/conditions/2-methyl-3-hydroxybutyric-acidemia

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Intellectual Disability
  https://medlineplus.gov/ency/article/001523.htm
- Health Topic: Developmental Disabilities
  https://medlineplus.gov/developmentaldisabilities.html
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Mitochondrial Diseases
  https://medlineplus.gov/mitochondrialdiseases.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- HSD10 disease
  https://rarediseases.info.nih.gov/diseases/10716/hsd10-disease

Additional NIH Resources

- National Heart, Lung, and Blood Institute: What is Cardiomyopathy?
  https://www.nhlbi.nih.gov/health-topics/cardiomyopathy

Educational Resources

- Centers for Disease Control and Prevention: Developmental Disabilities
  https://www.cdc.gov/ncbddd/developmentaldisabilities/
- Centers for Disease Control and Prevention: Facts About Intellectual Disability
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/intellectualdisability.pdf
- MalaCards: 2-methyl-3-hydroxybutyric aciduria
  https://www.malacards.org/card/2_methyl_3_hydroxybutyric_aciduria
- Medical Home Portal
  https://www.medicalhomeportal.org/newborn/2m3hba-deficiency
- Merck Manual Consumer Version: Intellectual Disability
  https://www.merckmanuals.com/home/children-s-health-issues/learning-and-developmental-disorders/intellectual-disability

- Orphanet: HSD10 disease
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=391417
- Orphanet: HSD10 disease, infantile type
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=391428
- Orphanet: HSD10 disease, neonatal type
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=391457
- United Mitochondrial Disease Foundation: What Is Mitochondrial Disease?
  https://www.umdf.org/what-is-mitochondrial-disease/

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD)
  https://www.aaidd.org/
- Children's Cardiomyopathy Foundation
  https://dev.childrenscardiomyopathy.org/
- Mito Action
  https://www.mitoaction.org/
- North American Mitochondrial Disease Consortium
  https://www.rarediseasesnetwork.org/cms/NAMDC
- United Mitochondrial Disease Foundation
  https://www.umdf.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%282-methyl-3-hydroxybutyric+aciduria%5BTIAB%5D%29+OR+%282-methyl-3-hydroxybutyryl-coa+dehydrogenase+deficiency%5BTIAB%5D%29+OR+%282m3hba%5BTIAB%5D%29+OR+%283-hydroxy-2-methylbutyryl-coa+dehydrogenase+deficiency%5BTIAB%5D%29+OR+%28mhbd+deficiency%5BTIAB%5D%29+OR+%28HSD10+disease%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- HSD10 MITOCHONDRIAL DISEASE
  http://omim.org/entry/300438

Medical Genetics Database from MedGen

- HSD10 disease, infantile type
  https://www.ncbi.nlm.nih.gov/medgen/798728
- HSD10 disease, neonatal type
  https://www.ncbi.nlm.nih.gov/medgen/799566

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