Congenital bile acid synthesis defect type 1

Description

Congenital bile acid synthesis defect type 1 is a disorder characterized by cholestasis, a condition that impairs the production and release of a digestive fluid called bile from liver cells. Bile is used during digestion to absorb fats and fat-soluble vitamins, such as vitamins A, D, E, and K. People with congenital bile acid synthesis defect type 1 cannot produce (synthesize) bile acids, which are a component of bile that stimulate bile flow and help it absorb fats and fat-soluble vitamins. As a result, an abnormal form of bile is produced.

The signs and symptoms of congenital bile acid synthesis defect type 1 often develop during the first weeks of life, but they can begin anytime from infancy into adulthood. Affected infants often have a failure to gain weight and grow at the expected rate (failure to thrive) and yellowing of the skin and eyes (jaundice) due to impaired bile flow and a buildup of partially formed bile. Excess fat in the feces (steatorrhea) is an additional feature of congenital bile acid synthesis defect type 1. As the condition progresses, affected individuals can develop liver abnormalities including an enlarged liver (hepatomegaly), inflammation, or chronic liver disease (cirrhosis). The spleen may also become enlarged (splenomegaly). The inability to absorb certain fat-soluble vitamins (vitamin D in particular) can result in softening and weakening of the bones (rickets) in some individuals.

If left untreated, congenital bile acid synthesis defect type 1 often leads to cirrhosis and death in childhood.

Frequency

The prevalence of congenital bile acid synthesis defect type 1 is unknown; however, it is the most common of all the congenital defects of bile acid synthesis. Together, these conditions are thought to have a prevalence of 1 to 9 per million people.

Causes

Mutations in the *HSD3B7* gene cause congenital bile acid synthesis defect type 1. The *HSD3B7* gene provides instructions for making an enzyme called 3 beta-hydroxysteroid dehydrogenase type 7 (3β-HSD7). This enzyme is found in liver cells that produce bile acids. Bile acids are produced from cholesterol in a multi-step process. The 3β-HSD7

enzyme is responsible for the second step in that process, which converts 7alpha(α)-hydroxycholesterol to 7α-hydroxy-4-cholesten-3-one.

HSD3B7 gene mutations result in a 3β-HSD7 enzyme with little or no function. Without enough functional 3β-HSD7 enzyme, the conversion of 7α-hydroxycholesterol to 7α-hydroxy-4-cholesten-3-one is impaired. The 7α-hydroxycholesterol instead gets converted into abnormal bile acid compounds that cannot be transported out of the liver into the intestine, where the bile acids are needed to digest fats. As a result, cholesterol and other fats build up in the liver and fat-soluble vitamins are not absorbed, which contribute to the signs and symptoms of congenital bile acid synthesis defect type 1.

Learn more about the gene associated with Congenital bile acid synthesis defect type 1

- HSD3B7

Inheritance

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

- 3beta-HSDH deficiency
- 3beta-hydroxy-delta-5-C27-steroid dehydrogenase deficiency
- 3beta-hydroxy-delta-5-C27-steroid oxidoreductase deficiency
- CBAS1

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Congenital bile acid synthesis defect 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1843116/)

Genetic and Rare Diseases Information Center

- Congenital bile acid synthesis defect type 1 (https://rarediseases.info.nih.gov/diseases/9813/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- BILE ACID SYNTHESIS DEFECT, CONGENITAL, 1; CBAS1 (https://omim.org/entry/607765)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28bile+acid+synthesis+defect%29+AND+%28HSD3B7%29+OR+%283beta-hydroxy-delta-5-C27-steroid+dehydrogenase+deficiency%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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