Congenital bile acid synthesis defect type 2

Description

Congenital bile acid synthesis defect type 2 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 2 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 2 often develop in infancy. Affected infants usually 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 another feature of congenital bile acid synthesis defect type 2. As the condition progresses, affected individuals can develop liver abnormalities including inflammation or chronic liver disease (cirrhosis). Some individuals with congenital bile acid synthesis defect type 2 cannot absorb certain fat-soluble vitamins, which can result in softening and weakening of the bones (rickets) or problems with blood clotting that lead to prolonged bleeding.

If left untreated, congenital bile acid synthesis defect type 2 typically leads to cirrhosis and death in childhood.

Frequency

The prevalence of congenital bile acid synthesis defect type 2 is unknown. Together, all congenital defects of bile acid synthesis are thought to have a prevalence of 1 to 9 per million people.

Causes

Mutations in the *AKR1D1* gene cause congenital bile acid synthesis defect type 2. The *AKR1D1* gene provides instructions for making an enzyme called 3-oxo-5- beta(β)-steroid 4-dehydrogenase. This enzyme is found in certain liver cells that produce bile acids. Bile acids are produced from cholesterol in a multi-step process. The 3-oxo-5-β-steroid 4-dehydrogenase enzyme is responsible for the third step in that process, which

converts 7alpha(α)-hydroxy-4-cholesten-3-one to 7α-hydroxy-5 β-cholesten-3-one.

AKR1D1 gene mutations result in a 3-oxo-5-β-steroid 4-dehydrogenase enzyme with severely reduced function. Without enough functional enzyme, the conversion of 7α-hydroxy-4-cholesten-3-one to 7α-hydroxy-5 β-cholesten-3-one is impaired. The 7α-hydroxy-4-cholesten-3-one 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 absorb fats and fat-soluble vitamins. As a result, cholesterol and abnormal bile acids 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 2.

Learn more about the gene associated with Congenital bile acid synthesis defect type 2

- AKR1D1

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

- CBAS2
- Cholestasis with delta(4)-3-oxosteroid 5-beta-reductase deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Congenital bile acid synthesis defect 2 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1856127/)

Genetic and Rare Diseases Information Center

- Congenital bile acid synthesis defect type 2 (https://rarediseases.info.nih.gov/diseases/10045/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Congenital bile acid synthesis defect type 2%22)

Catalog of Genes and Diseases from OMIM

- BILE ACID SYNTHESIS DEFECT, CONGENITAL, 2; CBAS2 (https://omim.org/entry/235555)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28bile+acid+synthesis+defect%29+AND+%28AKR1D1%29+OR+%28delta4-3-oxosteroid+5beta-reductase+deficiency%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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