MPV17-related hepatocerebral mitochondrial DNA depletion syndrome

Description

MPV17-related hepatocerebral mitochondrial DNA depletion syndrome is an inherited disorder that can cause liver disease and neurological problems. The signs and symptoms of this condition begin in infancy and typically include vomiting, diarrhea, and an inability to grow or gain weight at the expected rate (failure to thrive). Many affected infants have a buildup of a chemical called lactic acid in the body (lactic acidosis) and low blood glucose (hypoglycemia). Within the first weeks of life, infants develop liver disease that quickly progresses to liver failure. The liver is frequently enlarged (hepatomegaly) and liver cells often have a reduced ability to release a digestive fluid called bile (cholestasis). Rarely, affected children develop liver cancer. After the onset of liver disease, many affected infants develop neurological problems, which can include developmental delay, weak muscle tone (hypotonia), and reduced sensation in the limbs (peripheral neuropathy). Individuals with *MPV17*-related hepatocerebral mitochondrial DNA depletion syndrome typically survive only into infancy or early childhood.

MPV17-related hepatocerebral mitochondrial DNA depletion syndrome is most frequently seen in the Navajo population of the southwestern United States. In this population, the condition is known as Navajo neurohepatopathy. People with Navajo neurohepatopathy tend to have a longer life expectancy than those with *MPV17*-related hepatocerebral mitochondrial DNA depletion syndrome. In addition to the signs and symptoms described above, people with Navajo neurohepatopathy may have problems with sensing pain that can lead to painless bone fractures and self-mutilation of the fingers or toes. Individuals with Navajo neurohepatopathy may lack feeling in the clear front covering of the eye (corneal anesthesia), which can lead to open sores and scarring on the cornea, resulting in impaired vision. The cause of these additional features is unknown.

Frequency

MPV17-related hepatocerebral mitochondrial DNA depletion syndrome is thought to be a rare condition. Approximately 30 cases have been described in the scientific literature, including seven families with Navajo neurohepatopathy. Within the Navajo Nation of the southwestern United States, Navajo neurohepatopathy is estimated to occur in 1 in 1, 600 newborns.

Causes

As the condition name suggests, mutations in the *MPV17* gene cause *MPV17*-related hepatocerebral mitochondrial DNA depletion syndrome. The protein produced from the *MPV17* gene is located in the inner membrane of cell structures called mitochondria. Mitochondria are involved in a wide variety of cellular activities, including energy production, chemical signaling, and regulation of cell growth, division, and death. Mitochondria contain their own DNA, known as mitochondrial DNA (mtDNA), which is essential for the normal function of these structures. It is likely that the MPV17 protein is involved in the maintenance of mtDNA. Having an adequate amount of mtDNA is essential for normal energy production within cells.

MPV17 gene mutations that cause *MPV17*-related hepatocerebral mitochondrial DNA depletion syndrome lead to production of a protein with impaired function. One mutation causes all cases of Navajo neurohepatopathy and results in the production of an unstable MPV17 protein that is quickly broken down. A dysfunctional or absent MPV17 protein leads to problems with the maintenance of mtDNA, which can cause a reduction in the amount of mtDNA (known as mitochondrial DNA depletion). Mitochondrial DNA depletion impairs mitochondrial function in many of the body's cells and tissues, particularly the brain, liver, and other tissues that have high energy requirements. Reduced mitochondrial function in the liver and brain lead to the liver failure and neurological dysfunction associated with *MPV17*-related hepatocerebral mitochondrial DNA depletion syndrome. Researchers suggest that the less mtDNA that is available in cells, the more severe the features of Navajo neurohepatopathy.

Learn more about the gene associated with MPV17-related hepatocerebral mitochondrial DNA depletion syndrome

- MPV17

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

- Mitochondrial DNA depletion syndrome 6
- MPV17-associated hepatocerebral MDS
- MTDPS6
- Navajo familial neurogenic arthropathy
- Navajo neurohepatopathy
- Navajo neuropathy

- NNH

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Mitochondrial DNA depletion syndrome 6 (hepatocerebral type) (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1850406/)

Genetic and Rare Diseases Information Center

- Navajo neurohepatopathy (https://rarediseases.info.nih.gov/diseases/3972/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- MITOCHONDRIAL DNA DEPLETION SYNDROME 6 (HEPATOCEREBRAL TYPE); MTDPS6 (https://omim.org/entry/256810)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28navajo+neurohepatopathy%5BTIAB%5D%29+OR+%28navajo+neuropathy%5BTIAB%5D%29+OR+%28MPV17%5BTI%5D%29+AND+%28mitochondrial+DNA%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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