Farber lipogranulomatosis

Farber lipogranulomatosis is a rare inherited condition involving the breakdown and use of fats in the body (lipid metabolism). In affected individuals, lipids accumulate abnormally in cells and tissues throughout the body, particularly around the joints.

Three classic signs occur in Farber lipogranulomatosis: a hoarse voice or a weak cry, small lumps of fat under the skin and in other tissues (lipogranulomas), and swollen and painful joints. Affected individuals may also have difficulty breathing, an enlarged liver and spleen (hepatosplenomegaly), and developmental delay.

Researchers have described seven types of Farber lipogranulomatosis based on their characteristic features.

Type 1 is the most common, or classical, form of this condition and is associated with the classic signs of voice, skin, and joint problems that begin a few months after birth. Developmental delay and lung disease also commonly occur. Infants born with type 1 Farber lipogranulomatosis usually survive only into early childhood.

Types 2 and 3 generally have less severe signs and symptoms than the other types. Affected individuals have the three classic signs and usually do not have developmental delay. Children with these types of Farber lipogranulomatosis typically live into mid- to late childhood.

Types 4 and 5 are associated with severe neurological problems. Type 4 usually causes life-threatening health problems beginning in infancy due to massive lipid deposits in the liver, spleen, lungs, and immune system tissues. Children with this type typically do not survive past their first year of life. Type 5 is characterized by progressive decline in brain and spinal cord (central nervous system) function, which causes paralysis of the arms and legs (quadriplegia), seizures, loss of speech, involuntary muscle jerks (myoclonus), and developmental delay. Children with type 5 Farber lipogranulomatosis survive into early childhood.

Types 6 and 7 are very rare, and affected individuals have other associated disorders in addition to Farber lipogranulomatosis.

Frequency

Farber lipogranulomatosis is a rare disorder. About 80 cases have been reported worldwide.

Causes

Mutations in the \textit{ASAH1} gene cause Farber lipogranulomatosis. The \textit{ASAH1} gene provides instructions for making an enzyme called acid ceramidase. This enzyme is found in cell compartments called lysosomes, which digest and recycle materials. Acid
Ceramidase breaks down fats called ceramides into a fat called sphingosine and a fatty acid. These two breakdown products are recycled to create new ceramides for the body to use. Ceramides have several roles within cells. For example, they are a component of a fatty substance called myelin that insulates and protects nerve cells.

Mutations in the ASAH1 gene lead to severe reduction in acid ceramidase, typically to below 10 percent of normal. As a result, the enzyme cannot break down ceramides properly and they build up in the lysosomes of various cells, including in the lung, liver, colon, muscles used for movement (skeletal muscles), cartilage, and bone. The buildup of ceramides along with the reduction of its fatty breakdown products in cells likely causes the signs and symptoms of Farber lipogranulomatosis. It is unclear whether the level of acid ceramidase activity is related to the severity of the disorder.

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

- AC deficiency
- acid ceramidase deficiency
- acylsphingosine deacylase deficiency
- ceramidase deficiency
- Farber disease
- Farber-Uzman syndrome
- Farber's disease
- Farber's lipogranulomatosis

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Farber disease

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Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Farber+lipogranulomatosis%22+OR+%22acid+ceramidase+deficiency%22+OR+%22acylsphingosine+deacylase+deficiency%22+OR+%22ceramidase+deficiency%22

Other Diagnosis and Management Resources

- GeneReview: ASAH1-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK488189

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Lipid Metabolism Disorders
  https://medlineplus.gov/lipidmetabolismdisorders.html

Genetic and Rare Diseases Information Center

- Farber's disease
  https://rarediseases.info.nih.gov/diseases/6426/farbers-disease

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Farber's Disease Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Farbers-Disease-Information-Page

- National Institute of Neurological Disorders and Stroke: Lipid Storage Diseases Fact Sheet
  https://www.ninds.nih.gov/Disorders/All-Disorders/Lipid-storage-diseases-Information-Page

Educational Resources

- MalaCards: farber lipogranulomatosis
  https://www.malacards.org/card/farber_lipogranulomatosis

- Orphanet: Farber disease
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=333

- Washington University, St. Louis: Neuromuscular Disease Center
  https://neuromuscular.wustl.edu/synmot.html#farber
Patient Support and Advocacy Resources

- Lysosomal Diseases New Zealand
  http://www.ldnz.org.nz/lysosomal-diseases/list-of-lysosomal-diseases/farber-disease/

- Metabolic Support UK
  https://www.metabolicsupportuk.org/

- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/farbers-disease/

Clinical Information from GeneReviews

- ASAH1-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK488189

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28farber+lipogranulomatosis%5BTIAB%5D%29+OR+%28acid+ceramidase+deficiency%5BTIAB%5D%29+OR+%28ceramidase+deficiency%5BTIAB%5D%29+OR+%28farber+disease%5BTIAB%5D%29+OR+%28farber's+disease%5BTIAB%5D%29+OR+%28farber's+lipogranulomatosis%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

- FARBER LIPOGRANULOMATOSIS
  http://omim.org/entry/228000

Sources for This Summary


Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1920510/


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