Farber lipogranulomatosis

Description

Farber lipogranulomatosis is a rare inherited condition involving the breakdown and use of fats in the body (a process known as lipid metabolism). In affected individuals, lipids accumulate abnormally in cells and tissues throughout the body, particularly around the joints. Researchers had previously categorized Farber lipogranulomatosis into subtypes based on characteristic features, but the condition is now thought to be a spectrum of overlapping signs of symptoms.

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. Signs and symptoms typically first develop in infancy.

In addition to the classic signs, Farber lipogranulomatosis often affects multiple body systems. Affected individuals can have developmental delay, behavioral problems, or seizures. In severe cases, people experience progressive decline in brain and spinal cord (central nervous system) function, a buildup of fluid in the brain (hydrocephalus), loss (atrophy) of brain tissue, paralysis of the arms and legs (quadriplegia), loss of speech, or involuntary muscle jerks (myoclonus).

People with Farber lipogranulomatosis often have enlarged liver, spleen, and immune system tissues due to massive lipid deposits. Lipid deposits may also occur in the eyes and lungs, leading to vision problems and breathing difficulty. Affected individuals may develop thinning of the bones (osteoporosis) that worsens over time.

Because of the severity of the signs and symptoms of the condition, individuals with Farber lipogranulomatosis generally do not survive past childhood.

Frequency

Farber lipogranulomatosis is a rare disorder. More than 150 cases have been reported worldwide.

Causes

Variants (also known as mutations) in the *ASAH1* gene cause Farber lipogranulomatosis. The *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. Ceramides are also part of the outer membrane surrounding cells, where they sense stress and other external factors and help the cells react.

Variants 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.

Learn more about the gene associated with Farber lipogranulomatosis

- ASAH1

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have variants. The parents of an individual with an autosomal recessive condition each carry one copy of the altered 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's disease
- Farber's lipogranulomatosis
- Farber-Uzman syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Farber lipogranulomatosis (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268255/)

Genetic and Rare Diseases Information Center

- Farber disease (https://rarediseases.info.nih.gov/diseases/6426/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Farber lipogranulomatosis%22)

Catalog of Genes and Diseases from OMIM

- FARBER LIPOGRANULOMATOSIS; FRBRL (https://omim.org/entry/228000)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?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)

References

- Alves MQ, Le Trionnaire E, Ribeiro I, Carpentier S, Harzer K, Levade T,Ribeiro MG. Molecular basis of acid ceramidase deficiency in a neonatal form ofFarber disease: identification of the first large deletion in ASAH1 gene. MolGenet Metab. 2013 Jul; 109(3):276-81. doi: 10.1016/j.ymgme.2013.04.019. Epub 2013May 4. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23707712)
- Bar J, Linke T, Ferlinz K, Neumann U, Schuchman EH, Sandhoff K. Molecularanalysis of acid ceramidase deficiency in patients with Farber disease. HumMutat. 2001 Mar;17(3):199-209. doi: 10.1002/humu.5. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11241842)
- Devi ARR, Gopikrishna M, Ratheesh R, Savithri G, Swarnalata G, Bashyam M. Farber lipogranulomatosis: clinical and molecular genetic analysis reveals anovel mutation in an Indian family. J Hum Genet. 2006;51(9):811-814. doi:10.1007/s10038-006-0019-z. Epub 2006 Sep 2. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16951918)

- Dyment DA, Bennett SAL, Medin JA, Levade T. ASAH1-Related Disorders.2018 Mar 29. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. GeneReviews(R) [Internet]. Seattle (WA): University ofWashington, Seattle; 1993-2025. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK488189/ Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/29595935)
- Ehlert K, Frosch M, Fehse N, Zander A, Roth J, Vormoor J. Farber disease:clinical presentation, pathogenesis and a new approach to treatment. PediatrRheumatol Online J. 2007 Jun 29;5:15. doi: 10.1186/1546-0096-5-15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17603888) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1920510/)
- Elsea SH, Solyom A, Martin K, Harmatz P, Mitchell J, Lampe C, Grant C, SelimL, Mungan NO, Guelbert N, Magnusson B, Sundberg E, Puri R, Kapoor S, Arslan N, DiRocco M, Zaki M, Ozen S, Mahmoud IG, Ehlert K, Hahn A, Gokcay G, Torcoletti M, Ferreira CR. ASAH1 pathogenic variants associated with acid ceramidasedeficiency: Farber disease and spinal muscular atrophy with progressive myoclonicepilepsy. Hum Mutat. 2020 Sep;41(9):1469-1487. doi: 10.1002/humu.24056. Epub 2020Jun 24. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/32449975)
- Farina F, Cappello F, Todaro M, Bucchieri F, Peri G, Zummo G, Stassi G. Involvement of caspase-3 and GD3 ganglioside in ceramide-induced apoptosis inFarber disease. J Histochem Cytochem. 2000 Jan;48(1):57-62. doi:10.1177/002215540004800106. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10653586)
- Yu FPS, Amintas S, Levade T, Medin JA. Acid ceramidase deficiency: Farberdisease and SMA-PME. Orphanet J Rare Dis. 2018 Jul 20;13(1):121. doi:10.1186/s13023-018-0845-z. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/30029679)

Last updated May 20, 2022