Sjögren-Larsson syndrome

Description

Sjögren-Larsson syndrome is a condition characterized by dry, scaly skin (ichthyosis); neurological problems; and eye problems. These symptoms are apparent by early childhood and usually do not worsen with age.

Affected infants tend to be born prematurely. At birth the skin is red (erythema), but later in infancy the skin becomes dry, rough, and scaly with a brownish or yellowish tone. Mild to severe itchiness (pruritus) is also common. These skin abnormalities are generally dispersed over the whole body, most severely affecting the nape of the neck, the torso, and the extremities. The skin of the face is usually not affected.

People with this condition may also have neurological signs and symptoms. Most affected individuals have leukoencephalopathy, which is a change in a type of brain tissue called white matter. White matter consists of nerve fibers covered by a substance (myelin) that insulates and protects the nerves. The leukoencephalopathy is thought to contribute to many of the neurological signs and symptoms in people with Sjögren-Larsson syndrome. Most affected individuals have intellectual disability that varies from mild to profound and is usually apparent by early childhood. People with Sjögren-Larsson syndrome have speech difficulties (dysarthria) and delayed speech. Usually they are able to produce only short sentences with poorly formed words. Rarely, people with this condition have normal intelligence. In addition, approximately 40 percent of people with Sjögren-Larsson syndrome have seizures.

Children with this condition often experience delayed development of motor skills (such as crawling and walking) due to abnormal muscle stiffness (spasticity) that is typically in their legs and, less commonly, also in their arms. About one-half of people with Sjögren-Larsson syndrome require wheelchair assistance and many others need some form of support to walk.

Affected individuals have tiny crystals in the light-sensitive tissue at the back of the eye (retina) that can be seen during an eye exam. Based on their appearance, these retinal crystals are often called glistening white dots. These white dots are usually apparent by early childhood, and it is unclear if they affect normal vision. People with Sjögren-Larsson syndrome may also have nearsightedness (myopia) or an increased sensitivity to light (photophobia).

Frequency

Sjögren-Larsson syndrome was first observed in Sweden, where the prevalence of this condition is 1 per 250,000 individuals. Outside Sweden, the prevalence of this condition is unknown.

Causes

Mutations in the *ALDH3A2* gene cause Sjögren-Larsson syndrome. The *ALDH3A2* gene provides instructions for making an enzyme called fatty aldehyde dehydrogenase (FALDH). The FALDH enzyme is part of a multistep process called fatty acid oxidation in which fats are broken down and converted into energy. Specifically, the FALDH enzyme breaks down molecules called fatty aldehydes to fatty acids.

ALDH3A2 gene mutations disrupt the normal process of fatty acid oxidation. Most mutations result in the production of a FALDH enzyme that is unable to break down fatty aldehyde molecules. As a result, fats that cannot be broken down build up in cells. Within skin cells, excess fat accumulation can interfere with the formation of membranes that act as protective barriers to control water loss. As a result of the loss of these protective barriers, the skin has difficulty maintaining its water balance, resulting in dry, scaly skin. In the brain, the consequences of excess fat accumulation are unclear, but it is likely that an abundance of fat disrupts the formation of myelin. Myelin is the covering that protects nerves and promotes the efficient transmission of nerve impulses. A lack of myelin can lead to neurological problems such as intellectual disability and walking difficulties. The cause of the eye problems is unclear, but it is also likely related to a disruption in the breakdown of fats.

Learn more about the gene associated with Sjögren-Larsson syndrome

- ALDH3A2

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

- Congenital icthyosis mental retardation spasticity syndrome
- FALDH deficiency
- Fatty aldehyde dehydrogenase deficiency
- Ichthyosis oligophrenia syndrome
- Sjogren-Larsson syndrome
- SLS

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Sjögren-Larsson syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0037231/)

Genetic and Rare Diseases Information Center

- Sjögren-Larsson syndrome (https://rarediseases.info.nih.gov/diseases/7654/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Sjögren-Larsson syndrome%22)

Catalog of Genes and Diseases from OMIM

- SJOGREN-LARSSON SYNDROME; SLS (https://omim.org/entry/270200)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Sjogren-Larsson+Syndrome%5BMAJR%5D%29+AND+%28Sjogren-Larsson+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

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