Christianson syndrome

Description

Christianson syndrome is a disorder that primarily affects the nervous system. This condition becomes apparent in infancy. Its characteristic features include delayed development, intellectual disability, an inability to speak, problems with balance and coordination (ataxia), and difficulty standing or walking. Individuals who do learn to walk lose the ability in childhood. Most affected children also have recurrent seizures (epilepsy), beginning between ages 1 and 2.

Other features seen in many people with Christianson syndrome include a small head size (microcephaly); a long, narrow face with prominent nose, jaw, and ears; an open mouth and uncontrolled drooling; and abnormal eye movements. Affected children often have a happy demeanor with frequent smiling and spontaneous laughter.

Frequency

Christianson syndrome is a rare condition, although the exact prevalence is unknown. The condition was first described in a South African family and has since been found people in other parts of the world.

Causes

Christianson syndrome is caused by mutations in the *SLC9A6* gene, which provides instructions for making a protein called sodium/hydrogen exchanger 6 (Na+/H+ exchanger 6 or NHE6). The NHE6 protein is found in the membrane surrounding endosomes, which are compartments within cells that recycle proteins and other materials. The NHE6 protein helps exchange positively charged atoms (ions) of sodium (Na+) with hydrogen ions (H+) across the endosomal membrane. By controlling the amount of hydrogen ions, the NHE6 protein helps regulate the relative acidity (pH) inside endosomes, which is important for the recycling function of these compartments. The NHE6 protein may have additional functions, such as helping to move proteins to the correct location in the cell (protein trafficking).

Mutations in the *SLC9A6* gene typically lead to an abnormally short NHE6 protein that is nonfunctional or that is broken down quickly in cells, resulting in the absence of functional NHE6 proteins. As a result, the pH in endosomes is not properly maintained. It is unclear how unregulated endosomal pH leads to neurological problems in people

with Christianson syndrome. Some studies have shown that protein trafficking by endosomes is important for learning and memory, but the role of endosomal pH or the NHE6 protein in this process has not been identified.

Learn more about the gene associated with Christianson syndrome

- SLC9A6

Inheritance

This condition is inherited in an X-linked recessive pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In X-linked recessive inheritance, a female with one mutated copy of the gene in each cell is called a carrier. She can pass on the altered gene but usually does not experience signs and symptoms of the disorder. Occasionally, however, females who carry an *SLC9A6* gene mutation have mild learning disabilities. It is unclear if these disabilities are related to the gene mutation or occur by chance.

Other Names for This Condition

- Angelman-like syndrome, X-linked
- Intellectual deficit, X-linked, South African type

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Christianson syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2678194/)

Genetic and Rare Diseases Information Center

- Christianson syndrome (https://rarediseases.info.nih.gov/diseases/10572/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- INTELLECTUAL DEVELOPMENTAL DISORDER, X-LINKED, SYNDROMIC, CHRISTIANSON TYPE; MRXSCH (https://omim.org/entry/300243)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28christianson+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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