Autosomal recessive spastic ataxia of Charlevoix-Saguenay

Description

Autosomal recessive spastic ataxia of Charlevoix-Saguenay, more commonly known as ARSACS, is a condition affecting muscle movement. People with ARSACS typically have abnormal tensing of the muscles (spasticity), problems with balance and coordination (cerebellar ataxia), and reduced sensation and weakness in the arms and legs (peripheral neuropathy).

Additional muscle problems that can occur in ARSACS include muscle wasting (amyotrophy), involuntary eye movements (nystagmus), and difficulty swallowing (dysphagia) and speaking (dysarthria). Other features of ARSACS involve high-arched feet (pes cavus), a spine that curves to the side (scoliosis), yellow streaks of fatty tissue in the light-sensitive tissue at the back of the eye (hypermyelination of the retina), urinary tract problems, intellectual disability, hearing loss, and recurrent seizures (epilepsy).

An unsteady walking style (gait) is the first symptom of ARSACS. Walking problems usually begin between the ages of 12 months and 18 months, as toddlers are learning to walk. These movement problems worsen over time, with increased spasticity and ataxia of the arms and legs. In some cases spasticity goes away, but this apparent improvement is thought to be due to the wasting away (atrophy) of nerves in the arms and legs. Most affected individuals require wheelchair assistance by the time they are in their thirties or forties.

While this condition was named after the area in which it was first seen, the Charlevoix-Saguenay region of Quebec, Canada, ARSACS has been identified in individuals worldwide.

Frequency

The incidence of ARSACS in the Charlevoix-Saguenay region is estimated to be 1 in 1, 500 to 2,000 individuals. Outside of Quebec, the incidence of ARSACS is unknown. About 200 individuals with ARSACS have been described in the scientific literature.

Causes

Mutations in the *SACS* gene cause ARSACS. The *SACS* gene provides instructions for producing a protein called sacsin. Sacsin is primarily found in cells in the brain, skin,

and muscles used for movement (skeletal muscles), but the specific function of the protein is unknown. Research suggests that sacsin plays a role in organizing proteins into bundles called intermediate filaments. Intermediate filaments provide support and strength to cells. In nerve cells (neurons), specialized intermediate filaments called neurofilaments comprise the structural framework that establishes the size and shape of nerve cell extensions called axons, which are essential for transmission of nerve impulses to other neurons and to muscle cells.

Mutations in the *SACS* gene cause the production of an unstable sacsin protein that does not function normally. It is unclear how the abnormal sacsin protein affects the brain and skeletal muscles but it likely impairs normal organization of intermediate filaments in cells, particularly neurofilaments, and disrupts neuron function. This decreased neuronal signaling may result in the signs and symptoms of ARSACS.

Learn more about the gene associated with Autosomal recessive spastic ataxia of Charlevoix-Saguenay

- SACS

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

- ARSACS
- Charlevoix-Saguenay spastic ataxia
- Spastic ataxia of Charlevoix-Saguenay
- Spastic ataxia, Charlevoix-Saguenay type

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Charlevoix-Saguenay spastic ataxia (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1849140/)

Genetic and Rare Diseases Information Center

- Autosomal recessive spastic ataxia of Charlevoix-Saguenay (https://rarediseases.info.nih.gov/diseases/4910/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Autosomal recessive spastic ataxia of Charlevoix-Saguenay%22)

Catalog of Genes and Diseases from OMIM

- SPASTIC ATAXIA, CHARLEVOIX-SAGUENAY TYPE; SACS (https://omim.org/entry/270550)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28ARSACS%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3240+days%22%5Bdp%5D)

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