Andermann syndrome

Description

Andermann syndrome is a disorder that damages the nerves used for muscle movement and sensation (motor and sensory neuropathy). The neuropathy in this condition is due to poor development of nerves, particularly nerves that control movement, which are half their normal size. Absence (agenesis) or malformation of the tissue connecting the left and right halves of the brain (corpus callosum) occurs in most people with this disorder. Because of these features, Andermann syndrome is sometimes referred to as hereditary motor and sensory neuropathy with agenesis of the corpus callosum (HMSN/ACC).

People affected by Andermann syndrome have abnormal or absent reflexes (areflexia) and weak muscle tone (hypotonia). They experience muscle wasting (amyotrophy), severe progressive weakness and loss of sensation in the limbs, and rhythmic shaking (tremors).

People with Andermann syndrome typically begin walking between ages 3 and 4, and worsening neuropathy causes them to lose this ability by their teenage years. As they get older, people with this disorder frequently develop joint deformities called contractures, which restrict the movement of certain joints. Most affected individuals also develop abnormal curvature of the spine (scoliosis), which may require surgery.

Andermann syndrome also results in abnormal function of certain cranial nerves, which emerge directly from the brain and extend to various areas of the head and neck. Cranial nerve problems may result in facial muscle weakness, drooping eyelids (ptosis), and difficulty following movements with the eyes (gaze palsy).

Individuals with Andermann syndrome usually have intellectual disability, which may be mild to severe, and some experience seizures. They may also develop psychiatric symptoms such as depression, anxiety, agitation, paranoia, and hallucinations, which usually appear in adolescence.

Some people with Andermann syndrome have atypical physical features such as widely spaced eyes (ocular hypertelorism); a wide, short skull (brachycephaly); a high arch of the hard palate at the roof of the mouth; a big toe that crosses over the other toes; and partial fusion (syndactyly) of the second and third toes.

Andermann syndrome is associated with a shortened life expectancy related to

respiratory insufficiency, but affected individuals typically live into adulthood.

Frequency

Andermann syndrome is most often seen in the French-Canadian population of the Saguenay-Lac-St.-Jean and Charlevoix regions of northeastern Quebec. In this population, Andermann syndrome occurs in almost 1 in 2,000 newborns. Only a few individuals with this disorder have been identified in other regions of the world.

Causes

Variants (also known as mutations) in the *SLC12A6* gene cause Andermann syndrome. The *SLC12A6* gene provides instructions for making a protein called KCC3, a K-Cl co-transporter. This protein is involved in moving charged atoms (ions) of potassium (K) and chlorine (Cl) across the cell membrane. The positively charged potassium ions and negatively charged chlorine ions are moved together (co-transported), so that the charges inside and outside the cell membrane are unchanged (electroneutral).

Electroneutral co-transport of ions across cell membranes is involved in many functions of the body. While the specific function of KCC3 is unknown, it seems to be critical for the development and maintenance of nerve tissue and for the regulation of axons, which are specialized extensions of neurons that transmit nerve impulses throughout the nervous system. KCC3 may be involved in regulating the amounts of potassium, chlorine, or water in cells and intercellular spaces. KCC3 may also help regulate the activity of other proteins that are sensitive to ion concentrations.

Variants in the *SLC12A6* gene that cause Andermann syndrome disrupt the function of the KCC3 protein. The lack of functional protein normally produced from the *SLC12A6* gene is believed to interfere with the development of the corpus callosum and maintenance of the nerves that transmit signals needed for movement and sensation, resulting in the signs and symptoms of Andermann syndrome.

Learn more about the gene associated with Andermann syndrome

- SLC12A6

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

- ACCPN
- Agenesis of corpus callosum with neuronopathy

- Agenesis of corpus callosum with peripheral neuropathy
- Agenesis of corpus callosum with polyneuropathy
- Charlevoix disease
- Hereditary motor and sensory neuropathy with agenesis of the corpus callosum
- HMSN/ACC

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Agenesis of the corpus callosum with peripheral neuropathy (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0795950/)

Genetic and Rare Diseases Information Center

- Corpus callosum agenesis-neuronopathy syndrome (https://rarediseases.info.nih.gov/diseases/1537/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- AGENESIS OF THE CORPUS CALLOSUM WITH PERIPHERAL NEUROPATHY; ACCPN (https://omim.org/entry/218000)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28andermann+syndrome%5BTIAB%5D%29+OR+%28accpn%5BTIAB%5D%29+OR+%28hmsn/acc%5BTIAB%5D%29+OR+%28charlevoix+disease%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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