Autosomal dominant cerebellar ataxia, deafness, and narcolepsy

Description

Autosomal dominant cerebellar ataxia, deafness, and narcolepsy (ADCADN) is a nervous system disorder with signs and symptoms that usually begin in mid-adulthood and gradually get worse.

People with ADCADN have difficulty coordinating movements (ataxia) and mild to moderate hearing loss caused by abnormalities of the inner ear (sensorineural deafness) . Most have excessive daytime sleepiness (narcolepsy). Narcolepsy is typically accompanied by cataplexy, which is a sudden brief loss of muscle tone in response to strong emotion (such as excitement, surprise, or anger). These episodes of muscle weakness can cause an affected person to slump over or fall, which occasionally leads to injury. These characteristic signs and symptoms of ADCADN typically begin in a person's thirties.

Eventually, people with ADCADN also experience a decline of intellectual function (dementia). The cognitive problems often begin with impairment of executive function, which is the ability to plan and implement actions and develop problem-solving strategies. Other features that can occur as the condition worsens include degeneration of the nerves that carry information from the eyes to the brain (optic atrophy); clouding of the lenses of the eyes (cataracts); numbness, tingling, or pain in the arms and legs (sensory neuropathy); puffiness or swelling (lymphedema) of the limbs; an inability to control the bowels or the flow of urine (incontinence); depression; uncontrollable crying or laughing (pseudobulbar signs); or a distorted view of reality (psychosis). Affected individuals usually survive into their forties or fifties.

Frequency

The prevalence of ADCADN is unknown. At least 24 affected individuals have been described in the medical literature.

Causes

ADCADN is caused by mutations in the *DNMT1* gene, which provides instructions for making an enzyme called DNA methyltransferase 1. This enzyme is involved in DNA methylation, which is the addition of methyl groups, consisting of one carbon atom and three hydrogen atoms, to DNA molecules. In particular, the enzyme helps add methyl

groups to DNA building blocks (nucleotides) called cytosines.

DNA methyltransferase 1 is active in the adult nervous system. Although its specific role in the nervous system is not well understood, the enzyme may help regulate nerve cell (neuron) maturation and specialization (differentiation), the ability of neurons to move (migrate) where needed and connect with each other, and neuron survival.

DNMT1 gene mutations that cause ADCADN affect a region of the DNA methyltransferase 1 enzyme that helps target the methylation process to the correct segments of DNA. As a result of these mutations, methylation is abnormal, which affects the expression of multiple genes. Maintenance of the neurons that make up the nervous system is disrupted, leading to the signs and symptoms of ADCADN.

Learn more about the gene associated with Autosomal dominant cerebellar ataxia, deafness, and narcolepsy

- DNMT1

Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

In most cases, an affected person inherits the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- ADCA-DN syndrome
- ADCADN
- Autosomal dominant cerebellar ataxia-deafness-narcolepsy syndrome
- Cerebellar ataxia, deafness, and narcolepsy, autosomal dominant

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Autosomal dominant cerebellar ataxia, deafness and narcolepsy (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4302668/)

Genetic and Rare Diseases Information Center

- Autosomal dominant cerebellar ataxia-deafness-narcolepsy syndrome (https://rarediseases.info.nih.gov/diseases/12372/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 dominant c erebellar ataxia, deafness, and narcolepsy%22)

Catalog of Genes and Diseases from OMIM

- CEREBELLAR ATAXIA, DEAFNESS, AND NARCOLEPSY, AUTOSOMAL DOMINANT; ADCADN (https://omim.org/entry/604121)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28autosomal+dominant+cerebel lar+ataxia,+deafness,+and+narcolepsy%5BTIAB%5D%29+AND+english%5Bla%5D +AND+human%5Bmh%5D)

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