Hereditary sensory and autonomic neuropathy type IE

Description

Hereditary sensory and autonomic neuropathy type IE (HSAN IE) is a disorder that affects the nervous system. It is characterized by three main features: hearing loss, a decline of intellectual function (dementia), and a worsening loss of sensation in the feet and legs (peripheral neuropathy).

People with HSAN IE develop hearing loss that is caused by abnormalities in the inner ear (sensorineural hearing loss). The hearing loss, which affects both ears, gets worse over time and usually progresses to moderate or severe deafness between the ages of 20 and 35.

Affected individuals experience dementia typically beginning in their thirties. In some people with HSAN IE, changes in personality, such as irritability, apathy, or lack of impulse control, become apparent before problems with thinking skills.

Peripheral neuropathy is caused by impaired function of nerve cells called sensory neurons, which transmit information about sensations such as pain, temperature, and touch. Loss of sensation in the feet and legs, which usually begins in adolescence or early adulthood in people with HSAN IE and worsens over time, can cause difficulty walking. Affected individuals may not be aware of injuries to their feet, which can lead to complications such as open sores and infections. If these complications are severe, amputation of the affected areas may be required.

Some people with HSAN IE also experience recurrent seizures (epilepsy) and sleep problems. The severity of the signs and symptoms of HSAN IE and their age of onset are variable, even among affected members of the same family.

Frequency

HSAN IE is a rare disorder; its prevalence is unknown. Small numbers of affected families have been identified in populations around the world.

Causes

HSAN IE 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.

DNA methylation is important in many cellular functions. These include determining whether the instructions in a particular segment of DNA are carried out or suppressed (gene silencing), regulating reactions involving proteins and fats (lipids), and controlling the processing of chemicals that relay signals in the nervous system (neurotransmitters). DNA methyltransferase 1 is active in the adult nervous system. Although its specific function is not well understood, the enzyme may help regulate neuron maturation and specialization (differentiation), the ability of neurons to migrate where needed and connect with each other, and neuron survival.

DNMT1 gene mutations that cause HSAN IE affect the enzyme's methylation function, resulting in abnormalities in the maintenance of the neurons that make up the nervous system. However, it is not known how the mutations cause the specific signs and symptoms of HSAN IE.

Learn more about the gene associated with Hereditary sensory and autonomic neuropathy type IE

- 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

- DNMT1-complex disorder
- DNMT1-related dementia, deafness, and sensory neuropathy
- Hereditary sensory and autonomic neuropathy type 1 with dementia and hearing loss
- Hereditary sensory neuropathy type IE
- HSAN1E
- HSN IE
- HSNIE

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Hereditary sensory neuropathy-deafness-dementia syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3279885/)

Genetic and Rare Diseases Information Center

- Hereditary sensory neuropathy-deafness-dementia syndrome (https://rarediseases.info.nih.gov/diseases/11927/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Hereditary sensory and autonomic neuropathy type IE%22)

Catalog of Genes and Diseases from OMIM

- NEUROPATHY, HEREDITARY SENSORY, TYPE IE; HSN1E (https://omim.org/entry/614116)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28hereditary+sensory+neuropathy%29+AND+%28deafness%29+AND+%28dementia%29%29+OR+%28%28dnmt1%29+AND+%28neuropathy%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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