Hereditary sensory and autonomic neuropathy type IE

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.

Inheritance Pattern

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

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Hereditary sensory neuropathy type IE
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3279885/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22hereditary+sensory+and+autonomic+neuropathy+type+IE%22+OR+%22Hereditary+Sensory+and+Autonomic+Neuropathies%22

Other Diagnosis and Management Resources

- GeneReview: DNMT1-Related Disorder
  https://www.ncbi.nlm.nih.gov/books/NBK84112
- University of Chicago: Center for Peripheral Neuropathy
  http://peripheralneuropathycenter.uchicago.edu/

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Dementia
  https://medlineplus.gov/ency/article/000739.htm
- Encyclopedia: Sensorineural Deafness
  https://medlineplus.gov/ency/article/003291.htm
- Health Topic: Degenerative Nerve Diseases
  https://medlineplus.gov/degenerativenervediseases.html
- Health Topic: Dementia
  https://medlineplus.gov/dementia.html
- Health Topic: Hearing Disorders and Deafness
  https://medlineplus.gov/hearingdisordersanddeafness.html
- Health Topic: Peripheral Nerve Disorders
  https://medlineplus.gov/peripheralnervedisorders.html

Genetic and Rare Diseases Information Center

- Hereditary sensory and autonomic neuropathy type 1E
  https://rarediseases.info.nih.gov/diseases/11927/hereditary-sensory-and-autonomic-neuropathy-type-1e

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Dementia Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Dementia-Information-Page

Educational Resources

- MalaCards: dnmt1-related dementia, deafness, and sensory neuropathy
  https://www.malacards.org/card/dnmt1_rela
  ted_dementia_deafness_and_sensory_neuropathy
- Orphanet: Hereditary sensory and autonomic neuropathy type 1
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=36386
- Washington University in St. Louis Neuromuscular Disease Center
  https://neuromuscular.wustl.edu/time/hsn.htm#dnmt1

Patient Support and Advocacy Resources

- Family Caregiver Alliance
  https://www.caregiver.org/
- Hearing Health Foundation
  https://hearinghealthfoundation.org/
- National Organization for Rare Disorders
  https://rarediseases.org/rare-diseases/hereditary-sensory-autonomic-neuropathy-type-1e/
- The Foundation for Peripheral Neuropathy
  https://www.foundationforpn.org/

Clinical Information from GeneReviews

- DNMT1-Related Disorder
  https://www.ncbi.nlm.nih.gov/books/NBK84112

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?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

Catalog of Genes and Diseases from OMIM

- NEUROPATHY, HEREDITARY SENSORY, TYPE IE
  http://omim.org/entry/614116

Medical Genetics Database from MedGen

- Hereditary sensory neuropathy type IE
  https://www.ncbi.nlm.nih.gov/medgen/481515

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