Distal hereditary motor neuropathy, type II

Description

Distal hereditary motor neuropathy, type II is a progressive disorder that affects nerve cells (neurons) in the brain and spinal cord. This condition specifically affects motor neurons, which are specialized cells that control muscle movement. Damage to motor neurons results in muscle weakness that worsens over time. Distal hereditary motor neuropathy, type II weakness primarily affects movement in the legs.

The signs and symptoms of distal hereditary motor neuropathy, type II often begin in adolescence to mid-adulthood. The initial symptoms of the disorder are cramps or weakness in the muscles of the big toe and, later, the entire foot. During the next 5 to 10 years, affected individuals experience a gradual loss of muscle tissue (atrophy) in the lower legs, which can lead to problems with walking (gait disturbance) and high arches (pes cavus). Over time, the lower legs may become paralyzed. The thigh muscles may also undergo muscle atrophy, although this generally occurs later and is less severe than the muscle atrophy in the lower legs.

Some individuals with distal hereditary motor neuropathy, type II can also experience weaken the muscles in the hands and forearms. This weakening is less severe than the weakening in the lower limbs and does not usually lead to paralysis. In rare cases, affected individuals experience hearing loss.

People with distal hereditary motor neuropathy, type II can have exaggerated reflexes (hyperreflexia) or other minor disturbances in the nerves used to detect sensations (sensory neuropathy). Sensory neuropathy is uncommon in people with distal hereditary motor neuropathy, type II and is typically a feature of a disorder calledCharcot-Marie-Tooth disease. These two disorders have overlapping features and can also share a genetic

Frequency

The prevalence of all types of distal hereditary motor neuropathy is estimated to be about 2 in 100,000 individuals. Distal hereditary motor neuropathy, type II accounts for 8 to 15 percent of all cases of distal hereditary motor neuropathy.

Causes

Variants (also called mutations) in multiple genes can cause distal hereditary motor neuropathy, type II. Most commonly, variants in the *HSPB1* and *HSPB8* genes cause this condition. These genes provide instructions for making proteins called heat shock proteins. Heat shock protein beta-1 is made from the *HSPB1* gene, and heat shock protein beta-8 is made from the *HSPB8* gene. Heat shock proteins help protect cells that are under stress from factors such as infection, inflammation, exposure to toxins, elevated temperature, injury, and disease. In addition, these proteins appear to be involved in stabilizing the cell's structural framework (the cytoskeleton), folding and stabilizing newly produced proteins, and repairing damaged proteins. Heat shock proteins also seem to play a role in the tensing of muscle fibers (muscle contraction).

Heat shock protein beta-1 and heat shock protein beta-8 are found in cells throughout the body. These proteins help fold newly produced proteins and refold damaged proteins. These proteins are also involved in maintaining the structure of neurons.

The *HSPB1* and *HSPB8* gene variants that cause distal hereditary motor neuropathy, type II typically lead to changes in single protein building blocks (amino acids) in the proteins. These changes can cause the proteins to form clusters (aggregates). These aggregates can build up and impair the function of cells, particularly motor neurons. In addition, neurons that do not have functional versions of these heat shock proteins are vulnerable to stress and cell damage. As a result, these cells are more likely to die off over time, leading to the signs and symptoms of distal hereditary motor neuropathy, type II.

In rare cases, variants in other genes can cause distal hereditary motor neuropathy, type II.

Learn more about the genes associated with Distal hereditary motor neuropathy, type II

- HSPB1
- HSPB8

Additional Information from NCBI Gene:

- FBXO38
- HSPB3

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.

Other Names for This Condition

- Distal hereditary motor neuronopathy, type II
- HMN II
- HMN2
- HMND2

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Neuronopathy, distal hereditary motor, type 2A (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1834692/)
- Genetic Testing Registry: Neuronopathy, distal hereditary motor, type 2B (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2608087/)
- Genetic Testing Registry: Neuronopathy, distal hereditary motor, type 2C (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3150619/)
- Genetic Testing Registry: Neuronopathy, distal hereditary motor, type 2D (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3888271/)

Genetic and Rare Diseases Information Center

- Distal hereditary motor neuropathy type 2 (https://rarediseases.info.nih.gov/diseases/16954/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Distal hereditary motor neuropathy, type II%22)

Catalog of Genes and Diseases from OMIM

- NEURONOPATHY, DISTAL HEREDITARY MOTOR, AUTOSOMAL DOMINANT 2; HMND2 (https://omim.org/entry/158590)
- NEURONOPATHY, DISTAL HEREDITARY MOTOR, AUTOSOMAL DOMINANT 3; HMND3 (https://omim.org/entry/608634)
- NEURONOPATHY, DISTAL HEREDITARY MOTOR, AUTOSOMAL DOMINANT 6; HMND6 (https://omim.org/entry/615575)

- NEURONOPATHY, DISTAL HEREDITARY MOTOR, AUTOSOMAL DOMINANT 4; HMND4 (https://omim.org/entry/613376)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28distal+hereditary+motor+neuropathy%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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