Distal hereditary motor neuropathy, type II

Description

Distal hereditary motor neuropathy, type II is a progressive disorder that affects nerve cells in the spinal cord. It results in muscle weakness and affects movement, primarily in the legs.

Onset of distal hereditary motor neuropathy, type II ranges from the teenage years through mid-adulthood. The initial symptoms of the disorder are cramps or weakness in the muscles of the big toe and later, the entire foot. Over a period of approximately 5 to 10 years, affected individuals experience a gradual loss of muscle tissue (atrophy) in the lower legs. They begin to have trouble walking and running, and eventually may have complete paralysis of the lower legs. The thigh muscles may also be affected, although generally this occurs later and is less severe.

Some individuals with distal hereditary motor neuropathy, type II have weakening of the muscles in the hands and forearms. This weakening is less pronounced than in the lower limbs and does not usually result in paralysis.

Frequency

The prevalence of distal hereditary motor neuropathy, type II is unknown. At least 25 affected families have been identified worldwide.

Causes

Mutations in the *HSPB1* and *HSPB8* genes cause distal hereditary motor neuropathy, type II. These genes provide instructions for making proteins called heat shock protein beta-1 and heat shock protein beta-8. Heat shock proteins help protect cells under adverse conditions such as infection, inflammation, exposure to toxins, elevated temperature, injury, and disease. They block signals that lead to programmed cell death. In addition, they appear to be involved in activities such as cell movement (motility), stabilizing the cell's structural framework (the cytoskeleton), folding and stabilizing newly produced proteins, and repairing damaged proteins. Heat shock proteins also appear 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 and are abundant in nerve cells. In nerve cells, heat shock protein beta-1 helps to organize a network of molecular threads called neurofilaments that maintain the

diameter of specialized extensions called axons. Maintaining proper axon diameter is essential for the efficient transmission of nerve impulses. The function of heat shock protein beta-8 is not well understood, but studies have shown that it interacts with heat shock protein beta-1.

The *HSPB1* and *HSPB8* gene mutations that cause distal hereditary motor neuropathy, type II change single protein building blocks (amino acids) in the protein sequence. If either protein is altered, they may be more likely to cluster together and form clumps (aggregates). Aggregates of heat shock proteins may block the transport of substances that are essential for the proper function of nerve axons. The disruption of other cell functions in which these proteins are involved may also contribute to the signs and symptoms of distal hereditary motor neuropathy, type II.

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

- HSPB1
- HSPB8

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

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/)

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)

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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