Distal hereditary motor neuropathy, type V

Distal hereditary motor neuropathy, type V is a progressive disorder that affects nerve cells in the spinal cord. It results in muscle weakness and affects movement of the hands and feet.

Symptoms of distal hereditary motor neuropathy, type V usually begin during adolescence, but onset varies from infancy to the mid-thirties. Cramps in the hand brought on by exposure to cold temperatures are often the initial symptom.

The characteristic features of distal hereditary motor neuropathy, type V are weakness and wasting (atrophy) of muscles of the hand, specifically on the thumb side of the index finger and in the palm at the base of the thumb. Foot abnormalities, such as a high arch (pes cavus), are also common, and some affected individuals eventually develop problems with walking (gait disturbance). People with this disorder have normal life expectancies.

Frequency

The incidence of distal hereditary motor neuropathy, type V is unknown. Only a small number of cases have been reported.

Causes

Mutations in the *BSCL2* and *GARS* genes cause distal hereditary motor neuropathy, type V.

The *BSCL2* gene provides instructions for making a protein called seipin, whose function is unknown. Mutations in the *BSCL2* gene likely alter the structure of seipin, causing it to fold into an incorrect 3-dimensional shape. Research findings indicate that misfolded seipin proteins accumulate in the endoplasmic reticulum, which is a structure inside the cell that is involved in protein processing and transport. This accumulation likely damages and kills motor neurons (specialized nerve cells in the brain and spinal cord that control muscle movement), leading to muscle weakness in the hands and feet.

The *GARS* gene provides instructions for making an enzyme called glycyl-tRNA synthetase, which is involved in the production (synthesis) of proteins. It is unclear how *GARS* gene mutations lead to distal hereditary motor neuropathy, type V. The mutations probably reduce the activity of glycyl-tRNA synthetase. A reduction in the activity of this enzyme may impair transmission of nerve impulses. As a result, nerve cells slowly lose the ability to communicate with muscles in the hands and feet.

Mutations in other genes may also cause distal hereditary motor neuropathy, type V.

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.

Some people who have the altered gene never develop the condition, a situation known as reduced penetrance.

Other Names for This Condition

- DHMN-V
- distal hereditary motor neuronopathy type 5
- distal hereditary motor neuronopathy, type V
- distal spinal muscular atrophy, type V
- DSMAV
- HMN V
- spinal muscular atrophy, distal type V
- spinal muscular atrophy, distal, with upper limb predominance

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Distal hereditary motor neuronopathy type 5
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1833308/
- Genetic Testing Registry: Distal hereditary motor neuronopathy type 5B
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3553656/

Other Diagnosis and Management Resources

- GeneReview: BSCL2-Related Neurologic Disorders/Seipinopathy
  https://www.ncbi.nlm.nih.gov/books/NBK1307
- GeneReview: GARS-Associated Axonal Neuropathy
  https://www.ncbi.nlm.nih.gov/books/NBK1242
- MedlinePlus Encyclopedia: High-Arched Foot
  https://medlineplus.gov/ency/article/001261.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: High-Arched Foot
  https://medlineplus.gov/ency/article/001261.htm
- Health Topic: Spinal Muscular Atrophy
  https://medlineplus.gov/spinalmuscularatrophy.html

Additional NIH Resources

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

Educational Resources

- MalaCards: distal hereditary motor neuropathy, type v
  https://www.malacards.org/card/distal_hereditary_motor_neuropathy_type_v_2
- Orphanet: Distal hereditary motor neuropathy type 5
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=139536

Patient Support and Advocacy Resources

- Hereditary Neuropathy Foundation
  https://www.hnf-cure.org/

Clinical Information from GeneReviews

- BSCL2-Related Neurologic Disorders/Seipinopathy
  https://www.ncbi.nlm.nih.gov/books/NBK1307
- GARS-Associated Axonal Neuropathy
  https://www.ncbi.nlm.nih.gov/books/NBK1242

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28distal%5BTIAB%5D+AND+spinal+muscular+atrophy%5BTIAB%5D+AND+type+v%5BTIAB%5D%29+OR+%28distal%5BTIAB%5D+AND+spinal+muscular+atrophy%5BTIAB%5D+AND+type+5%5BTIAB%5D%29+OR+%28DHMN-V%5BTIAB%5D%29+OR+%28HMN+V%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- NEURONOPATHY, DISTAL HEREDITARY MOTOR, TYPE VA
  http://omim.org/entry/600794
- NEURONOPATHY, DISTAL HEREDITARY MOTOR, TYPE VB
  http://omim.org/entry/614751

Medical Genetics Database from MedGen

- Distal hereditary motor neuronopathy type 5
  https://www.ncbi.nlm.nih.gov/medgen/318838

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