Spastic paraplegia type 2

Spastic paraplegia type 2 is part of a group of genetic disorders known as hereditary spastic paraplegias. These disorders are characterized by progressive muscle stiffness (spasticity) and the development of paralysis of the lower limbs (paraplegia). Hereditary spastic paraplegias are divided into two types: pure and complex. The pure types involve the lower limbs. The complex types involve the lower limbs and can also affect the upper limbs to a lesser degree; the structure or functioning of the brain; and the nerves connecting the brain and spinal cord to muscles and sensory cells that detect sensations such as touch, pain, heat, and sound (the peripheral nervous system). Spastic paraplegia type 2 can occur in either the pure or complex form.

People with the pure form of spastic paraplegia type 2 experience spasticity in the lower limbs, usually without any additional features. People with the complex form of spastic paraplegia type 2 have lower limb spasticity and can also experience problems with movement and balance (ataxia); involuntary movements of the eyes (nystagmus); mild intellectual disability; involuntary, rhythmic shaking (tremor); and degeneration (atrophy) of the optic nerves, which carry information from the eyes to the brain. Symptoms usually become apparent between the ages of 1 and 5 years; those affected are typically able to walk and have a normal lifespan.

Frequency

The prevalence of all hereditary spastic paraplegias combined is estimated to be 2 to 6 in 100,000 people worldwide. Spastic paraplegia type 2 likely accounts for only a small percentage of all spastic paraplegia cases.

Causes

Mutations in the \( PLP1 \) gene cause spastic paraplegia 2. The \( PLP1 \) gene provides instructions for producing proteolipid protein 1 and a modified version (isoform) of proteolipid protein 1, called DM20. Proteolipid protein 1 and DM20 are primarily located in the brain and spinal cord (central nervous system) and are the main proteins found in myelin, the fatty covering that insulates nerve fibers. A lack of proteolipid protein 1 and DM20 can cause a reduction in the formation of myelin (dysmyelination) which can impair nervous system function, resulting in the signs and symptoms of spastic paraplegia type 2.

Inheritance Pattern

This condition is inherited in an X-linked recessive pattern. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes. In males (who have only one X chromosome), one
altered copy of the gene in each cell is sufficient to cause the condition. Because females have two copies of the X chromosome, one altered copy of the gene in each cell usually leads to less severe symptoms in females than in males, or may cause no symptoms at all. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In X-linked recessive inheritance, a female with one altered copy of the gene in each cell is called a carrier. She can pass on the gene, but generally does not experience signs and symptoms of the disorder. Some females who carry a PLP1 mutation, however, may experience muscle stiffness and a decrease in intellectual function. Females with one PLP1 mutation have an increased risk of experiencing progressive deterioration of cognitive functions (dementia) later in life.

Other Names for This Condition

- Hereditary X-linked Recessive Spastic Paraplegia
- spastic paraplegia 2
- X linked Recessive Hereditary Spastic Paraplegia

Diagnosis & Management

Genetic Testing Information

- What is genetic testing? /primer/testing/genetictesting

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov https://clinicaltrials.gov/ct2/results?cond=%22spastic+paraplegia++type+2%22+OR+%22Spastic+Paraplegia%2C+Hereditary%22+OR+%22Spastic+Paraplegia%22

Other Diagnosis and Management Resources

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Neurologic Diseases
  https://medlineplus.gov/neurologicdiseases.html
- Health Topic: Neuromuscular Disorders
  https://medlineplus.gov/neuromusculardisorders.html
- Health Topic: Paralysis
  https://medlineplus.gov/paralysis.html

Genetic and Rare Diseases Information Center

- Spastic paraplegia 2

Additional NIH Resources

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

Educational Resources

- MalaCards: spastic paraplegia 2, x-linked
  https://www.malacards.org/card/spastic_paraplegia_2_x_linked
- Merck Manual Consumer Version
- Orphanet: Hereditary spastic paraplegia
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=685
- Orphanet: Spastic paraplegia type 2
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=99015

Patient Support and Advocacy Resources

- National Ataxia Foundation
  https://ataxia.org/
- National Organization for Rare Disorders (NORD): Hereditary Spastic Paraplegia
  https://rarediseases.org/rare-diseases/hereditary-spastic-paraplegia/
- RareConnect
  https://www.rareconnect.org/en/community/hereditary-spastic-paraplegia
Clinical Information from GeneReviews

- Hereditary Spastic Paraplegia Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1509
- PLP1 Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1182

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28spastic+paraplegia+2%5BTIAB%5D%29+OR+%28SPG2%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- SPASTIC PARAPLEGIA 2, X-LINKED
  http://omim.org/entry/312920

Medical Genetics Database from MedGen

- Hereditary spastic paraplegia 2

Sources for This Summary

  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735361/