Hereditary neuralgic amyotrophy

Description

Hereditary neuralgic amyotrophy is a disorder characterized by episodes of severe pain and muscle wasting (amyotrophy) in one or both shoulders and arms. Pain is felt along the path of one or more nerves (neuralgia) and often has no obvious physical cause. The network of nerves involved in hereditary neuralgic amyotrophy, called the brachial plexus, controls movement and sensation in the shoulders and arms.

People with hereditary neuralgic amyotrophy usually begin experiencing pain episodes in their twenties, but pain episodes have occurred in children as young as 1 year old. The episodes may be spontaneous, or they may be triggered by stress such as strenuous exercise, childbirth, surgery, exposure to cold, infections, immunization, or emotional disturbance. While the frequency of the episodes tends to decrease with age, affected individuals are often left with residual problems, such as chronic pain and impaired movement, that accumulate over time.

Typically, an attack begins with severe pain on one or both sides of the body; the pain most commonly occurs on the right side of the body. About one-third of individuals with hereditary neuralgic amyotrophy have pain in both shoulders or arms. The pain typically starts out sharp and may become more of an ache over time, and the pain lasts about a month. It may be difficult to control the pain with medication. Over a period of a few hours to a couple of weeks, the muscles in the affected area begin to weaken and waste away (atrophy), and movement becomes difficult. Muscle wasting may cause changes in posture or in the appearance of the shoulder, back, and arm. In particular, weak shoulder muscles tend to make the shoulder blades (scapulae) stick out from the back, a common sign known as scapular winging. Additional features of hereditary neuralgic amyotrophy may include decreased sensation (hypoesthesia) and abnormal sensations in the skin such as numbness or tingling (paresthesias). Areas other than the shoulder and arm may also be involved.

In a few affected families, individuals with hereditary neuralgic amyotrophy also have unusual physical characteristics including short stature, excess skin folds on the neck and arms, an opening in the roof of the mouth (cleft palate), a split in the soft flap of tissue that hangs from the back of the mouth (bifid uvula), and partially webbed or fused fingers or toes (partial syndactyly). They may also have distinctive facial features including eyes set close together (ocular hypotelorism), a narrow opening of the eyelids (short palpebral fissures) with a skin fold that covers the inner corner of the eye (epicanthal fold), a long nasal bridge, a narrow mouth, and differences between one side

of the face and the other (facial asymmetry).

Frequency

Hereditary neuralgic amyotrophy is a rare disorder, but its specific prevalence is unknown.

Causes

Variants (also called mutations) in the *SEPTIN9* gene cause hereditary neuralgic amyotrophy. The *SEPTIN9* gene provides instructions for making a protein called septin-9, which belongs to a group of proteins called septins. Septins are involved in a process called cytokinesis, which is the step in cell division when the fluid inside the cell (cytoplasm) divides to form two separate cells.

The *SEPTIN9* gene seems to be found in cells throughout the body. Approximately 15 slightly different versions (isoforms) of the septin-9 protein may be produced from this gene. Different types of cells make different isoforms. However, the specific distribution of these isoforms in the body's tissues is not well understood. Septin-9 isoforms interact with other septin proteins and help them perform their functions.

Variants in the *SEPTIN9* gene may change the sequence of protein building blocks (amino acids) in certain septin-9 isoforms in ways that interfere with their function. These variants may also change the distribution of septin-9 isoforms and their interactions with other septin proteins in some of the body's tissues. This change in the functioning and location of the various septin-9 proteins seems to particularly affect the brachial plexus, but the reason for this is unknown.

Because many of the triggers for hereditary neuralgic amyotrophy also affect the immune system, researchers believe that an overactive immune response may be involved in this disorder. However, the relationship between *SEPTIN9* gene variants and immune function is unclear. The signs and symptoms of hereditary neuralgic amyotrophy may be the result of chronic inflammation caused by an overactive immune response in the nerves in the brachial plexus.

At least 15 percent of families affected by hereditary neuralgic amyotrophy do not have *SEPTIN9* gene variants. In these cases, the genetic cause of the disorder has not been identified.

Learn more about the gene associated with Hereditary neuralgic amyotrophy

- SEPTIN9

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

- Amyotrophic neuralgia
- Brachial neuralgia
- Brachial neuritis
- Brachial plexus neuritis
- Familial brachial plexus neuritis
- Hereditary brachial plexus neuropathy
- Heredofamilial neuritis with brachial plexus predilection
- HNA
- NAPB
- Neuralgic amyotrophy
- Neuritis with brachial predilection
- Shoulder girdle neuropathy

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Amyotrophic neuralgia (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1834304/)

Genetic and Rare Diseases Information Center

- Amyotrophy, hereditary neuralgic (https://rarediseases.info.nih.gov/diseases/3955/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- AMYOTROPHY, HEREDITARY NEURALGIC; HNA (https://omim.org/entry/162100)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=(Brachial+Plexus+Neuritis%5BMAJR%5D)+AND+(hereditary+neuralgic+amyotrophy%5BTIAB%5D)+OR+(amyotrophic+neuralgia%5BTIAB%5D)+OR+(hereditary+brachial+plexus+neuropathy%5BTIAB

%5D)+OR+(neuralgic+amyotrophy%5BTIAB%5D)+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+5000+days%22%5Bdp%5D)

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Last updated August 20, 2024