



Giant axonal neuropathy

Giant axonal neuropathy is an inherited condition characterized by abnormally large and dysfunctional axons called giant axons. Axons are specialized extensions of nerve cells (neurons) that transmit nerve impulses. Symptoms of the disorder first become apparent in the peripheral nervous system, in which long axons connect the brain and spinal cord (central nervous system) to muscles and to sensory cells that detect sensations such as touch, pain, heat, and sound. However, axons in the central nervous system are affected as well.

The signs and symptoms of giant axonal neuropathy generally begin in early childhood and get worse over time. Most affected individuals first have problems with walking. Later they may lose sensation, strength, and reflexes in their limbs; experience difficulty coordinating movements (ataxia); and require wheelchair assistance. Visual and hearing problems may also occur. Many individuals with this condition have extremely kinky hair as compared to others in their family.

Giant axonal neuropathy can also impact the autonomic nervous system, which controls involuntary body processes. Affected individuals may experience problems with the release of urine (neurogenic bladder), constipation, heat intolerance, and reduction in or loss of the ability to sweat.

As the disorder worsens, paralysis, seizures, and a gradual decline in mental function (dementia) can also occur. Most people with giant axonal neuropathy do not survive past their twenties.

Frequency

Giant axonal neuropathy is a very rare disorder; only about 50 affected families have been described in the medical literature. The condition is thought to be underdiagnosed because its early symptoms resemble those of other, more common disorders affecting the peripheral nervous system, such as Charcot-Marie-Tooth disease.

Genetic Changes

Giant axonal neuropathy is caused by mutations in the *GAN* gene, which provides instructions for making a protein called gigaxonin. Gigaxonin is part of the ubiquitin-proteasome system, which is a process that identifies and gets rid of excess or damaged proteins within cells. In particular, gigaxonin plays a role in the breakdown of neurofilaments, which comprise the structural framework that establishes the size and shape of axons.

The *GAN* gene mutations that have been identified in people with giant axonal neuropathy result in an unstable gigaxonin protein that breaks down more easily than normal, resulting in much less gigaxonin in cells. In neurons without enough functional gigaxonin, neurofilaments that would otherwise have been broken down by the ubiquitin-proteasome system accumulate. The neurofilaments become densely packed in the giant axons of people with giant axonal neuropathy. These giant axons do not transmit signals properly and eventually deteriorate, resulting in the death of neurons. The loss of nerve cells leads to problems with walking and sensation in people with giant axonal neuropathy.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- *GAN*
- giant axonal disease

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Giant axonal neuropathy
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1850386/>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Peripheral Nerve Disorders
<https://medlineplus.gov/peripheralnervedisorders.html>

Genetic and Rare Diseases Information Center

- Giant axonal neuropathy
<https://rarediseases.info.nih.gov/diseases/6500/giant-axonal-neuropathy>

Additional NIH Resources

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

Educational Resources

- Disease InfoSearch: Giant Axonal Neuropathy
<http://www.diseaseinfosearch.org/Giant+Axonal+Neuropathy/3042>
- MalaCards: giant axonal neuropathy
http://www.malacards.org/card/giant_axonal_neuropathy
- Neuromuscular Disease Center, Washington University
<https://neuromuscular.wustl.edu/time/child.html#gan>
- Orphanet: Giant axonal neuropathy
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=643

Patient Support and Advocacy Resources

- Child Neurology Foundation
<http://www.childneurologyfoundation.org/>
- Hannah's Hope Fund
<http://www.hannahshopefund.org/>
- National Organization for Rare Disorders (NORD)
<https://rarediseases.org/rare-diseases/giant-axonal-neuropathy/>
- The Foundation for Peripheral Neuropathy
<https://www.foundationforpn.org/>

GeneReviews

- Giant Axonal Neuropathy
<https://www.ncbi.nlm.nih.gov/books/NBK1136>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22giant+axonal+neuropathy%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28giant+axonal+neuropathy%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2520+days%22%5Bdp%5D>

OMIM

- GIANT AXONAL NEUROPATHY 1, AUTOSOMAL RECESSIVE
<http://omim.org/entry/256850>

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