CONDITION

Childhood giant axonal neuropathy

Learn how childhood giant axonal neuropathy affects the nerves, movement, sensation, swallowing, and breathing, and how genetic testing and supportive care can help.

WHAT IT IS
Rare inherited progressive nerve disorder

BODY SYSTEM
Nervous system

MAIN SYMPTOMS
Muscle weakness, poor balance and coordination, loss of sensation, swallowing or breathing difficulty

WHAT CAUSES IT
Inherited GAN gene changes

HOW IT IS DIAGNOSED
Genetic testing

MAIN TREATMENT
Supportive care

CAN IT BE CURED?
No, no approved treatment stops progression

IS IT AN EMERGENCY?
Sometimes, with severe difficulty breathing

LONG-TERM OUTLOOK
Progressive, with effects generally increasing over time

Overview

Childhood giant axonal neuropathy, often shortened to GAN, is a rare inherited disorder that affects the nervous system. It usually begins in early childhood and progresses over time.

GAN mainly damages axons, the long fibers that carry signals between nerve cells and the rest of the body. In this condition, some axons become enlarged because proteins called intermediate filaments build up inside them. These filaments normally help maintain the shape and structure of cells. The enlarged axons do not transmit signals normally and may eventually break down.

Both the peripheral and central nervous systems can be affected. The peripheral nervous system includes nerves outside the brain and spinal cord. Damage to these nerves can cause

weakness, reduced reflexes, and loss of sensation. Changes in the brain and spinal cord can affect balance, coordination, speech, swallowing, thinking, vision, and breathing.

GAN is a progressive condition, meaning its effects generally increase over time. The course varies among children, including the age when symptoms begin and how quickly they change. There is currently no approved treatment that corrects the underlying genetic cause. Care focuses on maintaining comfort, movement, communication, nutrition, breathing, and participation in daily life.

Symptoms

Symptoms often begin during the first few years of life. Early signs may include frequent falls, an unsteady walk, or difficulty running and climbing stairs. A child may appear clumsy or may lose physical skills that had already developed.

Peripheral nerve damage can cause:

As GAN affects the central nervous system, a child may develop poor balance and coordination, known as ataxia. Speech may become slow, unclear, or difficult to produce. Some children develop muscle stiffness, called spasticity, especially later in the condition.

Other possible features include abnormal eye movements, reduced vision, hearing changes, seizures, and changes in learning or thinking. Not every child develops all of these symptoms.

Swallowing can become difficult. A child may cough during meals, take longer to eat, or have trouble maintaining weight. Food, liquid, or saliva may enter the airway instead of the esophagus, which is the tube leading to the stomach. This is called aspiration.

Weakness may eventually involve the muscles used for breathing. Early signs can include a weak cough, repeated chest infections, morning headaches, restless sleep, or unusual daytime sleepiness.

Many children with GAN have tightly curled, coarse, or "kinky" hair that differs from the hair of other family members. This can be a useful clue, but it is not present in everyone and cannot confirm the diagnosis by itself.

- Muscle weakness, often beginning in the legs
- Low muscle tone, also called hypotonia
- Reduced or absent reflexes
- Numbness or reduced awareness of pain, temperature, or body position
- Foot deformities or difficulty lifting the front of the foot

- Problems with fine motor tasks, such as writing or using utensils

Causes and risk factors

GAN is caused by disease-causing changes in the GAN gene. This gene provides instructions for making gigaxonin, a protein that helps cells remove or organize certain structural proteins. When gigaxonin does not work properly, intermediate filaments build up in nerve cells and other cells.

The condition follows an autosomal recessive inheritance pattern. A child must usually inherit one altered copy of the GAN gene from each biological parent to develop the disorder. Parents who carry one altered copy generally do not have symptoms.

When both parents are carriers, each pregnancy has a chance of resulting in a child who has GAN, a child who is a carrier, or a child who inherited neither familial variant. These chances start again with each pregnancy. A genetics professional can explain the probabilities for a specific family without assuming that all genetic test results have the same meaning.

GAN affects people of different sexes and ethnic backgrounds. Having an affected sibling or known GAN variants in the family is the main recognized risk factor. The condition is genetic; it is not caused by parenting, diet, an infection, or something a child did.

Diagnosis

A diagnosis usually begins with a detailed medical and developmental history. The clinician may ask when the child first sat, walked, ran, or began having falls. They will also ask about changes in speech, swallowing, school performance, sensation, sleep, and breathing.

A neurological examination assesses muscle strength and tone, reflexes, sensation, coordination, walking, eye movements, and speech. Hair texture may be noted, but it is only one part of the evaluation.

Genetic testing is the main way to confirm GAN. Testing may examine the GAN gene alone or use a panel that includes genes associated with neuropathy, ataxia, or childhood neurodegeneration. Broader testing, such as exome or genome sequencing, may be considered when the initial results are unclear.

A genetic result should be interpreted by a clinician or genetics professional. Some gene changes are classified as variants of uncertain significance, which means available evidence does not yet show whether they cause disease. Such a result does not confirm GAN by itself.

Other tests may help define how the nervous system is affected:

A nerve biopsy can show the enlarged axons that gave the condition its name. However, biopsy is invasive and may not be necessary when genetic testing provides a clear diagnosis.

Several other conditions can resemble GAN, including inherited peripheral neuropathies, leukodystrophies, mitochondrial disorders, and other causes of childhood ataxia. The pattern of symptoms, test results, and genetic findings helps the care team distinguish among them.

- Nerve conduction studies and electromyography evaluate how well peripheral nerves and muscles carry electrical signals.
- Brain and spinal magnetic resonance imaging, or MRI, can show changes in white matter, the cerebellum, or other nervous-system structures.
- Swallowing studies can check whether food or liquid is entering the airway.
- Breathing tests and sleep studies can look for weak respiratory muscles or reduced breathing during sleep.
- Vision, hearing, nutrition, and developmental assessments identify needs that may benefit from treatment.

Treatment and management

There is no approved treatment that has been shown to stop or reverse GAN. Treatment is supportive and is tailored to the child's current abilities, symptoms, and family goals. Clinical trials have studied gene-transfer approaches, but these remain investigational. Participation in a trial should be discussed with a specialist who can explain possible risks, requirements, and unknowns.

Care often involves pediatric neurology, rehabilitation medicine, physical and occupational therapy, pulmonology, nutrition, speech-language pathology, orthopedics, and genetics.

Physical therapy can support safe movement, joint flexibility, positioning, and comfort. Gentle stretching may help limit contractures, which are joints that become fixed in a bent or shortened position. Braces, walkers, adapted seating, or wheelchairs may improve safety and independence. Mobility equipment is not a sign that therapy has failed; it can conserve energy and help a child participate in school, family activities, and the community.

Occupational therapy can help with dressing, writing, eating, bathing, and access to electronic devices. Home and school adaptations may reduce falls and make daily tasks easier.

A speech-language pathologist can evaluate speech and swallowing. Communication support may include strategies for clearer speech, picture boards, switches, or speech-generating

devices. Introducing communication tools before speech becomes severely limited gives a child time to learn them.

Swallowing management may involve changes in food texture, eating position, pacing, or equipment. If eating no longer provides enough nutrition or cannot be done safely, the care team may discuss tube feeding. This decision should consider safety, comfort, nutrition, and the child's and family's goals.

Respiratory care may include assisted coughing, airway-clearance techniques, treatment of infections, or noninvasive ventilation delivered through a mask during sleep. The specific approach depends on breathing tests, sleep findings, symptoms, and the child's tolerance.

Seizures, pain, constipation, sleep problems, muscle stiffness, and mood or behavioral concerns can be treated individually. Medicines should be selected and monitored by clinicians familiar with the child's neurological and respiratory status.

Educational planning is also important. A child may need physical access support, extra time, assistive technology, communication services, or changes in workload. Physical disability does not by itself show what a child understands, so learning and communication should be assessed carefully.

Complications

Progressive weakness can reduce mobility and increase the risk of falls, joint contractures, hip problems, and scoliosis, which is a side-to-side curve of the spine. Reduced movement may also increase the risk of pressure injuries unless seating and positioning are reviewed regularly.

Swallowing problems can lead to poor nutrition, dehydration, or aspiration. Repeated aspiration may contribute to lung infections. Respiratory muscle weakness can make it harder to cough, clear mucus, or breathe deeply, especially during sleep or an infection.

Communication can become difficult even when a child continues to understand what others are saying. Early access to reliable communication methods can reduce frustration and support decision-making.

The condition may also affect emotional health and family life. Social work, counseling, respite services, and palliative care can be helpful. Pediatric palliative care is not limited to the final stage of illness. It can be provided alongside other treatment to address symptoms, comfort, practical needs, and family goals.

Follow up

Regular follow-up helps the care team identify changes early and adjust support. The timing depends on the child's symptoms and rate of progression. Visits may review strength, mobility, joint range, spine alignment, swallowing, weight, communication, sleep, breathing, vision, hearing, and seizure control.

Families should contact the care team promptly if a child develops coughing or choking during meals, reduced food or fluid intake, unexplained weight loss, a weaker cough, new morning headaches, unusual daytime sleepiness, or repeated chest infections. These symptoms may need an urgent assessment, but they are not always an emergency.

Seek emergency care for severe difficulty breathing, blue or gray lips or skin, choking with inability to breathe, loss of consciousness, or a seizure that lasts longer than the child's emergency plan allows. Follow the child's established seizure or respiratory action plan when one is available.

Genetic counseling may be useful after diagnosis and again when family members are considering testing or pregnancy. Testing can sometimes clarify whether siblings or other relatives are carriers. Reproductive options may include prenatal testing or testing embryos created through in vitro fertilization when the familial variants are known.

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