CONDITION

Giant axonal disease

Giant axonal disease is a rare inherited condition that progressively damages nerves in the brain, spinal cord, and body.

WHAT IT IS
Rare inherited condition causing progressive nerve damage

BODY SYSTEM
Nervous system

MAIN SYMPTOMS
Walking difficulty, weakness, poor coordination, reduced sensation

WHAT CAUSES IT
Inherited changes in the GAN gene

HOW IT IS DIAGNOSED
Genetic testing confirming two disease-causing GAN variants

MAIN TREATMENT
Supportive multidisciplinary care and symptom management

CAN IT BE CURED?
No - current treatments cannot reverse nerve damage

IS IT AN EMERGENCY?
Sometimes - severe breathing, choking, or seizure symptoms

LONG-TERM OUTLOOK
Progressive disability and often shortened lifespan

Overview

Giant axonal disease is better known as giant axonal neuropathy , or GAN. It is a rare inherited condition that damages nerves throughout the body. It can affect peripheral nerves, which carry signals between the brain, spinal cord, muscles, and skin. It can also affect the brain and spinal cord.

The condition gets its name from unusually enlarged nerve fibres called giant axons. An axon is the long part of a nerve cell that carries electrical signals. In GAN, proteins and other materials build up inside axons, interfering with how the nerves work.

Symptoms usually begin in childhood, often with clumsiness or difficulty walking. Over time, the condition may affect movement, sensation, coordination, speech, swallowing, thinking, and breathing. The rate of change is not the same for everyone. Less commonly, symptoms begin

later and follow a milder course.

GAN is a serious, lifelong condition. There is currently no treatment proven to stop or reverse it. Care focuses on maintaining function, managing symptoms, supporting communication and nutrition, and preventing avoidable complications.

Symptoms

Early signs often involve the legs and walking. A child may fall frequently, have an unsteady walk, or struggle with running and climbing stairs. These changes can resemble other inherited nerve or muscle conditions.

Possible symptoms include:

Some people have tightly curled, pale, or unusually coarse hair that differs from their relatives' hair. This can be a clue, but it is not present in everyone and cannot confirm the condition.

Symptoms generally become more extensive over time. Some people eventually need braces, walking aids, or a wheelchair. Swallowing and breathing muscles may also weaken during the later course.

- Muscle weakness, usually beginning in the legs
- Reduced or absent reflexes
- Numbness or reduced ability to feel touch, pain, or temperature
- Poor balance and coordination
- Foot shape changes, including high arches
- Tight or stiff muscles as the brain and spinal cord become involved
- Curvature of the spine, called scoliosis
- Difficulty speaking or swallowing
- Abnormal eye movements or reduced vision
- Seizures
- Changes in learning, memory, attention, or behaviour

Causes and risk factors

GAN is caused by harmful changes, called pathogenic variants, in the GAN gene. This gene provides instructions for making gigaxonin, a protein that helps nerve cells organise and

remove other proteins. When gigaxonin does not work properly, structural proteins build up inside axons. The enlarged axons then become damaged and may stop carrying signals normally.

The condition follows an autosomal recessive inheritance pattern. This means a person usually has a disease-causing GAN variant in both copies of the gene.

Parents of someone with GAN are usually carriers. A carrier has one altered copy and one working copy of the gene and generally does not have symptoms. When both parents are carriers, each pregnancy has:

These chances apply separately to every pregnancy. GAN affects people of any sex or ethnic background. Having a family history increases the chance, but a family may not know that the altered gene is present until a child is diagnosed.

- A 1 in 4 chance of a child having GAN
- A 1 in 2 chance of a child being an unaffected carrier
- A 1 in 4 chance of a child inheriting neither altered copy

Diagnosis

Diagnosis starts with the pattern of symptoms, a neurological examination, and family history. The examination may assess muscle strength, reflexes, sensation, balance, coordination, eye movements, and thinking skills.

A genetic test that identifies disease-causing variants in both copies of the GAN gene confirms the diagnosis. Testing may use a panel covering many neuropathy or movement-related genes, or a broader test such as exome or genome sequencing.

Other tests help show which parts of the nervous system are affected:

A nerve biopsy may show enlarged axons filled with structural proteins. However, an invasive biopsy is often unnecessary when genetic testing provides a clear answer.

Several other conditions can cause childhood weakness, poor coordination, or loss of sensation. Genetic confirmation helps distinguish GAN from inherited neuropathies, ataxias, leukodystrophies, and some metabolic conditions.

Genetic counselling can help a family understand test results, carrier testing, and what the findings may mean for relatives.

- Nerve conduction studies and electromyography measure nerve and muscle signals
- Brain and spinal magnetic resonance imaging, or MRI, looks for characteristic changes

- Swallowing, breathing, hearing, vision, and developmental assessments check specific functions

Treatment and management

There is no approved treatment that cures GAN or reliably stops its progression. Management is tailored to the functions affected and usually involves a team with experience in inherited neurological conditions.

Physical therapy can help maintain comfortable movement, flexibility, and safe transfers. Stretching, braces, supportive seating, and mobility equipment may reduce strain and help a person remain involved in daily activities. Occupational therapy can suggest practical ways to support dressing, bathing, writing, schoolwork, and computer access.

Speech and language therapy may support clearer communication. Communication devices can help if speech becomes difficult. Swallowing assessments are important when eating takes longer, coughing occurs during meals, or weight becomes difficult to maintain. Changes in food texture or a feeding tube may be considered when they improve nutrition or reduce food entering the airway.

Breathing care may include lung-function monitoring, assisted coughing, airway-clearance equipment, or non-invasive ventilation delivered through a mask. These measures support breathing but do not correct the underlying genetic change.

Medicines may be used for individual problems such as seizures, muscle stiffness, pain, constipation, or excessive saliva. Orthopaedic care may be needed for scoliosis, tight joints, or foot changes.

Experimental gene-replacement treatment has been studied in clinical trials. Research participation is not the same as established treatment, and possible benefits and risks remain under evaluation.

Complications

Progressive weakness and reduced coordination can lead to falls, joint tightness, and loss of independent mobility. Spending long periods in one position can increase the risk of pressure injuries, discomfort, and reduced bone strength.

Swallowing weakness may cause poor nutrition or aspiration, meaning food, liquid, or saliva enters the airway. Aspiration can contribute to chest infections. Breathing-muscle weakness can make it harder to cough, clear mucus, or maintain normal breathing during sleep and later

while awake.

Other possible complications include scoliosis, seizures, loss of vision, communication difficulties, and increasing support needs. Not everyone experiences every complication, and the timing differs among individuals.

Regular planned assessments can identify changes before they cause a crisis. These may include reviews of mobility, seating, nutrition, swallowing, breathing, communication, vision, and seizure control.

Prevention

GAN cannot currently be prevented in someone who has inherited two disease-causing GAN variants. It is not caused by diet, activity, parenting, infection, or something that happened during pregnancy.

Once the genetic variants in a family are known, carrier testing may be available to adult relatives. People planning a pregnancy may choose to discuss prenatal testing, testing of embryos during in vitro fertilisation, donor eggs or sperm, adoption, or pregnancy without testing. These are personal choices rather than required steps.

Genetic counselling provides information about these options without deciding what is right for a family.

Living with it and what to expect

GAN usually progresses over years. In the more common childhood-onset form, walking and coordination problems become more noticeable during childhood. Many affected people later lose independent walking and require a wheelchair, although the timing cannot be predicted from the diagnosis alone.

Weakness, stiffness, communication changes, swallowing difficulty, and breathing problems may increase through adolescence or adulthood. Learning and thinking abilities can also change. Some people have later-onset or milder forms and retain abilities for longer.

Life expectancy is often shortened, especially when breathing or swallowing complications become severe. Published descriptions mainly involve small numbers of people, so they cannot predict one person's course with certainty.

People with GAN can continue to take part in family life, education, recreation, and relationships, although the way they participate may change. Accessible housing, mobility

equipment, communication technology, school support, and personal assistance can help preserve choice and involvement.

Routine follow-up is different from emergency care. Planned visits should monitor gradual changes such as increasing falls, weight loss, slower eating, daytime tiredness, new stiffness, or declining mobility. Families may also benefit from social work, psychological support, respite services, and age-appropriate planning for future care.

When to get medical help

Arrange a routine review if there are new or gradually worsening problems with walking, falls, pain, stiffness, vision, communication, eating, sleep, or daily activities. Coughing during meals, unexplained weight loss, morning headaches, restless sleep, or increasing daytime sleepiness should also be assessed because they may point to swallowing or breathing changes.

Seek urgent medical care for:

Call emergency services for severe trouble breathing, blue or grey lips, loss of consciousness, a prolonged seizure, or choking that blocks breathing. Follow any existing seizure, respiratory, or choking emergency plan while help is arriving.

- Repeated choking or sudden inability to swallow safely
- A new seizure, or a seizure lasting longer than the person's emergency plan allows
- Signs of dehydration or inability to keep down fluids
- Fever with worsening cough, chest discomfort, or unusual breathing difficulty

Common questions

Is giant axonal disease the same as giant axonal neuropathy?

Yes. Giant axonal neuropathy is the standard medical name. "Neuropathy" means damage to nerves. Because GAN can also affect the brain and spinal cord, some specialists use the broader term GAN-related neurodegeneration.

Is GAN contagious?

No. GAN is inherited through gene variants and cannot spread between people through contact, coughing, food, blood, or bodily fluids.

Does curly hair mean someone has GAN?

No. Tightly curled or coarse hair can occur with GAN, but many people with curly hair do not

have the condition, and some people with GAN do not have this hair feature. Diagnosis requires clinical assessment and genetic testing.

Can gene therapy cure GAN?

No gene therapy has yet been proven to cure GAN. Gene-replacement treatment has been studied in an early clinical trial, but its safety and long-term effects are still being evaluated. Experimental treatment should not be assumed to stop existing nerve damage.

Will brothers or sisters have it too?

If both biological parents are carriers, each full sibling has a 1 in 4 chance of having GAN. A sibling's result cannot be predicted from another child's result. Genetic testing can clarify whether a sibling is affected, a carrier, or has not inherited the family variants.

Is GAN always fatal in childhood?

No. The course is not identical for everyone, and some people live into adulthood, particularly with milder forms. However, the usual childhood-onset form is progressive and can shorten life because of neurological, swallowing, or breathing complications.

Sources

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