Spastic paraplegia type 7

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Spastic paraplegia type 7 (SPG7) 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 7 can occur in either the pure or complex form [Spastic paraplegia type 7, NIH Genetics Home Reference, 2018]. Mutations in SPG7, a gene causing recessive hereditary spastic paraplegia, has emerged as a relatively common cause of recessive cerebellar ataxia [Ataxia UK Medical Guidelines, 2016].

What are the symptoms?

SPG7 is characterized by progressive muscle stiffness (spasticity) and the development of paralysis of the lower limbs (paraplegia). Like all hereditary spastic paraplegias, spastic paraplegia type 7 involves spasticity of the leg muscles and increased muscle weakness. People with this form of spastic paraplegia can also experience exaggerated reflexes (hyperreflexia) in the arms; speech difficulties (dysarthria); difficulty swallowing (dysphagia); involuntary movements of the eyes (nystagmus); mild hearing loss; abnormal curvature of the spine (scoliosis); high-arched feet (pes cavus); numbness, tingling, or pain in the arms and legs (sensory neuropathy); disturbance in the nerves used for muscle movement (motor neuropathy); and muscle wasting (amyotrophy) [Spastic paraplegia type 7, NIH Genetics Home Reference, 2018].

What causes SPG7?

Mutations in the *SPG7* gene cause spastic paraplegia type 7. The *SPG7* gene provides instructions for producing a protein called paraplegin. Located within the inner membrane of the energy-producing centers of cells (mitochondria), paraplegin is one of the proteins that form a complex called the m-AAA protease. The m-AAA protease is responsible for assembling ribosomes (cellular structures that process the cell's genetic instructions to create proteins) and removing nonfunctional proteins in the mitochondria. When there is a mutation in paraplegin, the m-AAA protease cannot function correctly. Nonfunctional m-AAA proteases cause a buildup of unusable proteins in the mitochondria of nerve cells, which can result in swelling of the cell, reduced cell signaling, and impaired cell movement, leading to the major signs and symptoms of spastic paraplegia type 7 [Spastic paraplegia type 7, NIH Genetics Home Reference, 2018].

How is SPG7 inherited?

SPG7 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 [Spastic paraplegia type 7, NIH Genetics Home Reference, 2018]. Each sibling of an affected individual has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier. Carrier testing for at-risk relatives, prenatal diagnosis for pregnancies at increased risk and preimplantation genetic diagnosis are possible if both pathogenic alleles have been identified in the family [Hereditary Spastic Paraplegia Overview, GeneReviews® [Internet], 2000].

When do symptoms start?

Onset is mostly in adulthood, although symptoms may start as early as age 11 years and as late as age 72 years. Severe disability of gait due to leg spasticity may develop as soon as eight years after onset of symptoms, and some individuals are confined to a wheelchair [Spastic Paraplegia 7, GeneReviews® [Internet], 2006].

How is SPG7 diagnosed?

Hereditary spastic paraplegias are diagnosed following a thorough clinical examination and the identification of typical symptoms. Other conditions that cause mobility problems and muscle stiffness and weakness, such as multiple sclerosis and cerebral palsy, need to be ruled out first. A number of specialised tests may be used during diagnosis, including (MRI scans of the brain and spine, cerebrospinal fluid analysis, nerve conduction tests and an EMG. In some cases, genetic testing may also be needed [Hereditary spastic paraplegia, NHS Health A-Z, 2016].

How common is SPG7?

The prevalence of all hereditary spastic paraplegias combined is estimated to be 2 to 6 in 100,000 people worldwide. Spastic paraplegia type 7 likely accounts for only a small percentage of all spastic paraplegia cases [Spastic paraplegia type 7, NIH Genetics Home Reference, 2018].

Management of SPG7

No specific drug treatments or cures for SPG7 exist. Drugs that may reduce spasticity and muscle tightness include baclofen, tizanidine, dantrolene, and diazepam. Management of spasticity by intrathecal baclofen or intramuscular botulinum toxin injections may be an option in selected individuals. Physical therapy and assistive walking devices often reduce contractures, provide support, and promote stability. Occupational therapy and speech therapy help with activities of daily living. Annual neurologic evaluation to identify potential complications of spasticity is also advised [Spastic Paraplegia 7, GeneReviews® [Internet], 2006].

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