Infantile-onset ascending hereditary spastic paralysis

Infantile-onset ascending hereditary spastic paralysis is one of a group of genetic disorders known as hereditary spastic paraplegias. These disorders are characterized by progressive muscle stiffness (spasticity) and eventual paralysis of the lower limbs (paraplegia). The spasticity and paraplegia result from degeneration (atrophy) of motor neurons, which are specialized nerve cells in the brain and spinal cord that control muscle movement. Hereditary spastic paraplegias are divided into two types: pure and complicated. The pure types involve only the lower limbs, while the complicated types involve additional areas of the nervous system, affecting the upper limbs and other areas of the body. Infantile-onset ascending hereditary spastic paralysis starts as a pure hereditary spastic paraplegia, with spasticity and weakness in the legs only, but as the disorder progresses, the muscles in the arms, neck, and head become involved and features of the disorder are more characteristic of the complicated type.

Affected infants are typically normal at birth, then within the first 2 years of life, the initial symptoms of infantile-onset ascending hereditary spastic paralysis appear. Early symptoms include exaggerated reflexes (hyperreflexia) and recurrent muscle spasms in the legs. As the condition progresses, affected children develop abnormal tightness and stiffness in the leg muscles and weakness in the legs and arms. Over time, muscle weakness and stiffness travels up (ascends) the body from the legs to the head and neck. Muscles in the head and neck usually weaken during adolescence; symptoms include slow eye movements and difficulty with speech and swallowing. Affected individuals may lose the ability to speak (anarthria). The leg and arm muscle weakness can become so severe as to lead to paralysis; as a result affected individuals require wheelchair assistance by late childhood or early adolescence. Intelligence is not affected in this condition.

A condition called juvenile primary lateral sclerosis shares many of the features of infantile-onset ascending hereditary spastic paralysis. Both conditions have the same genetic cause and significantly impair movement beginning in childhood; however, the pattern of nerve degeneration is different. Because of their similarities, these conditions are sometimes considered the same disorder.

Frequency

Infantile-onset ascending hereditary spastic paralysis is a rare disorder, with at least 30 cases reported in the scientific literature.
Genetic Changes

Infantile-onset ascending hereditary spastic paralysis is caused by mutations in the 
*ALS2* gene. This gene provides instructions for making the alsin protein. Alsin is
produced in a wide range of tissues, with highest amounts in the brain, particularly
in motor neurons. Alsin turns on (activates) multiple proteins called GTPases that
convert a molecule called GTP into another molecule called GDP. GTPases play
important roles in several cell processes. The GTPases that are activated by alsin are
involved in the proper placement of the various proteins and fats that make up the cell
membrane, the transport of molecules from the cell membrane to the interior of the
cell (endocytosis), and the development of specialized structures called axons and
dendrites that project from neurons and are essential for the transmission of nerve
impulses.

Mutations in the *ALS2* gene alter the instructions for making alsin, often resulting in
the production of an abnormally short alsin protein that is unstable and rapidly broken
down. It is unclear exactly how *ALS2* gene mutations cause infantile-onset ascending
hereditary spastic paralysis. Research suggests that a lack of alsin and the subsequent
loss of GTPase functions, such as endocytosis and the development of axons and
dendrites, contribute to the progressive atrophy of motor neurons that is characteristic
of this condition.

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

- IAHSP
- infantile-onset ascending hereditary spastic paraplegia
- infantile onset ascending spastic paralysis

Diagnosis & Management

These resources address the diagnosis or management of infantile-onset ascending
hereditary spastic paralysis:

- GeneReview: ALS2-Related Disorders
  http://www.ncbi.nlm.nih.gov/books/NBK1243
- Genetic Testing Registry: Infantile-onset ascending hereditary spastic paralysis
These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

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

Additional Information & Resources

MedlinePlus

- Health Topic: Degenerative Nerve Diseases
  https://medlineplus.gov/degenerativenervediseases.html
- Health Topic: Neuromuscular Disorders
  https://medlineplus.gov/neuromusculardisorders.html

Genetic and Rare Diseases Information Center

- Infantile-onset ascending hereditary spastic paralysis
  http://rarediseases.info.nih.gov/gard/4914/infantile-onset-ascending-hereditary-spastic-paralysis/resources/1

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Hereditary Spastic Paraplegia Information Page
- National Institute of Neurological Disorders and Stroke: Motor Neuron Diseases Information Page
Educational Resources

- Disease InfoSearch: Infantile-onset ascending hereditary spastic paralysis
  http://www.diseaseinfosearch.org/Infantile-onset+ascending+hereditary+spastic+paralysis/3819
- MalaCards: infantile-onset ascending hereditary spastic paralysis
  http://www.malacards.org/card/infantile_onset_ascending_hereditary_spastic_paralysis
- National Health Service (NHS): Hereditary Spastic Paraplegia (UK)
- Orphanet: Infantile-onset ascending hereditary spastic paralysis
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=293168

Patient Support and Advocacy Resources

- Motor Neurone Disease Association (UK)
  http://www.mndassociation.org/
- National Organization for Rare Disorders (NORD): Hereditary Spastic Paraplegia
  http://rarediseases.org/rare-diseases/hereditary-spastic-paraplegia/
- RareConnect: Hereditary Spastic Paraplegia
  https://www.rareconnect.org/en/community/hereditary-spastic-paraplegia
- Spastic Paraplegia Foundation
  http://sp-foundation.org/

GeneReviews

- ALS2-Related Disorders
  http://www.ncbi.nlm.nih.gov/books/NBK1243

Genetic Testing Registry

- Infantile-onset ascending hereditary spastic paralysis

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22infantile-onset+ascending+hereditary+spastic+paralysis%22
Scientific articles on PubMed

- PubMed
  http://www.ncbi.nlm.nih.gov/pubmed?term=%28%28infantile-onset+ascending+hereditary+spastic+paralysis%29+OR+%28infantile-onset+ascending+hereditary+spastic+paraplegia%29+AND+english%5Blia%5D+AND+human%5Bmh%5D

OMIM

- SPASTIC PARALYSIS, INFANTILE-ONSET ASCENDING
  http://omim.org/entry/607225

Sources for This Summary


- GeneReview: ALS2-Related Disorders
  http://www.ncbi.nlm.nih.gov/books/NBK1243


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