

Spinal muscular atrophy with progressive myoclonic epilepsy

Description

Spinal muscular atrophy with progressive myoclonic epilepsy (SMA-PME) is a neurological condition that begins in childhood. SMA-PME causes muscle weakness and wasting (atrophy) and a combination of seizures and uncontrollable muscle jerks (myoclonic epilepsy).

In individuals with SMA-PME, spinal muscular atrophy results from a loss of specialized nerve cells, called motor neurons, in the spinal cord and the part of the brain that is connected to the spinal cord (the brainstem). After a few years of normal development, affected children begin experiencing muscle weakness and atrophy in the lower limbs, causing difficulty walking and frequent falls. The muscles in the upper limbs are later affected, and soon the muscle weakness and atrophy spreads throughout the body. Once weakness reaches the muscles used for breathing and swallowing, affected individuals develop life-threatening breathing problems and increased susceptibility to pneumonia.

A few years after the muscle weakness begins, affected individuals start to experience recurrent seizures (epilepsy). Most people with SMA-PME have a variety of seizure types. In addition to myoclonic epilepsy, they may have generalized tonic-clonic seizures (also known as grand mal seizures), which cause muscle rigidity, convulsions, and loss of consciousness. Affected individuals can also have absence seizures, which cause loss of consciousness for a short period that may or may not be accompanied by muscle jerks. In SMA-PME, seizures often increase in frequency over time and are usually not well-controlled with medication. Individuals with SMA-PME may also have episodes of rhythmic shaking (tremors), usually in the hands; these tremors are not thought to be related to epilepsy. Some people with SMA-PME develop hearing loss caused by nerve damage in the inner ear (sensorineural hearing loss).

Individuals with SMA-PME have a shortened lifespan; they generally live into late childhood or early adulthood. Near the end of their lives, affected individuals often have limited mobility, difficulty swallowing, and decline in cognitive functioning. The cause of death is often respiratory failure or pneumonia.

Frequency

SMA-PME is a rare disorder; approximately 50 affected individuals have been described in the scientific literature.

Causes

SMA-PME is caused by variants (also called mutations) in the *ASAH1* gene. This gene provides instructions for making an enzyme called acid ceramidase. This enzyme is found in lysosomes, which are cell compartments that digest and recycle materials. Within lysosomes, acid ceramidase breaks down fats called ceramides into a fat called sphingosine and a fatty acid. These two breakdown products are recycled to create new ceramides for the body to use. Ceramides have several roles within cells. For example, they are a component of a fatty substance called myelin that insulates and protects nerve cells.

ASAH1 gene variants that cause SMA-PME result in a reduction of acid ceramidase activity to a level less than one-third of normal. Inefficient breakdown of ceramides and impaired production of its breakdown products likely play a role in the nerve cell damage that leads to the features of SMA-PME, but the exact mechanism is unknown.

[Learn more about the gene associated with Spinal muscular atrophy with progressive myoclonic epilepsy](#)

- *ASAH1*

Inheritance

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

Other Names for This Condition

- Hereditary myoclonus with progressive distal muscular atrophy
- Jankovic-Rivera syndrome
- SMA-PME
- SMAPME

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Spinal muscular atrophy-progressive myoclonic epilepsy syndrome (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1834569/>)

Genetic and Rare Diseases Information Center

- Spinal muscular atrophy-progressive myoclonic epilepsy syndrome (<https://raredise>)

ases.info.nih.gov/diseases/3875/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

Catalog of Genes and Diseases from OMIM

- SPINAL MUSCULAR ATROPHY WITH PROGRESSIVE MYOCLONIC EPILEPSY; SMAPME (<https://omim.org/entry/159950>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28hereditary+myoclonus%5BTIAB%5D%29+AND+%28progressive+distal+muscular+atrophy%5BTIAB%5D%29+OR+%28sma-pme%5BTIAB%5D%29+OR+%28spinal+muscular+atrophy%5BTIAB%5D%29+AND+%28progressive+myoclonic+epilepsy%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>)

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