Intranuclear rod myopathy

Description

Intranuclear rod myopathy is a disorder that primarily affects skeletal muscles, which are muscles that the body uses for movement. People with intranuclear rod myopathy have severe muscle weakness (myopathy) and poor muscle tone (hypotonia) throughout the body. Signs and symptoms of this condition are apparent in infancy and include feeding and swallowing difficulties, a weak cry, and difficulty with controlling head movements. Affected babies are sometimes described as "floppy" and may be unable to move on their own.

The severe muscle weakness that occurs in intranuclear rod myopathy also affects the muscles used for breathing. Individuals with this disorder may take shallow breaths (hypoventilate), especially during sleep, resulting in a shortage of oxygen and a buildup of carbon dioxide in the blood. Frequent respiratory infections and life-threatening breathing difficulties can occur. Because of the respiratory problems, most affected individuals do not survive past infancy. Those who do survive have delayed development of motor skills such as sitting, crawling, standing, and walking.

The name intranuclear rod myopathy comes from characteristic abnormal rod-shaped structures that can be seen in the nucleus of muscle cells when muscle tissue is viewed under a microscope.

Frequency

Intranuclear rod myopathy is a rare disorder that has been identified in only a small number of individuals. Its exact prevalence is unknown.

Causes

Intranuclear rod myopathy is caused by a mutation in the *ACTA1* gene. This gene provides instructions for making a protein called skeletal alpha (α)-actin, which is part of the actin protein family. Actin proteins are important for cell movement and the tensing of muscle fibers (muscle contraction). Thin filaments made up of actin molecules and thick filaments made up of another protein called myosin are the primary components of muscle fibers and are important for muscle contraction. Attachment (binding) and release of the overlapping thick and thin filaments allows them to move relative to each other so that the muscles can contract.

ACTA1 gene mutations that cause intranuclear rod myopathy result in the accumulation of rods of skeletal α-actin in the nucleus of muscle cells. Normally, most actin is found in the fluid surrounding the nucleus (the cytoplasm), with small amounts in the nucleus itself. Researchers suggest that the *ACTA1* gene mutations that cause intranuclear rod myopathy may interfere with the normal transport of actin between the nucleus and the cytoplasm, resulting in the accumulation of actin in the nucleus and the formation of intranuclear rods. Abnormal accumulation of actin in the nucleus of muscle cells and a corresponding reduction of available actin in muscle fibers may impair muscle contraction and lead to the muscle weakness seen in intranuclear rod myopathy.

In some people with intranuclear rod myopathy, no *ACTA1* gene mutations have been identified. The cause of the disorder in these individuals is unknown.

Learn more about the gene associated with Intranuclear rod myopathy

- ACTA1

Inheritance

Intranuclear rod myopathy is an autosomal dominant condition, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Most cases are not inherited; they result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- Intranuclear nemaline rod myopathy
- Nemaline myopathy with exclusively intranuclear rods

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Actin accumulation myopathy (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3711389/)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- CONGENITAL MYOPATHY 2A, TYPICAL, AUTOSOMAL DOMINANT; CMYP2A (https://omim.org/entry/161800)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28intranuclear+rod+myopathy%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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Last updated April 1, 2012