Myofibrillar myopathy

Description

Myofibrillar myopathy refers to a group of disorders that are characterized by muscle weakness (myopathy) that worsens over time. Myofibrillar myopathy primarily affects the skeletal muscles, which are the muscles that the body uses for movement. In some cases, the heart (cardiac) muscle is also affected.

The signs and symptoms of myofibrillar myopathy vary widely among affected individuals. People with this disorder typically begin to develop myopathy in mid-adulthood. However, the features of this condition can appear anytime between infancy and late adulthood. Myopathy most often begins in the hands, forearms, feet, and lower legs (distal muscles), but some people first experience weakness in the muscles near the center of the body (proximal muscles). The weakness can spread to other muscles.

Other signs and symptoms of myofibrillar myopathy can include muscle pain (myalgia) or weakness and loss of sensation in the limbs (peripheral neuropathy). Affected individuals may also have skeletal problems, which can include joint stiffness (contractures) and abnormal side-to-side curvature of the spine (scoliosis). Some people with myofibrillar myopathy develop clouding in the lenses of the eyes (cataracts).

Some people with myofibrillar myopathy develop cardiomyopathy, which is a weakening of the heart muscle. In some cases, cardiomyopathy is the first sign of the disorder.

In rare cases, the muscles used for speaking, swallowing, or breathing are affected in people with myofibrillar myopathy. When the muscles used for breathing are involved, affected individuals may experience extreme tiredness (fatigue), breathing difficulties, and, in severe cases, respiratory failure.

Frequency

Although myofibrillar myopathy is considered a rare disorder, the exact number of people who have the condition is unknown.

Causes

Variants (also called mutations) in several genes can cause myofibrillar myopathy. These genes provide instructions for making proteins that play an important role in muscle contraction. Within muscle fibers, structures called sarcomeres generate the

force needed for muscles to contract. Structures called Z-discs link neighboring sarcomeres together to form myofibrils, which are the basic units of muscle fibers. The organization of sarcomeres and myofibrils provides the strength and stability that is needed during repeated cycles of muscle contraction and relaxation. Many of the genes that are associated with myofibrillar myopathy provide instructions for making proteins that are involved in the function of Z-discs.

Variants in the *DES*, *MYOT*, and *LDB3* genes are among the main causes of myofibrillar myopathy. Variants in these genes cause cells to produce proteins that do not function properly. Because these abnormal proteins do not interact with Z discs as they should, the coordinated arrangement of sarcomeres and myofibrils is disrupted. Myofibrils that are not formed correctly break down and form clumps (aggregates) of abnormal proteins within the sarcomere, which leads to the myopathy seen in people with myofibrillar myopathy.

Approximately 30 to 50 percent of affected individuals do not have variants in the genes known to be associated with myofibrillar myopathy. In these cases, the cause of the condition is unknown.

Learn more about the genes associated with Myofibrillar myopathy

- DES
- HSPB8
- LDB3
- MYOT
- TTN

Additional Information from NCBI Gene:

- BAG3
- CRYAB
- FLNC

Inheritance

Myofibrillar myopathy has different inheritance patterns depending on which gene is involved.

The condition is typically inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Some cases of myofibrillar myopathy result from new (de novo) variants in the gene that occur during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or during early embryonic development.

In rare cases, myofibrillar myopathy is inherited in an autosomal recessive pattern,

which means both copies of the gene in each cell must have a variant to cause the disorder. 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

- Myofibrillar myopathies

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Desmin-related myofibrillar myopathy (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1832370/)
- Genetic Testing Registry: Myofibrillar myopathy 10 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C5436656/)
- Genetic Testing Registry: Myofibrillar myopathy 11 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C5543038/)
- Genetic Testing Registry: Myofibrillar myopathy 2 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1837317/)
- Genetic Testing Registry: Myofibrillar myopathy 4 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4721886/)
- Genetic Testing Registry: Myofibrillar myopathy 5 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1836050/)
- Genetic Testing Registry: Myofibrillar myopathy 6 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2751831/)
- Genetic Testing Registry: Myofibrillar myopathy 7 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4310711/)
- Genetic Testing Registry: Myofibrillar myopathy 8 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4310645/)
- Genetic Testing Registry: Myofibrillar myopathy (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2678065/)
- Genetic Testing Registry: Myofibrillar myopathy 3 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3714934/)

Genetic and Rare Diseases Information Center

- Myofibrillar myopathy (https://rarediseases.info.nih.gov/diseases/10529/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Myofibrillar myopathy%22)

Catalog of Genes and Diseases from OMIM

- MYOFIBRILLAR MYOPATHY 10; MFM10 (https://omim.org/entry/619040)
- MYOPATHY, MYOFIBRILLAR, 11; MFM11 (https://omim.org/entry/619178)
- MYOPATHY, MYOFIBRILLAR, 12, INFANTILE-ONSET, WITH CARDIOMYOPATHY; MFM12 (https://omim.org/entry/619424)
- MYOPATHY, MYOFIBRILLAR, 13, WITH RIMMED VACUOLES; MFM13 (https://omim.org/entry/621078)
- MYOPATHY, MYOFIBRILLAR, 1; MFM1 (https://omim.org/entry/601419)
- MYOPATHY, MYOFIBRILLAR, 2A, ADULT-ONSET; MFM2A (https://omim.org/entry/608810)
- MYOPATHY, MYOFIBRILLAR, 2B, INFANTILE-ONSET; MFM2B (https://omim.org/entry/613869)
- MYOPATHY, MYOFIBRILLAR, 3; MFM3 (https://omim.org/entry/609200)
- MYOPATHY, MYOFIBRILLAR, 4; MFM4 (https://omim.org/entry/609452)
- MYOPATHY, MYOFIBRILLAR, 5; MFM5 (https://omim.org/entry/609524)
- MYOPATHY, MYOFIBRILLAR, 6; MFM6 (https://omim.org/entry/612954)
- MYOPATHY, MYOFIBRILLAR, 7; MFM7 (https://omim.org/entry/617114)
- MYOPATHY, MYOFIBRILLAR, 8; MFM8 (https://omim.org/entry/617258)
- MYOPATHY, MYOFIBRILLAR, 9, WITH EARLY RESPIRATORY FAILURE; MFM9 (https://omim.org/entry/603689)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28myofibrillar+myopathy%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D)

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