LAMA2-related muscular dystrophy

Description

LAMA2-related muscular dystrophy is a disorder that causes weakness and wasting (atrophy) of muscles used for movement (skeletal muscles). This condition varies in severity, from a severe, early-onset type to a milder, late-onset form.

Early-onset *LAMA2*-related muscular dystrophy is apparent at birth or within the first few months of life. It is considered part of a class of muscle disorders called congenital muscular dystrophies and is sometimes called congenital muscular dystrophy type 1A. Affected infants may have severe muscle weakness, lack of muscle tone (hypotonia), little spontaneous movement, and joint deformities (contractures). Weakness of the muscles in the face and throat can result in feeding difficulties and an inability to grow and gain weight at the expected rate. Respiratory insufficiency, which occurs when muscles in the chest are weakened, causes a weak cry and breathing problems that can lead to frequent, potentially life-threatening lung infections.

As affected children grow, they often develop an abnormal, gradually worsening side-to-side curvature of the spine (scoliosis) and inward curvature of the back (lordosis). Children with early-onset *LAMA2*-related muscular dystrophy often do not develop the ability to walk. Difficulty with speech may result from weakness of the facial muscles and an enlarged tongue. Seizures occur in about a third of individuals with early-onset *LAMA2*-related muscular dystrophy; rarely, heart complications occur in this form of the disorder.

Symptoms of late-onset *LAMA2*-related muscular dystrophy become evident later in childhood or adulthood, and are similar to those of a group of muscle disorders classified as limb-girdle muscular dystrophies. In late-onset *LAMA2*-related muscular dystrophy, the muscles most affected are those closest to the body (proximal muscles), specifically the muscles of the shoulders, upper arms, pelvic area, and thighs. Children with late-onset *LAMA2*-related muscular dystrophy sometimes have delayed development of motor skills such as walking, but generally achieve the ability to walk without assistance. Over time, they may develop rigidity of the back, joint contractures, scoliosis, and breathing problems. However, most affected individuals retain the ability to walk and climb stairs.

Frequency

The prevalence of *LAMA2*-related muscular dystrophy is estimated at between 1 in 50, 000 and 1 in 400,000 individuals worldwide. This condition is thought to be the most common type of congenital muscular dystrophy, accounting for between 30 and 40 percent of total cases.

Causes

As its name suggests, *LAMA2*-related muscular dystrophy is caused by mutations in the *LAMA2* gene. This gene provides instructions for making a part (subunit) of certain members of a protein family called laminins. Laminin proteins are made of three different subunits called alpha, beta, and gamma. There are several forms of each subunit, and each form is produced from instructions carried by a different gene. The *LAMA2* gene provides instructions for the alpha-2 subunit. This subunit is found in the laminin 2 protein, also known as merosin; it is also part of another laminin protein called laminin 4.

Laminins are found in an intricate lattice of proteins and other molecules that forms in the spaces between cells (the extracellular matrix). Laminin 2 and laminin 4 play a particularly important role in the skeletal muscles. The laminins attach (bind) to other proteins in the extracellular matrix and in the membrane of muscle cells, which helps maintain the stability of muscle fibers.

Most *LAMA2* gene mutations that cause the severe, early-onset form of *LAMA2*-related muscular dystrophy result in the absence of functional laminin alpha-2 subunit. Mutations that cause the milder, later-onset form usually result in a reduction (deficiency) of functional laminin alpha-2 subunit. Deficiency or absence of the laminin alpha-2 subunit results in a corresponding lack of laminin 2 and laminin 4, reducing the strength and stability of muscle tissue and leading to the signs and symptoms of *LAMA2*-related muscular dystrophy.

Learn more about the gene associated with LAMA2-related muscular dystrophy

- LAMA2

Inheritance

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

- LAMA2 MD
- Laminin alpha 2 deficiency

- Laminin alpha-2 deficient muscular dystrophy
- MDC1A
- Merosin-deficient muscular dystrophy
- Muscular dystrophy due to LAMA2 deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Congenital muscular dystrophy due to partial LAMA2 deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1842898/)
- Genetic Testing Registry: Merosin deficient congenital muscular dystrophy (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1263858/)

Genetic and Rare Diseases Information Center

- Laminin subunit alpha 2-related congenital muscular dystrophy (https://rarediseases.info.nih.gov/diseases/3843/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22LAMA2-related muscular dystrophy%22)

Catalog of Genes and Diseases from OMIM

- MUSCULAR DYSTROPHY, CONGENITAL MEROSIN-DEFICIENT, 1A; MDC1A (https://omim.org/entry/607855)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28muscular+dystrophy%29+AND+%28lama2%29%29+OR+%28merosin-deficient%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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