LMNA-Related Congenital Muscular Dystrophy

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LMNA-related congenital muscular dystrophy (L-CMD) is a condition that primarily affects muscles used for movement (skeletal muscles). It is part of a group of genetic conditions called congenital muscular dystrophies, which cause weak muscle tone (hypotonia) and muscle wasting (atrophy) beginning very early in life.

Keywords: genetic conditions

1. Introduction

In people with L-CMD, muscle weakness becomes apparent in infancy or early childhood and can worsen quickly. The most severely affected infants develop few motor skills, and they are never able to hold up their heads, roll over, or sit. Less severely affected children may learn to sit, stand, and walk before muscle weakness becomes apparent. First the neck muscles weaken, causing the head to fall forward (dropped-head syndrome). As other skeletal muscles become weaker, these children may ultimately lose the ability to sit, stand, and walk unassisted.

Other features of L-CMD often include spinal rigidity and abnormal curvature of the spine (scoliosis and lordosis); joint deformities (contractures) that restrict movement, particularly in the hips and legs; and an inward-turning foot. People with L-CMD also have an increased risk of heart rhythm abnormalities (arrhythmias).

Over time, muscle weakness causes most infants and children with L-CMD to have trouble eating and breathing. The breathing problems result from restrictive respiratory insufficiency, which occurs when muscles in the chest are weakened and the ribcage becomes increasingly rigid. This problem can be life-threatening, and many affected children require support with a machine to help them breathe (mechanical ventilation).

2. Frequency

L-CMD is a rare disorder. Only about 50 affected individuals have been described in the medical literature.

3. Causes

L-CMD is caused by mutations in the *LMNA* gene. This gene provides instructions for making very similar proteins called lamins. These proteins play an important role in determining the shape of the nucleus within cells. Lamins are an essential supporting (scaffolding) component of the nuclear envelope, which is the membrane that surrounds the nucleus. The nuclear envelope regulates the movement of molecules into and out of the nucleus, and researchers believe it may play a role in regulating the activity of certain genes.

Mutations in the *LMNA* gene lead to the production of abnormal lamins. These malfunctioning proteins alter the structure of the nuclear envelope in ways that are not well understood. Researchers are working to determine how these changes affect muscle cells and lead to muscle weakness and atrophy in people with L-CMD.

3.1. The gene associated with LMNA-related congenital muscular dystrophy

- LMNA

4. Inheritance

L-CMD is considered an autosomal dominant disorder, which means one copy of the altered gene in each cell is sufficient to cause the condition. All known cases of L-CMD have resulted from new (de novo) mutations in the gene. These mutations occur during the formation of reproductive cells (eggs or sperm) or in early embryonic development. Affected individuals have no history of the disorder in their family.

5. Other Names for This Condition

- L-CMD
- LMNA-related CMD
- MDCL
- muscular dystrophy, congenital, LMNA-related

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