SMA-LED

Subjects: Genetics & Heredity
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Spinal muscular atrophy with lower extremity predominance (SMA-LED) is characterized by muscle weakness and wasting (atrophy) in the lower limbs, most severely affecting the thigh muscles (quadriceps). (In SMA-LED, the "D" stands for dominant, which refers to the inheritance pattern of this condition.) The loss of nerve cells that control muscle movement (motor neurons) leads to atrophy of the muscles in the lower limbs. Affected individuals often have a waddling or unsteady walk and walk on the balls of their feet. They may have difficulty rising from a seated position and climbing stairs. Some people with SMA-LED also have weakness in upper limb muscles.
Joint deformities (contractures) in the hips, knees, feet, and ankles can occur in SMA-LED, and in severe cases are present from birth and can impair walking. Some individuals with this disorder have rigidity of joints (arthrogryposis) in their shoulders, elbows, and hands.
In most people with SMA-LED, the muscle problems are apparent in infancy or early childhood; however, about one-quarter of affected individuals do not develop muscle weakness until adulthood. The muscle weakness and related health problems typically do not worsen over time.

genetic conditions

1. Introduction

Joint deformities (contractures) in the hips, knees, feet, and ankles can occur in SMA-LED, and in severe cases are present from birth and can impair walking. Some individuals with this disorder have rigidity of joints (arthrogryposis) in their shoulders, elbows, and hands.

In most people with SMA-LED, the muscle problems are apparent in infancy or early childhood; however, about one-quarter of affected individuals do not develop muscle weakness until adulthood. The muscle weakness and related health problems typically do not worsen over time.

2. Frequency

SMA-LED is thought to be a rare condition; its prevalence is unknown.

3. Causes

SMA-LED is caused by mutations in the *DYNC1H1* gene or *BICD2* gene. When this condition is caused by mutations in the *DYNC1H1* gene, it is often known as SMA-LED type 1 or SMA-LED1, and when it is caused by

mutations in the *BICD2* gene, the condition is often known as SMA-LED type 2 or SMA-LED2.

The *DYNC1H1* gene provides instructions for making a protein that is part of a group (complex) of proteins called dynein. This complex is part of a network that moves (transports) proteins and other materials within cells. The protein produced from the *BICD2* gene attaches (binds) to the dynein complex, turning it on (activating it) and helping it bind to other cellular materials for transport. The BICD2 protein and the dynein complex help neighboring neurons communicate by transporting sac-like structures called synaptic vesicles that contain chemical messengers. The BICD2 protein also helps maintain the structure of a cell component called the Golgi apparatus, in which newly produced proteins are modified so they can carry out their functions.

DYNC1H1 and *BICD2* gene mutations that cause SMA-LED disrupt the function of the dynein complex. As a result, transport of proteins, synaptic vesicles, and other materials within cells is reduced. Decreased synaptic vesicle transport in motor neurons, leading to impaired growth of neurons, is thought to contribute to the muscle weakness and atrophy experienced by people with SMA-LED. It is unclear why this condition primarily affects the lower limbs.

Additionally, *BICD2* gene mutations impair the BICD2 protein's ability to maintain the structure of the Golgi apparatus within cells. As a result, the Golgi apparatus breaks down into small fragments and the altered BICD2 protein becomes trapped within these fragments. Loss of these cell components likely further contributes to the signs and symptoms of SMA-LED.

3.1 The genes associated with Spinal muscular atrophy with lower extremity predominance

- BICD2
- DYNC1H1

4. Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

In some cases, an affected person inherits the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- autosomal dominant childhood-onset proximal spinal muscular atrophy with contractures
- Kugelberg-Welander syndrome, autosomal dominant
- lower extremity-predominant autosomal dominant proximal spinal muscular atrophy with contractures
- SMA-LED

- spinal muscular atrophy, childhood, proximal, autosomal dominant
- spinal muscular atrophy, juvenile, proximal, autosomal dominant
- spinal muscular atrophy, lower extremity, autosomal dominant
- spinal muscular atrophy, lower extremity, dominant

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