X-linked infantile spinal muscular atrophy

Description

X-linked infantile spinal muscular atrophy is a condition that affects only boys and is characterized by severe muscle weakness and absent reflexes (areflexia). Affected children often have multiple joint deformities (contractures) from birth that cause joint stiffness (arthrogryposis) and impair movement. In severe cases, affected infants are born with broken bones. The muscle weakness worsens over time; affected children reach some early motor developmental milestones, such as sitting unassisted, but these skills are often lost (developmental regression).

Additional features of X-linked infantile spinal muscular atrophy include an unusually small chin (micrognathia), abnormal curvature of the spine (scoliosis or kyphosis), and undescended testes (cryptorchidism).

Weakness of the chest muscles used for breathing often leads to life-threatening breathing problems. Children with X-linked infantile spinal muscular atrophy usually do not survive past early childhood due to respiratory failure, although, in rare cases, affected individuals can survive into adolescence.

Frequency

X-linked infantile spinal muscular atrophy is thought to be a rare condition; its prevalence is unknown.

Causes

Mutations in the *UBA1* gene cause X-linked infantile spinal muscular atrophy. The *UBA1* gene provides instructions for making the ubiquitin-activating enzyme E1. This enzyme is necessary for a process that targets damaged or unneeded proteins to be broken down (degraded) within cells. Protein degradation helps to maintain the proper balance of protein production and breakdown (protein homeostasis) that cells need to function and survive.

UBA1 gene mutations lead to a decrease in enzyme production or the production of an enzyme with reduced or abnormal function. As a result, damaged or unneeded proteins build up inside cells instead of being degraded, which may damage cells and contribute to cell death. This buildup also disrupts protein homeostasis. Old proteins must be removed before cells can make new proteins. If these damaged or unneeded proteins

are not degraded, they can impair normal cell functions by stopping the production of new proteins. An imbalance in protein production and breakdown can ultimately lead to cell death. Specialized nerve cells that control muscle movement (motor neurons) are particularly susceptible to disruptions in cell function, likely due to their large size. Loss of these cells causes many of the signs and symptoms of X-linked infantile spinal muscular atrophy.

Learn more about the gene associated with X-linked infantile spinal muscular atrophy

- UBA1

Inheritance

This condition is inherited in an X-linked recessive pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- AMCX1
- Arthrogryposis multiplex congenita, distal, X-linked
- Arthrogryposis, X-lined, type I
- Distal X-linked AMC
- Infantile X-linked SMA
- SMAX2
- Spinal muscular atrophy, infantile X-linked
- Spinal muscular atrophy, X-linked 2
- Spinal muscular atrophy, X-linked lethal infantile
- X-linked arthrogryposis multiplex congenita
- X-linked arthrogryposis type I
- X-linked lethal infantile SMA
- XL-SMA
- XLSMA

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Infantile-onset X-linked spinal muscular atrophy (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1844934/)

Genetic and Rare Diseases Information Center

- Infantile-onset X-linked spinal muscular atrophy (https://rarediseases.info.nih.gov/diseases/8521/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- SPINAL MUSCULAR ATROPHY, X-LINKED 2; SMAX2 (https://omim.org/entry/301830)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28X-linked+infantile+spinal+muscular+atrophy%29+OR+%28SMAX2%29+OR+%28XLSMA%29+OR+%28spinal+muscular+atrophy,+X-linked+2%29+OR+%28infantile+X-linked+SMA%29+OR+%28X-linked+spinal+muscular+atrophy%29%29+NOT+%28%28bulbar%29+OR+%28Kennedy%29+OR+%28spinobulbar%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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