Atelosteogenesis type 3

Description

Atelosteogenesis type 3 is a disorder that affects the development of bones throughout the body. Affected individuals are born with inward- and upward-turning feet (clubfeet) and dislocations of the hips, knees, and elbows. Bones in the spine, rib cage, pelvis, and limbs may be underdeveloped or in some cases absent. As a result of the limb bone abnormalities, individuals with this condition have very short arms and legs. Their hands and feet are wide, with broad fingers and toes that may be permanently bent (camptodactyly) or fused together (syndactyly). Characteristic facial features include a broad forehead, wide-set eyes (hypertelorism), and an underdeveloped nose. About half of affected individuals have an opening in the roof of the mouth (a cleft palate.)

Individuals with atelosteogenesis type 3 typically have an underdeveloped rib cage that affects the development and functioning of the lungs. As a result, affected individuals are usually stillborn or die shortly after birth from respiratory failure. Some affected individuals survive longer, usually with intensive medical support. They typically experience further respiratory problems as a result of weakness of the airways that can lead to partial closing, short pauses in breathing (apnea), or frequent infections. People with atelosteogenesis type 3 who survive past the newborn period may have learning disabilities and delayed language skills, which are probably caused by low levels of oxygen in the brain due to respiratory problems. As a result of their orthopedic abnormalities, they also have delayed development of motor skills such as standing and walking.

Frequency

Atelosteogenesis type 3 is a rare disorder; its exact prevalence is unknown. About two dozen affected individuals have been identified.

Causes

Mutations in the *FLNB* gene cause atelosteogenesis type 3. The *FLNB* gene provides instructions for making a protein called filamin B. This protein helps build the network of protein filaments (cytoskeleton) that gives structure to cells and allows them to change shape and move. Filamin B attaches (binds) to another protein called actin and helps the actin to form the branching network of filaments that makes up the cytoskeleton. It also links actin to many other proteins to perform various functions within the cell,

including the cell signaling that helps determine how the cytoskeleton will change as tissues grow and take shape during development.

Filamin B is especially important in the development of the skeleton before birth. It is active (expressed) in the cell membranes of cartilage-forming cells (chondrocytes). Cartilage is a tough, flexible tissue that makes up much of the skeleton during early development. Most cartilage is later converted to bone (a process called ossification), except for the cartilage that continues to cover and protect the ends of bones and is present in the nose, airways (trachea and bronchi), and external ears. Filamin B appears to be important for normal cell growth and division (proliferation) and maturation (differentiation) of chondrocytes and for the ossification of cartilage.

FLNB gene mutations that cause atelosteogenesis type 3 change single protein building blocks (amino acids) in the filamin B protein or delete a small section of the protein sequence, resulting in an abnormal protein. This abnormal protein appears to have a new, atypical function that interferes with the proliferation or differentiation of chondrocytes, impairing ossification and leading to the signs and symptoms of atelosteogenesis type 3.

Learn more about the gene associated with Atelosteogenesis type 3

- FLNB

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. Most cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- AOIII
- Atelosteogenesis type III

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Atelosteogenesis type III (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3668942/)

Genetic and Rare Diseases Information Center

- Atelosteogenesis type III (https://rarediseases.info.nih.gov/diseases/10608/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- ATELOSTEOGENESIS, TYPE III; AO3 (https://omim.org/entry/108721)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28atelosteogenesis+type+3%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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