Fibrochondrogenesis

Subjects: Genetics & Heredity
Contributor: Nicole Yin

Fibrochondrogenesis is a very severe disorder of bone growth. Affected infants have a very narrow chest, which prevents the lungs from developing normally. Most infants with this condition are stillborn or die shortly after birth from respiratory failure. However, some affected individuals have lived into childhood.

Keywords: genetic conditions

1. Introduction

Fibrochondrogenesis is characterized by short stature (dwarfism) and other skeletal abnormalities. Affected individuals have shortened long bones in the arms and legs that are unusually wide at the ends (described as dumbbell-shaped). People with this condition also have a narrow chest with short, wide ribs and a round and prominent abdomen. The bones of the spine (vertebrae) are flattened (platyspondyly) and have a characteristic pinched or pear shape that is noticeable on x-rays. Other skeletal abnormalities associated with fibrochondrogenesis include abnormal curvature of the spine and underdeveloped hip (pelvic) bones.

People with fibrochondrogenesis also have distinctive facial features. These include prominent eyes, low-set ears, a small mouth with a long upper lip, and a small chin (micrognathia). Affected individuals have a relatively flat-appearing midface, particularly a small nose with a flat nasal bridge and nostrils that open to the front rather than downward (anteverted nares). Vision problems, including severe nearsightedness (high myopia) and clouding of the lens of the eye (cataract), are common in those who survive infancy. Most affected individuals also have sensorineural hearing loss, which is caused by abnormalities of the inner ear.

2. Frequency

Fibrochondrogenesis appears to be a rare disorder. About 20 affected individuals have been described in the medical literature.

3. Causes

Fibrochondrogenesis can result from mutations in the *COL11A1* or *COL11A2* gene. When the condition is caused by *COL11A1* gene mutations, it is designated as type 1; when it is caused by *COL11A2* gene mutations, it is designated as type 2. Both of these genes provide instructions for making components of type XI collagen, which is a complex molecule that gives structure and strength to the connective tissues that support the body's joints and organs. Specifically, type XI collagen is found in cartilage, a tough but flexible tissue that makes up much of the skeleton during early development. Most cartilage is later converted to bone, except for the cartilage that continues to cover and protect the ends of bones and is present in the nose and external ears. Type XI collagen is also part of the inner ear; the vitreous, which is the clear gel that fills the eyeball; and the nucleus pulposus, which is the center portion of the discs between vertebrae.

Mutations in the *COL11A1* or *COL11A2* gene impair the assembly of type XI collagen, in most cases leading to the production of abnormal collagen molecules. The defective collagen weakens connective tissues, impairing the formation of bones throughout the skeleton and causing changes in the eye and inner ear that lead to vision and hearing problems.

3.1. The Genes Associated with Fibrochondrogenesis

- COL11A1
- COL11A2

4. Inheritance

Fibrochondrogenesis is generally 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 usually do not show signs and symptoms of the condition. In a few reported cases, parents of children with fibrochondrogenesis have had mild features that may be related to the condition, including slightly short stature, myopia, cataracts, joint pain, and hearing loss.

In at least one case of fibrochondrogenesis caused by a *COL11A2* gene mutation, the condition was inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In this case, the condition resulted from a new (de novo) mutation in the gene that occurred during the formation of reproductive cells (eggs or sperm) in one of the affected individual's parents. There was no history of the disorder in the family.

5. Other Names for This Condition

- FBCG1
- FBCG2
- fibrochondrogenesis-1
- fibrochondrogenesis-2

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