Acrocallosal Syndrome

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Acrocallosal syndrome is a rare condition characterized by a brain abnormality called agenesis of the corpus callosum, the presence of extra fingers and toes (polydactyly), and distinctive facial features. The signs and symptoms of this disorder are present at birth, and their severity varies widely among affected individuals.

genetic conditions

1. Introduction

Agenesis of the corpus callosum occurs when the tissue that connects the left and right halves of the brain (the corpus callosum) fails to form normally during the early stages of development before birth. Other brain abnormalities, including the growth of large cysts in brain tissue, have also been reported in people with acrocallosal syndrome. The changes in brain structure associated with this condition lead to delayed development and intellectual disability, which is most often moderate to severe. Some affected individuals also experience seizures.

Extra fingers and toes are common in people with acrocallosal syndrome. The extra digits can be on the same side of the hand or foot as the pinky or little toe (postaxial polydactyly) or on the same side as the thumb or great toe (preaxial polydactyly). Some affected individuals also have webbed or fused skin between the fingers or toes (syndactyly).

Distinctive facial features that can occur with acrocallosal syndrome include widely spaced eyes (hypertelorism) and a high, prominent forehead. Many affected individuals also have an unusually large head size (macrocephaly).

2. Frequency

This condition appears to be rare. Only a few dozen cases have been reported in the medical literature.

3. Causes

Mutations in the *KIF7* gene have been found to cause acrocallosal syndrome. Mutations in another gene, *GLI3*, can also cause features of this disorder. However, the signs and symptoms overlap significantly with those of a similar disorder called Greig cephalopolysyndactyly syndrome (which is also caused by *GLI3* gene mutations), so

acrocallosal syndrome resulting from *GLI3* gene mutations is sometimes considered a severe form of that condition.

The proteins produced from the *KIF7* and *GLI3* genes play critical roles in the normal shaping (patterning) of many tissues and organs before birth. The proteins are part of a chemical signaling pathway called Sonic Hedgehog signaling. This pathway is involved in cell growth, cell specialization, and the patterning of structures such as the brain and limbs.

Mutations in either the *KIF7* or *GLI3* gene are thought to impair Sonic Hedgehog signaling, which has wide-ranging effects on development before birth. The roles of these genes in brain and limb patterning may help explain why mutations lead to agenesis of the corpus callosum, polydactyly, and the other features of acrocallosal syndrome.

3.1. The genes associated with Acrocallosal syndrome

- GLI3
- KIF7

4. Inheritance

When acrocallosal syndrome is caused by *KIF7* gene mutations, it is 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 typically do not show signs and symptoms of the condition.

Acrocallosal syndrome (or severe Greig cephalopolysyndactyly syndrome) resulting from *GLI3* gene mutations is considered autosomal dominant , which means one copy of the altered gene in each cell is sufficient to cause the disorder. This condition results from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) or in early embryonic development. These cases occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- ACLS
- hallux duplication, postaxial polydactyly, and absence of corpus callosum
- Schinzel acrocallosal syndrome
- Schinzel syndrome 1

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