Craniofacial-Deafness-Hand Syndrome

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Craniofacial-deafness-hand syndrome is characterized by distinctive facial features, profound hearing loss, and hand abnormalities.

Keywords: genetic conditions

1. Introduction

The distinctive facial features of people with craniofacial-deafness-hand syndrome result from a variety of developmental abnormalities involving the skull (cranium) and face. Affected individuals often have underdeveloped or absent nasal bones resulting in a small nose, thin nostrils, and a flattened mid-face with a flat nasal bridge. Individuals with this condition typically also have widely spaced eyes (ocular hypertelorism), narrowed openings of the eyes (narrowed palpebral fissures), a small upper jaw (hypoplastic maxilla), and a small mouth with pursed lips.

People with this condition also have profound hearing loss that is caused by abnormalities in the inner ear (sensorineural deafness). Hearing loss in these individuals is present from birth.

In affected individuals, a common abnormality of the muscles in the hand is a malformation in which all of the fingers are angled outward toward the fifth finger (ulnar deviation). People with craniofacial-deafness-hand syndrome may also have permanently bent third, fourth, and fifth fingers (camptodactyly), which can limit finger movement and lead to joint deformities called contractures. Contractures in the wrist can further impair hand movements.

2. Frequency

Craniofacial-deafness-hand syndrome is an extremely rare condition. Only a few cases have been reported in the scientific literature.

3. Causes

Craniofacial-deafness-hand syndrome is caused by mutations in the *PAX3* gene. The *PAX3* gene plays a critical role in the formation of tissues and organs during embryonic development. To perform this function, the gene provides instructions for making a protein that attaches (binds) to specific areas of DNA to help control the activity of particular genes. During embryonic development, the *PAX3* gene is active in cells called neural crest cells. These cells migrate from the developing spinal cord to specific regions in the embryo. The protein produced from the *PAX3* gene directs the activity of other genes that signal neural crest cells to form specialized tissues or cell types. These include some nerve tissues, bones in the face and skull (craniofacial bones), and muscle tissue.

At least one *PAX3* gene mutation has been identified in individuals with craniofacial-deafness-hand syndrome. This mutation appears to affect the ability of the PAX3 protein to bind to DNA. As a result, the PAX3 protein cannot control the activity of other genes and cannot regulate the differentiation of neural crest cells. A lack of specialization of neural crest cells leads to the impaired growth of craniofacial bones, nerve tissue, and muscles seen in craniofacial-deafness-hand syndrome.

3.1. The Gene Associated with Craniofacial-Deafness-Hand Syndrome

- PAX3

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.

5. Other Names for This Condition

- CDHS

References

1. Asher JH Jr, Sommer A, Morell R, Friedman TB. Missense mutation in the paired domain of PAX3 causes craniofacial-deafness-hand syndrome. Hum Mutat.1996;7(1):30-5.
2. Birrane G, Soni A, Ladias JA. Structural basis for DNA recognition by thehuman PAX3 homeodomain. Biochemistry. 20 09 Feb 17;48(6):1148-55. doi:10.1021/bi802052y.
3. Sommer A, Bartholomew DW. Craniofacial-deafness-hand syndrome revisited. Am J Med Genet A. 2003 Nov 15;123A (1):91-4.