Oral-facial-digital syndrome

Description

Oral-facial-digital syndrome is actually a group of related conditions that affect the development of the oral cavity (the mouth and teeth), facial features, and digits (fingers and toes).

Researchers have identified at least 13 potential forms of oral-facial-digital syndrome. The different types are classified by their patterns of signs and symptoms. However, the features of the various types overlap significantly, and some types are not well defined. The classification system for oral-facial-digital syndrome continues to evolve as researchers find more affected individuals and learn more about this disorder.

The signs and symptoms of oral-facial-digital syndrome vary widely. However, most forms of this disorder involve problems with development of the oral cavity, facial features, and digits. Most forms are also associated with brain abnormalities and some degree of intellectual disability.

Abnormalities of the oral cavity that occur in many types of oral-facial-digital syndrome include a split (cleft) in the tongue, a tongue with an unusual lobed shape, and the growth of noncancerous tumors or nodules on the tongue. Affected individuals may also have extra, missing, or defective teeth. Another common feature is an opening in the roof of the mouth (a cleft palate). Some people with oral-facial-digital syndrome have bands of extra tissue (called hyperplastic frenula) that abnormally attach the lip to the gums.

Distinctive facial features often associated with oral-facial-digital syndrome include a split in the lip (a cleft lip); a wide nose with a broad, flat nasal bridge; and widely spaced eyes (hypertelorism).

Abnormalities of the digits can affect both the fingers and the toes in people with oral-facial-digital syndrome. These abnormalities include fusion of certain fingers or toes (syndactyly), digits that are shorter than usual (brachydactyly), or digits that are unusually curved (clinodactyly). The presence of extra digits (polydactyly) is also seen in most forms of oral-facial-digital syndrome.

Other features occur in only one or a few types of oral-facial digital syndrome. These features help distinguish the different forms of the disorder. For example, the most common form of oral-facial-digital syndrome, type I, is associated with polycystic kidney

disease. This kidney disease is characterized by the growth of fluid-filled sacs (cysts) that interfere with the kidneys' ability to filter waste products from the blood. Other forms of oral-facial-digital syndrome are characterized by neurological problems, particular changes in the structure of the brain, bone abnormalities, vision loss, and heart defects.

Frequency

Oral-facial-digital syndrome has an estimated incidence of 1 in 50,000 to 250,000 newborns. Type I accounts for the majority of cases of this disorder. The other forms of oral-facial-digital syndrome are very rare; most have been identified in only one or a few families.

Causes

Only one gene, *OFD1*, has been associated with oral-facial-digital syndrome. Mutations in this gene cause oral-facial-digital syndrome type I. *OFD1* gene mutations were also found in an affected family whose disorder was classified as type VII; however, researchers now believe that type VII is the same as type I.

The *OFD1* gene provides instructions for making a protein whose function is not fully understood. It appears to play an important role in the early development of many parts of the body, including the brain, face, limbs, and kidneys. Mutations in the *OFD1* gene prevent cells from making enough functional OFD1 protein, which disrupts the normal development of these structures. It is unclear how a shortage of this protein causes the specific features of oral-facial-digital syndrome type I.

Researchers are actively searching for the genetic changes responsible for the other forms of oral-facial-digital syndrome.

Learn more about the gene associated with Oral-facial-digital syndrome

- OFD1

Inheritance

Oral-facial-digital syndrome type I is inherited in an X-linked dominant pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell is sufficient to cause the disorder. Some cells produce a normal amount of OFD1 protein and other cells produce none. The resulting overall reduction in the amount of this protein leads to the signs and symptoms of oral-facial-digital syndrome type I.

In males (who have only one X chromosome), mutations result in a total loss of the OFD1 protein. A lack of this protein is usually lethal very early in development, so very few males are born with oral-facial-digital syndrome type I. Affected males usually die before birth, although a few have lived into early infancy.

Most of the other forms of oral-facial-digital syndrome are inherited in an autosomal recessive pattern, which suggests that both copies of a causative 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.

Other Names for This Condition

- Dysplasia linguofacialis
- OFDS
- Oro-facio-digital syndrome
- Orodigitofacial dysostosis
- Orodigitofacial syndrome
- Orofaciodigital syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Orofacial-digital syndrome III (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0406726/)
- Genetic Testing Registry: Orofacial-digital syndrome IV (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0406727/)
- Genetic Testing Registry: Orofaciodigital syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0029294/)
- Genetic Testing Registry: Orofaciodigital syndrome I (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1510460/)
- Genetic Testing Registry: Orofaciodigital syndrome type 6 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2745997/)
- Genetic Testing Registry: Orofaciodigital syndrome V (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1868118/)
- Genetic Testing Registry: Orofaciodigital syndrome VIII (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0796101/)

Genetic and Rare Diseases Information Center

- Orofaciodigital syndrome (https://rarediseases.info.nih.gov/diseases/10692/index)
- Orofaciodigital syndrome type 1 (https://rarediseases.info.nih.gov/diseases/4121/index)
- Orofaciodigital syndrome type 2 (https://rarediseases.info.nih.gov/diseases/3701/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Oral-facial-digital syndrome%22)

Catalog of Genes and Diseases from OMIM

- OROFACIODIGITAL SYNDROME X; OFD10 (https://omim.org/entry/165590)
- OROFACIODIGITAL SYNDROME VI; OFD6 (https://omim.org/entry/277170)
- OROFACIODIGITAL SYNDROME II; OFD2 (https://omim.org/entry/252100)
- OROFACIODIGITAL SYNDROME VIII; OFD8 (https://omim.org/entry/300484)
- OROFACIODIGITAL SYNDROME I; OFD1 (https://omim.org/entry/311200)
- OROFACIODIGITAL SYNDROME III; OFD3 (https://omim.org/entry/258850)
- OROFACIODIGITAL SYNDROME IV; OFD4 (https://omim.org/entry/258860)
- OROFACIODIGITAL SYNDROME IX; OFD9 (https://omim.org/entry/258865)
- OROFACIODIGITAL SYNDROME V; OFD5 (https://omim.org/entry/174300)
- OROFACIODIGITAL SYNDROME VII; OFD7 (https://omim.org/entry/608518)
- OROFACIODIGITAL SYNDROME XI; OFD11 (https://omim.org/entry/612913)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Orofaciodigital+Syndromes%5BMAJR%5D%29+AND+%28%28oral-facial-digital%5BTIAB%5D%29+OR+%28orofaciodigital%5BTIAB%5D%29+OR+%28oral+facial+digital%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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