Tooth Agenesis

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Subdivisions of Tooth Agenesis

- hypodontia
- oligodontia
- anodontia

General Discussion

Tooth agenesis is a condition in which teeth are missing. Anodontia is a genetic disorder defined as the absence of all teeth. It usually occurs as part of a syndrome that includes other abnormalities. Also rare but more common than anodontia are hypodontia and oligodontia. Hypodontia is genetic in origin and usually involves the absence of from 1 to 5 teeth. Oligodontia is genetic as well and is the term used to describe a condition in which six or more teeth are missing.

Hypodontia/oligodontia/anodontia might be considered as a unique clinical entity but with increasing severity.

These conditions may involve either the primary or permanent sets of teeth, but most cases involve the permanent teeth. Tooth agenesis occurs following a specific pattern of missing teeth. Not only the number of missing teeth, but also the type of missing teeth, must be considered.

Tooth agenesis is often associated with a group of conditions affecting the development or function of the teeth, hair, nails and sweat glands called ectodermal dysplasias.

Signs & Symptoms

Hypo/oligodontia is characterized by partial and anodontia by complete absence of teeth. Since all primary teeth are usually present by the age of three, their absence is usually noted and a dentist consulted. With the exception of wisdom teeth, all permanent teeth are usually present by the ages 12 to 14. When teeth have not appeared by the appropriate age, dental panoramic X-rays are usually taken.

When hypo/oligodontia and surely anodontia occur, abnormalities of hair, nails, and sweat glands may also be present. In many cases, hypo/oligodontia is a component of one of the ectodermal dysplasias, a group of hereditary disorders.

Causes

Several different genes have been found to be associated with hypo/oligodontia and anodontia including the *EDA, EDAR* and *EDARADD* genes.

The same genes are involved in so called isolated hypo/oligodontia (only missing teeth) or associated hypo/oligodontia with other symptoms in syndromes like ectodermal dysplasias. *EDA, EDAR* and *EDARADD* genes are indeed responsible both for isolated or syndromic hypo/oligodontia.

Many other genes are involved in hypo/oligodontia such as *MSX1, PAX9, IRF6, GREM2, AXIN2, LRP6, SMOC2, LTBP3, PITX2,* and *WNT10B. WNT10A* is now recognized as being the major gene involved in the etiology of hypodontia/oligodontia.

Depending on the gene involved, inheritance can follow different modes of inheritance. Most genetic diseases are determined by the status of the two copies of a gene, one received from the father and one from the mother.

Recessive genetic disorders occur when an individual inherits a non-working gene from each parent. If an individual receives one working gene and one non-working gene for the disease, the person will be a carrier for the disease, but usually will not show symptoms. The risk for two carrier parents to both pass the non-working gene and, therefore, have an affected child is 25% with each pregnancy. The risk to have a child who is a carrier, like the parents, is 50% with each pregnancy. The chance for a child to receive working genes from both parents is 25%. The risk is the same for males and females.

Parents who are close relatives (consanguineous) have a higher chance than unrelated parents to both carry the same abnormal gene, which increases the risk to have children with a recessive genetic disorder.

Dominant genetic disorders occur when only a single copy of a non-working gene is necessary to cause a particular disease. The non-working gene can be inherited from either parent or can be the result of a mutated (changed) gene in the affected individual. The risk of passing the non-working gene from an affected parent to an offspring is 50% for each pregnancy. The risk is the same for males and females.

In some individuals, the disorder is due to a spontaneous (de novo) genetic mutation that occurs in the egg or sperm cell. In such situations, the disorder is not inherited from the parents.

X-linked genetic disorders are conditions caused by a non-working gene on the X chromosome and manifest mostly in males. Females that have a non-working gene present on one of their X chromosomes are carriers for that disorder. Carrier females usually do not display symptoms because females have two X chromosomes and only one carries the non-working gene. Males have one X chromosome that is inherited from their mother and if a male inherits an X chromosome that contains a non-working gene he will develop the disease.

Female carriers of an X-linked disorder have a 25% chance with each pregnancy to have a carrier daughter like themselves, a 25% chance to have a non-carrier daughter, a 25% chance to have a son affected with the disease and a 25% chance to have an unaffected son.

If a male with an X-linked disorder is able to reproduce, he will pass the non-working gene to all of his daughters who will be carriers. A male cannot pass an X-linked gene to his sons because males always pass their Y chromosome instead of their X chromosome to male offspring.

X-linked dominant disorders are caused by a non-working gene on the X chromosome and occur mostly in females. Females with these rare conditions are affected when they have an X chromosome with the non-working gene for a particular disease. Males with a non-working gene for an X-linked dominant disorder are more severely affected than females and often do not survive.

Affected Populations

The prevalence of anodontia is unknown. This condition affects males and females in equal numbers. The prevalence of hypodontia is 2 to 8% of the general population (excluding third molar) and oligodontia is 0.09%. to 0.3%.

Related Disorders

The ectodermal dysplasias are a group of hereditary, non-progressive conditions affecting the development or function of the teeth, hair, nails and sweat glands, salivary glands, mammary glands, nasolacrimal ducts. (For more information, choose “Ectodermal Dysplasia” as your search term in the Rare Disease Database).

Hypo/oligodontia might also be associated to cleft lip and palate in certain syndromes and associated with mutations is several different genes (*MSX1, IRF6, LRP6*...).

A rare association was discovered linking tooth agenesis and susceptibility to colorectal cancer (*AXIN2* gene mutations).

Diagnosis

The diagnosis of hypo/oligodontia or anodontia may be confirmed by dental X-rays. Other signs might be associated such as smaller teeth, peg shape lateral incisors, conical teeth, taurodontic molars, and spaced dentition.

Genetic testing is available to identify mutations in 560 known and candidate genes involved in orodental diseases.

Standard Therapies

Treatment
Treatment of hypo/oligodontia or anodontia consists of artificial dentures. Artificial dentures are removable teeth that may aid in chewing and can improve appearance of the mouth. In case of oligodontia or according to the patient need, treatment might be started early. Removable prosthesis could be proposed for children who are 3-4 years old. These prostheses can be renewed as the child grows.

If only front teeth are missing in hypodontia or oligodontia, a flexible system allowing slight movement of a bridge can be created by bonding an acrylic tooth to the supporting structure (abutments) by means of three orthodontic wires. Permanent options to replace missing teeth include dental implants.

Therapeutic management of patients with hypo/oligodontia requires a multidisciplinary team including the pediatric dentist, orthodontist, a specialist in prosthodontics, and a maxillofacial surgeon.

Investigational Therapies

Information on current clinical trials is posted on the Internet at www.clinicaltrials.gov All studies receiving U.S. government funding, and some supported by private industry, are posted on this government web site.

For information about clinical trials being conducted at the NIH Clinical Center in Bethesda, MD, contact the NIH Patient Recruitment Office:

Tollfree: (800) 411-1222
TTY: (866) 411-1010
Email:

Some current clinical trials also are posted on the following page on the NORD website: https://rarediseases.org/for-patients-and-families/information-resources/info-clinical-trials-and-research-studies/

For information about clinical trials sponsored by private sources, contact: http://www.centerwatch.com/

For information about clinical trials conducted in Europe, contact:

https://www.clinicaltrialsregister.eu/

Supporting Organizations

- Genetic and Rare Diseases (GARD) Information Center
  PO Box 8126
  Gaithersburg, MD 20898-8126
  Phone: (301) 251-4925
  Toll-free: (888) 205-2311
  Website: http://rarediseases.info.nih.gov/GARD/
- NIH/National Institute of Dental and Craniofacial Research
  Building 31, Room 2C39
  31 Center Drive, MSC 2290
  Bethesda, MD 20892 USA
  Phone: (301) 496-4261
  Toll-free: (866) 232-4528
  Email:
  Website: http://www.nidcr.nih.gov/

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