

Rare Case Reports of Non Syndromic Hypodontia – Genes at Work

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Received February 13, 2014; Revised May 21, 2014; Accepted May 21, 2014

Abstract Agenesis of one or more permanent teeth is a common developmental dental anomaly in human beings. In the literature, many terms are used to describe missing teeth like oligodontia, anodontia, aplasia of teeth, congenitally missing teeth, absence of teeth, agenesis of teeth and lack of teeth. The etiology of missing teeth may be environmental factors like infection, trauma, drugs, chemotherapy or radiotherapy or may be genetic. The most often missing permanent teeth, excluding third molars, are the second premolars and the lateral incisors. Here we report two cases of hypodontia of permanent teeth which are familial and without the presence of any syndrome. We have also reviewed literature of similar cases published till date.

Keywords: hypodontia, familial, tooth agenesis

Cite This Article: Arati Paranjpe, Priyanka Sawant, Avinash Kshar, and Raghvendra Byakodi, "Rare Case Reports of Non Syndromic Hypodontia – Genes at Work." *Oral Surgery, Oral Medicine, Oral Radiology*, vol. 2, no. 2 (2014): 14-16. doi: 10.12691/oral-2-2-2.

1. Introduction

Hypodontia is the condition in which a person has missing teeth as a result of failure of the teeth to develop. It is the congenital absence of less than six teeth excluding third molars. Patients with six or more missing teeth are said to be having oligodontia; anodontia refers to complete absence of teeth. There are two types of hypodontia. Syndromic hypodontia refers to tooth agenesis in individuals who have an underlying recognizable clinical syndrome. Examples are Down syndrome, ectodermal dysplasia, Ehlers-Danlos syndrome, Rieger syndrome, Witkop syndrome, oral-facial-digital syndrome, Sturge-Weber syndrome, Turner syndrome. The non-syndromic or familial form is the one where tooth agenesis is the primary condition and is the most common reason for congenital absence of tooth [1].

The reduction in number of teeth is attributed to the reduction in the size of the jaw in human evolution and believed to be a continuing evolutionary trend. [2] The incidence of hypodontia ranged from 2.3 to 9.6%, excluding the third molars. [3] The most often missing permanent teeth, excluding third molars, are the second premolars and the lateral incisors. Agenesis of tooth has been attributed to various etiologic factors such as changes of the dental lamina formation, failure of tooth germ to develop at the optimal time, space limitation, systemic condition and genetic factors [4].

The aim of this paper is to document two cases of hypodontia involving missing permanent teeth in three generations as an isolated non-syndromic trait with a strong role of heredity.

1.1. Case Report 1

A 19 years old female patient reported to the department of Oral Medicine and Radiology with the chief complaint of spacing in the front region of the upper jaw. When questioned about similar presentation in the family, it was found that the patient's mother, younger brother and the maternal grandfather and many family members had spacings in their teeth. The patient's past medical and dental history were not significant. General examination did not suggest any syndrome present. Intraoral examination showed presence of retained deciduous right maxillary lateral incisor. The permanent maxillary lateral incisors were missing clinically. An orthopantomogram (OPG) was taken which confirmed retained deciduous right maxillary lateral incisor and missing maxillary permanent lateral incisors (Figure 1 A).

During next visit, patient's mother and younger brother were called for examination to confirm a familial pattern. The patient's younger brother aged 16 years on examination gave no significant past medical and dental history. On intraoral examination had mixed dentition which showed absence of all 4 permanent mandibular incisors, maxillary lateral incisors and all 4 maxillary premolars. Also showed presence of retained deciduous right maxillary lateral incisor same as his sister. An OPG showed agenesis of all clinically missing teeth (Figure 1 B).

Patient's mother aged 36 years on examination gave no significant past medical history. Intraoral examination showed missing mandibular central incisors and maxillary lateral incisors. Patient's dental history was positive with restorative and endodontic treatment for molars, patient

gave negative history for extractions. An OPG showed agenesis of mandibular central incisors and maxillary lateral incisors.



Figure 1. A. Clinical photograph of patient showing retained deciduous maxillary right lateral incisor, and Orthopantomogram of patient showing missing 12, 22. B. Clinical photograph of patient's brother, and, Orthopantomogram of patient's younger brother showing missing 12, 22, 14, 15, 24, 25, 31, 32, 41, 42

1.2. Case Report 2

Another 15 years old male patient with chief complaint of spacing in the front region of the jaw reported. The family history revealed many multiple missing teeth in patient's mother and younger brother. The patient's past medical and dental history were not significant. General examination did not suggest any syndrome present. Intraoral examination showed presence of retained deciduous maxillary lateral incisors bilaterally. All permanent lateral incisors were missing clinically. There was presence of ankyloglossia as was also seen in other case report. [2] An orthopantomogram (OPG) was taken which confirmed retained deciduous maxillary lateral incisors bilaterally and missing all permanent lateral incisors and maxillary third molars (Figure 2 A).

Patient's younger brother and mother gave non-contributory past medical and dental history. The patient's younger brother aged 12 years on intraoral examination had mixed dentition which showed absence of 4 permanent teeth namely all second premolars. An OPG showed agenesis of all permanent second premolars along with all third molars. All permanent second molars tooth buds were seen (Figure 2 B).



Figure 2. A. Clinical photograph of patient showing retained deciduous maxillary right and left lateral incisors, and Orthopantomogram of patient showing missing 12, 22, 32, 42. B. Clinical photograph of patient's brother and Orthopantomogram of patient's younger brother showing missing 15, 25, 35, 45

Patient's mother aged 40 years on clinical examination had retained deciduous mandibular right central incisor

and deciduous mandibular left second molar were seen. There was absence of 5 permanent teeth namely mandibular right central incisor, mandibular left second premolar, second molars except mandibular right second molar. An OPG showed agenesis of all suspected missing permanent teeth along with all third molars.

All the members of the family were investigated for any other anomaly, but no significant findings were noted. Hence a diagnosis of non-syndromic familial hypodontia was made. The patients were enrolled for orthodontic, pedodontic and prosthetic treatment for esthetic management.

2. Discussion

A tooth is said to be congenitally missing if it has not erupted in the oral cavity and is not visible in the radiograph. The term congenitally missing tooth is a misnomer, as permanent teeth which are most commonly missing are not present in the mouth at birth. Rather the term tooth agenesis is more informative because it also implies the underlying developmental defects [5].

There are a few proposed theories for the cause of agenesis of a tooth. The primary cause is heredity or familial distribution. A reduction in the dentition is regarded as nature's attempt to fit the shortened dental arches as an evolutionary trend. Finally, localized inflammation or infections in the jaw and disturbance of the endocrine system destroying the tooth buds [6].

As in our two cases missing teeth were seen in males and females in 3 generations it indicates an autosomal dominant pattern of inheritance (Figure 3). Heredity is seen to play a role as missing teeth are also found in relatives of those affected. The congenital absence of teeth is the result of one or more point mutations in a closely linked polygenic system. Most commonly transmitted in an autosomal dominant pattern with incomplete penetrance and variable expressivity [7].

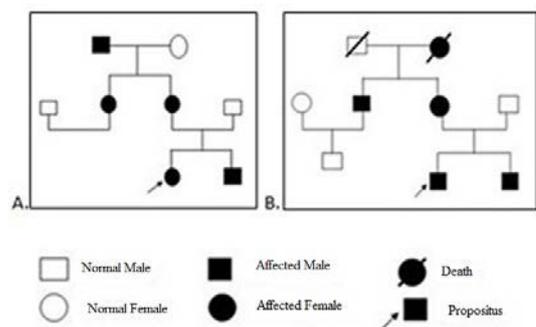


Figure 3. Pedigree of two families showing autosomal dominant inheritance pattern of non-syndromic familial hypodontia. A. Case 1 and B. Case 2

The recent developments in molecular genetics are revealing the roles of the homeobox genes in the control of the complex epithelial/mesenchymal interactions that occur during dental development [8]. Genes involved in dental development are the muscle-specific homeobox genes, PAX9, MSX1, MSX2, DLX, LHX and recently IRF6, TGFA, FGFR1 have been implicated. Also AXIN2 mutations, EDA, LTBP3 and WNT10A mutations have been associated with non-syndromic hypodontia [9,10,11,12,13].

The prevalence of missing lateral incisor is 2.1% in maxilla and is significantly lower in males than in females. In the present case report, all permanent lateral incisors of male patients were missing in case 1 and 2. Also maxillary lateral incisors were missing in female patient of case 1.

The prevalence of missing second premolars is 1.9%. In our cases, patient's younger brother is having agenesis of all the permanent second premolars in case 2. Maxillary second premolars were missing in patient's younger brother in case 1.

Table 1. shows review of literature only of those case reports showing familial hypodontia [6,14,15,16]

AUTHOR	YEAR	FAMILY MEMBER	MISSING TEETH	
Ranta R [14]	1985	Mother	765	567
		Son 1	765	567
		Son 2	765	567
SP Lyngstadaas et al [12]	1996	Father	5	5
		Mother	2	2
		Older Daughter	542	542
		Younger Daughter	5	5
Newman & Newman	1998	Mother		12
		Daughter 1		12
		Daughter 2		12
		Daughter 3	21	12
Ran Tao et al [16]	2006	Grand father	5432	2345
			5321	1235
		Paternal aunt	2	2
		Grand Son	542	245
			21	12

Hypodontia in young patients can cause esthetic, functional, and psychological problems. More so particularly if teeth of anterior region are involved. Treatment of hypodontia requires long term multidisciplinary management. Regular dental visits and genetic counseling are necessary. Orthodontic and prosthetic treatments are started at an early age to improve esthetics and function and to minimize any psychological problem. Dental implants can be used to support dentures, and can be placed after the growth period. With proper dental treatment patients can hope to have a functional and esthetic dentition.

Hypodontia has a polygenic multifactorial etiology. Studies have confirmed that environmental or epigenetic factors can modify phenotype expression. However, the

specific epigenetic factors involved and their interaction with genotype are poorly understood [7].

3. Conclusion

Any case of hypodontia should be evaluated for a familial pattern as heredity plays a strong role. Patients with hypodontia have functional problems as well as psychological distress which requires early diagnosis. Careful evaluation and multidisciplinary treatment planning of hypodontia should be made.

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