CASE REPORT

A Rare Incidence of Nonsyndromic Mandibular Incisor Agenesis in a Three-generation Family: Case Report and Literature Review

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Abstract

Hypodontia is an inherited condition involving the absence of one to six teeth. The permanent dentition is the most frequently affected; however, it may also affect the primary dentition. A congenitally missing tooth (CMT) is the most common dental abnormality, with the missing mandibular second premolar, maxillary lateral incisor, maxillary second premolar, and mandibular central incisor accounting for 90% of CMT in hypodontia studies. The etiology of CMT has been attributed to environmental and genetic contributing factors, with the latter having a strong influence. It may occur in isolation or in association with syndromes. Congenitally missing mandibular incisor is more common in the Asian population and females. Depending on the number and location of missing teeth, hypodontia may be a considerable issue for the clinician since it may impact occlusal balance, mastication, speech, and esthetics and often requires a multidisciplinary approach. Missing mandibular incisors are of particular interest to orthodontists because of the possibility of mandibular retrognathism, the potential for the development of malocclusion, and difficulty in achieving a balanced occlusion. This case report describes the skeletal and dental features of a nonsyndromic familial occurrence of missing mandibular incisors in three generations. A comprehensive literature search was also performed to review the familial cases with missing mandibular incisors.

Keywords: Congenitally missing teeth, Familial tooth agenesis, Hypodontia, Mandibular incisor.

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Introduction

Tooth agenesis is one of the most prevalent developmental disturbances of permanent dentition.[1,2] Hypodontia (OMIM #106600) is the congenital absence of one to six teeth with a population prevalence of 6.4%.[2–4] It is observed that mandibular second premolars are the most commonly missing teeth, followed by maxillary lateral, maxillary second premolars, mandibular central incisors, and mandibular lateral incisors.[5] There are ethnic variations reported in prevalence as well as the type of teeth affected. Prevalence is highest in Africa (13.4%), followed by Europe (7%) and Asia (6.3%).[6] Mandibular second premolars are most affected in the Caucasian population, whereas mandibular incisors are commonly involved in Asian Populations.[7–9] Females have a higher prevalence than males.[5] It could be attributed to their smaller jaws, which might interfere with tooth bud formation.[10]

Congenitally missing teeth (CMT) may occur as an isolated entity or a component of a syndrome. Also >60 syndromes have been known to be associated with this condition.[4,11] The etiology of tooth agenesis is often a genetic cause, with an autosomal dominant pattern of transmission, incomplete penetrance, and variable expressivity.[12] According to Graber, "It's the dental clinician's challenge to recognize the congenital absence of teeth and evaluate other family members for possible manifestations of this primary inheritable condition."[13] With just a few cases previously recorded, hereditary or familial transmission has been considered the main cause of mandibular incisor agenesis.[13–15] The other possible causes may include disturbances in mandibular symphysis development leading to congenital absence of lower incisor tooth bud or a manifestation of an evolutionary trend.[13,14] Various studies reported mandibular incisor agenesis in two-generation and among siblings.[13,16,17] However, only one incidence was reported in the literature with a missing mandibular incisor in a three-generation Japanese family.[18] This paper reviews the literature on nonsyndromic familial mandibular incisor agenesis cases and reports the condition in a three-generation family.

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Case Description

An 11-year-old boy of North Indian ethnicity and the first child of healthy nonconsanguineous parents presented to the orthodontic clinic with the chief complaint of spacing between the upper and

lower teeth. Medical history was noncontributory, and the patient's dental history was uneventful. In addition, there was no history of infection, trauma, or drug therapy throughout the mother's pregnancy. There was a history of normal delivery at term, and neonatal history was noncontributory. The family history revealed that both his father and grandfather have agenesis of permanent mandibular incisors and retained deciduous teeth.

The patient's height, weight, and build on general examination correlated with his chronological age. There was no delay in achieving the developmental milestones. History revealed mouth breathing habits, particularly during sleep. The extraoral features showed an apparently symmetrical face with potentially competent lips, a deep mentolabial sulcus, and a prominent chin. Intraoral examination revealed that the patient was in the late mixed dentition stage. The maxillary incisors were proclined with generalized spaces between them. The mandibular central incisors were missing clinically with an over-retained deciduous incisor. The molar was in half-cusp Class II relation bilaterally. There was a 9 mm overjet and a traumatic deep bite (100% overbite) with lower incisors impinging on the palatal surface (type 1 Akerly classification). The dental arches were symmetrical. The palate was deep, with an exaggerated curve of Spee in the mandibular arch. The frenal attachments were normal, with no soft tissue abnormalities. The oral hygiene was satisfactory except for proximal caries in the deciduous maxillary left second molar. The panoramic radiographic confirmed the congenital absence of the mandibular central incisors and all the third molar tooth buds. The lateral cephalogram showed enlarged adenoids, retrognathic mandible, steep mandibular plane, proclined upper incisors, prominent chin, and retrusive lips (Fig. 1).

The patient's 41-year-old father had a congenitally missing permanent mandibular central incisor with a retained deciduous mandibular incisor tooth that was mobile. The molar relation was Angle's Class I with proclined incisors. The skeletal base was Class I with a prominent chin button, deep mentolabial sulcus, and retrusive lips (Fig. 2). Likewise, the patient's 66-year-old grandfather had congenitally missing permanent mandibular central incisors and a mobile retained deciduous mandibular incisors. The molar relation was Angle's Class I bilaterally with age-related changes such as attrition of teeth and interdental spacing. The skeletal bases were in Angle's Class I relationship with a flat mandibular plane. The incisors were retroclined, and the lips were thin and retrusive (Fig. 3). Both were medically fit, and no contributing history or condition was present that was relevant to their missing permanent mandibular central incisors. The pedigree analysis revealed that the trait that is, congenitally missing mandibular incisors, was present in all three generations with the male-to-male transmission, essentially showing an autosomal dominant inheritance pattern. The developmental history and a thorough dysmorphic physical examination by a clinical geneticist did not reveal any other congenital deformity; therefore, a provisional diagnosis of a nonsyndromic condition was made in all three cases. Further, the family was not made to undergo additional genetic testing due to financial constraints.

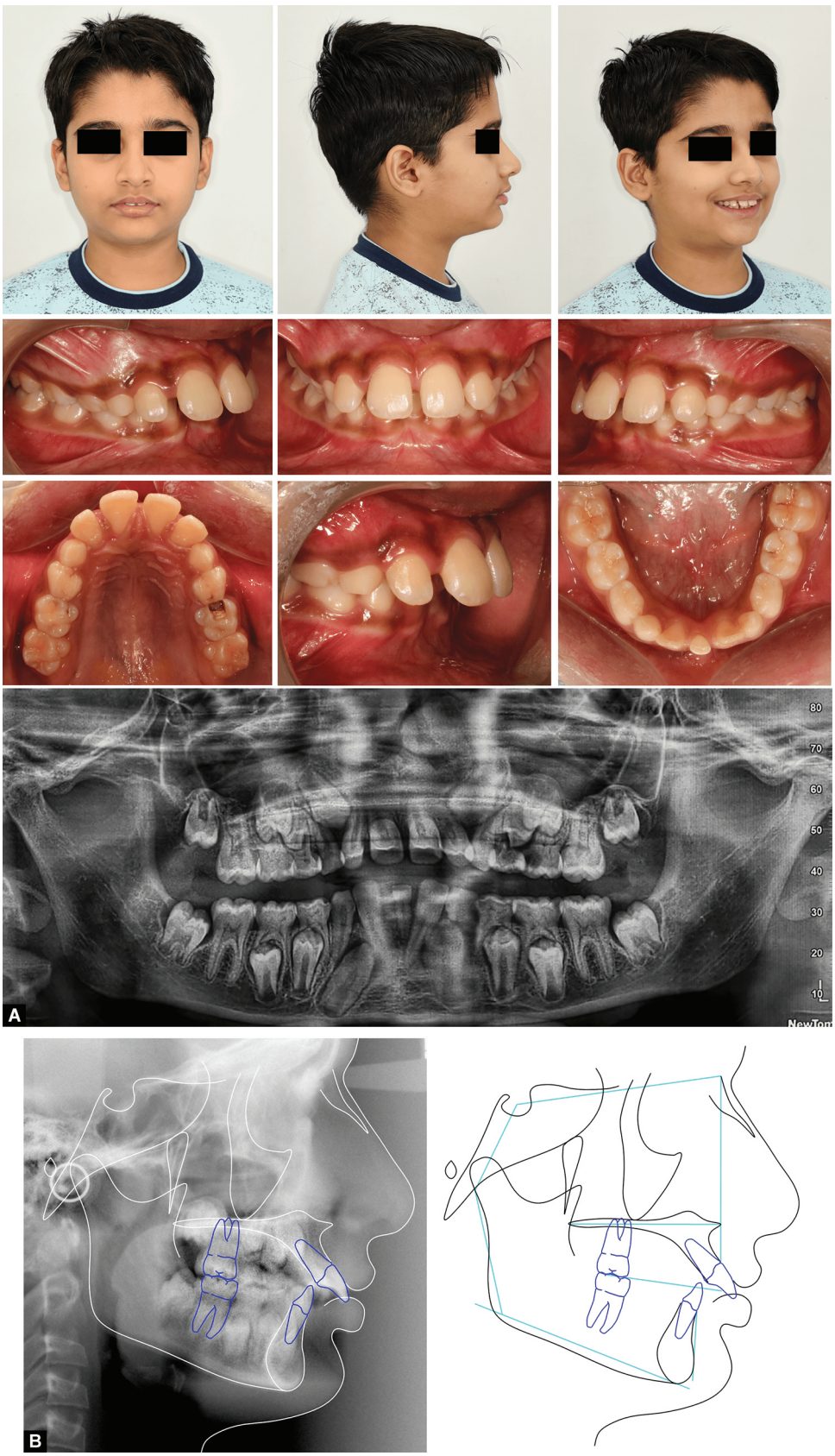
Literature Review

The literature search on familial cases of mandibular incisor agenesis was conducted using various databases (PubMed, Embase, Scopus, Web of Science, and Ovid MEDLINE) till March 2022 with no language or time restrictions. The search terms used in various databases were ("lower incisor" or "mandibular incisor" or "mandibular anterior" or "lower anterior") and (hypodontia or "missing" or "agenesis" or anodontia or oligodontia or absent) and (congenital or familial or genetic or hereditary) and ("nonsyndromic" or non-syndromic). Only articles with the familial occurrence of missing mandibular incisors were included in this study. In addition, articles in which patients had a history of extracted permanent mandibular incisors, impacted mandibular incisors, missing primary mandibular incisors, history of facial trauma, craniofacial anomalies, and syndromes were excluded. A search through various databases yielded a total of 292 studies. Out of these 292 articles, 115 articles were screened after removing duplicates. Based on titles and abstracts, 33 full-text articles were reviewed. Of these 33 articles, 29 had nonfamilial/generation, syndromic, and multiple missing teeth and did not meet the selection criteria. Lastly, four articles were considered after a full-text review (Flowchart 1).[13,16–18] The following data were extracted—author, year of publication, number and age of patients, gender, race/ethnicity, missing teeth, malocclusion, affected family members, and other findings (Table 1). The two authors (MS and KS) performed the study identification and data extraction and were reviewed by the senior authors (VS and RD).

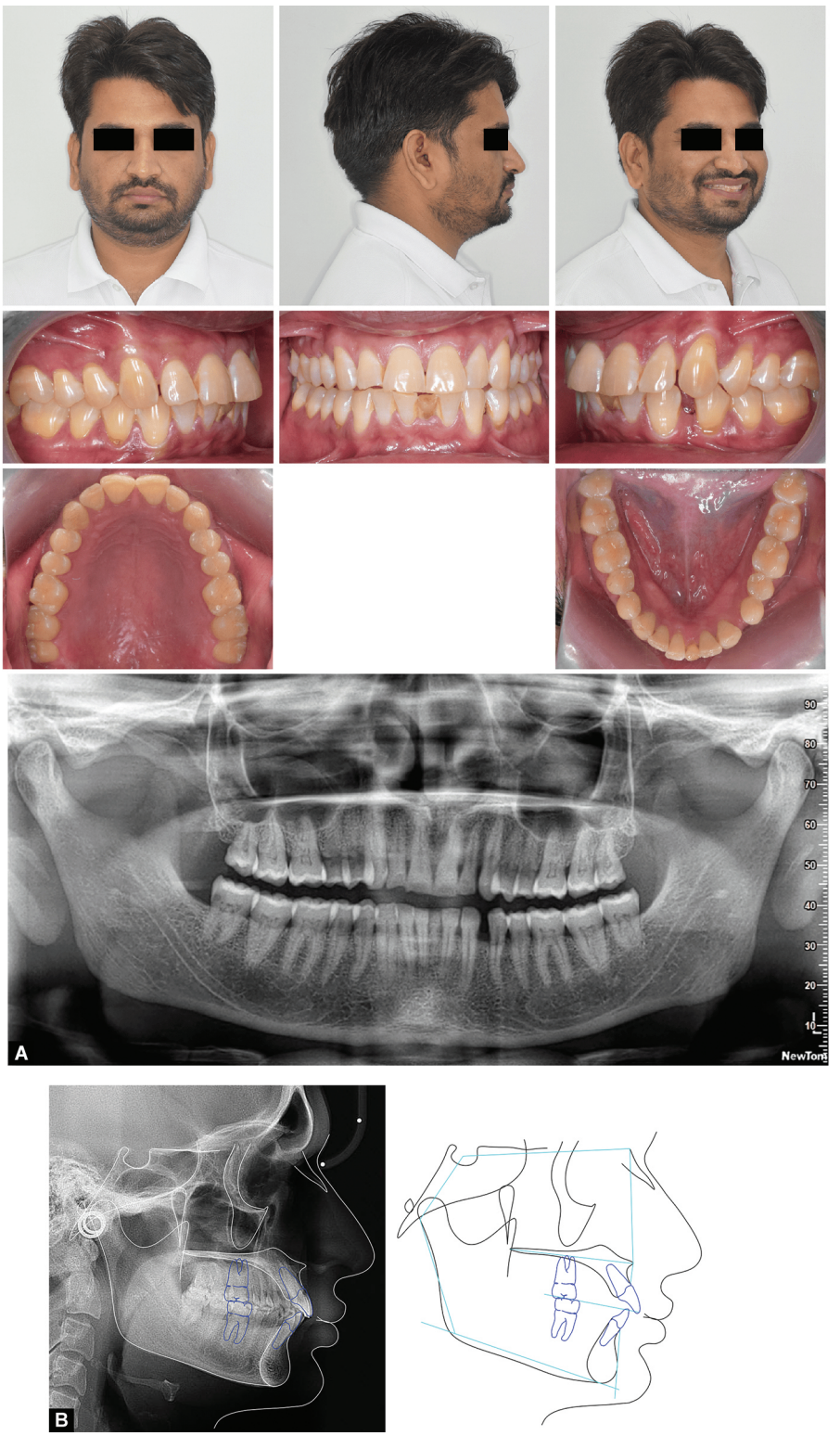
Miller et al. reported three generations of missing one mandibular incisor in a Japanese family. Based on pedigree analysis, autosomal dominant inheritance was suggested. The congenital absence of missing teeth was confirmed using an intraoral periapical radiograph.[18] Newman et al. reported a case of an Indian mother and her three daughters with congenitally missing mandibular incisors. All of them displayed a relatively balanced facial profile on extraoral assessment; however, the cephalometric study revealed the lower jaw to be retruded. Besides, one of the daughters had an Angle's Class III subdivision molar relationship, while the others had Angle's Class I molar relationships. The treatment of missing mandibular incisors by orthodontic space closure was described.[13] Frazier-Bowers et al. screened records of 700 people of Vietnamese descent in the age group of 5–49 years. A total of 20 patients were identified, comprising eight male and twelve female patients. A total of 16 patients had a familial history of at least one affected first-degree relative. Around 10 patients showed bilateral mandibular only one presented with missing maxillary third molars. The affected patients also showed morphological variations—12 had shovel-shaped incisors, and one presented with a fusion of primary teeth (72 and 73). Fifteen patients had a Class III occlusal relationship, possibly due to mesial migration of the mandibular posterior teeth consequent to incisor hypodontia. Pedigree analysis showed an autosomal dominant inheritance with incomplete penetrance. Based on the mutational analysis of *paired box 9 (PAX9)* and *msh homeobox 1 (MSX1)*, it was uncertain whether these genes caused mandibular incisor agenesis in this population.[16] Korkut et al. presented two cases (one male and one female) with the familial transmission of a bilaterally missing mandibular incisor. Father and siblings were also affected by the same condition. Additionally, the female patient presented with multiple congenitally missing teeth.[17]

Discussion

Congenitally missing teeth (CMT) is a dental disability affecting personal appearance, functional problems and overall quality of life.[19,20] Several explanations have been proposed to explain the cause of tooth agenesis. The most mesial tooth in each field are considered more genetically stable, but the teeth at the end of each field are less genetically stable and thus more likely to get affected.[21] Role of evolution has also been proposed, which

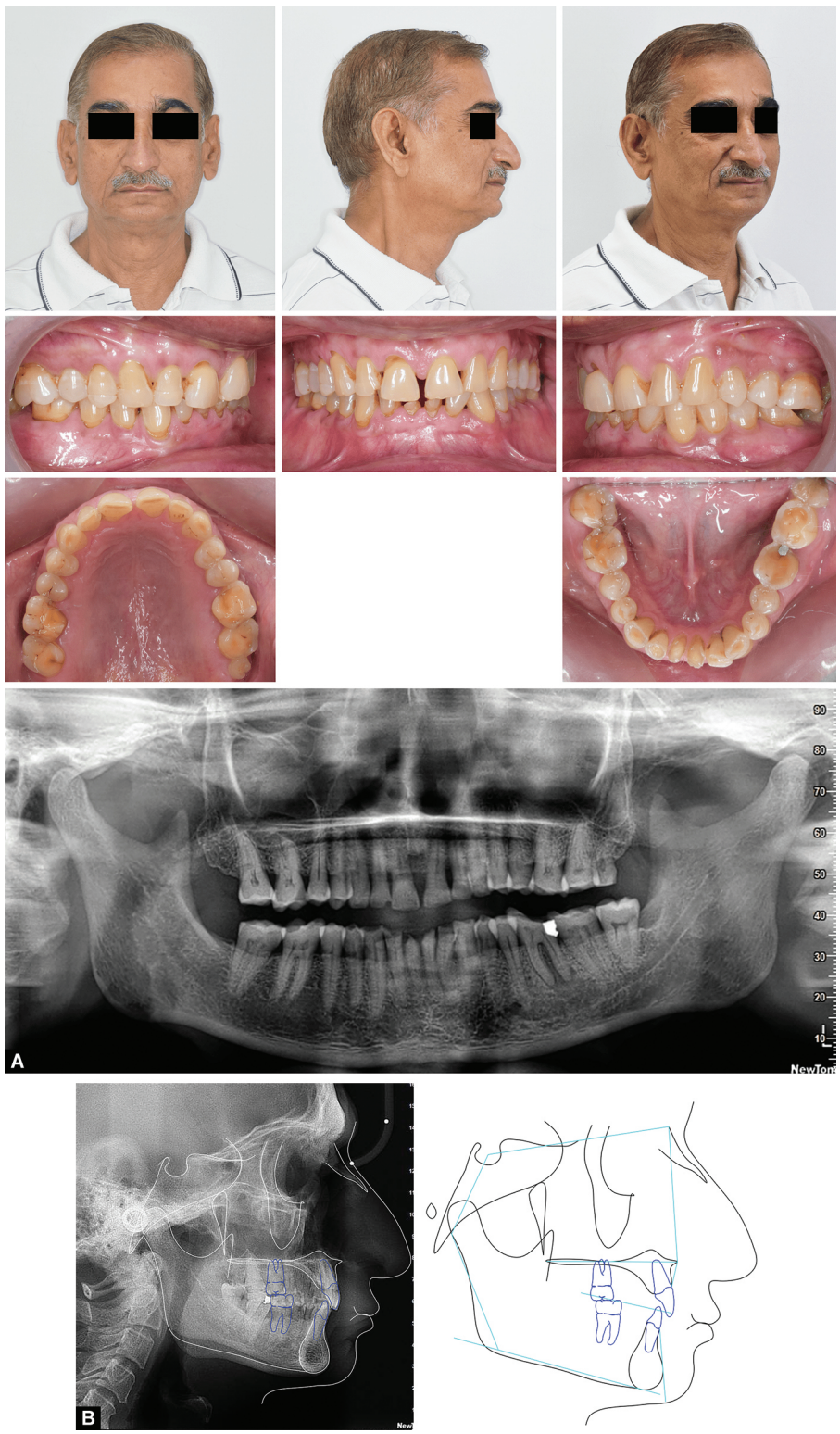


Figs 1A and B: (A) Extraoral and intraoral clinical photographs and panoramic radiograph of the patient (proband); (B) Cephalometric radiograph and tracing of the patient



Figs 2A and B: (A) Extraoral and intraoral clinical photographs and panoramic radiographs of the patient's father; (B) Cephalometric radiograph and tracing of the patient's father

states that the evolutionary process produces a steady decline in human dentition as each quadrant loses a tooth.[10,22] Apart from the genetic influence and evolutionary mechanism, environmental factors such as endocrine disorders, local trauma, and radiation have been implicated in the etiology of hypodontia.[3] Early odontogenesis is influenced by several overlapping molecular processes during the signal transduction between the epithelium and neural-crest-derived mesenchyme.[23,24] High levels of oxidative stress can affect the neural cells, disrupting these odontogenesis processes.[25] Children receiving radiation and chemotherapy have

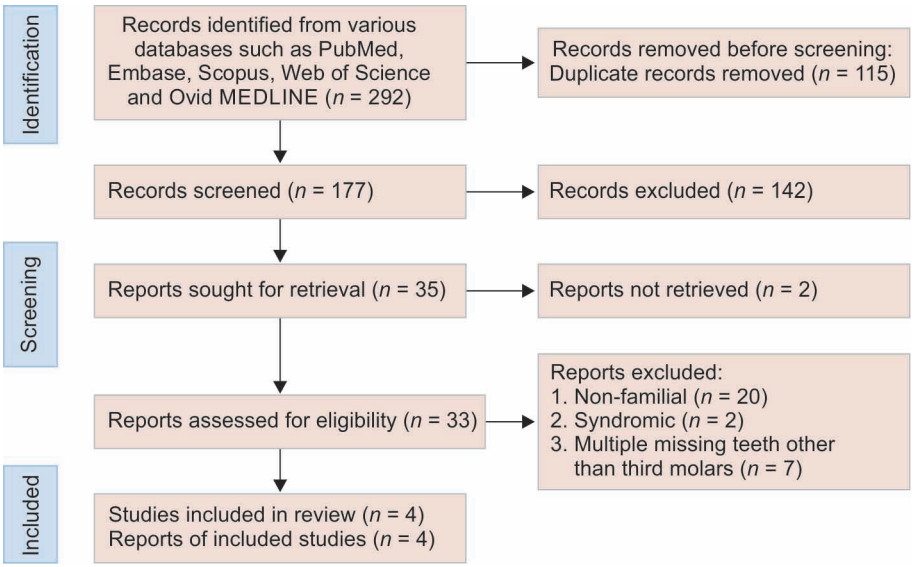


Figs 3A and B: (A) Extraoral and intraoral clinical photographs and panoramic radiographs of the patient's grandfather; (B) Cephalometric radiograph and tracing of the patient's grandfather

also been linked to the occurrence of hypodontia.[26] Additionally, thalidomide embryopathy (7.7%) has a higher prevalence than normal children (0.4%).[27,28]

Nonsyndromic tooth agenesis is one of the most common dental problems; however, it can also be associated with various syndromes, including van der Woude syndrome, ectodermal dysplasia, oromandibular limb hypogenesis syndromes and hypoglossia-hypodactyly or Hanhart's syndrome.[29,30] Selective tooth agenesis is known to be associated with variants of *PAX9, ectodysplasin A (EDA), MSX1, ectodysplasin A receptor (EDAR)*

Flowchart 1: Flow diagram illustrating the search process



associated death domain, wingless-type Mouse mammary tumor virus integration site family member 10A (WNT10A), bone morphogenetic protein 2 (BMP2), EDAR, axis inhibition protein 2 (AXIN2), DAN family BMP antagonist (GREM2) and gremlin 2.[7,27,29,31,32] Defects in MSX1 and PAX9 appear particularly sensitive to posterior teeth.[33] On the other hand, it has been demonstrated that autosomal-dominant *AXIN2* mutations can lead to a severe type of multiple-tooth agenesis. In contrast, EDA variants can cause hypo-hidrotic ectodermal dysplasia, and nonsyndromic tooth agenesis favors the anterior dentition.[3,34] During the bell stage of lower incisor formation, *BMP2* is expressed, and single nucleotide mutations in the gene are thought to enhance the chance of mandibular incisor agenesis.[7] As a result, the varying sensitivity of distinct dentition types could be influenced by the variable expression of associated genes, indicating differing roles for these genes during normal tooth development.

In Chinese individuals with nonsyndromic hypodontia, Wang et al. discovered two unique missense variants in the *PAX9* gene. Both mutations *(G6R* and *S43K)* are found in PAX9's paired domain and are likely to disrupt amino acid residues that are highly conserved. *G6R* mutations were linked to missing mandibular incisors, while *S43K* mutations were related to multiple missing teeth.[35] Yamaguchi et al. determined the genetic causes of selective mandibular incisor agenesis (SMIA), which is common in Asian populations. Exome analysis revealed variations in the genes *EDA, AXIN2, PAX9, BMP2, WNT10A,* and *EDAR* linked to tooth agenesis. In addition, the lately discovered genes such as family with sequence similarity 65 member A, nuclear factor of activated T-cells 3, and cadherin-related 23 gene have been linked to SMIA.[7]

Mandibular incisor agenesis significantly impacts the growth and shape of the mandibular symphysis. The constant growth of the mandibular symphysis, which results in vertical and horizontal development, is facilitated by tooth eruption.[36] A disruption in tongue-lip pressure balance and a loss of lingual support are also outcomes of agenesis of both mandibular incisors, further leading to mandibular retrognathia associated with a severe anterior deep bite.[14] Noncoinciding dental midline and often broad spacing in the anterior area contribute to an unattractive appearance. In different studies, the association between tooth agenesis and craniofacial morphology has generated conflicting results. However, sagittal skeletal relationships are minimally affected by missing mandibular incisors.[37] Disturbances in tooth morphology and size, hypoplastic enamel, delayed eruption, prolonged retention of primary teeth, tooth impaction or eruption, and transposed teeth due to migration abnormalities are often associated with dental malformations linked with hypodontia.[11]

Our report describes a rare familial occurrence of mandibular incisor agenesis in three generations of people with intact retained deciduous incisors. There was no syndromic relationship in the clinical evaluation of the patient and their family members. However, the importance of genome sequencing in detecting any abnormalities cannot be overlooked. In such cases, genome sequencing aims to detect any *AXIN2* gene-like variations linked to intestinal polyposis and colorectal cancer.[7] The proband patient showed the features of mandibular retrognathia. However, the facial balance in the father and grandfather revealed that the mandibular retrognathia in the proband patient could be due to environmental causes such as increased resistance in nasal breathing leading to chronic mouth breathing.[38] The interception of habit followed by unlocking the mandible is the first line of treatment in such patients. Calculating the Bolton ratio and virtual setup may help orthodontic treatment planning and predict future arch coordination.[39] If orthodontic space reopening is performed, a temporary removable partial denture may be advised to serve the purpose of retainer and space maintainer until a definitive prosthesis is planned. The congenital absence of mandibular incisors can result in atrophy of the anterior alveolar bone ridge, which could be disadvantageous to placing an endosseous prosthetic implant.[40] For this reason, orthodontic space opening for prosthetic placement is avoided during the mixed dentition stage. Treatment planning should be based on the patient's age, facial morphology, the amount of molar and incisor correction required, alveolar bone status, and the patient's desire.

Conclusion

A familial case of congenitally missing mandibular incisors is a sporadic condition. The cause of nonsyndromic tooth agenesis

Table 1: Characteristics of cases reported in the literature with congenitally missing mandibular incisors in two and three-generations family

Author (Year)	*Generations affected*	*Family members affected*	*Race*	*Age*	*Missing teeth*	*Other findings*
Miller et al. (1941)[18]	Three generations	Grandmother, mother and one son and daughter	Japanese	Not known	Single mandibular lateral incisor in all the three generations	Not known
Newman et al. (1998)[13]	Two generations	Mother and three daughters	Indian	9 years (daughter 1)	Two mandibular incisors	Third molars absent
				10 years (daughter 2)	Mandibular left central incisor	–
				12 years (daughter 3)	Mandibular left incisor	Third molars absent
				26 years (mother)	Mandibular left incisor	–
Frazier-Bowers et al. (2003)[16]	Eleven families (16 out of 20 patients had at least one first degree relative affected)	Variable	Vietnamese	Age ranging from 5 to 32 years	Around 10 patients had bilateral mandibular incisor missing. Remaining 10 patients had single incisor missing	Third molar absent in one patient. Class III molar relation in most of the patients
Korkut et al. (2016)[17]	Two generations	Daughter, siblings and father	Not reported	9 years (daughter–proband)	Bilateral mandibular central incisors	Premature birth missing second premolars and molars and upper first molar
				Not reported (siblings)	Bilateral mandibular central incisors	–
				Not reported (father)	Bilateral mandibular central incisors	–
	Two generations	Son and father	Not reported	9 years (son–proband)	Bilateral mandibular central incisors	–
				Not reported (father)	Mandibular central incisors	–
Current study	Three generations	One family (grandfather, father, and son)	Indian	11 years (son–proband)	Bilateral mandibular central incisor	Retained deciduous mandibular incisor and Class II skeletal base
				41 years (father)	Mandibular central incisor	Retained deciduous mandibular incisor
				66 years (grandfather)	Bilateral mandibular central incisor	Retained deciduous mandibular incisors

is multifactorial but most commonly due to genetic variation; however, the specific genes responsible for mandibular incisor agenesis have not been identified. A prompt diagnosis based on history, clinical examination, radiographic evaluation, and the patient's realistic expectations should be the foundation for treatment planning. Genetic testing may be warranted in cases showing familial tooth agenesis to exclude any syndromic association or predict risk for disease such as adulthood neoplasms.

Ethical Statement

Informed written consent was obtained from the patients and guardians to publish their photographs and radiographs.

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References

1. Kirac D, Eraydin F, Avcilar T, et al. Effects of PAX9 and MSX1 gene variants to hypodontia, tooth size and the type of congenitally missing teeth. Cell Mol Biol (Noisy-le-grand) 2016;62(13):78–84. DOI: 10.14715/cmb/2016.62.13.14
2. Matalova E, Fleischmannova J, Sharpe PT, et al. Tooth agenesis: from molecular genetics to molecular dentistry. J Dent Res 2008;87(7): 617–623. DOI: 10.1177/154405910808700715
3. De Coster PJ, Marks LA, Martens LC, et al. Dental agenesis: genetic and clinical perspectives. J Oral Pathol Med 2009;38(1):1–17. DOI: 10.1111/j.1600-0714.2008.00699.x

4. Online Mendelian Inheritance in Man, OMIM®. Johns Hopkins University, Baltimore, MD. MIM Number: #106600: last edited 13/06/2022:https://omim.org/
5. Polder BJ, Van't Hof MA, Van der Linden FP, et al. A meta-analysis of the prevalence of dental agenesis of permanent teeth. Community Dent Oral Epidemiol 2004;32(3):217–226. DOI: 10.1111/j.1600-0528.2004.00158.x
6. Khalaf K, Miskelly J, Voge E, et al. Prevalence of hypodontia and associated factors: a systematic review and meta-analysis. J Orthod 2014;41(4):299–316. DOI: 10.1179/1465313314Y.0000000116
7. Yamaguchi T, Hosomichi K, Yano K, et al. Comprehensive genetic exploration of selective tooth agenesis of mandibular incisors by exome sequencing. Hum Genome Var 2017;4:17005. DOI: 10.1038/hgv.2017.5
8. Zhang R, Bai Y, Li S. Use of Forsus fatigue-resistant device in a patient with Class I malocclusion and mandibular incisor agenesis. Am J Orthod Dentofacial Orthop 2014;145(6):817–827. DOI: 10.1016/j.ajodo.2013.08.021
9. Endo T, Yoshino S, Ozoe R, et al. Association of advanced hypodontia and craniofacial morphology in Japanese orthodontic patients. Odontology 2004;92(1):48–53. DOI: 10.1007/s10266-004-0034-5
10. Rakhshan V, Rakhshan H. Meta-analysis and systematic review of the number of non-syndromic congenitally missing permanent teeth per affected individual and its influencing factors. Eur J Orthod 2016;38(2):170–177. DOI: 10.1093/ejo/cjv008
11. Rakhshan V. Congenitally missing teeth (hypodontia): a review of the literature concerning the etiology, prevalence, risk factors, patterns and treatment. Dent Res J 2015;12(1):1–13. DOI: 10.4103/1735-3327.150286
12. Pirinen S, Kentala A, Nieminen P, et al. Recessively inherited lower incisor hypodontia. J Med Genet 2001;38(8):551–556. DOI: 10.1136/jmg.38.8.551
13. Newman GV, Newman RA. Report of four familial cases with congenitally missing mandibular incisors. Am J Orthod Dentofacial Orthop 1998;114(2):195–207. DOI: 10.1053/od.1998.v114.a87015
14. Endo T, Ozoe R, Kojima K, et al. Congenitally missing mandibular incisors and mandibular symphysis morphology. Angle Orthod 2007;77(6):1079–1084. DOI: 10.2319/020106-37.1
15. Goldenberg M, Das P, Messersmith M, et al. Clinical, radiographic, and genetic evaluation of a novel form of autosomal-dominant oligodontia. J Dent Res 2000;79(7):1469–1475. DOI: 10.1177/00220345000790070701
16. Frazier-Bowers SA, Pham KY, Le EV, et al. A unique form of hypodontia seen in Vietnamese patients: clinical and molecular analysis. J Med Genet 2003;40(6):79e. DOI: 10.1136/jmg.40.6.e79
17. Korkut E, Gezgin O, Turkoglu S, et al. Bilateral agenesis of permanent mandibular central incisors: two familial case reports. Dent Adv Res 2016;1:105. DOI: 10.29011/2574-7347.100005
18. Miller MA. An inherited dental anomaly in a Japanese family. J Hered 1941;32(9):313–314. DOI: 10.1093/oxfordjournals.jhered.a105074
19. Batista MJ, Rihs LB, Sousa Mda L. Risk indicators for tooth loss in adult workers. Braz Oral Res 2012;26(5):390–396. DOI: 10.1590/s1806-83242012000500003
20. Kaur P, Singh S, Mathur A, et al. Impact of dental disorders and its influence on self esteem levels among adolescents. J Clin Diagn Res 2017;11(4):ZC05–ZC08. DOI: 10.7860/JCDR/2017/23362.9515
21. Townsend G, Harris EF, Lesot H, et al. Morphogenetic fields within the human dentition: A new, clinically relevant synthesis of an old concept. Arch Oral Biol 2009;54(Suppl 1):S34–S44. DOI: 10.1016/j.archoralbio.2008.06.011
22. Vastardis H. The genetics of human tooth agenesis: New discoveries for understanding dental anomalies. Am J Orthod Dentofacial Orthop 2000;117(6):650–656.
23. Thesleff I, Nieminen P. Tooth morphogenesis and cell differentiation. Curr Opin Cell Biol 1996;8(6):844–850. DOI: 10.1016/s0955-0674(96)80086-x
24. Thesleff I, Vaahtokari A, Vainio S, et al. Molecular mechanisms of cell and tissue interactions during early tooth development. Anat Rec 1996;245(2):151–1561. DOI: 10.1002/(SICI)1097-0185(199606)245:2<151::AID-AR4>3.0.CO;2-#
25. Fitriasari S, Trainor PA. Diabetes, oxidative stress, and dna damage modulate cranial neural crest cell development and the phenotype variability of craniofacial disorders. Front Cell Dev Biol 2021;9:644410. DOI: 10.3389/fcell.2021.644410
26. Kılınç G, Bulut G, Ertuğrul F, et al. Long-term Dental Anomalies after Pediatric Cancer Treatment in Children. Turk J Haematol 2019;36(3):155–161. DOI: 10.4274/tjh.galenos.2018.2018.0248
27. Brook AH. Multilevel complex interactions between genetic, epigenetic and environmental factors in the aetiology of anomalies of dental development. Arch Oral Biol 2009;54(Suppl 1):S3–17. DOI: 10.1016/j.archoralbio.2009.09.005
28. Gilbert-Barness E. Teratogenic causes of malformations. Ann Clin Lab Sci 2010;40(2):99–114.
29. Kapadia H, Mues G, D'Souza R. Genes affecting tooth morphogenesis. Orthod Craniofac Res 2007;10(4):237–244. DOI: 10.1111/j.1601-6343.2007.00407.x
30. Turri de Castro Ribeiro T, Doneux Van der Laan H, Massaro C, et al. Orthodontic treatment of mandibular incisor agenesis with Herbst appliance in a patient with Hanhart syndrome: a 12-year follow-up. Am J Orthod Dentofacial Orthop 2022;161(6):866–877. DOI: 10.1016/j.ajodo.2021.01.035
31. Ye X, Attaie AB. Genetic basis of nonsyndromic and syndromic tooth agenesis. J Pediatr Genet 2016;5(4):198–208. DOI: 10.1055/s-0036-1592421
32. Pan Y, Lu T, Peng L, Zeng Q, et al. Functional analysis of ectodysplasin-a mutations in X-linked nonsyndromic hypodontia and possible involvement of X-chromosome inactivation. Stem Cells Int 2021;2021:e7653013. DOI: 10.1155/2021/7653013
33. Tallón-Walton V, Manzanares-Céspedes MC, Carvalho-Lobato P, et al. Exclusion of PAX9 and MSX1 mutation in six families affected by tooth agenesis. A genetic study and literature review. Med Oral Patol Oral Cir Bucal 2014;19(3):e248. DOI: 10.4317/medoral.19173
34. Pääkkönen K, Cambiaghi S, Novelli G, et al. The mutation spectrum of the EDA gene in X-linked anhidrotic ectodermal dysplasia. Hum Mutat 2001;17(4):349. DOI: 10.1002/humu.33
35. Wang J, Sun K, Shen Y, et al. DNA methylation is critical for tooth agenesis: implications for sporadic non-syndromic anodontia and hypodontia. Sci Rep 2016;6:19162. DOI: 10.1038/srep19162
36. Buschang PH, Julien K, Sachdeva R, et al. Childhood and pubertal growth changes of the human symphysis. Angle Orthod 1992;62(3):203–210. DOI: 10.1043/0003-3219(1992)062<0203:CAPGCO>2.0.CO;2
37. Chen DD, Cheng JH, Hsu CS. Relationship between craniofacial morphology and congenitally missing mandibular incisors. J Dent Sci 2022;17(2):928–934. DOI: 10.1016/j.jds.2021.12.009
38. Zhao Z, Zheng L, Huang X, et al. Effects of mouth breathing on facial skeletal development in children: a systematic review and meta-analysis. BMC Oral Health 2021;21(1):108. DOI: 10.1186/s12903-021-01458-7
39. Aulakh R. The anterior ratio: the missing link between orthodontics and aesthetic dentistry. Case Rep Dent 2013;2013:470637. DOI: 10.1155/2013/470637
40. Kang HG, Huh YH, Park CJ, et al. Rehabilitation of a patient with non-syndromic partial oligodontia. J Adv Prosthodont 2016;8(3):241–250.