Journal of Dental Sciences (2018) 13, 60—67

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jds.com

Original Article

Concomitant hypo-hyperdontia: A rare entity

Yin-Lin Wang [a,b,c], Hsing-Han Pan [a,b], Hsiao-Hua Chang [a,b,c], Guay-Fen Huang [a,b,c*]

[a] Department of Dentistry, School of Dentistry National Taiwan University, No. 1, Changde St., Taipei City, 10048, Taiwan
[b] Department of Pediatric Dentistry, National Taiwan University Children's Hospital, No. 8, Zhongshan S. Rd., Taipei City, 10041, Taiwan
[c] Graduate Institute of Clinical Dentistry, School of Dentistry National Taiwan University, No. 1, Changde St., Taipei City, 10048, Taiwan

Received 23 December 2017
Available online 13 February 2018

KEYWORDS
Tooth agenesis;
Supernumerary;
Numeric anomaly;
Premaxillary

Abstract *Background/purpose:* Concomitant hypo-hyperdontia (CHH) is a rare numeric dental anomaly characterized by congenital missing teeth and supernumerary teeth occurring in the same individual. Due to its rarity and sporadicity, the causes of CHH have been completely unknown. Detailed characterization and presentation of more CHH cases not only strengthen clinical diagnosis and treatment for the patients but facilitate the search for etiological factors of the disorder.
Materials and methods: From a pedodontic patient population, 21 CHH subjects, with a mean age of 6 years 10 months, were identified and characterized. Dental records and radiographs were scrutinized and analyzed for the distribution and frequencies of involved teeth and concurrent dental anomalies. Through further literature review, 59 CHH cases with supernumeraries in the premaxillary region were retrieved for comparative analyses.
Results: The boys were affected twice as often as the girls. While most cases were unrelated and sporadic, two sisters and a pair of identical twins from two unrelated families were presented. Of all cases, only one was of syndromic CHH carrying Duchenne muscular dystrophy. Bimaxillay CHH, with anomalies involving two jaws, occurred more than 4 times as often as maxillary CHH. While all supernumeraries were found in premaxillary region, hypodontia frequently involved lateral incisors and premolars of both jaws.
Conclusion: As genetic contribution to CHH is strongly suggested by its familial occurrence and syndromic cases, environmental factors seem to play certain roles in modifying disease

* Corresponding author. Department of Dentistry, School of Dentistry, National Taiwan University, No. 1, Changde St., Taipei City 10048, Taiwan.
E-mail address: 000841@ntuh.gov.tw (G.-F. Huang).

https://doi.org/10.1016/j.jds.2018.01.001

phenotypes. Judicious use of radiographs during early mixed dentition stage enhances clinical diagnosis and treatment of CHH.

Introduction

Tooth development requires intricate genetic and molecular regulations to establish accurate tooth number and precise location, size, morphology, and composition of each tooth. Disturbances during early tooth development can lead to anomalies of tooth number, namely congenital missing teeth or supernumerary teeth.[1,2] While "Hypodontia" has been used as a generic term to describe the condition of developmental tooth absence, "hyperdontia" refers to the presence of extra teeth to a normal dentition. These two conditions are considered as the opposite extremes in the development of a dentition. Paradoxically, hypodontia and hyperdontia can occur in the same individual, and the condition has been described as "concomitant hypodontia and hyperdontia" by Camilleri[3] or simply "concomitant hypo-hyperdontia," coined by Gibson.[4]

Concomitant hypo-hyperdontia (CHH) has been regarded as a rare mixed numeric anomaly of dentitions with a prevalence ranging from 0.002% to 0.7%.[5] In 1979, Gibson characterized and presented 20 patients with CHH, which has been the largest case study to date.[4] He classified this condition into premaxillary, maxillary, mandibular, and bimaxillary subdivisions, based upon the distribution of anomalies. While maxillary and mandibular CHHs have both missing and supernumerary teeth within one of respective jaws, bimaxillary CHH affects two jaws. Premaxillary CHH refers to a particular condition in which the anomalies occur in the upper incisor (premaxillary) region, although the hypodontia can sometimes extend beyond the premaxilla. Furthermore, CHH has also been divided into syndromic and non-syndromic variants, since this numeric abnormality was observed in patients with defined congenital anomalies or syndromes.[5,6]

Due to the rarity and sporadicity of the disease, the etiology of CHH has been completely unknown. Despite that genetic contribution, environmental influence, and a combination of both have been proposed for explanation,[5–7] detailed characterization of more cases are imperative to test these hypotheses and search for etiological factors of CHH. Therefore, the aim of this study was to characterize CHH patients identified from our clinic and retrieve specific cases from the literature for analyses, with an attempt to search for the etiology of this numeric dental anomaly.

Materials and methods

Selection of CHH patients

This study selected 21 subjects with CHH from a specific pedodontic population of ~300 patients visiting Department of Pediatric Dentistry at National Taiwan University Children's Hospital from 2009 to 2017 and undergoing surgical removal of premaxillary supernumeraries. The patients' basic information, including age and gender, and general health were carefully recorded during clinical examination. The presence and absence of teeth and tooth morphology were scrutinized through reviewing panoramic radiograph of all cases and with available cone-beam computed tomography (CBCT) of some cases. Hyperdontia was registered when at least one supernumerary was detected with radiograph and later confirmed during surgical removal. Hypodontia was assigned when congenital absence of a tooth and its germ, excluding third molars, was evidently present and consensually diagnosed by three pediatric dentists. Parents as well as available siblings were interviewed and sometimes clinically examined to obtain a family history of potential dental anomalies, particularly numerical aberrations.

Retrieval of premaxillary CHH cases from English literature

A comprehensive search for reported CHH cases in English literature was conducted by querying PubMed, Medline, Embase, and Google database. The searching keywords

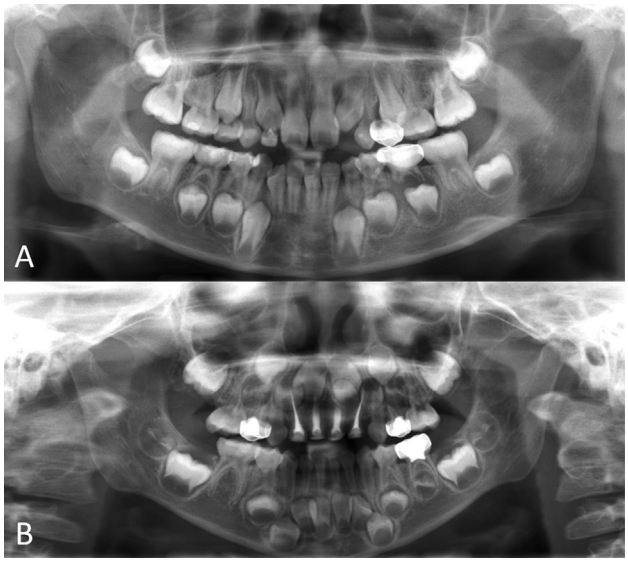

Figure 1 Panoramic radiographs of two sisters with CHH. ***A:*** The elder sister (Case 14) had an inverted supernumerary in the apical area of tooth number 9 and absent tooth germs of all upper premolars (tooth numbers 4, 5, 12, 13). Bilateral maxillary permanent canines were ectopically erupting to a more distal position. ***B:*** The younger sister (Case 15) had an inverted supernumerary around developing crown of tooth number 9 and 2 missing tooth germs (tooth numbers 4, 29).

included "concomitant," "hypo-hyperdontia," "hypo-hyperdontia," "hypodontia," "oligodontia," "tooth agenesis," "missing teeth," "hyperdontia," "supernumerary teeth," and their various combinations. Case studies, case series, and case reports with descriptive characterization of CHH patients were included. Studies with only epidemiological and statistical data but no individual specification of patients were excluded. Overall, 7 case studies/series and 45 case reports from January 1967 to October 2017 were included, and a total of 109 CHH cases were carefully reviewed. Subsequently, cases whose supernumeraries occurred at upper incisor (premaxillary) area, without regard to the distribution of missing teeth, were of our interest and particularly retrieved for further analyses. From 4 case series[4,5,7,8] and 26 reports,[3,9–33] 59 "premaxillary hypo-hyperdontia" cases were identified and scrutinized. Whenever available, the patients' age, gender, medical condition, and the distribution and frequencies of involved teeth (supernumeraries and missing teeth) were recorded, compiled, and analyzed.

Results

From a pedodontic patient population in Taiwan, 21 cases of concomitant hypo-hyperdontia (CHH) were identified, consisting of 14 boys and 7 girls with a gender ratio of 2:1 in favor of males. The mean age of diagnosis was 6 years 10 months with a range from 4 years 3 months—9 years 3 months. While most cases (17 out of 21) were unrelated and sporadic, without contributory family history, there were 2 siblings (Case 14, 15) (Fig. 1) and a pair of identical twins (Case 16, 17) (Fig. 2). All subjects were generally healthy, except that case 21 was diagnosed with Duchenne muscular dystrophy (Fig. 3). The distribution and frequencies of involved teeth as well as other concurrent dental anomalies were summarized in Table 1.

While 15 cases (71%) had only one supernumerary tooth, the other 6 (29%) had two or more, giving a total of 28 supernumeraries. All these teeth were present at premaxillary area, between right and left upper lateral incisors, with 17 of them being mesiodens. Lateral incisors were absent in 10 cases (48%), and premolars in the rest (52%), with a total of 40 missing teeth. Noticeably, primary teeth were found absent in 2 cases (Case 3, 5). In 17 cases (81%) the numerical anomalies involved both jaws, namely "bimaxillary hypo-hyperdontia," and in the other 4 cases (19%) only maxilla, maxillary hypo-hyperdontia. Fusion of primary incisors, premolar central cusps, and molar taurodontism were also found in some cases, in addition to the numeric anomalies.

Searching for CHH cases with premaxillary involvement in the English literature, we identified four case studies and 26 case reports involving 59 patients reported to have congenital missing teeth associated with premaxillary supernumeraries. Of these cases, 34 (58%) were male and the remaining (42%) female, with a male bias of 1.36 to 1. Excluding 6 cases with no specification of patients' age,[8,10] the mean age of reported patients was 10.25 years. While the majority of cases were reported to be non-syndromic, six cases were of other genetic disorders or congenital abnormalities.[14,16,20,22,29] Familial occurrence was reported in 2 case reports, one of which presented a pair of identical twin boys[25] and the other characterized dental anomalies of two siblings with Ellis—van Creveld syndrome.[20] Table 2 summarized the descriptive analysis of the 59 reported cases.

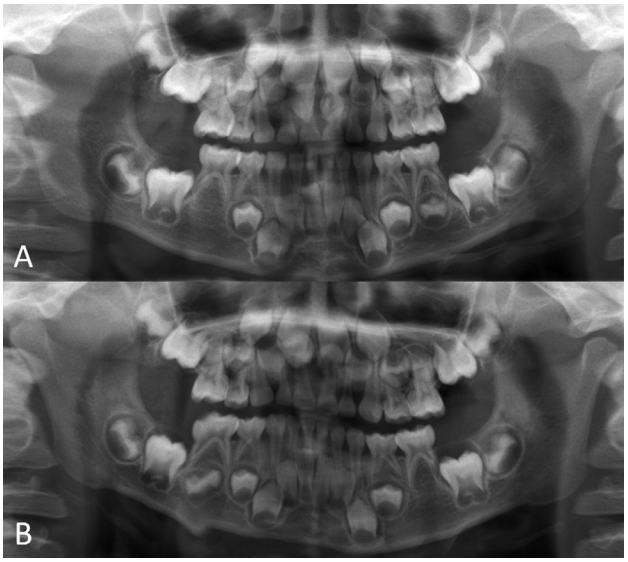

Figure 2 Panoramic radiographs of a pair of identical twins with CHH. ***A:*** One twin brother (Case 16) had 3 supernumeraries in the upper central incisor region. While the tooth germ of tooth number 20 was evident, that of tooth number 29 was not observed. Tooth germs of all third molars were not present either. ***B:*** The other twin brother (Case 17) had 2 supernumeraries in similar premaxillary region and absent tooth germ of tooth number 20. Tooth germs of all third molars were not present either.

While one supernumerary tooth was present in 47 cases (80%), two or more extra teeth were found in the other 12 (20%), giving a total of 73 supernumeraries. In 19 cases (32%) the missing teeth were only incisors, primarily

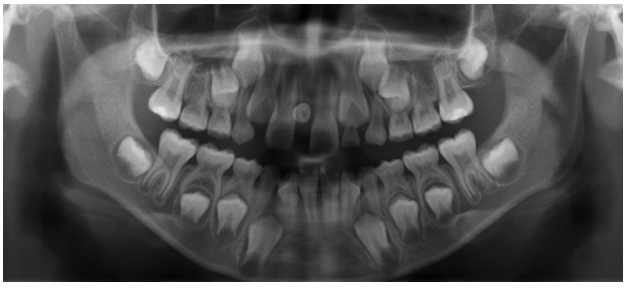

Figure 3 Panoramic radiograph of a CHH patient with Duchenne muscular dystrophy. Case 21 was an 8-year-old boy diagnosed with Duchenne muscular dystrophy at an early age. The radiograph revealed a horizontally-impacted mesiodens, causing a diastema between upper central incisors. Tooth germs of bilateral maxillary second bicuspids (tooth numbers 4, 13) were not observed, although they should be detectable at patient's age. An elongated root trunk with enlarged pulp chamber (taurodontism) was evident of all permanent first molars.

Table 1 Distribution of congenital missing teeth and supernumerary teeth in patients of concomitant hypo-hyperdontia (CHH). The symbles (* & #) indicate the sibilings of the same family. "§" indicates the patient with genetic disorder.

Case no.	Sex	Age	Hyperdontia (ISO System)	Hypodontia (ISO System)	Other dental anomalies (ISO System)
1	F	9Y3M	1 (mesiodens)	32	
2	M	7Y4M	1 (mesiodens)	32	72, 73 fusion
3	F	5Y1M	2 (mesiodens)	72, 82, 32, 42	Lower premolar central cusps
4	M	5Y9M	2 (mesiodens, 21 region)	32, 42	72, 73 fusion; 82, 83 fusion; premolar central cusps
5	M	5Y11M	1 (mesiodens)	82, 42	72, 73 fusion
6	M	7Y3M	1 (mesiodens)	32, 42	Molar taurodontism
7	M	8Y4M	2 (mesiodens)	42	
8	M	8Y6M	1 (22 region)	22	21 macrodontia
9	F	7Y2M	1 (11 region)	32	Lower premolar central cusps; molar taurodontism
10	M	7Y8M	1 (11 region)	32	
11	M	7Y10M	1 (mesiodens)	14, 15, 24, 25, 35, 45	
12	M	7Y2M	1 (mesiodens)	25, 35, 45	Molar taurodontism
13	M	7M6M	1 (mesiodens)	35	Short roots of primary molars
14*	F	8M5M	1 (mesiodens)	14, 15, 24, 25	*(sister of Case 15)
15*	F	4M3M	1 (21 region)	15, 45	*(sister of Case 14)
16#	M	5Y10M	3 (1 at 11 region, 2 at 21 region)	45	#(identical twin with Case 17)
17#	M	5Y10M	2 (11, 21 regions)	35	#(identical twin with Case 16)
18	F	6Y0M	1 (mesiodens)	15, 27	Molar taurodontism
19	F	5Y7M	2 (mesiodens, 21 region)	35	
20	M	5Y7M	1 (mesiodens)	45	Molar taurodontism
21§	M	8Y9M	1 (mesiodens)	15, 25	Molar taurodontism;§(Duchenne muscular dystrophy)

laterals, and in 30 cases (51%) only premolars, with majority of them being second bicuspids. Of all 138 missing teeth, primary teeth were reported in 3 cases.[5,23,29] For jaw involvement, 41 cases (69%) were bimaxillary and 18 cases (31%) maxillary, with usually premaxillary supernumeraries and missing upper lateral incisors or second bicuspids.

Discussion

It has been documented that premaxilla is the most frequently involved area of supernumerary teeth in cases of concomitant hypo-hyperdontia (CHH). In a total of 109 CHH patients, from 7 case studies and 45 case reports, 59 (54%) were reported to have premaxillary supernumeraries.[3–5,7–33] The 21 cases we presented in this study further expanded this number to 80. Consistent with the male bias reported in the literature,[6] our cases showed a male to female ratio of 2:1. However, while the average age of reported patients was 10.25 years, our cases were diagnosed with CHH at a much younger age (6.9 years in average), presumably due to common panoramic radiographic examinations for pedodontic patients of early mixed dentition in Taiwan. In most cases, CHH was diagnosed during a regular dental examination. For the distribution and frequencies of involved teeth, of all 80 cases to date, 62 cases (77.5%) had one supernumerary and the remaining (22.5%) two or more, with majority of them being mesiodens. Upper lateral incisors, lower incisors, and premolars were most frequently absent teeth, while canines and molars were also involved in a few cases. The numeric anomalies affected both jaws (bimaxillary hypo-hyperdontia) in about three fourth of the cases (58/80), and only maxilla (maxillary hypo-hyperdontia) in the remaining one fourth (22/80).

The etiology of CHH has been completely unknown, primarily due to the rarity and sporadicity of this disorder.[5–7] Two siblings with Ellis–van Creveld syndrome in Jordan[20] and two identical twin boys in India[25] have been reported to have CHH, suggesting a genetic contribution to this condition. In this study, we further presented two sisters and a pair of identical twins with non-syndromic CHH from two unrelated families. In the family of two sisters, while none of their parents had extra or missing teeth, both of them had a premaxillary supernumerary and missing premolars. This familial occurrence made *de novo* mutations, a common cause of sporadic genetic conditions, a less plausible etiology of CHH. Instead, a recessive inheritance or a dominant inheritance with incomplete penetrance might better explain the condition. However, while both sisters had a premaxillary supernumerary, the pattern of their missing teeth was different, suggesting a significant influence from environmental factors and potential genetic modifiers on the disease expressivity and phenotype. This hypothesis was supported by the phenotypic variance from our identical twin cases. Despite their presumably identical genetic backgrounds, one boy had 3 supernumeraries and missing tooth number 29, while the other had 2 supernumeraries and missing tooth number 20, indicating the environmental contribution to the condition. More interestingly, for Case 3 in this study, while none of her family members was reported to have CHH, her elder brother had a mesiodens but no missing teeth. This concurrence of two

Table 2 Distribution of congenital missing teeth and supernumerary teeth in cases of concomitant hypo-hyperdontia (CHH) from literature review.

Author	Year	Sex	Age	Hyperdontia (ISO System)	Hypodontia (ISO System)	Medical and family history
Camilleri[3]	1967	F	17	1 (mesiodens)	12, 22	
Nathanail[9]	1970	F	11	1 (mesiodens)	35, 45	
Brook and Winter[10]	1970	F		1 (mesiodens)	12	
Mercer[11]	1970	M	20	1 (mesiodens)	15, 35, 45	
Spyropoulos et al.[12]	1979	M	15	1 (mesiodens)	13, 45	
		M	13	1 (supplemental 22)	31	
Gibson[4]	1979	M	8	1 (mesiodens)	12	
		M	9	1 (mesiodens)	22	
		M	11	1 (mesiodens)	22, 15	
		F	13	1 (mesiodens)	15, 25	
		F	11	1 (supplemental 22)	15	
		F	8	1 (supplemental 22)	45	
		F	13	1 (mesiodens)	15, 25, 35	
		F	10	1 (mesiodens)	45	
		M	13	1 (mesiodens)	35, 45	
		F	9	1 (supplemental 22)	15, 25, 35, 45	
		M	10	1 (mesiodens)	22, 23, 25, 35, 31, 41, 45	
Moore[13]	1980	M	11	1 (between 11, 12)	13, 23	
Ranta[14]	1987	F	6.1	2 (supplemental 52, 12)	16, 15, 25, 26, 35	Dubowitz syndrome
Symons[15]	1992	M	8	3 (11 and 13 regions)	31, 41	
Trotman and McNamara[16]	1994	F	9	3 (supplemental 11, 21, 31)	15	Cleft palate and abnormalities of cervical vertebra
Hewson et al.[17]	1995	M	9	1 (supplemental maxillary central incisor)	45	
Scheiner and Sampson[18]	1997	F	8	2 (mesiodens)	35, 45	
Segura and Jimenez-Rubio[19]	1998	M	13	1 (mesiodens)	22	
Hattab et al.[20]	1998	M	9	1 (mesiodens)	12, 22, 31, 32, 33, 41, 42, 43	Ellis-van Creveld syndrome (siblings)
		F	8	1 (11 region)	12, 22, 31, 32, 41, 42	
Matsumoto et al.[21]	2001	F	8	1 (22 region)	25, 32	
Acerbi et al.[22]	2001	M	12	1 (mesiodens)	15, 25, 34, 35, 45	Down syndrome
Oliveira et al.[23]	2002	F	9	1 (mesiodens)	35, 45	
Patchett et al.[24]	2006	M	9	2 (supplemental 11, palatal supernumerary tooth)	35, 45	
Anthonappa et al.[5]	2008	M	9	1 (supplemental 21)	15, 35	
		M	5	1 (mesiodens)	71, 81, 42	
		M	7	2 (11, 21 region)	31, 41	
		F	5	1 (mesiodens)	72, 32	
		M	6	1 (mesiodens)	35, 45	

Sharma[25]	2008	M	7	2 (mesiodens)	25	Identical twins
		M	7	1 (mesiodens)	35	
Lertsirivorakul[26]	2009	F	9	1 (supplemental 22)	15, 14, 25, 35, 36, 45, 46, 47	
Varela et al.[8]	2009	M		1 (mesiodens)	22	
		F		1 (supplemental 62)	22	
		F		2 (supplemental 52, 12)	22	
		M		1 (mesiodens)	35, 45	
		M		1 (supplemental 12)	35	
Manjunatha et al.[27]	2011	M	26	1 (supplemental 22)	31, 41	
Sharma[28]	2012	F	9	1 (supplemental 12)	35, 45	
		M	8	1 (mesiodens)	32, 42	
Zadurska et al.[7]	2012	M	8	2 (mesiodens)	15, 25	
		M	10	1 (supplemental 22)	15	
		F	11	1 (supplemental 12)	15, 25	
		M	9	1 (odontoma)	15, 13, 12, 35, 41, 45	
		F	10	1 (supplemental 12)	35	
		M	12	1 (mesiodens)	35, 45	
		F	17	1 (supplemental 22)	15, 14, 24, 25, 35, 45	
Mallineni et al.[29]	2012	M	5	2 (51, 61 region)	82, 42	Marfan syndrome
Nirmala et al.[30]	2013	F	9	1 (mesiodens)	13, 23	
Gupta and Popat[31]	2013	M	11	1 (mesiodens)	31, 41	
Kariya et al.[32]	2017	M	10	2 (mesiodens, 21 region)	31, 41	
Tewari et al.[33]	2017	M	13	2 (mesiodens, 21 region)	35	
		F	10	1 (mesiodens)	45	

conditions in the same family suggested that isolated hyperdontia and CHH might actually result from the same genetic mutation but be phenotypically affected by environmental factors and potential genetic modifiers.

Although the majority of documented CHH cases were non-syndromic, there were 20 cases reported to be associated with different syndromes.[6] For CHH with premaxillary supernumeraries, we retrieved 6 cases from the literature, involving Dubowitz syndrome,[14] cleft palate and abnormalities of cervical vertebra,[16] Ellis—van Creveld syndrome,[20] Down syndrome,[22] and Marfan syndrome.[29] Like cases of familial occurrence, these syndromic CHH cases also demonstrated a genetic contribution to this numeric anomaly. In this study, we presented a patient of Duchenne muscular dystrophy (DMD) having a mesiodens and missing upper second bicuspids. DMD is an X-linked recessive disorder characterized by severe muscle wasting. It is caused by mutations of *DMD* (dystrophin) gene on X chromosome.[34] Our case was an 8-year-old boy carrying a hemizygous *DMD* splice site mutation (c.6913-1 G>A), which presumably caused a non-functional truncated dystrophin protein. He was diagnosed with DMD at an early age, while CHH was an accidental finding during regular dental examination. This case suggested that dystrophin might play a role in early tooth development and that loss-of-function mutations in *DMD* might cause numeric dental anomalies. Interestingly, Symons et al. previously characterized dental and orofacial phenotypes of 23 DMD patients and found 6 cases (17%) had missing, microdontic, and/or hypoplastic second bicuspids,[35] which supported our hypothesis.

The most puzzling aspect of CHH is its coexistence of hypodontia and hyperdontia, which are considered as opposite extremes in the development of a dentition. Mutations in *MSX1*, *PAX9*, *AXIN2*, *EDA*, *WNT10A*, and *LRP6* have been reported to cause human non-syndromic tooth agenesis (hypodontia and oligodontia).[2] In contrast, no mutations or genes have been identified in patients with non-syndromic hyperdontia, probably due to its low prevalence. Juuri and Balic recently reviewed the molecular and cellular mechanisms regulating successional tooth formation and discussed the biology underlying tooth number abnormalities in humans.[2] For tooth agenesis, a complete absence or arrested development of a successional dental lamina was proposed. On the other hand, a continued successional tooth formation was suggested to explain the occurrence of a mesiodens. However, it remains puzzling that an arrest and a continuation of successional tooth formation can happen in the same individual and presumably result from the same genetic aberration. Arguably, it is possible that the genetic regulation of early tooth development is region-dependent. A genetic variance that disturbs premolar development might adversely facilitate a continued successional tooth formation from incisors. This hypothesis might be partly supported by several mouse models. For example, mice with depletion of BMP4 in dental mesenchyme showed tooth agenesis of mandibular molars, but not maxillary ones and incisors.[36] Furthermore, whereas loss-of-function mutations in *WNT10A* cause tooth agenesis in humans, mice with *Wnt10a* ablation have extra molars, but not incisors.[37,38] These phenotypic differences between regions of a dentition and species might provide plausible explanations to the biology underlying CHH.

Tooth number abnormalities are usually linked to altered tooth size and shape. It has been documented that tooth agenesis is frequently associated with small teeth (microdontia) and dysmorphology of crown (molars with fewer cusps) and root (molar taurodontism).[1,2] Fusion teeth are also a frequent observation in hypodontia cases, particularly in primary dentition. On the other hand, dentitions with supernumeraries may have larger teeth (macrodontia) and crowns with additional cusps and grooves.[1,2] In our 21 CHH cases, molar taurodontism was evident in 6 cases (29%), being the most frequently-observed concurrent dental anomaly of CHH. In 3 cases, fusion of primary lower lateral incisors and canines was found, which was all linked to missing permanent lower laterals. Furthermore, central cusps of premolars were clearly identifiable from panoramic radiograph of 3 cases, one of which also exhibited molar taurodontism. Macrodontia of tooth number 9 was found in Case 8, who had a premaxillary supernumerary and missing tooth number 10. These concurrent dental aberrations suggested that molecular and cellular mechanisms regulating tooth number also play significant roles in tooth morphogenesis. However, more cases and further investigations are required to determine the prevalence of these concurrent anomalies in CHH patients.

In summary, we presented here 21 cases of CHH, including 4 cases with familial occurrence and a syndromic case, and scrutinized their dental phenotypes. The results not only expanded the documentation of this rare disease entity but also supported a significant genetic contribution as well as environmental influences to the condition. Genetic analyses on these patients, particularly familial cases, at molecular level are imperative to further unravel the genetic etiology and disease mechanism of CHH.

Conflicts of interest

All authors declare that there are no conflicting interests.

Acknowledgments

We thank Drs. Ming-Kuang Guo and Jan Hu for critical review of the manuscript. This work was supported by NTUH Grant 106-N3424.

References

1. Cobourne MT, Sharpe PT. Diseases of the tooth: the genetic and molecular basis of inherited anomalies affecting the dentition. *Wiley Interdiscip Rev Dev Biol* 2013;2:183—212.
2. Juuri E, Balic A. The biology underlying abnormalities of tooth number in humans. *J Dent Res* 2017;96:1248—56.
3. Camilleri GE. Concomitant hypodontia and hyperodontia. Case report. *Br Dent J* 1967;123:338—9.
4. Gibson AC. Concomitant hypo-hyperodontia. *Br J Orthod* 1979; 6:101—5.
5. Anthonappa RP, Lee CK, Yiu CK, King NM. Hypohyperdontia: literature review and report of seven cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008;106:e24—30.

6. Mallineni SK, Nuvvula S, Cheung A, Kunduru R. A comprehensive review of the literature and data analysis on hypo-hyperdontia. *J Oral Sci* 2014;56:295—302.
7. Zadurska M, Sieminska-Piekarczyk B, Maciejak D, Wyszomirska-Zdybel B, Kurol J. Concomitant hypodontia and hyperodontia: an analysis of nine patients. *Acta Odontol Scand* 2012;70:154—9.
8. Varela M, Arrieta P, Ventureira C. Non-syndromic concomitant hypodontia and supernumerary teeth in an orthodontic population. *Eur J Orthod* 2009;31:632—7.
9. Nathanail P. Letter to the editor. *Br Dent J* 1970;129:309.
10. Brook AH, Winter GB. Letter to the editor. *Br Dent J* 1970;129:195.
11. Mercer AE. Letter to the editor. *Br Dent J* 1970;129:402.
12. Spyropoulos ND, Patsakas AJ, Angelopoulos AP. Simultaneous presence of partial anodontia and supernumerary teeth. *Oral Surg Oral Med Oral Pathol* 1979;48:53—6.
13. Moore R. Hypo-hyperodontia—report of a rare case. *Br J Orthod* 1980;7:95—6.
14. Ranta R. The Dubowitz syndrome development of teeth and jaws. *Med Sci Res* 1987;15:851—2.
15. Symons AL. Ectopic eruption of a maxillary canine following trauma. *Endod Dent Traumatol* 1992;8:255—8.
16. Trotman CA, McNamara T. Four maxillary incisors: a case report. *Spec Care Dentist* 1994;14:112—5.
17. Hewson A, McCue J, Kavanagh P, McNamara T. Supernumerary central incisor: orthodontic management. *J Ir Dent Assoc* 1995;41:34—5.
18. Scheiner MA, Sampson WJ. Supernumerary teeth: a review of the literature and four case reports. *Aust Dent J* 1997;42:160—5.
19. Segura JJ, Jimenez-Rubio A. Concomitant hypohyperdontia: simultaneous occurrence of a mesiodens and agenesis of a maxillary lateral incisor. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998;86:473—5.
20. Hattab FN, Yassin OM, Sasa IS. Oral manifestations of Ellis-van Creveld syndrome: report of two siblings with unusual dental anomalies. *J Clin Pediatr Dent* 1998;22:159—65.
21. Matsumoto M, Nakagawa Y, Sobue S, Ooshima T. Simultaneous presence of a congenitally missing premolar and supernumerary incisor in the same jaw: report of case. *ASDC J Dent Child* 2001;68. 63—66, 32.
22. Acerbi AG, de Freitas C, de Magalhaes MH. Prevalence of numeric anomalies in the permanent dentition of patients with Down syndrome. *Spec Care Dentist* 2001;21:75—8.
23. Oliveira LM, Primo LG, Barcelos R, Portela MB, Bastos EP. Radiographic diagnosis of supernumerary teeth: report of six unusual cases. *ASDC J Dent Child* 2002;69. 175—179, 25.
24. Patchett C, Sargison AE, Cole BO. Management of a patient exhibiting concomitant supernumerary teeth and hypodontia. *Int J Paediatr Dent* 2006;16(s1):3.
25. Sharma A. A rare case of concomitant hypo-hyperdontia in identical twins. *J Indian Soc Pedod Prev Dent* 2008;26(Suppl. 2):S79—81.
26. Lertsirivorakul J. Concomitant oligodontia and supplemental maxillary lateral incisor: a case report. *J Dent Assoc Thai* 2009;59:75—81.
27. Manjunatha BS, Nagarajappa D, Singh SK. Concomitant hypo-hyperdontia with dens invaginatus. *Indian J Dent Res* 2011;22:468—71.
28. Sharma A. Concomitant hypo-hyperdontia: report of two cases. *Indian J Dent Res* 2012;23:700.
29. Mallineni SK, Jayaraman J, Yiu CK, King NM. Concomitant occurrence of hypohyperdontia in a patient with Marfan syndrome: a review of the literature and report of a case. *J Investig Clin Dent* 2012;3:253—7.
30. Nirmala SV, Mallineni SK, Nuvvula S. Pre-maxillary hypo-hyperdontia: report of a rare case. *Rom J Morphol Embryol* 2013;54:443—5.
31. Gupta S, Popat H. A clinical report of nonsyndromic concomitant hypo-hyperdontia. *Case Rep Dent* 2013;2013:598727.
32. Kariya PB, Singh S, Kulkarni N, Arora A. Bimaxillary concomitant hypohyperdontia in a 10-year-old child. *BMJ Case Rep* 2017;2017.
33. Tewari N, Pandey RK, Singh S. Concomitant hypodontia and hyperdontia: a report of two cases. *Natl J Maxillofac Surg* 2017;8:75—7.
34. Tuffery-Giraud S, Beroud C, Leturcq F, et al. Genotype-phenotype analysis in 2,405 patients with a dystrophinopathy using the UMD-DMD database: a model of nationwide knowledgebase. *Hum Mutat* 2009;30:934—45.
35. Symons AL, Townsend GC, Hughes TE. Dental characteristics of patients with Duchenne muscular dystrophy. *ASDC J Dent Child* 2002;69. 277—283, 34.
36. Jia S, Zhou J, Gao Y, et al. Roles of Bmp4 during tooth morphogenesis and sequential tooth formation. *Development* 2013;140:423—32.
37. Yang J, Wang SK, Choi M, et al. Taurodontism, variations in tooth number, and misshapened crowns in Wnt10a null mice and human kindreds. *Mol Genet Genomic Med* 2015;3:40—58.
38. Xu M, Horrell J, Snitow M, et al. WNT10A mutation causes ectodermal dysplasia by impairing progenitor cell proliferation and KLF4-mediated differentiation. *Nat Commun* 2017;8:15397.