Association of Agenesis of Mandibular Lateral Incisors with Other Dental Anomalies in a Japanese Population

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ABSTRACT

Purpose: The purpose of this study was to explore the association of mandibular incisor agenesis with other dental anomalies in Japanese orthodontic patients.

Methods: A total of 52 subjects with 1 or 2 congenitally missing permanent mandibular lateral incisors (group A) were selected and divided into group 1a (26 subjects with 1 lateral incisor missing) and group 2a (26 subjects with 2 lateral incisors missing). Fifty two sex-matched subjects without agenesis of the mandibular lateral incisor served as controls (group C). Radiographs, study models, and medical and dental records were used to identify anomalies of teeth.

Results: The prevalence rate of agenesis of teeth other than the mandibular lateral incisors and third molars was significantly increased in group A. Agenesis of the maxillary second premolars was significantly increased in groups 2a and A. Significantly increased prevalence rates of symmetrical tooth agenesis, with third molars excluded, and third molar agenesis were observed in group 1a and A.

Conclusions: Japanese subjects with agenesis of 1 or 2 permanent mandibular lateral incisors have significantly increased prevalence rates of other permanent tooth agenesis and symmetrical tooth agenesis. (J Dent Child 2013;80(1):9-15)

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KEYWORDS: MANDIBULAR INCISOR AGENESIS, THIRD MOLAR AGENESIS, DENTAL ANOMALY

Tooth agenesis is one of the most common dental anomalies in the permanent dentition.[1] The reported prevalence rates of tooth agenesis, excluding third molars, range from approximately 4% in the American population[2] to 10% in the Norwegian population.[3] In Japanese populations, the tooth agenesis rate ranges from approximately 7% to 9%.[4,5] Types of the most commonly missing teeth are strongly influenced by ethnicity. In Caucasian populations, the most commonly congenitally missing teeth (third molars excluded) are the mandibular second premolars, followed by either the permanent maxillary lateral incisors[1,2] or the maxillary second premolars.[3,6] Niswander and Sujaku,[4] and Davis[7] reported that the permanent mandibular incisors were the most commonly missing teeth in Japanese and Chinese populations, respectively. Endo et al.[5] characterized hypodontia in a Japanese population by a high prevalence of permanent mandibular lateral incisor agenesis in children with minor hypodontia. A high prevalence of permanent mandibular lateral incisor agenesis might be a characteristic of Asian populations, including the Japanese.

There may be associations between agenesis of specific teeth and other dental anomalies.[8-11] Garib et al.[8] showed associations between second premolar agenesis with agenesis of other permanent teeth, microdontia, primary molar infraocclusion, and ectopic eruption. Garib et al.[9] also showed that permanent tooth agenesis, maxillary lateral incisor microdontia, palatally displaced canines, and distoangulation of mandibular second premolars

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were frequently associated with maxillary lateral incisor agenesis. Abe et al.[10] reported that permanent maxillary first molar agenesis is associated with other congenitally missing permanent teeth and severe tooth agenesis, but not with supernumerary teeth, tooth-shape abnormalities and ectopic eruption. Garn and Lewis[11] showed that third molar agenesis was significantly associated with agenesis of permanent lateral incisors and second premolars. No studies have addressed the association of permanent mandibular incisor agenesis with other dental anomalies in any ethnic groups.

The purpose of this study was to explore the association of permanent mandibular incisor agenesis with other dental anomalies in a Japanese orthodontic population.

METHODS

This study was approved by the Research Ethics Committee of the Nippon Dental University at Niigata, Japan (ECNG-H-100). Japanese subjects with 1 or 2 congenitally missing mandibular lateral incisors who had been treated in the orthodontic clinic at Nippon Dental University Niigata Hospital were part of the tooth agenesis group (group A). On the first visit, each subject was given a registration number. When mandibular incisor agenesis was found, the next subject without agenesis was included in a control group (group C), which was sex- and age-matched to those in group A.

Group A was further divided into 2 subgroups: the first consisted of subjects with agenesis of 1 mandibular lateral incisor (group 1a); and the second was made up of subjects with agenesis of 2 mandibular lateral incisors (group 2a). The distinction between congenital absence of the mandibular central and lateral incisors was made based on the size and symmetry of the crown morphology of the remaining incisors. Subjects diagnosed with conditions such as ectodermal dysplasia or cleft lip or palate, or who had previously undergone orthodontic treatment in other orthodontic clinics were excluded from this study.

Panoramic and periapical radiographs, study models, and medical and dental records were used by one of the investigators to identify anomalies of permanent teeth in number, shape, and position.

ANOMALIES IN NUMBER

Tooth agenesis was evaluated mainly using panoramic radiographs, which were taken at the initial visit or later with the same panoramic machine (Veraviewepocs 2D, Morita, Kyoto, Japan) and the same subject positioning. Agenesis was diagnosed when no mineralization of the tooth crown could be identified on the panoramic radiographs and when there was no evidence of tooth extraction. The study models and medical and dental records were used as reference materials to avoid an erroneous diagnosis of tooth agenesis due to extraction of the permanent teeth. To exclude the cases of late mineralized teeth, panoramic radiographs of the subjects who were at least 14 years old were examined. This critical age of 14 was adopted following Garn and Lewis'[11] suggestion that third molar agenesis could not be confirmed in patients younger than 14 years old. Third molars were included in this study. Supernumerary teeth and mesiodens were diagnosed on the panoramic radiographs.

ANOMALIES IN SHAPE

Fused, concrescent, and geminated teeth, and peg-shaped maxillary lateral incisors were identified on the periapical radiographs and study models. The peg-shaped maxillary lateral incisor was defined as a severe, conical, crown-size reduction in diameter from the cervix to the incisor edge.[12]

ANOMALIES IN POSITION

Diagnosis of palatally or labially displaced maxillary canines was made on the panoramic radiographs and intraoral examinations immediately before their emergence into the oral cavity. Images obtained by computed tomographic scanning were also used when it was difficult to determine canine displacement.

Transposed teeth were defined as the positional interchange of 2 adjacent teeth—particularly of the roots—or the development or eruption of a tooth in a position occupied normally by a nonadjacent tooth on the panoramic radiographs.[13]

All dental anomalies were re-examined by the aforementioned investigator as well as another investigator independently after an interval of 1 month. Both intraexaminer and interexaminer reproducibility were 100% in the identification of all dental anomalies.

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS 17.0J for Mac (SPSS Japan Inc, Tokyo, Japan). The chi-square test or Fisher's exact test was used to determine the significant differences in the prevalence rate of dental anomalies between the groups. The Kruskal-Wallis test and test for equality were used to determine whether significant differences in the distribution of subjects by the number of missing teeth occurred among the groups 1a, 2a, and C and between groups A and C, respectively. All statistical tests were performed at the $P<.05$ level of significance. The odds ratio (**OR**) was calculated at the 95% confidence interval to measure the strength of associations between mandibular incisor agenesis and the other dental anomalies investigated.

RESULTS

Group A consisted of 52 subjects (7 males and 45 females) with 1 or 2 congenitally missing permanent mandibular lateral incisors. Group 1a consisted of 26 subjects (2 males and 24 females) with agenesis of 1 mandibular lateral incisor and group 2a was made up of 26 subjects (5 males and 21 females) with agenesis of 2

mandibular lateral incisors. Group 1a comprised 15 subjects with agenesis of the mandibular right lateral incisor and 11 with agenesis of the mandibular left lateral incisor. Group C consisted of 52 subjects (7 males and 45 females) without agenesis of permanent mandibular lateral incisors, who were almost age matched to those in group A.

ANOMALIES IN NUMBER

Table 1 shows that the prevalence rate of subjects with agenesis of teeth other than mandibular lateral incisors and third molars was significantly higher in group A (~23%) than in group C (~8%). There were significant differences in the prevalence rate of subjects with: maxillary second premolar agenesis between group C

Table 1. Number of Subjects with Dental Anomalies

Anomalies	Group 1a (N=26) N (%)	Group 2a (N=26) N (%)	Group A (N=52) N (%)	Group C (N=52) N (%)	Chi-square test or Fisher's exact test/*P*-value			
					Group 1a vs 2a	Group 1a vs C	Group 2a vs C	Group A vs C
Tooth agenesis (excluding third molars)	6 (23)	6 (23)	12 (23)	4 (8)	>.99	<.08	<.08	.03*
Maxillary lateral incisor agenesis	2 (8)	2 (8)	4 (8)	2 (4)	>.99	<.60	<.60	<.68
Maxillary second premolar agenesis	4 (15)	5 (19)	9 (17)	1 (2)	>.99	.04*	>.01*	.008†
Mandibular second premolar agenesis	4 (15)	3 (12)	7 (14)	1 (2)	>.99	.04*	<.11	.06
Symmetrical tooth agenesis (excluding third molars)	6 (23)	5 (19)	11 (21)	3 (6)	>.73	>.05	<.11	.00‡
Third molar agenesis	6 (23)	4 (15)	10 (19)	3 (6)	>.48	>.05	>.21	>.07
Symmetrical third molar agenesis	4 (15)	3 (12)	5 (10)	5 (10)	>.99	>.47	>.99	.76
Supernumerary tooth (excluding mesiodens)	0 (0)	0 (0)	0 (0)	0 (0)	-	-	-	-
Mesiodens	0 (0)	0 (0)	0 (0)	0 (0)	-	-	-	-
Fused tooth	0 (0)	0 (0)	0 (0)	0 (0)	-	-	-	-
Concrescent tooth	0 (0)	0 (0)	0 (0)	0 (0)	-	-	-	-
Geminated tooth	0 (0)	0 (0)	0 (0)	0 (0)	-	-	-	-
Peg-shaped lateral incisor	1 (4)	2 (8)	3 (6)	3 (6)	>.99	>.99	>.99	>.99
Palatal or labial displacement of maxillary canine	0 (0)	1 (4)	1 (2)	6 (12)	>.99	>.17	>.41	>.11
Transposed teeth	0 (0)	0 (0)	0 (0)	1 (2)	-	>.99	>.99	>.99

** P<.05.* *† P<.01.* *‡ P<.001.*

Table 2. Number of Subjects with Agenesis and Oligodontia Cases

No. of missing teeth (excluding third molars and mandibular incisors)	Group 1a (N=26) N (%)	Group 2a (N=26) N (%)	Group A (N=52) N (%)	Group C (N=52) N (%)	Statistical comparisons
					Kruskal-Wallis test/*P*-value
0	20 (77)	20 (77)	40 (77)	48 (92)	>.07
1	0 (0)	1 (4)	1 (2)	1 (2)	Test for equality/*P*-value
2	2 (8)	2 (8)	4 (8)	2 (4)	>.19
3	1 (4)	0 (0)	1 (2)	1 (2)	
4	1 (4)	2 (8)	3 (6)	0 (0)	
5	0 (0)	0 (0)	0 (0)	0 (0)	
6	2 (8)	1 (4)	3 (6)	0 (0)	

					Fisher's exact test/*P*-value			
					Group 1a vs 2a	Group 1a vs C	Group 2a vs C	Group A vs C
No. of subjects with oligodontia (including missing mandibular incisors)	2 (8)	3 (12)	5 (10)	0 (0)	>.99	<.11	.03*	<.06

** P<.05.*

and the other groups; and mandibular second premolar agenesis between groups 1a and C. The prevalence rate of subjects with symmetrical tooth agenesis, excluding third molars and mandibular lateral incisors, was significantly higher in group A than in group C ($P<.01$). There were no significant differences in the prevalence rate of subjects with either third molar agenesis or symmetrical third molar agenesis between groups. No subjects had supernumerary teeth or mesiodentes in the study groups.

Table 2 shows no significant differences in the distribution of the subjects by the number of congenitally missing teeth between groups. The prevalence of oligodontia, which is defined as 6 or more missing permanent teeth excluding third molars,[14] was approximately 12% in group 2a, with a significant difference from group C ($P<.05$).

Table 3 shows that the prevalence rate of tooth agenesis, excluding the mandibular lateral incisors and third molars, was significantly higher in each tooth agenesis group than in group C ($P<.01$). The most commonly missing teeth were maxillary and mandibular second premolars in each tooth agenesis group. The prevalence rate of symmetrical tooth agenesis, excluding the mandibular lateral incisors and third molars, was significantly higher in each tooth agenesis group than in group C, and symmetrical agenesis was seen more frequently with maxillary and mandibular second premolars.

There were no significant differences in the distribution of subjects by the number of missing third molars between groups, and prevalence rate of agenesis and symmetrical agenesis of maxillary and/or mandibular third molars between groups (Table 4).

As shown in Table 5, the prevalence rate of subjects with agenesis of teeth other than the mandibular lateral incisors and third molars was significantly increased in group A (OR=3.6); the rate of maxillary second premolar agenesis was significantly increased in groups 2a (OR=12.14) and A (OR=10.67); the rates of symmetrical tooth agenesis with third molars excluded and third molar agenesis were significantly increased in groups 1a (OR=4.9 in each) and A (OR=4.38 and 3.89, respectively).

ANOMALIES IN SHAPE

There were no subjects with fused, concrescent, or geminated teeth and no significant differences in the prevalence rate of subjects with the peg-shaped lateral incisors (Table 1).

ANOMALIES IN POSITION

There were no significant differences in the prevalence rates of subjects with palatally or labially displaced maxillary canines or transposed teeth between groups (Table 1).

DISCUSSION

Our results show that, excluding third molars, subjects with mandibular incisor agenesis presented agenesis of the maxillary second premolars (17%), as well as of other teeth (23%) and which represent a 10.7-fold and a 3.6-fold increase in occurrence, respectively, compared with subjects without mandibular incisor agenesis. This significantly increased prevalence rate of maxillary second premolar agenesis in the subjects with mandibular incisor agenesis is consistent with the findings of Garib et al.,[8] which showed strong associations between agenesis of second premolars and agenesis of other permanent teeth. This study and others[8-10] show that agenesis of some specific teeth, such as second premolars, maxillary lateral incisors, and maxillary first molars, is associated with agenesis of other permanent teeth, meaning that the phenotype represented by a specific tooth may be concurrent with the high prevalence of other missing teeth in the same subjects.

In this study, subjects with bilateral agenesis of mandibular incisors presented significantly higher prevalence rates of oligodontia, excluding third molars, than those without mandibular incisor agenesis. Abe et al.[10] showed that bilateral maxillary first molar agenesis was significantly associated with severe tooth agenesis; their results and ours suggest that bilateral agenesis of some specific type of tooth is associated with oligodontia. There were 5 subjects with oligodontia in the tooth agenesis groups. Peres et al.[14] reported that individuals affected by PAX mutation have severe tooth agenesis with most molars, second premolars, and some incisors congenitally missing.

Previous researchers pointed out that symmetrical tooth agenesis occurred at a high frequency, mostly involving the maxillary and mandibular second premolars.[1,5] Subjects with bilateral agenesis of maxillary first molars had a significantly high prevalence rate of symmetrical tooth agenesis of the maxillary and mandibular second premolars as well as maxillary lateral incisors.[10] These observations support our findings that those subjects with mandibular incisor agenesis had significantly high prevalence rates of symmetrical agenesis of maxillary and mandibular second premolars, representing a 4.4-fold increase in occurrence of symmetrical tooth agenesis, with third molars excluded, compared with those without mandibular incisor agenesis.

Previous studies showed significant associations of agenesis of second premolars, lateral incisors, and maxillary first molars with third molar agenesis.[8-11] Some investigators showed that MSX1 mutations predominantly affected agenesis of both second premolars and third molars.[15] Others showed that PAX9 mutations caused bilateral agenesis of maxillary first molars and third molars in a family with advanced tooth agenesis.[16] In this study, subjects with agenesis of 1 or 2 mandibular incisors represented a 3.9-fold increased occurrence

Table 3. Number and Type of Congenitally Missing Teeth and Symmetrical Tooth Agenesis

		Group 1a (N=26) N (%)	Group 2a (N=26) N (%)	Group A (N=52) N (%)	Group C (N=52) N (%)	Chi-square test or Fisher's exact test/ *P*-value			
						Group 1a vs 2a	Group 1a vs C	Group 2a vs C	Group A vs C
Tooth agenesis pattern									
Maxilla	Central incisors	0 (0)	0 (0)	0 (0)	0 (0)				
	Lateral incisors	3 (13)	3 (16)	6 (14)	2 (25)				
	Canines	0 (0)	0 (0)	0 (0)	3 (38)				
	First premolars	2 (9)	0 (0)	2 (5)	0 (0)				
	Second premolars	7 (30)	6 (32)	13 (31)	2 (25)				
	First molars	2 (9)	2 (11)	4 (10)	0 (0)				
	Second molars	0 (0)	1 (5)	1 (2)	0 (0)				
	Subtotal	**14 (61)**	**12 (63)**	**26 (62)**	**7 (88)**				
Mandible	Central incisors	0 (0)	0 (0)	0 (0)	0 (0)				
	Canines	0 (0)	0 (0)	0 (0)	0 (0)				
	First premolars	0 (0)	0 (0)	0 (0)	0 (0)				
	Second premolars	8 (35)	5 (26)	13 (31)	1 (13)				
	First molars	0 (0)	0 (0)	0 (0)	0 (0)				
	Second molars	1 (4)	2 (11)	3 (7)	0 (0)				
	Subtotal	**9 (39)**	**7 (37)**	**16 (38)**	**1 (13)**				
	Total	**23 (100)**	**19 (100)**	**42 (100)**	**8 (100)**	**>.53**	**<.001***	**<.001***	**<.001***
Symmetrical tooth agenesis pattern									
Maxilla	Lateral incisors	1 (10)	1 (13)	2 (11)	1 (33)				
	Canines	0 (0)	0 (0)	0 (0)	1 (33)				
	First premolars	1 (10)	0 (0)	1 (6)	0 (0)				
	Second premolars	3 (30)	3 (38)	6 (33)	1 (33)				
	First molars	1 (10)	1 (13)	2 (11)	0 (0)				
	Subtotal	6 (60)	5 (63)	11 (61)	3 (100)				
Mandible	Second premolars	4 (40)	2 (25)	6 (33)	0 (0)				
	Second molars	0 (0)	1 (13)	1 (6)	0 (0)				
	Subtotal	**4 (40)**	**3 (38)**	**7 (39)**	**0 (0)**				
	Total	**10 (100)**	**8 (100)**	**18 (100)**	**3 (100)**	**>.63**	**.001†**	**.006†**	**.001†**

** P<.001.* *† P<.01.*

Table 4. Distribution of Third Molar Agenesis in Each Group

	Group 1a (N=26) N (%)	Group 2a (N=26) N (%)	Group A (N=52) N (%)	Group C (N=52) N (%)	Statistical comparisons			
No. of subjects by the no. of missing third molars					Kruskal-Wallis test/*P*-value			
0	20 (77)	22 (85)	42 (81)	44 (85)	>.69			
1	2 (8)	0 (0)	2 (4)	3 (6)	Test for equality/ *P*-value			
2	2 (8)	4 (15)	6 (12)	2 (4)	>.12			
3	2 (8)	0 (0)	2 (4)	0 (0)				
4	0 (0)	0 (0)	0 (0)	3 (6				
					Chi-square test or Fisher's exact test/ *P*-value			
No. of different missing third molars					1a vs 2a	1a vs C	2a vs C	A vs C
Maxillary third molars	8 (16)	7 (14)	15 (14)	13 (13)	.78	<.62	<.87	<.69
Mandibular third molars	4 (8)	1 (2)	5 (5)	6 (6)	>.36	>.73	<.43	<.76
Total	12 (12)	8 (8)	20 (10)	19 (9)	<.35	>.50	<.67	<.87
Symmetrical third molar agenesis								
Maxillary third molars	2 (8)	3 (12)	5 (10	5 (10	>.99	>.99	>.99	>.99
Mandibular third molars	2 (8)	0 (0)	2 (4)	3 (6)	.49	>.99	<.55	>.99
Total	**4 (8)**	**3 (6)**	**7 (7)**	**8 (8)**	**>.99**	**>.99**	**>.75**	**<.79**

Table 5. Odds Ratio and 95% Confidence Interval

Anomalies in number	Group 1a vs C		Group 2a vs C		Group A vs C	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
Tooth agenesis (excluding third molars)	3.60	(0.92-14.15)	3.60	(0.92-14.15)	3.60	(1.08-12.04)
Oligodontia (including missing mandibular incisors)	-	-	-	-	-	-
Maxillary lateral incisor agenesis	2.08	(0.28-15.70)	2.08	(0.28-15.70)	2.08	(0.37-11.91)
Maxillary second premolar agenesis	9.27	(0.98-87.77)	12.14	(1.34-110.29)	10.67	(1.30-87.65)
Mandibular second premolar agenesis	9.27	(0.98-87.77)	6.65	(0.66-67.43)	7.93	(0.94-66.98)
Symmetrical tooth agenesis (excluding third molars)	4.90	(1.12-21.53)	3.89	(0.85-17.78)	4.38	(1.15-16.77)
Third molar agenesis	4.90	(1.12-21.53)	2.97	(0.61-14.41)	3.89	(1.01-15.07)
Symmetrical third molar agenesis	1.71	(0.42-6.99)	1.23	(0.27-5.58)	1.46	(0.43-4.94)
Supernumerary tooth (excluding mesiodens)	-	-	-	-	-	-
Mesiodens	-	-	-	-	-	-
Fused tooth	-	-	-	-	-	-
Concrescent tooth	-	-	-	-	-	-
Geminated tooth	-	-	-	-	-	-
Peg-shaped lateral incisor	0.65	(0.07-6.61)	1.36	-	1.00	(0.19-5.20)
Palatal or labial displacement of maxillary canine	-	-	0.31	(0.04-2.70)	0.15	(0.02-1.30)
Transposed teeth	-	-	-	-	-	-

of third molar agenesis compared with the controls (Table 5), although there was no significant difference in the prevalence rate between the 2 groups (Table 1). Pan et al.[17] reported no significant differences in the allele and genotype frequencies of 4 PAX9 gene polymorphisms between subjects without tooth agenesis and those only with mandibular incisor agenesis.

Some researchers showed significantly increased occurrences of agenesis of premolars,[8,18-20] maxillary lateral incisors,[9] and third molars[19]; peg-shaped maxillary lateral incisors[19,20]; infraocclusion of primary molars[18,20]; ectopic eruption of maxillary first molars[18]; and enamel hypoplasia[20] associated with palatal displacement (ectopic eruption) of maxillary canines. By contrast, our study showed no significant association between mandibular lateral incisor agenesis and supernumerary teeth and anomalies in tooth shape and position.

CONCLUSIONS

Based on this study's results, the following conclusions can be made for Japanese subjects:

1. Those with agenesis of 1 or 2 permanent mandibular lateral incisors have significantly increased prevalence rates of other permanent tooth agenesis and symmetrical tooth agenesis;
2. There was no association between mandibular lateral incisor agenesis and supernumerary teeth, and anomalies in tooth shape and position.

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