Original Article

Maxillary first molar agenesis and other dental anomalies

Ryota Abe[a]; Toshiya Endo[b]; Shohachi Shimooka[c]

ABSTRACT

Objective: To explore the association of maxillary first molar agenesis with other dental anomalies in Japanese orthodontic patients.

Materials and Methods: A total of 32 subjects with one or two congenitally missing maxillary first molars (group M) were selected and divided into group 1M (12 subjects with one maxillary first molar missing) and group 2M (20 subjects with two maxillary first molars missing). As controls, 32 sex-matched subjects without agenesis of maxillary first molars were collected (group C). Panoramic and periapical radiographs, cephalograms, study models, intraoral photographs, and anamnestic data were used to identify anomalies of permanent teeth. Chi-square, Fisher's exact, Kruskal-Wallis, and Steel-Dwass tests were used to make statistical comparisons.

Results: The prevalence rates of tooth agenesis other than the maxillary first molars and advanced tooth agenesis, with third molars excluded, were significantly higher in group 2M than in group C. The absence of second premolars was most common. The prevalence rate of third molar agenesis was significantly higher in groups 1M and 2M than in group C. The occurrence of symmetrical agenesis of the mandibular third molars was particularly notable in group 2M as compared to group 1M, in which maxillary third molar agenesis was predominant. There was no significant association between maxillary first molar agenesis and other dental anomalies, except for agenesis of teeth other than maxillary first molars.

Conclusion: Agenesis of maxillary first molars is associated with a higher prevalence of other permanent tooth agenesis and advanced tooth agenesis. (*Angle Orthod.* 2010;80:1002–1009.)

KEY WORDS: Maxillary first molar agenesis; Third molar agenesis; Advanced tooth agenesis; Dental anomaly

INTRODUCTION

Agenesis of maxillary first molars does not occur frequently in general and orthodontic populations.[1] The reported prevalence rate of maxillary first molar agenesis was 2.9% of the total number of missing teeth in a general population[1] and has been reported to vary from 0.4%[2] to 4%[3] in orthodontic patients. Maxillary first molar agenesis accounts for about 0.5% of orthodontic patients with tooth agenesis.[2] Despite the low prevalence rate, maxillary first molar agenesis presents clinically significant problems affecting treatment planning and outcome, because first molars play an important role in the mastication of food, in supporting the vertical dimension of the face, and as anchorage teeth against orthodontic forces.

Subjects with maxillary first molar agenesis showed more remarkable skeletal and dental deviations than those without agenesis of this class of tooth.[4] Some studies show that the prevalence of maxillary first molar agenesis is relatively high in orthodontic patients with advanced tooth agenesis.[1,3,5] The prevalence rates of maxillary first molar agenesis are 4% and 9.2% in Japanese orthodontic populations with tooth agenesis and advanced tooth agenesis, respectively.[3,5] These rates are higher than those reported in previous studies dealing with other ethnic groups,[1,2,6] thus suggesting that the maxillary first molars are more commonly missing in Japanese people.

Several studies have reported an association between tooth agenesis and other dental anoma-

[a] Assistant Professor, Orthodontic Dentistry, The Nippon Dental University Niigata Hospital, Niigata, Japan.

[b] Professor and Chairman, Orthodontic Dentistry, The Nippon Dental University Niigata Hospital, Niigata, Japan.

[c] Professor and Chairman, Department of Pediatric Dentistry, The Nippon Dental University School of Life Dentistry at Niigata, Niigata, Japan.

Corresponding author: Dr Toshiya Endo, Professor and Chairman, Orthodontic Dentistry, The Nippon Dental University Niigata Hospital, 1-8 Hamaura-cho, Chuo-ku, Niigata 951-8580, Japan
(e-mail: endoto@ngt.ndu.ac.jp)

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Table 1. Numbers and Mean Ages (Standard Deviation) of Subjects at Registration

	Group 1M	Group 2M	Group M	Group C
Number of subjects	12	20	32	32
Age	10 y (1 y 10 mo)	13 y 6 mo (4 y 2 mo)	12 y (4 y 1 mo)	8 y 10 mo (1 y 6 mo)

lies.[1,2,6,7] Garib et al.[7] statistically evaluated the prevalence of other dental anomalies in orthodontic patients with second premolar agenesis and provided evidence that agenesis of other permanent teeth, microdontia, deciduous molar infraocclusion, and certain dental ectopias are the products of the same genetic mechanisms that cause second premolar agenesis. Garn and Lewis[8] reported that third molar agenesis was significantly associated with agenesis of lateral incisors and second premolars. No literature on the association of maxillary first molar agenesis with other dental anomalies was found in a PubMed search.

Several studies have furnished sufficient evidence that genes play a critical role in the etiology of tooth agenesis.[6,9,10] Grahnen[6] stated that in sibling relationships in which the patients or the parents had six or more missing teeth, the penetrance appeared to have been high, thus supporting the hypothesis that tooth agenesis is genetically determined. Vastardis et al.[9] reported that a MSX1 homeodomain missense mutation caused selective agenesis of the second premolars and third molars in an American family with a severe form of autosomal-dominant tooth agenesis. Stockton et al.[10] associated a frameshift mutation in PAX9 with autosomal-dominant oligodontia, which involved the absence of most permanent molars.

The purpose of the present study was to explore the association of maxillary first molar agenesis with other dental anomalies in Japanese orthodontic patients.

MATERIALS AND METHODS

A total of 32 Japanese subjects with one or two congenitally missing maxillary first molars (the agenesis group, Group M) were selected from the files of orthodontic patients who had visited the orthodontic clinic at Nippon Dental University Niigata Hospital. The group comprised 7 male and 25 female patients. On the first visit, each subject was given a registration number. Where maxillary first molar agenesis was found, the adjacent number of the same sex was included in a control group (Group C). Group M was further divided into two groups. One group consisted of 12 subjects (4 male and 8 female) with agenesis of one maxillary first molar (Group 1M), and the other was made up of 20 subjects (3 male and 17 female) with agenesis of both maxillary first molars (Group 2M). Group 1M comprised seven subjects with agenesis of the maxillary right first molar and five with agenesis of the maxillary left first molar. The number and mean ages of the subjects in each group at the time of registration are shown in Table 1. Subjects who had such developmental anomalies as ectodermal dysplasia or cleft lip and/or palate or who had undergone orthodontic treatment were excluded from this study.

Panoramic and periapical radiographs, lateral cephalograms, study models, intraoral photographs, and anamnestic data were used to identify the dental anomalies of permanent teeth in number, shape, and position (see Table 2). The dental anomalies were examined by a single investigator.

Anomalies in Number

Tooth agenesis was examined mainly using longitudinal panoramic radiographs, which were available for most patients receiving orthodontic treatments. A tooth was diagnosed as presenting agenesis when no mineralization of the tooth crown could be identified on the panoramic radiographs and when no evidence of its having been extracted was recognized. The study models and anamnestic data were used as reference materials to prevent wrong diagnoses. To exclude any cases of late mineralized teeth, panoramic radiographic examinations were performed only on subjects who were at least 14 years old. This critical age was adopted following the suggestions of Garn and Lewis[8] that third molar agenesis could not be confirmed in patients under 14 years of age. Third molars were included in this study. Agenesis of the maxillary first molars was diagnosed when the most anterior maxillary molars looked more like maxillary second molars than maxillary first molars in crown morphology and root development and erupted at the age of 9 to 10 years, and when only one or two molars were identified in the affected quadrants.[1,5] Supernumerary teeth and mesiodentes were diagnosed on the panoramic radiographs.

Anomalies in Shape

The occlusal surface morphology of maxillary first and second molars that had erupted was evaluated on study models in each group according to the classification of Dahlberg.[11] The occlusal surface patterns were divided into four classes according to the number and size of the cusps (Figure 1).

Fused, concrescent, and geminated teeth were determined using periapical radiographs and study

Table 2. Numbers and Percentages of Subjects with Different Anomalies and Statistical Comparisons

	Group 1M[a] (N = 12)	Group 2M[a] (N = 20)	Group M[a] (N = 32)	Group C[a] (N = 32)	Chi-Square Test or Fisher's Exact Test/*P* Value			
					1M vs 2M	1M vs C	2M vs C	M vs C
Anomalies of number								
Tooth agenesis (excluding third molars)	2 (16.7)	8 (40.0)	10 (31.3)	2 (6.3)	.248	.297	.004**	.010*
Maxillary lateral agenesis	0 (0.0)	3 (15.0)	3 (9.4)	0 (0.0)	.274	-	.052	.238
Second premolar agenesis	2 (16.7)	7 (35.0)	9 (28.1)	2 (6.3)	.422	.297	.019*	.020*
Symmetrical tooth agenesis	0 (0.0)	8 (40.0)	8 (40.0)	1 (3.1)	.014*	>.999	.001***	.026*
Third molar agenesis	9 (75.0)	13 (65.0)	22 (68.8)	7 (21.9)	.703	.003**	.002**	.000***
Supernumerary tooth (excluding mesiodens)	0 (0.0)	2 (10.0)	2 (6.3)	1 (3.1)	.516	>.999	.551	>.999
Mesiodens	1 (8.3)	0 (0.0)	1 (3.1)	1 (3.1)	.375	.476	>.999	>.999
Anomalies of shape								
Fused tooth	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-	-
Concrescent tooth	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-	-
Geminated tooth	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-	-
Peg-shaped lateral incisor	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.1)	-	>.999	>.999	>.999
Shovel-shaped incisor	0 (0.0)	2 (10.0)	2 (6.3)	1 (3.1)	.516	>.999	.551	>.999
Incisor tubercle	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-	-
Canine tubercle	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-	-
Central cusp	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-	-
Paramolar tubercle	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-	-
Carabelli's cusp	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.1)	-	>.999	>.999	>.999
Anomalies of position								
Displacement of maxillary canine	1 (8.3)	2 (10.0)	3 (9.4)	3 (9.4)	>.999	>.999	>.999	>.999
Mesial angulation of maxillary canine	1 (8.3)	0 (0.0)	1 (3.1)	0 (0.0)	.375	.273	-	>.999
Distal angulation of mandibular second premolar	4 (33.3)	7 (35.0)	11 (34.4)	12 (37.5)	>.999	>.999	.855	.794
Ectopic eruption of molar	0 (0.0)	2 (10.0)	2 (6.3)	1 (3.1)	.516	>.999	.551	>.999
Transposed teeth	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-	-

[a] Percentages in parentheses. N indicates number of subjects.
* $P < .05$; ** $P < .01$; *** $P < .001$.

models. Peg-shaped lateral incisors, incisor and canine tubercles, and central cusps, paramolar tubercles, and Carabelli's cusps were identified on the study models.

Anomalies in Position

Anomalies in position were diagnosed mainly using panoramic radiographs taken at nearly the same age for the agenesis and control groups. Diagnosis of palatally or buccally displaced canines was made on the panoramic radiographs and lateral cephalograms.

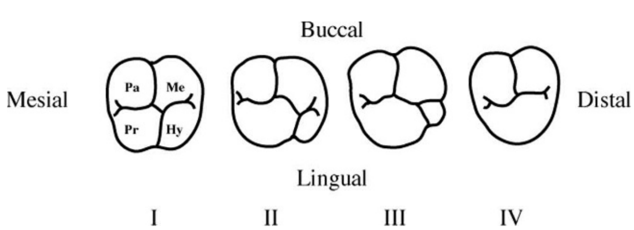

Figure 1. Four classes of maxillary first molar occlusal surface patterns. Class I features four well-developed cusps. Class II has a reduced hypocone. Class III has a cuspule on the distal border. Class IV has no hypocone. Pa indicates paracone; Me, metacone; Pr, protocone; and Hy, hypocone.

Images obtained by computed tomographic scanning were also used when it was difficult to determine canine displacements. Dislocation of a maxillary canine was regarded as mesial angulation when the distal angle formed between the long axis of the canine and the occlusal plane (defined by the mesiobuccal crests of the maxillary right and left first [second] permanent molars) was 57.4 degrees or less on the panoramic radiographs. The decision of this critical angle was based on the findings by Grande et al.[12] that the mean mesial inclination of displaced and retained maxillary canines was 57.4 degrees (SD 13.3). Diagnosis for mesial angulation of maxillary canines was performed on subjects who were at least 10 years old. This critical age was adopted on the basis of the findings by Ericson and Kurol[13] that radiographic examinations of patients under the age of 10 did not provide a reliable basis for prognosis of a future unfavorable eruption path of the maxillary canines.

A mandibular second premolar was diagnosed as presenting distal angulation when the distal angle formed between the long axis of the second premolar and a tangent to the inferior border of the mandibular body was 73.9 degrees or less on the panoramic

Table 3. Numbers and Percentages of Subjects by Number of Missing Teeth and with Advanced Tooth Agenesis and Statistical Comparisons

	Group 1M[a] (N = 12)	Group 2M[a] (N = 20)	Group M[a] (N = 32)	Group C[a] (N = 32)	Statistical Comparisons			
Number of missing teeth (excluding third molars and maxillary first molars)					Kruskal-Wallis Test/*P* Value			
0	10 (83.3)	12 (60.0)	22 (68.8)	30 (93.8)	.010**			
1	2 (16.7)	0 (0.0)	2 (6.3)	1 (3.1)	Steel-Dwass Test/Significant Comparison/*P* Value			
2	0 (0.0)	2 (10.0)	2 (6.3)	1 (3.1)	Group 2M vs Group C	.011*		
3	0 (0.0)	1 (5.0)	1 (3.1)	0 (0.0)	Group M vs Group C	.044*		
4	0 (0.0)	2 (10.0)	2 (6.3)	0 (0.0)				
5	0 (0.0)	2 (10.0)	2 (6.3)	0 (0.0)				
6	0 (0.0)	1 (5.0)	1 (3.1)	0 (0.0)				
					Fisher's Exact Test/*P* Value			
					1M vs 2M	1M vs C	2M vs C	M vs C
Number of subjects with advanced tooth agenesis (including missing maxillary first molars)	0 (0.0)	6 (30.0)	6 (18.8)	0 (0.0)	.061	-	.002**	.024*

[a] Percentages in parentheses. N indicates number of subjects.
* $P < .05$; ** $P < .01$.

radiographs of subjects who were at least 10 years old. This critical angle was based on the findings of Shalish et al.[14] that the mean distal inclination of mandibular second premolars was 85.5 degrees (SD 5.8). This angle of 73.9 degrees—11.6 degrees smaller than 2 SDs from the mean—was used as a threshold for the clinical significance of distal inclination. Ectopic eruption of molars and transposed teeth were identified on the panoramic radiographs.

All dental anomalies were reexamined by the same investigator and another investigator independently after an interval of 1 month. Either intraexaminer or interexaminer reproducibility was 100% in the identification of all dental anomalies.

Statistical Analysis

Statistical analyses were performed by the use of SPSS for the Macintosh, Version 17.0J (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 and Steel-Dwass tests were used to determine whether and where significant differences in the distribution of dental anomalies occurred between the groups. All statistical tests were performed at the $P < .05$ level of significance.

RESULTS

Anomalies in Number

Table 2 shows that the prevalence rate of agenesis of teeth other than maxillary first and third molars was significantly higher in groups 2M (40.0%) and M (31.3%) than in group C (6.3%). Table 3 shows significant differences in the distribution of subjects by the number of missing teeth between groups 2M and C and between groups M and C. Table 3 also shows that the prevalence of advanced tooth agenesis, which is defined as five or more missing permanent teeth, including maxillary first molars and excluding third molars,[3] was calculated at 30% and 18.8% in groups 2M and M, respectively, with significant differences between groups 2M and C and between groups M and C. As shown in Table 4, the most commonly missing teeth were maxillary and mandibular second premolars (22.6% for each), followed by maxillary lateral incisors (19.4%) in group 2M, while in groups 1M and C the only missing tooth was mandibular second premolars. Table 2 shows that the prevalence rate of second premolar agenesis was significantly higher in groups 2M and M than in group C, while that of maxillary lateral incisor agenesis was not significantly different between groups. Table 2 also shows that the prevalence rates of symmetrical tooth agenesis, excluding third molars and maxillary first molars, were significantly different between groups 1M and 2M, between groups 2M and C, and between groups M and C. The most common symmetrical agenesis was exhibited by maxillary lateral incisors and second premolars, followed by mandibular second premolars (Table 4).

Table 2 shows that the prevalence rate of third molar agenesis was significantly lower in group C than in the other groups. Table 5 shows significant differences in the distribution of subjects by the number of missing third molars between group C and the other groups. As shown in Table 5, there were significant differences in the prevalence rate of missing maxillary

Table 4. Numbers and Percentages of Different Missing Teeth and Symmetrical Tooth Agenesis

		Group 1M[a] (N = 12)	Group 2M[a] (N = 20)	Group M[a] (N = 32)	Group C[a] (N = 32)	Chi-Square Test or Fisher's Exact Test/*P* Value 1M vs 2M	1M vs C	2M vs C	M vs C
FDI tooth number									
Maxilla	11 or 21	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)				
	12 or 22	0 (0.0)	6 (19.4)	6 (18.2)	0 (0.0)				
	13 or 23	0 (0.0)	2 (6.5)	2 (6.1)	0 (0.0)				
	14 or 24	0 (0.0)	1 (3.2)	1 (3.0)	0 (0.0)				
	15 or 25	0 (0.0)	7 (22.6)	7 (21.2)	0 (0.0)				
	17 or 27	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)				
	Subtotal	0 (0.0)	16 (51.6)	16 (48.5)	0 (0.0)				
Mandible	31 or 41	0 (0.0)	2 (6.5)	2 (6.1)	0 (0.0)				
	32 or 42	0 (0.0)	2 (6.5)	2 (6.1)	0 (0.0)				
	33 or 43	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)				
	34 or 44	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)				
	35 or 45	2 (100.0)	7 (22.6)	9 (27.3)	3 (100.0)				
	36 or 46	0 (0.0)	2 (6.5)	2 (6.1)	0 (0.0)				
	37 or 47	0 (0.0)	2 (6.5)	2 (6.1)	0 (0.0)				
	Subtotal	2 (100.0)	15 (48.4)	17 (51.5)	3 (100.0)				
	Total	2 (100.0)	31 (100.0)	33 (100.0)	3 (100.0)	.000***	.618	.000***	.000***
Symmetrical tooth agenesis pattern									
Maxilla	12 and 22	0 (0.0)	3 (15.0)	3 (9.4)	0 (0.0)				
	13 and 23	0 (0.0)	1 (5.0)	1 (3.1)	0 (0.0)				
	15 and 25	0 (0.0)	3 (15.0)	3 (9.4)	0 (0.0)				
	Subtotal	0 (0.0)	7 (5.8)	7 (3.6)	0 (0.0)				
Mandible	31 and 41	0 (0.0)	1 (5.0)	1 (3.1)	0 (0.0)				
	35 and 45	0 (0.0)	2 (10.0)	2 (6.3)	1 (3.1)				
	36 and 46	0 (0.0)	1 (5.0)	1 (3.1)	0 (0.0)				
	37 and 47	0 (0.0)	1 (5.0)	1 (3.1)	0 (0.0)				
	Subtotal	0 (0.0)	5 (3.6)	5 (2.2)	0 (0.0)				
	Total	0 (0.0)	12 (4.6)	12 (2.9)	1 (0.2)	.005**	> .999	.000***	.002**

[a] Percentages in parentheses. FDI indicates Fédération Dentaire Internationale.
** $P < .01$; *** $P < .001$.

third molars between groups 1M and 2M, between groups 1M and C, and between groups M and C; significant differences in the rate of missing mandibular third molars between groups 1M and 2M and between group C and the other groups; and significant differences in the rate of missing maxillary and mandibular third molars between group C and the other groups. Table 5 also shows that there were significant differences in the prevalence rates of subjects with symmetrical third molar agenesis, symmetrical agenesis of mandibular third molars, and symmetrical agenesis of combined maxillary and mandibular third molars between groups 2M and C and between groups M and C. Table 6 shows no significant associations between agenesis of third molars and other teeth, or between agenesis of third molars and mandibular second premolars in each group.

There were no significant differences in the prevalence rate of supernumerary teeth or mesiodentes between groups (Table 2).

Anomalies in Shape and Position

There were no significant differences in the prevalence rates of peg-shaped lateral incisors, shovel-shaped incisors, Carabelli's cusps, displacement or mesial angulation of maxillary canines, distal angulation of mandibular second premolars, and ectopic eruption of molars between groups (Table 2).

Table 7 shows significant differences in the distribution of occlusal surface patterns between the maxillary first molars of group C and the maxillary second molars of each group.

DISCUSSION

In this study, subjects with bilateral agenesis of maxillary first molars presented significantly higher prevalence rates of agenesis of other teeth, excluding third molars (Table 2), and advanced tooth agenesis (Table 3) than those without agenesis of maxillary first molars. Aside from the third molar, the most commonly absent tooth was the second premolar (Table 4). Part of these results may be consistent with the findings of Garib et al.[7] that there were strong associations between agenesis of second premolars and other permanent teeth. Bergstrom[1] reported that, of six children with the absence of maxillary and/or mandibular first molars, two pairs of siblings had the absence of two maxillary first molars and four second premolars

Table 5. Distribution of Third Molar Agenesis in Each Group

	Group 1M[a] (N = 12)	Group 2M[a] (N = 20)	Group M[a] (N = 32)	Group C[a] (N = 32)	Statistical Comparisons			
Number of subjects by the number of missing third molars					Kruskal-Wallis Test/*P* Value			
0	3 (25.0)	7 (35.0)	10 (31.3)	25 (78.1)	.001***			
1	3 (25.0)	0 (0.0)	3 (9.4)	2 (6.3)	Steel-Dwass Test/Significant Comparison/*P* Value			
2	3 (25.0)	7 (35.0)	10 (31.3)	3 (9.4)	Group 1M vs Group C 0.012*			
3	2 (16.7)	4 (20.0)	6 (18.8)	1 (3.1)	Group 2M vs Group C 0.007**			
4	1 (8.3)	2 (10.0)	3 (9.4)	1 (3.1)	Group M vs Group C 0.002**			
					Chi-Square Test or Fisher's Exact Test/*P* Value			
Number of different missing third molars[b]					1M vs 2M	1M vs C	2M vs C	M vs C
18 or 28	12 (50.0)	10 (25.0)	22 (34.4)	9 (14.1)	.041*	.000***	.160	.007**
38 or 48	7 (29.2)	24 (60.0)	31 (48.4)	6 (9.4)	.017*	.038*	.000***	.000***
Total	19 (39.6)	34 (42.5)	53 (41.4)	15 (11.7)	.746	.000***	.000***	.000***
Number of subjects with symmetrical third molar agenesis	5 (41.7)	12 (60.0)	17 (53.1)	5 (15.7)	.314	.105	.001***	.002**
Symmetrical third molar agenesis pattern[b]								
18 and 28	3 (25.0)	3 (15.0)	6 (18.8)	4 (12.5)	.647	.369	> .999	.491
38 and 48	3 (25.0)	11 (55.0)	14 (43.8)	2 (6.3)	.098	.116	.000***	.001***
Total	6 (25.0)	14 (35.0)	20 (31.3)	6 (9.4)	.403	.081	.001***	.002**

[a] Percentages in parentheses. N indicates number of subjects.
[b] 18, 28, 38, and 48 indicate Fédération Dentaire Internationale tooth numbers.
* $P < .05$; ** $P < .01$; *** $P < .001$.

coincidently, thus supporting our results. From a genetic point of view, our results were in agreement with the findings of Stockton et al.[10] and Kapadia et al.[15] that individuals with bilateral agenesis of maxillary first molars had congenitally missing maxillary and/or mandibular premolars in a family, a unique form of advanced tooth agenesis in an autosomal-dominant manner caused by PAX9 mutations. Other investigators stated that maxillary first molar agenesis occurred in individuals with advanced tooth agenesis,[1,3,5] as evidenced by this study. Still other researchers reported that advanced tooth agenesis was caused by MSX1 mutations, with an average of 11.0 teeth/person,[9] 8.4 teeth/person,[16] and 12.2 teeth/person,[17] and by PAX9 mutations, with an average of 13.7 teeth/person,[10] 15.5 teeth/person,[15] and 12.7 teeth/person.[18]

Previous studies suggested that subjects with advanced hypodontia had various types of symmetri-

Table 6. Number of Subjects[a] with Other Tooth Agenesis (Excluding Maxillary First Molars) and Mandibular Second Premolar Agenesis by Third Molar Agenesis

	Group 1M (12)		Group 2M (20)		Group M (32)		Group C (32)	
	With Third Molar Agenesis (9)	Without Third Molar Agenesis (3)	With Third Molar Agenesis (13)	Without Third Molar Agenesis (7)	With Third Molar Agenesis (22)	Without Third Molar Agenesis (10)	With Third Molar Agenesis (7)	Without Third Molar Agenesis (25)
With other tooth agenesis	2	0	4	4	6	4	0	2
Without other tooth agenesis	7	3	9	3	16	6	7	23
Fisher's exact test/*P* value	> .999		.356		.683		> .999	
With second premolar agenesis	2	0	3	4	5	4	0	2
Without second premolar agenesis	7	3	10	3	17	6	7	23
Fisher's exact test/*P* value	> .999		.174		.407		> .999	

[a] Number of subjects in parentheses.

Table 7. Distribution of Maxillary Molar Occlusal Surface Patterns

	Group 1M (N = 12)[a]	Group 2M (N = 40)[a]	Group M (N = 52)[a]	Group C (N = 64)[a]			
	Second Molars (S)[b]	Second Molars (S)[b]	Second Molars (S)[b]	First Molars (F)	Second Molars (S)	Statistical Comparisons	
Class I	2 (16.7)	6 (15.0)	8 (15.4)	60 (93.8)	16 (25.0)	Kruskal-Wallis Test/*P* Value	.000***
Class II	1 (8.3)	10 (25.0)	11 (21.2)	4 (6.3)	20 (31.3)	Steel-Dwass Test/Significant	
Class III	4 (33.3)	5 (12.5)	9 (17.3)	0 (0.0)	13 (20.3)	Comparison/*P* Value	.000***
Class IV	5 (41.7)	19 (47.5)	24 (46.2)	0 (0.0)	15 (23.4)	Group 1M (S) vs Group C (F)	.000***
						Group 2M (S) vs Group C (F)	
						Group M (S) vs Group C (F)	.000***
						Group C (S) vs Group C (F)	.000***

[a] N indicates number of teeth examined.
[b] Second molars located in the affected quadrants.
*** $P < .001$.

cal tooth agenesis.[6,9,10,15–18] In our study, those subjects with bilateral agenesis of maxillary first molars had a significantly higher prevalence rate of symmetrical tooth agenesis, with third molars excluded, than those with unilateral agenesis and without agenesis of maxillary first molars (Tables 2 and 4). These results were consistent with the findings of previous investigators[10,15,18] that, in subjects with advanced tooth agenesis caused by PAX mutations, most patterns of tooth agenesis, including maxillary first molar agenesis, were bilaterally symmetrical.

In this study, those subjects with unilateral and bilateral agenesis of maxillary first molars had a significantly higher prevalence rate of third molar agenesis than those without agenesis of maxillary first molars. These results may suggest that maxillary first molar agenesis and third molar agenesis are different phenotypes of the same genetic defect and support several other studies[10,15,18] demonstrating that as a result of PAX9 mutations, almost all individuals with bilateral agenesis of maxillary first molars had bilateral agenesis of maxillary and mandibular third molars in a family with advanced tooth agenesis.

From a clinical perspective, our finding that the subjects with bilateral agenesis of maxillary first molars predominantly had symmetrical agenesis of mandibular third molars may be convenient for orthodontists to treat malocclusions with maxillary first molar agenesis, because there is no need to extract molars if maxillary third molars are present and mandibular third molars are absent. On the other hand, our finding that the subjects with unilateral agenesis of maxillary first molars predominantly had maxillary third molar agenesis may indicate a possibility of the eruption of only one molar in each of the maxillary quadrants.

Previous studies showed a significant association of third molar agenesis with agenesis of other teeth, particularly second premolars and lateral incisors.[7,8] Some investigators showed that MSX1 mutations predominantly affected agenesis of both second premolars and third molars.[16,17] Their findings[7,8,16,17] may not support our results that there were no statistically significant associations between agenesis of third molars and agenesis of other teeth, including second premolars and excluding maxillary first molars (Table 6). Different phenotypes between MSX1[9,16,17] and PAX9[10,15,18] mutations may account for the fact that agenesis of both first and second molars is observed in families with the PAX9 mutation, thus indicating that PAX9 mutations play a critical role in severe molar agenesis.

Our study found no significant associations between maxillary first molar agenesis and other dental anomalies, except for agenesis of other teeth. These findings disagreed with those of the study published by Garib et al.,[7] who observed statistically significant associations of second premolar agenesis with other dental anomalies, including microdontia, deciduous molar infraocclusion, and certain dental ectopias as well as other permanent tooth agenesis.

Agenesis of the maxillary first molars is differentiated from delayed eruption of the maxillary first molars due to immature formation.[19] Our results showed significant differences in the distribution of occlusal surface patterns between the maxillary first molars of the control subjects (group C) and the maxillary second molars of those with tooth agenesis (groups 1M and 2M). These results reconfirmed our previous findings that the most anterior maxillary molars located in the affected quadrants were the early erupted second molars caused by the first molar agenesis rather than the late erupted first molars caused by immature tooth formation.

CONCLUSIONS

- Agenesis of maxillary first molars is associated with a higher prevalence of other permanent tooth agenesis and advanced tooth agenesis.

- There is no association between maxillary first molar agenesis and supernumerary teeth, tooth shape abnormalities, and tooth ectopia.

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