Mandibular lateral incisorcanine transposition, concomitant dental anomalies, and genetic control

Sheldon Peck, DDS, MScD; Leena Peck, DMD, MSD; Matti Kataja, PhD

Tooth transposition is an anomaly of eruption characterized by interchanged positions of two adjacent teeth. In some cases, transposition is caused by intraosseous migration and eruption of a single tooth into a distantly ectopic position, one ordinarily occupied by a nonadjacent tooth. It is an uncommon phenomenon, usually occurring unrelated to and independent of the commonplace condition of dental crowding. As such, tooth transposition is a designation applied to extreme types of ectopic eruption, each causing a change in the natural order of the permanent teeth. These relatively rare permutations of tooth order have been observed to occur at several specific sites in the

human maxilla and mandible.

Mandibular tooth transpositions are seen less frequently and with less variety than those in the maxilla. Based upon data from published surveys,¹⁻⁵ we can estimate that transpositions involving teeth in the mandible account for 15% to 30% of all tooth transpositions. Five anatomical types of maxillary transpositions have been identified and described.⁶ In comparison, only two kinds of mandibular transpositions occur typically:

- 1. Mandibular lateral incisor–canine (abbreviated here as Mn.I2.C)
- 2. Mandibular canine transmigrated/erupted (Mn.C transerupted), which is a transposition

Abstract

Mandibular lateral incisor-canine (Mn.I2.C) transposition is a rare developmental disturbance of tooth order characterized by positional interchange of the two teeth. In children with Mn.I2.C anomaly, the mandibular lateral incisor shows distal ectopic eruption and the adjacent canine subsequently erupts mesial to it. A sample of 60 orthodontic patients with Mn.I2.C transposition was studied using roentgenograms taken at the time of diagnosis. Two age-related phenotypes of the anomaly were identified: early-stage (median age, 9 years) and mature-stage (median age, 12 years). Mn.I2.C transposition occurred bilaterally in 10 subjects (17%) and favored female expression (sex ratio, M1:F3) and right-side occurrence (68% of unilateral cases). Statistically significant associations were found between Mn.I2.C transposition and increased frequency of tooth agenesis (M3, p<0.01; MnP2, p<0.01) and peg-shaped maxillary lateral incisors (p<0.0001). The results from this study and the analysis of 50 previously published cases provide evidence that Mn.I2.C transposition is a disturbance of tooth order and eruptive position probably caused by genetic influences. The Mn.I2.C anomaly likely results from genetic mechanisms similar to those responsible for occurrences of its associated dental anomalies, such as tooth agenesis and peg-shaped maxillary lateral incisors. In an appendix, clinical orthodontic management of Mn.I2.C transposition is discussed, based on treatment data derived from the study sample.

Key Words

Tooth transposition • Tooth eruption, ectopic • Tooth abnormalities • Malocclusion • Genetics, clinical

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Peck; Peck; Kataja



Figure 1A

Figure 1A-J

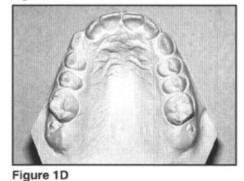
Mandibular lateral incisor-canine (Mn.I2.C) transposition, bilateral expression, in a 10.7-year-old girl (subject 02) with Class II Division 1 malocclusion.

A-H: Dental casts, including close-ups of the mandibular cast, focusing on the transposed teeth.

I-J: Periapical roentgenograms showing transposed teeth, right and left sides. Orthodontic treatment was performed on a nonextraction basis, keeping the transposed order of the teeth.



Figure 1B



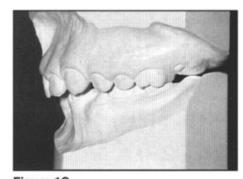


Figure 1C



Figure 1E

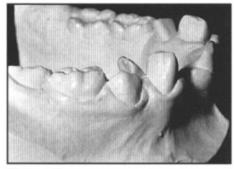


Figure 1F



Figure 1G



Figure 1H

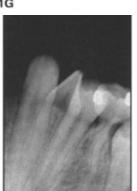


Figure 11

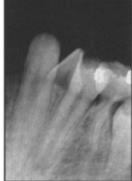


Figure 1J

caused by the ectopic eruption of an impacted mandibular canine after intraosseous transmigration across the symphyseal midline. Less than 20% of all transmigrating mandibular canines finally erupt and become transpositions; the rest of them remain as nonerupted, impacted teeth.⁵

Both types of mandibular tooth transposition are very rare. The prevalence rate for Mn.I2.C transposition, calculated using data from two population surveys, 1,2 is 0.03% (or 3 cases per 10,000 individuals). Mn.C transcrupted transposition is likely found at a prevalence rate of less than 0.02%.5

Because of their rareness, tooth transpositions in the mandible were overlooked by most early observers. In his exhaustive treatise on dental anomalies published in 1877, Magitot⁷ wrote that "the lower teeth seemed to have escaped totally any transposition involvement" and he published no examples of mandibular transposition. Angle⁸ in 1907 was one of the first to recognize mandibular tooth transposition, describing the orthodontic management of a malocclusion involving an Mn.I2.C abnormality. Since then, Mn.I2.C transposition has become known largely through occasional published reports, the most extensive of which documented 13 cases. Recently, a published report described monozygotic twins who each expressed the Mn.I2.C anomaly.

The clinical appearance of Mn.I2.C transposition typically shows severe distal tipping, displacement and rotation of the mandibular lateral incisor as it erupts ectopically into the area normally reserved for the same-side canine and first premolar (Figure 1). Later, the mandibular canine erupts on the alveolar ridge transposed mesially to the ectopic lateral incisor. Thus, the resulting tooth order in an affected mandibular quadrant is central incisor, canine, lateral incisor and first premolar.

The aim of this article is to examine the nature of Mn.I2.C transposition and its associated features, because the abnormality presents an unusual and challenging orthodontic problem. A sample of subjects with Mn.I2.C transposition was assembled for study. For comparison, an additional sample was gathered from published Mn.I2.C case reports. Furthermore, a section on clinical orthodontic management of the anomaly is appended to this article. This is the fourth of a series^{5,6,11} of comprehensive studies that systematically examine all human tooth-transposition ectopia of typical occurrence and clinical interest.

Materials and methods

A sample of 60 subjects with the Mn.I2.C transposition anomaly was collected from 44 orthodontists practicing in North America and one orthodontist practicing in Japan. This grouping is the largest sample assembled to this time of persons affected with the Mn.I2.C transposition abnormality. In epidemiological terms, a sample of 60 Mn.I2.C subjects is consistent with the expected yield from a dental population screening of approximately 200,000 children.

Seven variables were recorded for each of the 60 subjects with Mn.I2.C transposition:

- 1. Mn.I2.C location: bilateral, unilateral right or left
- 2. sex
- 3. age at diagnosis, to the nearest whole year
- 4. self-identified racial group
- 5. Angle's classification of molar occlusion
- 6. agenesis of any permanent teeth, including third molars (M3)
- 7. presence of peg-shaped maxillary lateral incisors (MxI2)

The sample contained 45 females and 15 males. The mean age at diagnosis was 11.9 years, the median age was 10.5 years and the age range was 7 to 45 years. Fifty-eight of the subjects identified as whites, one as black, and one as Asian. No history of dentofacial trauma was noted for any of the participants.

Panoramic or full-mouth periapical roentgenograms, or both, taken at the time of diagnosis of the transpositions, were the primary study materials. These films, along with clinical information and photographs from the case-contributing orthodontists, were used to identify accurately the Mn.I2.C transpositions. Furthermore, the dental roentgenograms were employed for determination of the occurrence of tooth agenesis and the peg-shaped MxI2 trait, two dental anomalies that have been earlier associated with other abnormalities of tooth position, such as maxillary canine-first premolar (Mx.C.P1) transposition¹¹ and the palatally displaced canine. ¹²⁻¹⁵ Most of the subjects were preadolescents, so for many of them additional panoramic roentgenograms were taken at older ages to confirm thirdmolar presence or absence.

Maxillary lateral incisors (MxI2) identified as having the peg-shape trait were defined as those having conical crown shape "reducing in diameter from the cervix to the incisal edge," according to criteria established by Le Bot and Salmon. Peg-shaped MxI2 represents an extreme form of tooth-size reduction that has been associated with agenesis of other teeth and reductions in tooth size throughout the dentition. In Since MxI2 emergence occurs relatively early (at approximately 8 years of age), its peg-shaped phenotype can become an easily recognized marker-trait often signaling the development of associated dental anomalies in the individual.

Data comparisons were performed between the findings from the Mn.I2.C transposition sample and normal population reference values. Statistical significance was set at the 0.05 probability level. The odds ratio was calculated to measure the strength of association between Mn.I2.C transposition and the occurrence of either concomitant tooth agenesis or peg-shaped MxI2.

Results

Characteristics of Mn.I2.C transposition

Examination of panoramic and/or full-mouth dental roentgenograms for the 60 subjects in this study indicated that Mn.I2.C transposition in children and adults may be observed at either of two age-related anatomical stages (Figure 2A-F):

(1) Early-stage transposition (n=36 subjects; median age=9 years; greater than 70% were 7 to

Figure 2A-F Panoral roentgenograms of six subjects (A to F), arranged according to age, with unilateral Mn.I2.C transposition to demonstrate the two age-related anatomical stages in the formation of the Mn.I2.C anomaly. The white arrow indicates location of the affected mandibular lateral incisor. Earlystage Mn.I2.C transposition is characterized by early distal tipping, coronal displacement and severe mesiolingual rotation of the affected, erupting mandibular lateral incisor. prompting the neighboring, unerupted canine to start migrating mesially away from it. Mature-stage Mn.I2.C transposition is characterized by ectopic eruption of the affected mandibular canine between same-side lateral and central incisors, with development of more clearly transposed crown and root relationships between the lateral incisor and canine. A: 7.7-year-old girl (subject no. 05), unilateral right Mn.l2.C, early stage.

B: 9.2-year-old girl (subject 25), unilateral right Mn.12.C, early stage.

C: 10.5-year-old girl (subject 19), unilateral right Mn.I2.C, early stage.

D: 10.5-year-old girl (subject 26), unilateral right Mn.I2.C, mature stage.

E: 11.7-year-old girl (subject 53), unilateral right Mn.I2.C, mature stage.

F: 16.4-year-old girl (subject 15), unilateral left Mn.I2.C, mature stage.

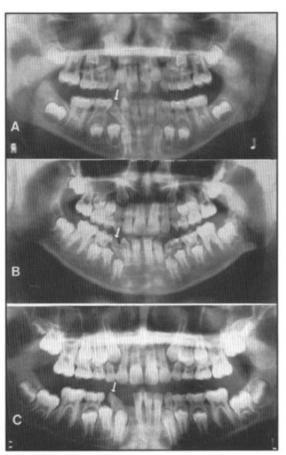


Figure 2A-C

10 years old). This stage of Mn.I2.C development is characterized by early distal tipping, coronal displacement and severe mesiolingual rotation (ranging from 60 to 120 degrees) of the mandibular lateral incisor, prompting the adjacent canine to develop transposed mesially to it. The deciduous first molar is often undermined by the ectopically developing lateral incisor and it usually exfoliates prematurely because of this. In the early stage, the Mn.I2.C anomaly shows transposition of the mandibular lateral incisor and canine crowns, but typically the roots of these teeth are not yet in a switched position.

(2) Mature-stage transposition (n=24 subjects; median age=12 years; greater than 90% were 11 years or older). This later stage of Mn.I2.C development is characterized by ectopic position of a mandibular canine between the same-side lateral and central incisors. The erupted mandibular lateral incisor is displaced distally and lingually with severe mesiolingual rotation ranging from 60 to 120 degrees. In most cases at this stage, the crowns of the canine and lateral incisor are clearly transposed and the roots have uprighted naturally to a superimposed or fully transposed relationship. Typically, by age 13 years, Mn.I2.C transposition matures to a com-

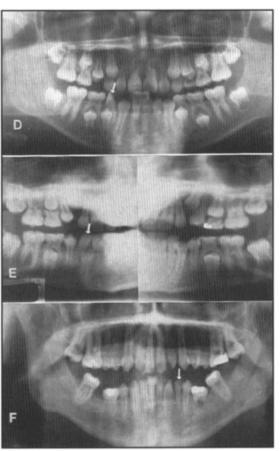


Figure 2D-F

plete root transposition.

The particular stage and age at which Mn.I2.C transposition is diagnosed for the individual patient could make a significant difference in the way the condition is treated orthodontically. (See the Appendix of this article for a section on "Clinical orthodontic management of Mn.I2.C transposition.")

Within the Mn.I2.C sample, the distribution of malocclusions according to Angle's classification appeared relatively normal for an orthodontic population. Thirty-nine (65%) of the cases were Class I, 16 (27%) were Class II Division 1, 5 (8%) were Class II Division 2, and none were Class III.

Pertinent data describing the Mn.I2.C transposition sample are shown in Table 1. For each subject, the tabulated factors are location of Mn.I2.C transposition, sex, age, racial grouping, and identification of associated permanent-tooth agenesis and peg-shaped MxI2.

Table 2 gives the distribution and relative frequency of Mn.I2.C transposition according to sidedness and sex. At least three notable characteristics of the sample may be ascertained from this table:

1. Bilateral expression. Occurring at a rate of 17% (10 subjects), bilateralism of the Mn.I2.C ab-

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56 X M 13 W - 57 X M 16 W 18,28,38,48 58 X F 11 W 18			Х					-	-	
57 X M 16 W 18,28,38,48 58 X F 11 W 18		Х						-	-	
57 X M 16 W 18,28,38,48 58 X F 11 W 18			Х					-	-	
58 X F 11 W 18		Χ			M	16	W	18,28,38,48	-	
			Χ		F				-	
7 1 17 17	59		Χ		F	17	W	18	-	
60 X F 11 W 18,28,38,48									-	
			16	10		•	•		6 subjects	
			(27%)						(10%)	

Table 2
Distribution and relative frequency of mandibular lateral incisor-canine (Mn.I2.C) transposition anomaly according to location and sex, N = 60 subjects.

Location	Female	Male
Right side	27	7 = 34 (56%)
Left side	11	5 = 16 (27%)
Bilateral	7	3 = 10 (17%)
	45 (75%)	15 (25%)

normality was elevated beyond chance occurrence.

- 2. Dominance of right-side occurrence. Right-side expression was seen in 34 of the 50 unilateral cases of Mn.I2.C, for a relative frequency of 68%. This laterality favoring right-side occurrence among unilateral cases prevailed also after subgrouping according to sex: male (58% right-sided) and female (71% right-sided).
- 3. Dominance of female occurrence. Girls comprised 75% (45 subjects) of the sample, yielding a sex ratio of M1:F3 for Mn.I2.C transposition.

Associated dental anomalies

Table 3 reports the frequency of tooth agenesis (including third molars) in Mn.I2.C transposition cases. The frequencies are displayed in descending order according to tooth type, sex, number of affected subjects and number of absent teeth. The mandibular and maxillary third molars were the most frequently missing teeth, showing the largest numbers of affected individuals and affected teeth, followed by the mandibular second premolar. The average number of teeth absent per case among the female Mn.I2.C subjects was over twice as high as that observed for the male subjects, a significant difference statistically (F=70/45=1.56; M=11/15=0.73; t-test value [Poisson distribution] = 2.85, d.f.=79, p<0.01).

Table 4 displays summary data on the prevalence of tooth agenesis (calculated for five epidemiological categories) and peg-shaped MxI2 anomaly found in the sample of 60 Mn.I2.C subjects. Twenty-four (40%) of the 60 subjects with Mn.I2.C transposition had associated hypodontia of one or more permanent teeth, including third molars. The most extreme case was a girl with 11 absent teeth; the mildest expressions of hypodontia were seen in seven subjects who each had one missing tooth. Six (10%) of the subjects expressed peg-shape anomaly of one or both MxI2. Several instances of small MxI2 went unrecorded, since the size and shape reductions were not severe enough to fit the "peg-shaped

crown" definition. In total, 27 (45%) of the 60 Mn.I2.C transposition subjects expressed missing and/or peg-shaped teeth.

Table 4 also shows data comparisons with normal population reference values 16,18,19 for prevalence of tooth agenesis and MxI2 peg-shape anomaly. Statistical testing of differences in prevalence was performed using the Chi-square test (χ^2). For the Mn.I2.C sample, statistically significant increases were observed in the prevalence of tooth agenesis in four of the five recorded categories, the exception being MxI2 agenesis which showed no difference (χ^2 =0.02, not significant). A five-fold increase was noted in the occurrence of MxI2 peg-shape anomaly among the Mn.I2.C subjects, a very highly significant difference statistically.

Strengths of associations between Mn.I2.C transposition and the expression of either tooth agenesis or MxI2 peg-shape anomaly were evaluated using the odds-ratio assessment (OR; 95% confidence interval; see Table 4). The odds ratio is a proportion of probabilities that in this study determined if the proportion of persons with either tooth agenesis or MxI2 peg-shape anomaly in the presence of Mn.I2.C transposition is greater than the proportion of persons with either anomaly in a normal population. The arithmetic value of the odds ratio is minimally influenced by sample size and, as such, it can function as a reliable indicator of clinical significance of trait associations, particularly of conditions occurring at low prevalence. The results of the odds-ratio assessments in this study added statistical evidence indicating the likelihood of clinical associations between Mn.I2.C transposition and all tested anomalous conditions except one: MxI2 agenesis. The odds-ratio value for this one anomaly suggested a lack of clinical association between occurrences of MxI2 agenesis and Mn.I2.C transposition.

Discussion

This study has identified mandibular lateral incisor–canine (Mn.I2.C) transposition as disturbance of tooth order that has at least two agerelated roentgenographic phenotypes and is found often accompanied by other dental anomalies.

The finding that a preponderance of occurrences of Mn.I2.C anomaly were in females (75%) is noteworthy. Greater expression in women than men is also the finding in studies of related dental abnormalities, such as hypodontia, ¹⁸⁻²³ peg-shaped MxI2 anomaly, ²⁴ palatally displaced canine (PDC) ^{14,25-27} and maxillary canine–first pre-

Table 3 Frequency of tooth agenesis in Mn.I2.C transposition cases, classified according to tooth type, sex, number of affected persons and number of absent teeth, N = 60 subjects. Tooth type Males, N=15 Females, N=45 M + F combined Ν Ν % Ν Ν Ν % % % Ν % subjects teeth subjects teeth subjects teeth MnM3 МхМЗ MnP2 MxP2 MxP1 MxI2 2.5 2.5 MnM2 MnP1 Mnl2 Total Mn=mandibular; Mx=maxillary

Table 4 Prevalence of tooth agenesis and peg-shaped Mxl2 in subjects with Mn.I2.C transposition anomaly (N = 60), compared with normal prevalence values								
Condition	Mn.I2.C (N=60) N cases %		Normal prevalence value	Difference	Odds ratio (OR)	95% confidence interval for odds ratio		
Any tooth agenesis (including M3)	24	40%	524/2061 = 25% Bredy, ¹⁸ 1991	$\chi^2 = 6.46$ $p < 0.05$	1.96	(1.17 - 3.28)		
M3 agenesis (1or more teeth)	22	37%	427/2061 = 21% Bredy, 18 1991	$\chi^2 = 8.89$ $\rho < 0.01$	2.22	(1.31 - 3.74)		
Tooth agenesis, excluding M3	7	12%	53/1064 = 5% Grahnén,¹º 1956	$\chi^2 = 5.02$ $p < 0.05$	2.52	(1.12 - 5.65)		
Mandibular P2 agenesis (1 or 2 teeth	5)	8%	25/1064 = 2% Grahnén, ¹⁹ 1956	$\chi^2 = 7.83$ $p < 0.01$	3.78	(1.49 - 9.59)		
Maxillary I2 agenesis (1 or 2 teeth	1	2%	109/5738 = 2% Le Bot,¹6 1977	$\chi^2 = 0.02$ n.s.	0.88	(0.12 - 6.37)		
Maxillary I2 peg-shape anomaly (1 or 2 teeth) n.s. = not significant	9 6	10%	91/5738 = 2% Le Bot, ¹⁶ 1977	$\chi^2 = 25.56$ $p < 0.0001$	6.90	(3.26 - 14.6)		

molar (Mx.C.P1) transposition.¹¹ Most of these cited studies used samples derived from the general population, but the samples in two studies^{11,14} were composed of orthodontic patients, who tend to reflect a moderate sex bias favoring girls.²⁸ Nevertheless, the strength of the M1:F3 sex ratio favoring female expression of MnI2.C would clearly override any possible orthodontic sampling bias in our study. A biologic explanation would seem to be the most likely factor

causing the observed higher female prevalence of Mn.I2.C anomaly.

Strong preference for right-side expression (68% of unilateral Mn.I2.C cases) is an interesting observation in this study. Laterality or sidedness is not an uncommon finding in studies of other orofacial anomalies. A tendency toward right-side preference has been found also in subjects with palatal displacement of canines. 14,25-27 Left-side preference has been found

Publication	R	L	Bilateral	Sex	Age†	Racial group	Tooth agenesis ‡ n=44	Peg-shaped MxI2 * n=44
Adler-Hradecky(ref.34),		X		F	12	W	-	-
1972	Х			М	11	W	12,22	-
Al-Shawaf(ref.35), 1988		Х		М	17	W	-	-
Ascher(ref.36), 1953		Х	V	M	18	W	-	-
			X X	М	11	W	- 15.05	-
			X	F	13 1 1	W W	15,25 -	-
Bradley(ref.37), 1990			X	M F	10	W	-	12, 22
Bradiey(161.57), 1990	Х		^	M	9	W	-	12, 22
	^		Х	M	9	w	-	_
Brownbill(ref.38), 1994			x	F	9	w	_	_
Florczyk(ref.39), 1971			X	F	11	W	-	-
Järvinen(ref.40), 1978		Х		F	9	W	-	-
Järvinen(ref.1), 1982	X			F	10	W	•	-
	Χ			F	10	W	-	12,22
		Х		M	11	W	15,13,35,45	-
Kryshtalskyj(ref.41), 1982			X	М	50	W	-	-
Lieberman(ref.42), 1983		Х		F	10	W	-	•
Maric(ref.43), 1987	X			М	7	W	?	?
Nakata(ref.44), 1989	X			M	10	A	?	?
Niczky(ref.2), 1967	Х	v		M	10	W	?	?
Pajoni(ref.45), 1990 Pifer(ref.46), 1973		Х	Х	M F	9 27	W W	- ?	?
Platzer(ref.47), 1968	•	Х	^	M	37	W	; ?	?
rialzer(rei.47), 1900		x		M	8	W	:	:
	X	^		M	9	W	<u>-</u>	_
	Α		Х	M	9	w	•	_
Parker(ref.48), 1990	X			F	10	w	_	_
. u		X		F	13	w	_	_
Shapira(ref.49), 1983			X	F	15	W	12	22
, , , , , , , , , , , , , , , , , , , ,		Χ		F	14	W	-	-
	X			M	12	W	-	-
	X			F	13	W	-	-
Shapira(ref.50), 1978			Х	М	11	W	-	12
Vichi(ref.9), 1986			Х	F	7	W	•	-
		X		F	7	W	-	-
	.,	X		F	8	W	-	-
	X	V		F	8	W	22	-
	v	Х		F F	8	W W	-	-
	Х	X		M	8 8	W	-	<u>-</u>
		X		F	9	W	- -	-
	X	^		F	9	W	- -	-
	X			F	9	w	-	-
	,,		Х	M	9	w	=	-
			X	F	9	w	22	-
	Χ			F	10	W	-	-
Werner(ref.51), 1989			X	F	11	?	•	-
Yaillen(ref.52), 1990	Χ			F	8	W	-	-
Zuckerberg(ref.53), 1982	Χ			М	45	?	?	?
Tatala	40	4.0	40	MOG			0 . 1.1	4
Totals	18	16	16	M22			6 subjects	4 subjects
N=50 cases	(36%)	(32%)	(32%)	F28			(14%) n=44	(9%) n=44
Notes: Tooth numbering according to Race: W=white, A=Asian, B=I † Age at diagnosis to neares: ‡ Excluding third molars * Maxillary lateral incisor	black	-digit syste	em					

Table 6 Aspects of orthodontic treatment for patients with Mn.I2.C transposition anomaly, comparing two-phase versus one-phase treatment approaches. N=60 subjects Type of treatment Age at Orthodontic Average time, diagnosis Finished diagnosis permanent-tooth to end of treatment tooth order (years) extraction (years, incomplete Mean age Median age Extraction Transposed Nonextraction data, n=25) Corrected Two-phase (N=28) 8.9 9.0 4 (14%) 24 (86%) 5.4 (n=14) 4 (14%) 24 (86%) One-phase (N=32) 14.3 12.0 11 (34%) 21 (66%) 3.5 (n=11) 12 (38%) 20 (62%) Total sample (N=60) 45 (75%) 11.9 10.5 15 (25%) 4.5 (n=25) 16 (27%) 44 (73%)

in individuals with Mx.C.P1 transposition^{11,29} and in cases of unilateral cleft lip with or without cleft palate.³⁰ This definite pattern favoring right-side expression of the Mn.I2.C abnormality is too dominant to be disregarded and it remains an unexplained finding at this time. In this light, an intriguing hypothesis for investigation would be that the strong sidedness preferences in genetically controlled anomalies may actually be triggered in some fashion by aspects of the genetic and developmental processes themselves.

Occlusal-view observation of the Mn.I2.C transposition anomaly shows severe mesiolingual rotation (mesiolinguoversion) of the transposed mandibular lateral incisor (see Figure 1). This characteristic pattern of tooth rotation does not seem related to any spatial pressures from neighboring deciduous or permanent teeth. Pathognomonic tooth rotations have been identified with other studied dental malpositions. For example, palatally displaced canines13 and winged maxillary central incisors31-33 also possess characteristic mesiolingual rotations. In contrast, the canine in Mx.C.P1 transposition is usually rotated mesiofacially.11 These specific orientations of tooth rotation occurring within dental anomaly patterns may be related to the basic nature of the development of the periodontal attachment apparatus.

The collective data from the present study provide evidence pointing to a strong genetic component in the etiology of Mn.I2.C transposition. The statistically significant increases in the occurrence of associated dental anomalies, particularly congenital absence of third molars (p<0.01) and mandibular second premolars (p<0.01) and the presence of the MxI2 peg-shape anomaly (p<0.0001), suggest a common genetic basis. Furthermore, the M1:F3 sex ratio, strongly implying a sex-linked etiologic factor, adds support for a heterogeneity of genetic controls underlying the formation of the Mn.I2.C transposition anomaly. Family studies would be helpful in confirming

more substantially a genetic origin for the Mn.I2.C abnormality. The only reported instance of familial occurrence of Mn.I2.C transposition involved a set of monozygotic twin girls, both exhibiting unilateral right expression. Unfortunately, the very low prevalence rate (0.03%) for the anomaly discourages the prospects for easy collection of other familial occurrences.

Analysis of previously published cases

To provide comparative data, a compilation of published documented cases of Mn.I2.C transposition was undertaken (Table 5). A world literature search uncovered 50 Mn.I2.C cases in 23 articles, 1,2,9, 34-53 each indicating at least information on the transposition site, proband's sex, and age at diagnosis (rounded to nearest whole year). The mean age was 12.6 years, the median age was 10 years and the age range was 7 to 50 years. Forty-four of the 50 case reports were accompanied by roentgenograms and photographs sufficient to determine permanent tooth agenesis (excluding M3) and presence of MxI2 peg-shape anomaly.

On analysis, the grouping of 50 published documented cases of Mn.I2.C transposition demonstrated most of the same trends identified in the sample of 60 Mn.I2.C subjects collected for this study. Bilateral expression was high (16 individuals, 32%) among the 50 published occurrences. Females predominated (sex ratio, M1:F1.3), although to a significantly lesser degree than in the study sample. Among 34 unilateral cases, right-side expression was slightly favored (R18:L16), but to a lesser degree than that observed in the study sample.

Of the 44 cases with published roentgenograms, tooth agenesis (excluding third molars) was found in six individuals (14%), almost a three-fold elevation beyond the normal prevalence rate¹⁹ (see Table 4). The frequency of hypodontia calculated according to tooth type shows a higher rate of maxillary lateral incisor absence (4 cases, 9%) than mandibular second premolar

absence (2 cases, 5%), a divergence from this study's findings. This discrepancy could be related to the fact that compilations of case reports provide an easy source of bias since cases are usually chosen for publication in part because of their visually striking features, like lateral incisor anomalies or bilateralism (almost double in this sample compared with the study sample). Peg-shape anomaly of the maxillary lateral incisor was noted in 4 cases (9%), over four times the normal rate of occurrence.¹⁶ These elevated frequencies of genetically controlled dental disturbances such as tooth agenesis or MxI2 pegshape anomaly parallel the associated findings from our study sample. Thus, further evidence becomes apparent, supporting genetic factors as a primary origin for the Mn.I2.C transposition anomaly.

The age-related anatomical dichotomy (mature stage versus early stage) identified from dental radiographic analysis of our study sample was corroborated by this sample of published Mn.I2.C cases. The six oldest individuals (14 to 50 years of age) in the subgroup of 44 cases with published roentgenograms showed mature-stage Mn.I2.C transpositions with completely transposed crown and root positions. In contrast, the published cases of younger patients, ranging in age from 7 to 10 years, showed severe distal tipping of the lateral incisor with its root superimposed over the unerupted canine, the typical appearance of early-stage Mn.I2.C anomaly formation.

Conclusions

The findings from this first large-sample study of mandibular lateral incisor-canine (Mn.I2.C) transposition have biological and clinical implications. Strong associations were found between this anomaly and the occurrence of tooth agenesis and MxI2 peg-shaped phenotype, both of which are known to be familial traits under genetic control. Thus, it is reasonable to speculate that the Mn.I2.C anomaly is controlled by similar genetic mechanisms. Family studies would provide more definitive evidence regarding a genetic basis, but such investigations may be remote due to the rareness of this type of tooth transposition. Recognition of the early stages in the formation of Mn.I2.C transposition can yield clinical advantages in the orthodontic management of this malocclusion (see Appendix).

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Author Address

Dr. Sheldon Peck

1615 Beacon Street

Newton, MA 02168 USA

E-mail: pecks@warren.med.harvard.edu

Sheldon Peck, Department of Orthodontics and Dentofacial Orthopedics, Harvard School of Dental Medicine, Boston, Mass.

Leena Peck, Department of Orthodontics and Dentofacial Orthopedics, Harvard School of Dental Medicine, Boston, Mass.

Matti Kataja, National Public Health Institute, Helsinki, Finland.

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Appendix 1: Clinical orthodontic management of Mn.I2.C transposition

Table 6 indicates aspects of orthodontic treatment for the 60 patients in this study of malocclusions involving Mn.I2.C transpositions. Clinical information was gathered from the 45 orthodontists who contributed case records to this study. For summary data tabulations, the sample was subdivided into two groups: those patients who received treatment in one continuous phase and those who received two-phase treatment, the first phase of which was an early-stage intervention. Other variables examined were (1) mean and median ages at diagnosis, (2) need for orthodontic permanenttooth extractions, (3) mean length of treatment from initial diagnostic records to final appliance removal, and (4) finished status of the transposition: corrected or left transposed.

The data clearly show that when Mn.I2.C transposition is recognized and treated in its early stage (for example, age 9 years in a two-phase treatment program) the transposition can be intercepted and easily corrected on a nonextraction basis utilizing fixed orthodontic appliances. Often, one or more same-side deciduous anterior teeth, especially the deciduous canine, require extraction to facilitate an early-stage corrective treatment. In contrast, older patients (over 12 years of age) with Mn.I2.C transposition are more likely to undergo one-phase orthodontic treatment, with greater chances of involving permanent-tooth extractions and maintaining, not correcting, the transposed tooth order, because of the increased difficulty in successfully correcting mature-stage transpositions. In all cases,

orthodontic treatment time was significantly longer than the customary two years experienced with more typical malocclusions.

One-quarter (15 subjects) of the sample underwent extraction of one or more permanent teeth (excluding third molars) as part of orthodontic treatment. This low extraction frequency discredits the often-assumed clinical notion that tooth transposition occurs as a result of severe dental crowding; in reality, the preponderance of Mn.I2.C cases showed arch-space adequacy in both jaws. In five unilateral cases, the affected lower lateral incisor was the only tooth extraction, effectively correcting the transposed tooth order. In 8 of the 15 extraction cases, two to four permanent teeth were in the extraction plan, usually including the transposed mandibular lateral incisor(s) and two or more first premolars. With the sample subdivided into two-phase (early) orthodontic intervention and one-phase treatment, the two-phase subgroup showed less than one-half the frequency of permanent-tooth extraction than that recorded for the one-phase subgroup (14% versus 34%), highlighting an apparent benefit of early recognition of the Mn.I2.C malocclusion.

As may have been expected, the two-phase early-intervention approach did lengthen total orthodontic treatment involvement by approximately two additional years (including time between phases), but it also resulted in a sharp increase in the chance for successful orthodontic correction of the transposed tooth order on finishing.