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A Morphological Study of the Oral and Maxillofacial Area in Patients with Williams Syndrome

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Williams syndrome was reported in 1961 by Williams and coworkers as a syndrome characterized by mental retardation, supravalvular aortic stenosis, and specific facies. It is thought to be a contiguous gene syndrome that is a neurocognitive disorder commonly caused by a 1.5 Mb deletion containing about 20 genes, for example the elastin gene, the LIM kinase 1 gene, on chromosome band 7q11.23. Accordingly, in the present study we conducted a morphological study of the oral and maxillofacial area in patients with Williams syndrome. The subjects were 15 patients found to have a microdeletion of chromosome 7q11.23 and diagnosed as having Williams syndrome. The methods used consisted of conducting analyses of cephalometric radiograms of the head and gnathostatic models, and the oral and radiographic findings. An analysis of cephalometric radiograms of the head revealed significantly higher values for mandibular arch, mandibular incisor protrusion, upper molar position, cranial length anterior, and lip protrusion than the mean values in Japanese, and as a result the facies of Williams syndrome patients appeared to be characterized by maxillary protrusion, labial inclination of the lower incisor, protrusion of the lower lip, and, in terms of facial description, a dolicofacial pattern. Analysis of gnathostatic models and the oral and radiographic findings showed congenitally missing teeth, microdontia, short-rooted teeth.

Key words: Williams syndrome, the oral and maxillofacial area, cephalometric radiograms

Introduction

Williams syndrome was reported in 1961 by Williams and coworkers[1] as a syndrome characterized by mental retardation, supravalvular aortic stenosis, and specific facies. It is also referred to as the "Elfin face syndrome", and it is thought to be a contiguous gene syndrome that is a neurocognitive disorder commonly caused by a 1.5 Mb deletion containing about 20 genes, for example the elastin gene, the LIM kinase 1 gene, on chromosome band 7q11.23[2].

Dental hypoplasia or aplasia and malocclusion are said to be common findings in the oral and maxillofacial area[1)3)], but there are still few precise reports, and a search of the Japanese and foreign literature failed to retrieve any reports of

Table 1 Clinical summary of the subjects of this study

Case	Sex/ Age (y)	Cardiovascular diseases	Other diseases or abnormalities	Mentality (IQ)
1	M/3	mild SVAS, central PS		48
2	M/8	SVAS, VSD (natural closure)	moyamoya disease, iris: pale brown and stellate sharp	42
3	M/9	PPS	iris: stellate sharp	under 40
4	M/10	SVAS		61
5	M/12	no cardiovascular disease	diabetes mellitus, iris: stellate sharp, contractures of fingers	45
6	M/12	mild SVAS, VSD (natural closure), LVH	iris: roughness, congenital auricular fistula, contractures of toes	under 40
7	M/13	mild SVAS, mild PPS, VSD (natural closure)	diabetes mellitus	51
8	F/6	SVAS (post ope.), Co A, branch PS, PLSVC	iris: pale brown and stellate sharp	49
9	F/7	SVAS, PPS, diffuse branch PS (bilateral)	iris: roughness, kyphosis, contractures of fingers	38
10	F/9	SVAS, MVP, MR	iris: pale brown and roughness, contractures of ankles	under 40
11	F/10	SVAS, MVP, MR	iris: pale brown and roughness, posterior vocal fold slit	48
12	F/13	PDA (post ope.), MVP	iris: pale brown and stellate sharp	under 40
13	F/13	SVAS	iris: stellate sharp, diabetes mellitus (border type), hoarseness	53
14	F/15	SVAS (post ope.)	diabetes mellitus	55
15	F/22	SVAS, PS (supravalvular and peripheral)		60

SVAS: supravalvular aortic stenosis, PS: pulmonary stenosis, VSD: ventricular septal defect, PPS: peripheral pulmonic stenosis, LVH: left ventricular hypertrophy, Co A: coarctation of the aorta, PLSVC: persistent left superior veua cava, MVP: mitral valve prolapse, MR: mitral regurgitation, PDA: patent ductus arteriosus.
IQ used methods for mentality: Tsumori (Case 1), '87 TK Binet (Case 2, 9), WISC or WAIS (Case 3 ~ 8, 10 ~ 15).

morphological studies of the oral and maxillofacial area, even though facial abnormalities are one of the characteristics of the syndrome.

Accordingly, in the present study we conducted a morphological study of the oral and maxillofacial area centered on an analysis of cephalometric radiograms of the head and gnathostatic models and included the oral and radiographic findings in patients with Williams syndrome.

Subjects and Methods

The subjects were 15 patients found to have a microdeletion of chromosome band 7q11.23 by FISH (fluorescence *in situ* hybridization) and diagnosed with Williams syndrome in the Department of Pediatric Cardiology, The Heart Institute of Japan affiliated with Tokyo Women's Medical University. There were 7 males and 8 females, and their ages ranged from 3 years to 22 years (mean: 10.8 years).

The 15 cases are outlined in Table 1. All 15 cases except one had cardiovascular disease, including supravalvular aortic stenosis (SVAS), and assessment of their mental development yielded IQ scores of 38~61 (mean: 47.3), and all of them were found to have moderate mental developmental delay. In addition, 10 cases had iris abnormalities, 4 had contractures of the hands and feet, and 3 had diabetes mellitus (type II), including border type diabetes.

The methods used consisted of conducting centered on an analysis of cephalometric radiograms of the head and gnathostatic models, and the oral and radiographic findings. Congenitally missing teeth and teeth anomalies were surveyed based on the oral findings. Bony impaction of congenitally missing teeth and absence of the tooth germs of permanent teeth in patients at ages when there are unerupted permanent teeth were checked based on the X-ray findings.

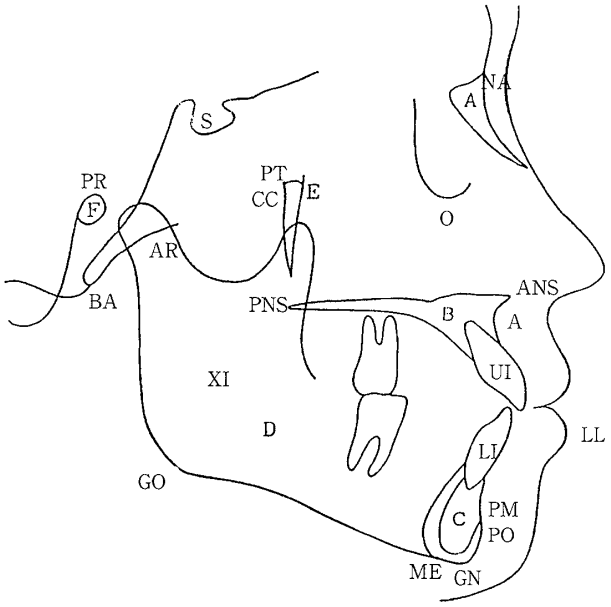

Fig. 1 Measurement points of cephalometric radiogram

A: nasal bone, B: maxilla, C: symphysis, D: mandible, E: pterygomaxillary fissure, F: external auditory meatus.

NA: nasion (the point at the anterior limit of the nasal and frontal sutures), O: orbitale (the lowest point on the perimeter of the orbit), A: A point (the most anterior point at the base of the maxillary alveolar base), ANS: anterior nasal spine (tip of the anterior nasal spine of the maxilla), PNS: posterior nasal spine (tip of the posterior nasal spine of the maxilla), UI: upper incisor (tip of the upper central incisors), LI: lower incisor (tip of the lower central incisors), PM: protuberance menti (superior border of the mental protuberance), ME: menton (the lowest point on the contour of the mandibular symphysis), PO: pogonion (the most protruding point in the mental protuberance), LL: lower lip (the most anterior point on the lower lip), *GN: gnathion (the point where the line that bisects the angle formed by the facial plane and the mandibular plane intersects the anterior border of the mental protuberance), *GO: gonion (the point where the line that bisects the angle formed by the tangent from AR to the posterior border of the mandibular ramus and the mandibular plane intersects the mandibular border), PT: pterygoido point (inferior border of the opening of the round foramen), *CC: center of cranium (point of intersection between the BA-NA plane and FX), BA: basion (the midpoint of the anterior border of the foramen magnum), *XI: XI point (the point at the center of the ramus of the mandible on tracings and close to the mandibular foramen, anatomically. Using the plane that passes through this point makes it possible to see the morphological features of the mandible), *AR: articulare (the point where the posterior border of the mandibular ramus intersects the inferior border of the temporal bone on radiogram), S: sella turcica (center of the sella turcica), PR: porion (superior border of the external auditory meatus).

* : Point shown on the drawing.

Ricketts method[4] was used to analyze the cephalometric radiograms of the head. In the Ricketts method growth is assumed to stop at 18 years of age in males and at 15 years of age in females, and sex differences are assumed not to exist. The measurement points used in this study are listed in Fig. 1.

And the parameters measured based on the above measurement points are listed in Fig. 2.

We assessed the results for the above parameters in the Williams syndrome group by comparing them with the mean values for Japanese reported by Nezu and coworkers[5)6)] and performed a single-sample significant difference test. Since there were no changes due to growth in 7 of the parameters: FX, LFH, L1-APO, ∠L1-APO, CD, RP, and LP, they were used unaltered. However, there were changes in 9 parameters due to growth: FD, MP, MA, PTA, UM-PTV, CLA, PFH, PL, and CL, and for these parameters we used ratios calculated by dividing the numerical values of each parameter by the mean value for Japanese of the same age according to Nezu and coworkers[5)6)].

Student's t test was used for the statistical analysis, and p values <0.05 were considered evidence of a significant difference.

Three dentists with 10 or more years of clinical experience judged cone-shaped teeth, peg-shaped teeth, and nodular teeth, and whenever all 3 judged that microdontia was present, the case was diagnosed as microdontia.

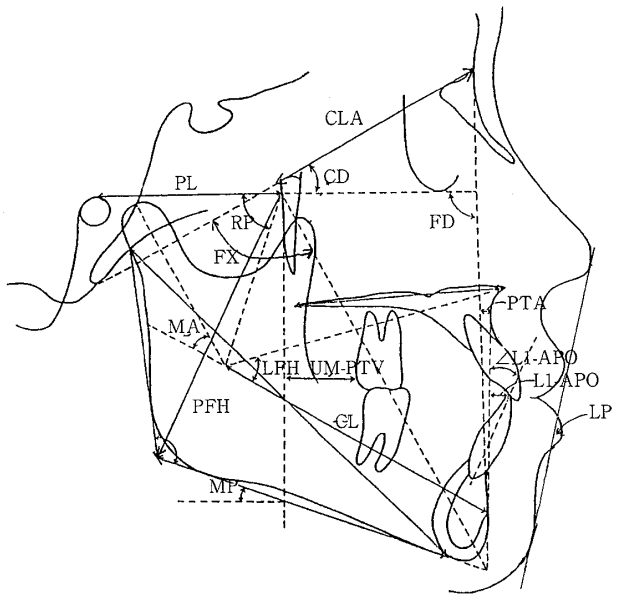

Fig. 2 Measurement parameters of cephalometric radiogram

The parameters measured based on the above measurement points are listed below. [ ] : the meanings of high values for each of the parameters. FX (°) : facial axis [severe anterior protrusion of the menton, and a small facial height radius], FD (°) : facial depth [anterior protrusion of the menton], MP (°) : mandibular plane angle [severe skeletal open bite attributable to the mandibular], LFH (°) : lower face height [severe skeletal open bite], MA (°) : mandibular arch [severe deep overbite and relative smallness of the mandibular in relation to the maxilla], PTA (mm) : convexity (extent of protrusion of the mandible) [severe maxillary protrusion], L1-APO (mm) : mandibular incisor protrusion (extent of protrusion of the lower central incisors) [severe protrusion labially of the lower central incisors], ∠L1-APO (°) : mandibular incisor inclination (angle of inclination of the lower central incisors) [severe inclination of the lower central incisors], UM-PTV (mm) : upper molar position [severe anterior position of the upper molar that is almost always attributable to an anteriorly positioned maxilla], CD (°) : cranial deflection [severe overgrowth of the mandible], CLA (mm) : cranial length anterior [severe maxillary protrusion attributable to a long anterior cranial base], PFH (mm) : posterior facial height [long ramus of the mandible], RP (°) : ramus position [severe anterior protrusion of the ramus of the mandible], PL (mm) : porion location [severe anterior protrusion of the porion], CL (mm) : corpus length [long body of the mandible], LP (mm) : lip protrusion [severe protrusion of the lower lip].

Table 2 Comparison with mean values in Japanese and Williams syndrome group

Parameters	Mean values in Japanese at 9 years [growth change/year]	Williams syndrome group
FX(°)	86.0±3.0	85.4±3.9
FD(°)	86.0±3.0[+0.3]	87.5±3.9
MP(°)	30.0±4.0[−0.2]	30.7±5.1
LFH(°)	49.0±4.0	48.7±4.7
MA(°)	25.0±4.0[+0.3]	31.0±6.0*
PTA(mm)	4.0±2.0[−0.2]	5.4±3.7
L1-APO(mm)	3.0±1.5	6.2±2.2*
∠L1-APO(°)	25.0±5.0	27.9±6.9
UM-PTV(mm)	11.0±2.0[+1.0]	16.1±5.4*
CD(°)	28.0±2.0	28.5±2.5
CLA(mm)	55.0±3.0[+0.8]	53.5±5.0*
PFH(mm)	57.0±4.0[+1.7]	57.5±7.5
RP(°)	75.0±3.0	73.9±4.6
PL(mm)	−39.0±2.0[−0.5]	−39.5±4.5
CL(mm)	63.0±3.0[+1.5]	66.1±7.2
LP(mm)	2±1.5	5.8±3.2*

*: significant difference $p < 0.05$.

Results

1. Analysis of cephalometric radiograms of the head and gnathostatic models

The values measured in the Williams syndrome group, the mean values for Japanese reported by Nezu and coworkers[5)6)], and the results of the statistical tests are shown in Table 2.

The values measured for 5 parameters in the Williams syndrome group, MA, L1-APO, UM-PTV, CLA, and LP, were all significantly greater than the mean values in Japanese.

The results of the analysis of the radiographs revealed bimaxillary protrusion in 2 cases (13.3%), maxillary protrusion and mandibular retrusion in 1 case (6.7%), maxillary protrusion in 6 cases (40%), mandibular protrusion in 1 case (6.7%), mandibular retrusion in 3 cases (20%), reversed occlusion in 2 cases (13.3%), and upper and lower lip protrusion in 6 cases (40%). Evaluation of facial description based on 5 parameters, i. e. FX, FD, MP, LFH, and MA, revealed a dolico-

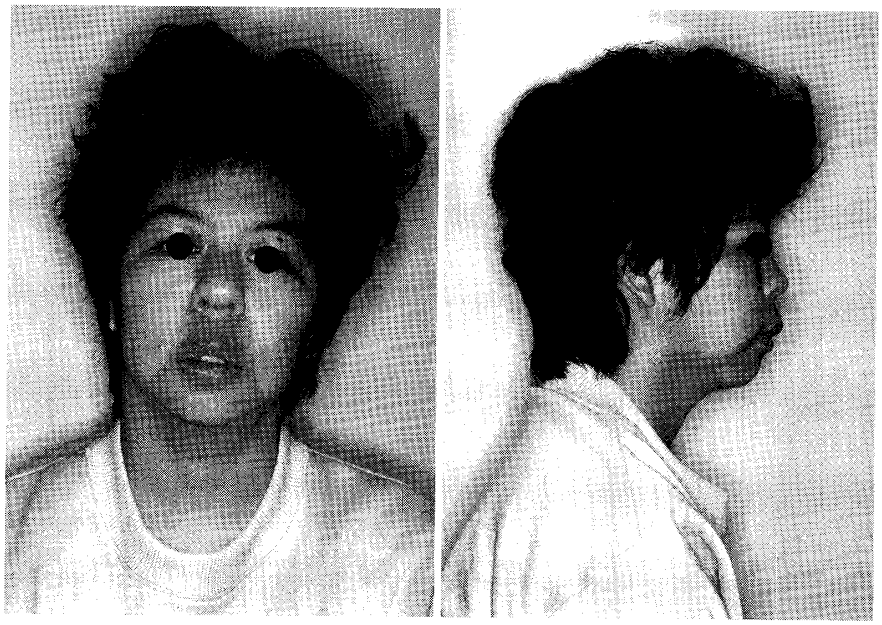

Fig. 3 A representative case of the facial finding of Williams syndrome (Case 8)
It shows elfin face, the dolicofacial type, and maxillary protrusion and upper and lower lip protrusion.

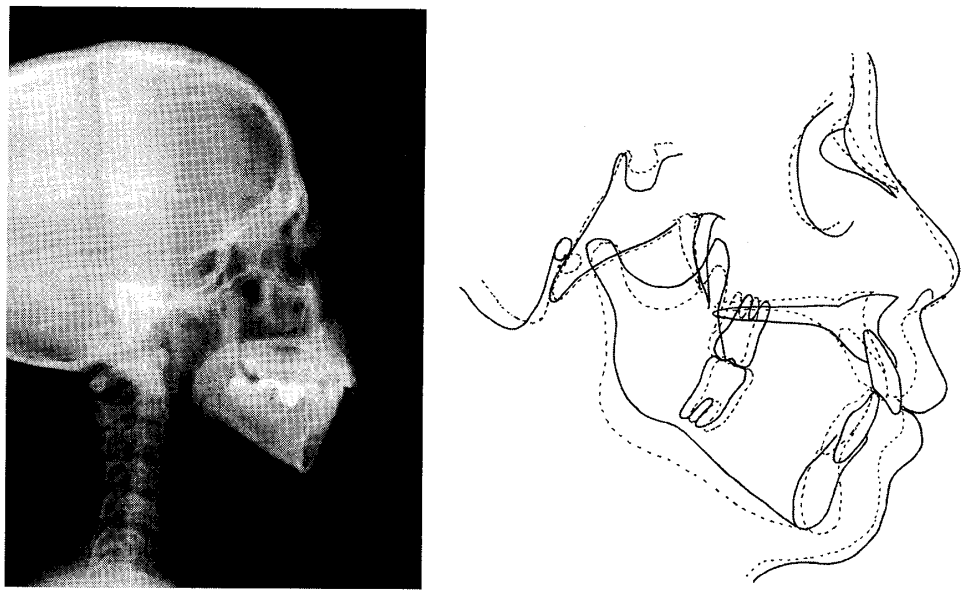

Fig. 4 A representative case of the cephalometric radiogram of the head of Williams syndrome (Case 8)
It shows the dolicofacial type and mandibular retrusion and upper and lower lip protrusion.
—— : Case 8, ------ : normal case.

facial pattern (long-face type) in 7 cases (46.7%), a mesiofacial pattern (normal face type) in 5 cases (33.3%), and a brachyofacial pattern (short-face type) in 3 cases (20%).

A representative case (Case 8) of the facial finding and the cephalometric radiogram of the head in a case with Williams syndrome is shown in Figs. 3, 4. It shows elfin face, the dolicofacial type,

Table 3 Results of analysis

Case	Cephalometric analysis	Facial description	Congenitally missing teeth	Tooth anomalies	
				Microdontia	Short-root
1	Mandibular retrusion	M	⌈A		
	Reversed occlusion				
	Palatal inclination of upper incisor				
2	Bimaxillary protrusion	M	$\frac{2\,\vert\,2}{2\,\vert\,2}$		
3	Maxillary protrusion	D	$\frac{}{2\,\vert\,2}$	$\underline{2\,\vert\,2}$	
4	Maxillary protrusion	D			
	Mandibular retrusion				
	Upper and lower lip protrusion				
5	Maxillary protrusion	B	$\overline{2\vert}$		$\frac{5+5}{5+5}$
	Upper and lower lip protrusion				
	Labial inclination of upper and lower incisor				
6	Mandibular retrusion	D			$\underline{5\,\vert\,5}$
	Upper and lower lip protrusion				
	Palatal inclination of upper incisor				
7	Maxillary protrusion	M	$\underline{5\ 3\vert}$		$\frac{41\ \vert\ 145}{1\ \vert\ 1}$
	Labial inclination of upper and lower incisor				
8	Maxillary protrusion	D	$\frac{}{5\ 2\ \vert\ 2}$	$\underline{2\vert 2\ 5}$	$\underline{5\vert}$
	Upper and lower lip protrusion				
9	Lingual inclination of lower incisor	D	$\overline{2\ 1\vert}$		
10	Maxillary protrusion	M			
11	Labial inclination of upper incisor	D		$\underline{2\vert 2}$	$\underline{5\vert}$
12	Mandibular protrusion	B	⌈2		$\frac{5\ \vert 5}{4\vert}$
	Reversed occlusion				
13	Mandibular retrusion	D	$\frac{53\ \vert\ 34}{542\ \vert\ 245}$	$\underline{42\vert 2}$	
	Upper and lower lip protrusion				
	Labial inclination of lower incisor				
14	Maxillary protrusion	M	$\underline{3\vert 3}$	$\underline{2\vert 2}$	
	Upper and lower lip protrusion				
15	Bimaxillary protrusion	B		$\underline{2\vert 2}$	

M: mesiofacial pattern, D: dolicofacial pattern, B: brachyofacial pattern.

and maxillary protrusion and upper and lower lip protrusion.

2. Analysis of the oral and radiographic findings

The findings in the Williams syndrome group are shown in Table 3. Congenitally missing teeth were noted in 10 cases (66.7%), and a total of 26 teeth were missing: 1 tooth in 3 cases (30%), 2 teeth in 5 cases (50%), and 3 teeth and 10 teeth in 2 cases each (10%). According to type of tooth, 11 (42.3%) of the 26 missing teeth were lower lateral incisors, 5 (19.2%) were upper canines, 3 (11.5%) were lower second premolars, 2 (7.7%) were an upper second premolar and lower first premolar, and 1 each (3.8%) was an lower central incisor, upper first premolar, and lower deciduous central incisor.

Tooth anomalies were observed in 10 cases (66.7%), and both microdontia and short-rooted teeth were present in 6 cases (40%). There was a total of 14 microdontia: both upper lateral incisors in 4 cases (66.7%), and both upper lateral incisors plus 1 upper premolar and both upper lateral incisors plus 1 upper second premolar in 1 case (16.7%) each. The majority of the microdontia were upper lateral incisors (12 teeth, 85.7%),

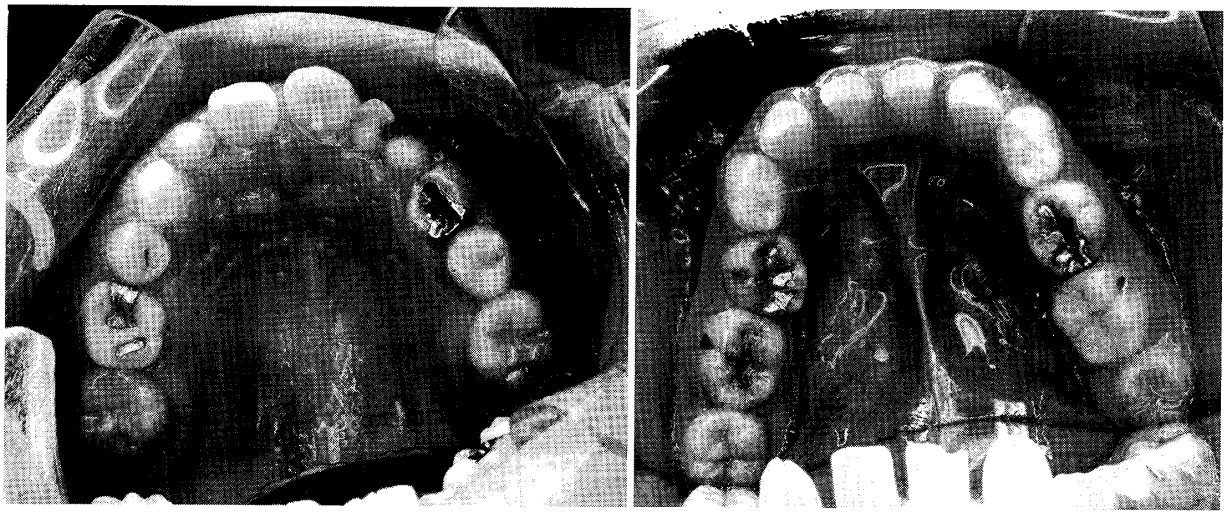

Fig. 5 A representative case of the oral findings of Williams syndrome (Case 13)
It shows congenitally missing teeth ($\frac{53\ |\ 34}{542\ |\ 245}$), and microdontia ($\underline{42\ |\ 2}$). (Congenitally missing teeth were confirmed by radiographic findings.)

and there was one upper first and second premolar each (7.1%). The 6 cases with short-rooted teeth had a total of 34 short-rooted teeth. They consisted of 1 cases each with 20, 7, 3, and 2 short-rooted teeth, and 2 cases with just one short-rooted tooth each. According to type of tooth, the short-rooted teeth consisted of 9 upper second premolars (26.5%), 4 upper and lower central incisors and upper first premolars each (11.8%), 3 lower first premolars (8.8%), and 2 upper and lower lateral incisors, upper and lower canines, and lower second premolars each (5.9%).

A representative case (Case 13) of the oral findings in a patient with Williams syndrome is shown in Fig. 5. It shows congenitally missing teeth, microdontia.

Discussion

Williams syndrome was reported by Williams and coworkers[1] as a syndrome consisting of mental retardation, supravalvular aortic stenosis, and specific facies. It is thought to be an contiguous gene syndrome caused by a 1.5 Mb deletion on chromosome band 7q11.23.

Characteristically mental retardation (IQ: 41 ~80), in the cardiovascular system, cardiovascular abnormalities of supravalvular aortic stenosis, hypertension, in the skeleton, short stature, joint contractures, kyphosis, and hoarseness, etc are also seen[1)~3)].

And the head and face are characterized by typical facies resembling that of the elves of Western folklore, with patients exhibiting a long face, broad forehead, thick inner eyebrows, hypotelorism, epicathus, strabismus, stellate iris, and puffy upper eyelids[1)~3)]. A flat root of the nose, saddle nose, upturned nares, long philtrum, hypoplastic cheeks that are full, thick lip with a lower lip that sags, and an open mouth are seen. Dental hypoplasia or missing teeth (especially upper lateral incisors) are also noted[1)~3)].

The cardiovascular abnormalities, hoarseness, dysplasia of ligaments and tendons observed in joint contractures, etc, and the characteristic facies are thought to be caused by deficiency of the elastin gene, and the visual space perception disorder is thought to be due to deficiency of the LIM kinase 1 gene[2)7)~9)]. The estimated incidence in Western countries is 1 in 7500~20,000 individuals[10)11)].

But facial abnormalities were only looking and

tooth anomalies were only oral findings in those reports[1)~3)], there has been no report of detailed analysis in the oral and maxillofacial area in Japan or abroad to the best of our knowledge.

We therefore conducted a study centered on an analysis of cephalometric radiograms of the head had been used for orthodontics[5)], it was very useful.

Based on the parameters of MA, L1-APO, UM-PTV, CLA, and LP for which significant differences were observed from the means values in Japanese, maxillary protrusion, labial inclination of the lower incisor, and protrusion of the lower lip appeared to characterize the facies in the cases of Williams syndrome.

Moreover, according to the our results, maxillary protrusion was present in 60% of the cases, and mandibular protrusion in 20%. Since the incidence of maxillary protrusion in Japan is 5.2%[12)], and the incidence of mandibular protrusion in Japan is 4～10% and 2～4% in Western countries[12)], these findings confirmed that the incidence of maxillary protrusion, in particular, was high.

The dolicofacial pattern was the most common type of facial description (46.7%), and since the mean value for Japanese is said to be 2.5%[5)], the dolicofacial pattern can be concluded to be characteristic of the facies in Williams syndrome.

Next, as regards missing teeth and tooth anomalies, congenitally missing deciduous teeth are rare, with incidences of 1.2～1.8% in Japan and 0.4～0.7% in other countries[12)13)], and lower deciduous lateral incisors are most often affected, followed by lower deciduous central incisors and upper deciduous lateral incisors[12)]. Among permanent teeth, excluding wisdom teeth, the incidence is 8.7% in Japan[12)]and 1.6～9.6% in other countries[14)], with 1 missing tooth accounting for 43.5～61.7%, two accounting for 29～35.8%, and three or more for less than 10%. The upper lateral incisors are said to be most often affected (40～45%), followed by the upper second premolars[12)]. The lower central and lateral incisors are also often missing, whereas the upper central incisors are said to be the least likely to be missing, and the upper and lower first molars are also said to seldom be missing[12)].

Microdontia, including cone-shaped teeth that have a small cone-shaped crown, peg-shaped teeth, nodular teeth, whose crowns appear nodular and bud-shaped, and bud-shaped teeth, are referred to by the general name " hypoplastic teeth", and they are said to represent a transitional form between normal morphology and congenitally missing teeth. If wisdom teeth are excluded, they are most common in the upper lateral incisors, 8.8%, followed by the second premolars, and are said to hardly ever occur in the lower lateral incisors[12)]. In addition, short-rooted teeth are most common in the upper central incisors, the second premolars, and the lower central incisors, and the roots of microdontia are said to exhibit short roots as well.

Congenitally missing teeth were noted in 66.7% of the our results, and 2 or more were missing in 46.7% of them. Moreover, the finding of both microdontia and short roots in 40% represents an extremely high rate in view of the incidences stated above. Outside Japan as well, Hertzberg[15)]and coworkers reported observing microdontia in 12.5% of the deciduous teeth and in 40.7% of the permanent teeth in 45 cases of Williams syndrome, and congenitally missing teeth and microdontia can be concluded to be a representative characteristic of the stomatognathic region in Williams syndrome.

Generally speaking, the etiology of the congenitally missing teeth and microdontia is unknown, the primordia of both the deciduous teeth and the permanent teeth form relatively early in the fetal period, but the hard tissue of the teeth is formed

and the teeth are actually completed some time after birth. Thus, since the development of both the deciduous teeth and the permanent teeth occurs over a long period of time, it is thought that a variety of factors come into play in the meantime, and that the occurrence of various developmental disorders, including missing teeth and tooth anomalies, depends on the strength, duration, and timing of these factors[12]. For this reason it is difficult to identify the factors that contribute to dental developmental disorders, and while the cardiovascular abnormalities, hoarseness, dysplasia of the ligaments and tendons observed in the joint contractures, and the characteristic facies seen in Williams syndrome are thought to be attributable to deficiency of the elastin gene[2].

The dentin in teeth is approximately 20% organic matter, and its principal component is collagen, but blood vessels are widely distributed throughout the dental pulp, and collagen and elastin are present. The periodontal fibers are also composed of collagen and elastin[16]. In Williams syndrome, it also appears possible that the teeth are in some way damaged as a result of the elastin deficiency in the dental development period described above, and that it induces the degenerative changes in the dental pulp and the periodontal ligament and results in congenitally missing teeth and the development of dental anomalies.

In view of this high rate of abnormalities in the maxillofacial and oral area, regular dental and oral surgery checkups and early dental and orthodontic treatment appear to be important in Williams syndrome.

Conclusions

A morphological study of the oral and maxillofacial area was conducted in Williams syndrome, and the following results were obtained.

1. An analysis of cephalometric radiograms of the head and gnathostatic models revealed significantly higher values for MA, L1-APO, UM-PTV, CLA, and LP than the mean values in Japanese, and as a result the facies of Williams syndrome patients appeared to be characterized by maxillary protrusion, labial inclination of the lower incisor, protrusion of the lower lip, and, in terms of facial description, a dolicofacial pattern.

2. The oral and radiographic findings showed that 26 teeth were congenitally missing in 10 case, and the lower lateral incisors were the most common site of absence (11 teeth; 42.3%).

3. Tooth anomalies were present in 10 case (14 teeth), with microdontia present in 6 cases (14 teeth), and short-rooted teeth in 6 cases (34 teeth). Microdontia was most common in the upper lateral incisors (12 teeth, 85.7%), and short-rooted teeth were most common in the upper second premolars (9 teeth, 26.5%).

4. It is suggested that a deletion of the elastin gene may contribute to the morphological abnormalities of the oral and maxillofacial area in patients with Williams syndrome.

References

1) **Williams JCP, Barratt-Boyes BG, Lowe JB**: Supravalvular aortic stenosis. Circulation **24**: 1311–1318, 1961
2) **Ewart AK, Morris CA, Atkinson D et al**: Hemizygosity at the elastin locus in a developmental disorder, Williams syndrome. Nature Genet **5**: 11–16, 1993
3) **Niikawa N**: A-14 Williams syndrome. *In* New Atlas of Congenital Malformation Syndromes. (Kajii M, Kuroki Y, Niikawa N eds), pp36–37, Nankodo Publishing Company, Tokyo (1998)
4) **Ricketts RM, Roth RH, Chaconas ST et al**: Orthodontic Diagnosis and Planning. Vol 1, 2, Rocky Mountain Orthodontics, Denver (1982)
5) **Nezu H, Nagata K, Yoshida Y et al**: Orthodontics Bioprogressive Diagnostics. Rocky Mountain Morita, Tokyo (1984)
6) **Nezu H, Nagata K, Yoshida Y et al**: Cephalometric comparison of olinical norms between the Japanese and Caucasians. J Jpn Orthod Soc **41**: 450–465, 1982
7) **Kimura M, Nishikawa T, Ishiyama S et al**:

Chromosomal deletion and phenotype correlation in patients with Williams syndrome. *In* Etiology and Morphogenesis of Congenital Heart Disease (Clark EB, Nakazawa M eds), pp381–384, Futura, New York (2000)
8) **Li DY, Brooke B, Davis EC et al**: Elastin is an essential determinant of arterial morphogenesis. Nature **393**: 276–280, 1998
9) **Meng Y, Zhang Y, Tregoubov V et al**: Abnormal spine morphology and enhanced LTP in LIMK-1 knockout mice. Neuron **35**: 121–133, 2002
10) **Korenberg JR, Chen XN, Hirota H et al**: VI. Genome structure and cognitive map of Williams syndrome. J Cogn Neurosci **12** (Suppl 1): 89–107, 2000
11) **Stromme P, Bjornstad PG, Ramstad K**: Prevalance estimation of Williams syndrome. J Child Neurol **17**: 269–271, 2002
12) **Ishikawa G, Akiyoshi M**: Oral Pathology I. pp31–32, Nagasueshoten, Kyoto (1989)
13) **Ravn JJ**: Aplasia, supernumerary teeth and fused teeth in the primary dentition. An epidemiological study. Scand J Dent Res **79**: 1–6, 1971
14) **Graber LW**: Congenital abscence of teeth: a review with emphasis on inheritance patterns. J Am Dent Assoc **96**: 266–275, 1978
15) **Hertzberg J, Nakisbendi L, Needleman HL et al**: Williams syndrome-oral presentation of 45 cases. Pediatr Dent **16**: 262–267, 1994
16) **Avery JK**: 5 Dental pulp. *In* Orban's Oral Histology and Embryology 8th ed. (Bhaskar SN ed), pp98–99, 137–152, Mosby, St. Louis (1976)

Williams 症候群患者における口腔顎顔面領域の形態学的検討

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Williams 症候群は，1961 年に Williams らが精神遅滞，大動脈弁上部狭窄および特異顔貌を有する症候群として報告した疾患で，染色体 7q11.23 にあるエラスチン遺伝子，LIM キナーゼ 1 遺伝子などを始めとする約 20 種類の遺伝子を含む領域の微小欠失が原因の隣接遺伝子症候群と考えられている．今回われわれは，本疾患群に対し口腔顎顔面領域の形態学的検討を行ったので報告する．対象は当院附属日本心臓血圧研究所循環器小児科で FISH 法により染色体 7q11.23 の微細欠失が確認され Williams 症候群と確定診断された患者 15 例で，方法は頭部 X 線規格写真，顎態模型，口腔内および X 線所見による分析を行い，頭部 X 線規格写真分析の方法は Ricketts 法を使用した．結果は，頭部 X 線規格写真分析では下顎のアーク，下顎中切歯突出量，上顎大臼歯の位置，前頭蓋底の長さ，下唇の突出量が高値で日本人平均値と比較し有意差を認め，その結果，上顎前突，下顎前歯の唇側傾斜，下唇の突出および顔面形態では dolicofacial pattern などが Williams 症例の顔貌上の特徴と考えられた．顎態模型，口腔内および X 線所見による分析では歯の先天性欠如が 10 例 26 歯に認められ，下顎側切歯が 11 歯（42.3%）と最も多かった．歯の奇形は 10 例（48 歯）に認め，矮小歯が 6 例（14 歯），短根歯が 6 例（34 歯）であり，矮小歯では上顎側切歯が 12 歯（85.7%）と最も多く，短根歯では上顎第二小臼歯が 9 歯（26.5%）と最も多かった．

このように顎顔面口腔領域の異常が高率に認められることから Williams 症候群においては定期的な歯科口腔外科的チェックと早期からの歯科矯正学的治療が重要であると考えられる．