CASE REPORT

Orthodontic treatment in a patient with Van der Woude's syndrome

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Van der Woude's syndrome (VDW; #OMIM 119300) is an autosomal dominant disease characterized by cleft lip and/or palate and lower lip pit (fistula). The precise skeletal characteristics are unclear, and there have been no case reports of orthodontic treatment of patients with VDW. The Japanese girl whose treatment is reported here had VDW, including bilateral cleft lip and palate and bilateral symmetric lower lip pits. Orthodontic treatment started when she was just 3 years old, with a removable maxillary expansion appliance, followed by an edgewise multibracket appliance in both arches. Retention began at 11 years of age, and a secondary bone graft was performed for the alveolar cleft. She received prosthetic treatment and achieved a desirable occlusion at 18 years of age. Early intervention helped achieve a satisfactory treatment result for our patient. In contrast, her mother also had VDW, with a severe Class III skeletal pattern, but she had not been treated orthodontically; she had an anterior and lateral crossbite even after prosthetic treatment. The pretreatment characteristics of 4 other subjects with VDW are discussed; they show wide variations in the sizes of the maxilla and the mandible, suggesting that a common skeletal pattern is not generally seen in VDW. (Am J Orthod Dentofacial Orthop 2006;129:696-705)

Van der Woude's syndrome (VDW) is an autosomal dominant disease characterized by the association of congenital lower lip pits (fistula) with cleft lip and/or palate.[1] VDW is the most frequent form of syndromic clefting and accounts for 2% of all cleft lip and palate cases.[2] Precise examination of the clefts and lower pits in the patients and their relatives is important for the diagnosis of this syndrome.[3-6] VDW is frequently accompanied by hypodontia, and the type of cleft is known to vary within the same family.[7] Recently, this disease was reported to be caused by mutations in the gene encoding interferon regulatory factor-6 (IRF6).[8]

A previous study reported that 66.2%, 16.5%, and 17.3% of VDW patients exhibited cleft lip and palate, cleft lip, and cleft palate, respectively.[9] Most also had bilateral lower lip pits (symmetric, 49.7%; asymmetric, 31.6%).[9] Regarding facial growth, the maxillary length and height are shorter in VDW patients than in nonsyndromic cleft lip and palate patients.[10] However, the precise skeletal characteristics are unclear, and there have been no case reports of orthodontic treatment of VDW patients. We describe the orthodontic treatment of a Japanese girl with VDW. She received early orthodontic intervention, beginning at 3 years of age, and achieved a desirable occlusion. We further consider the characteristics of her mother and 4 other VDW patients.

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DIAGNOSIS AND ETIOLOGY

This Japanese girl was born to a mother with VDW who had bilateral cleft lip and palate and lower lip pits. Neither her father nor her brother had congenital anomalies. Her maternal grandmother had lower lip pits but no cleft lip or palate.

At birth, the patient was 51 cm in height and weighed 3212 g. She had bilateral cleft lip and palate, and bilateral symmetric lower lip pits (Fig 1). Bilateral lip repair and palatal closure were performed at 4 months of age and 1 year 6 months of age, respectively. She was seen at our dental hospital at 3

Fig 1. Pretreatment frontal and lateral facial photographs at 3 years 2 months of age, and bilateral symmetric pits on lower lip.

Fig 2. Pretreatment intraoral photographs.

years 2 months of age. Her profile photograph showed a protruded lower lip and mandible, and a flat nasal alae and a depressed nasal tip were noted in the frontal facial photograph. Deciduous dentition with bilateral alveolar cleft between the maxillary central incisors and canines was seen (Figs 2 and 3). The lingual tipped premaxilla and the narrowed and collapsed maxillary arch had resulted in a crossbite of the anterior teeth and molars, with –5 mm of overjet. Deepbite was noted with 5 mm of overbite. A frontal cephalogram and a panoramic radiograph showed the complete alveolar cleft and congenitally missing deciduous and permanent maxillary lateral incisors (Fig 4). A lateral cephalogram showed a retroclined premaxilla and deciduous maxillary central incisors (Fig 4). The SNA and ANB angles were larger than the Japanese female norm[11] (Table I). This was because the lingual tipped premaxilla placed Point A in an anterior position, which is frequently seen in bilateral cleft lip and palate patients.

TREATMENT OBJECTIVES AND ALTERNATIVES

The treatment objectives were to correct her anterior and lateral crossbite and to level and align both arches. In addition to better occlusion, improve-

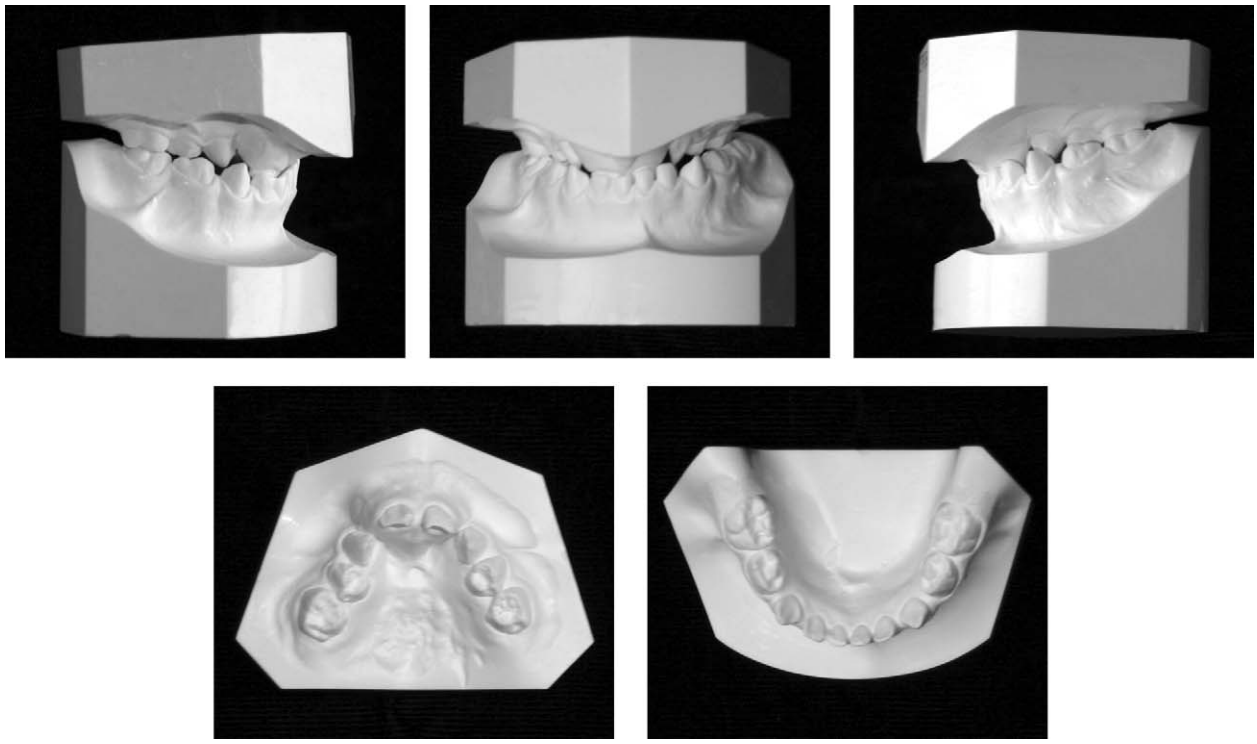

Fig 3. Pretreatment dental casts.

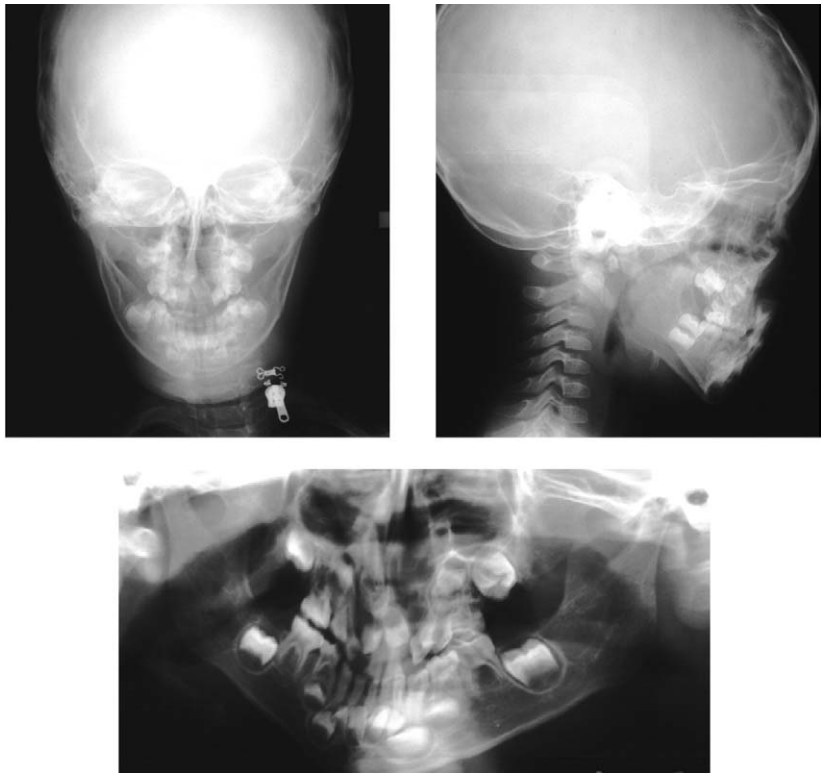

Fig 4. Pretreatment radiographs.

Table I. Analytical measurements before treatment (°)

Angle	*Value*	*Japanese norm ± SD*[11]
SNA	93.3	80.1 ± 3.4
SNB	85.5	76.0 ± 3.5
ANB	7.8	4.1
U-1 to FH plane	71.5	96.6 ± 6.5
L-1 to mandibular plane	105.3	85.7 ± 4.1
Mandibular plane	30.6	29.5 ± 3.4
Gonial	133.8	130.0 ± 5.3

S, sella turcica; *N,* nasion; *A,* Point A; *SNA,* angle between SN and NA; *B,* Point B; *SNB,* angle between SN and NB; *U-1,* long axis of deciduous maxillary central incisor; *U-1 to FH plane,* angle between U-1 and FH (Frankfort horizontal) plane; *L-1,* long axis of decidous mandibular central incisor; *L-1 to mandibular plane,* angle between L-1 and mandibular plane; *Mandibular plane,* angle between mandibular plane and FH plane; *Gonial,* angle between mandibular plane and ramus plane.

Fig 5. Intraoral photograph during first phase of treatment with removable expansion appliance at 3 years 7 months of age.

ment of her profile was also crucial. Because she had surgical lip repair and palatal closure, careful observation of the maxillary growth was required.

To accomplish these objectives, labial tipping of the premaxilla was planned, followed by lateral expansion of the buccal dentition and molars after eruption of the permanent teeth. Her facial profile was expected to be improved after these treatments. Lip and nose revisions were also considered. It was presumed that the labial and lateral expansions would enlarge the maxillary alveolar clefts between the premaxilla and the lateral segments, and a secondary bone graft was planned to close these clefts at an appropriate stage. Dental implants or prosthetic treatment was planned for the missing teeth after the orthodontic treatment.

As a treatment alternative, orthognathic surgery without intensive maxillary arch expansion was considered. This plan would correct the crossbite and improve the facial profile, but any orthognathic

Fig 6. Panoramic radiograph after first phase of treatment. In addition to the missing permanent maxillary right and left lateral incisors, congenitally missing maxillary right second premolar is noted.

Table II. Analytical measurements after treatment (°)

Angle	*After first phase of treatment (9y 10mo)*	*After prosthetic treatment (18y 5mo)*
SNA	82.6 (80.9 ± 3.1)	84.1 (82.3 ± 3.5)
SNB	78.0 (76.2 ± 2.8)	81.1 (78.9 ± 3.5)
ANB	4.6 (4.8)	3.0 (3.4)
U-1 to FH plane	101.5 (109.8 ± 5.3)	122.9 (111.1 ± 5.5)
L-1 to mandibular plane	86.8 (93.8 ± 5.9)	89.4 (96.3 ± 5.8)
Mandibular plane	31.5 (32.0 ± 2.4)	29.1 (28.8 ± 5.2)
Gonial	123.4 (129.2 ± 4.7)	125.4 (122.2 ± 4.6)

S, sella turcica; *N,* nasion; *A,* Point A; *SNA,* angle between SN and NA; *B,* Point B; *SNB,* angle between SN and NB; *U-1,* long axis of deciduous maxillary central incisor; *U-1 to FH plane,* angle between U-1 and FH (Frankfort horizontal) plane; *L-1,* long axis of decidous mandibular central incisor; *L-1 to mandibular plane,* angle between L-1 and mandibular plane; *Mandibular plane,* angle between mandibular plane and FH plane; *Gonial,* angle between mandibular plane and ramus plane. Parentheses denote norm ± SD of age- and sex-matched Japanese norm.[11]

surgery during the growth period has a serious risk of impairing skeletal growth. Therefore, we decided on early orthodontic intervention. We expected that expansion of the maxillary arch at this stage would help normal skeletal growth, also improving her facial profile. We planned to include orthognathic surgery later, if the result after orthodontic treatment was not acceptable.

TREATMENT PROGRESS

For the first phase of treatment, a removable appliance with a sagittal expansion screw was placed at 3 years 7 months of age with instructions to activate it once a week (Fig 5). The appliance was refined a few times, and the anterior crossbite was

Table III. Skeletal characteristics of patients before orthodontic treatment and congenitally missing teeth

	Patient 1	*Patient 2*	*Patient 3*	*Patient 4*	*Present patient*	*Untreated mother*
Age	9y 0mo	9y 7mo	10y 7mo	11y 8mo	9y 10mo	27y 3mo
Sex	Male	Male	Female	Female	Female	Female
Type of cleft	BCLP	BCLP	CP	RCLP	BCLP	BCLP
S-N	−0.5	−0.6	−1.5	−1.2	0.1	
S-Ba	−0.3	−1.0	0.0	−2.0	0.0	
ANS-PNS	0.7	2.5	−2.4	0.1	−1.2	
Ar-Go	0.0	−1.4	0.0	0.6	−0.2	
Go-Pog	−1.1	1.4	−0.1	1.3	1.3	
Number of congenitally missing teeth	3	2	4	1	3	4
Missing teeth (FDI tooth number)	12, 22, 25	12, 22	15, 12, 22, 25	12	15, 12, 22	15, 12, 22, 25

BCLP, bilateral cleft lip and palate; *CP,* cleft palate; *RCLP,* right cleft lip and palate; *S,* sella turcica; *N,* nasion; *Ba,* basion; *ANS,* anterior nasal spine; *PNS,* posterior nasal spine; *Ar,* articulare; *Go,* gonion; *Pog,* pogonion. Each value is represented by following formula: (value − mean)/SD. Mean value and SD were from age- and sex-matched Japanese norm.[13]

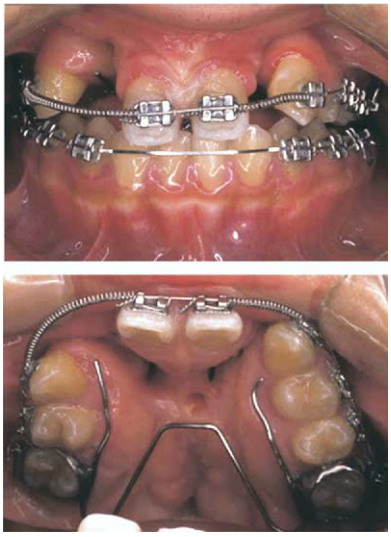

Fig 7. Intraoral photographs during second phase of treatment with Porter-type expansion appliance and edgewise multibracket appliance at 10 years of age.

corrected at 4 years of age. Because the permanent central incisors erupted in an edge-to-edge position at 6 years 5 months of age, labial tipping of the incisors was performed with a removable appliance. Surgical removal of the lower pits was performed at this stage. Panoramic radiograph at 9 years 10 months of age showed a congenitally missing maxillary permanent right second premolar in addition to the lateral incisors (Fig 6). The premaxilla had moved labially, and the profile had improved slightly. Table II shows that the ANB angle was 4.6°, which is similar to the Japanese norm.[11] There was a decrease in the SNA angle due to the labial tipping of maxilla (Tables I and II).

For the second phase of treatment, a Porter-type expansion appliance was used to expand the maxillary arch laterally, and an edgewise multibracket appliance was placed in the maxillary and mandibular arches (Fig 7). This phase of treatment lasted 1 year 8 months, and retention began at 11 years 6 months of age (Fig 8). Removable retainers were used in both arches for retention. A panoramic radiograph showed an enlarged alveolar cleft between the maxillary central incisors and canines on both sides. Because she was still in the pubertal growth spurt, careful observation of the mandibular growth and the occlusion was necessary. To minimize mandibular growth, a chincup was used in addition to removable retainers from 13 years 7 months to 16 years of age.

TREATMENT RESULTS

A secondary bone graft was performed to repair the alveolar cleft and stabilize the maxillary segments at 16 years of age. Before this surgery, a palatal arch was placed to prevent relapse in the maxillary arch. At 18 years of age, she received prosthetic treatment for the missing maxillary lateral incisors. Stable and functional occlusion was achieved at the end of treatment (Figs 9-11). An improved profile was noted in the cephalograms, although the deviated nasal septum was still seen. The alveolar clefts were filled with newly formed bone. Table II shows the proclined maxillary incisors; ANB angle was 3.0°. ANB angle decreased slightly during the second phase of treatment and the retention period, as is the Japanese norm.[11] The increment in SNB angle was 3.1° during this period (78.0° and 81.1° after the first phase of treatment and the prosthetic treatment, respectively), which was almost equivalent to the Japanese norm[11] (2.7°,

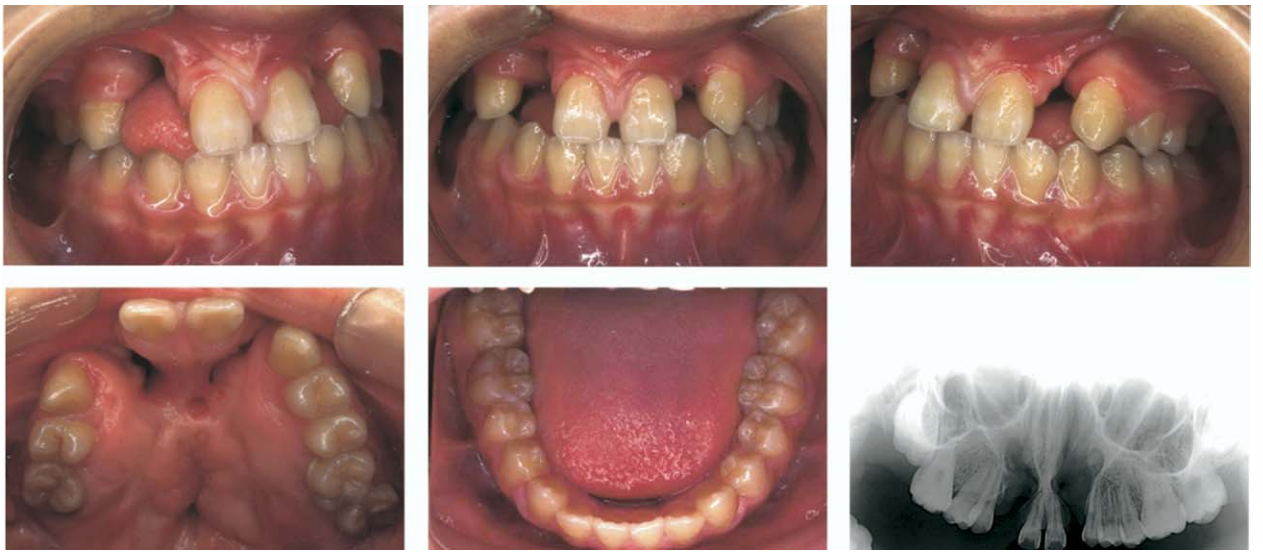

Fig 8. Intraoral photographs and panoramic radiograph after second phase of treatment at 11 years 6 months of age.

Fig 9. Intraoral photographs after secondary bone graft and prosthetic treatment at 18 years 5 months of age.

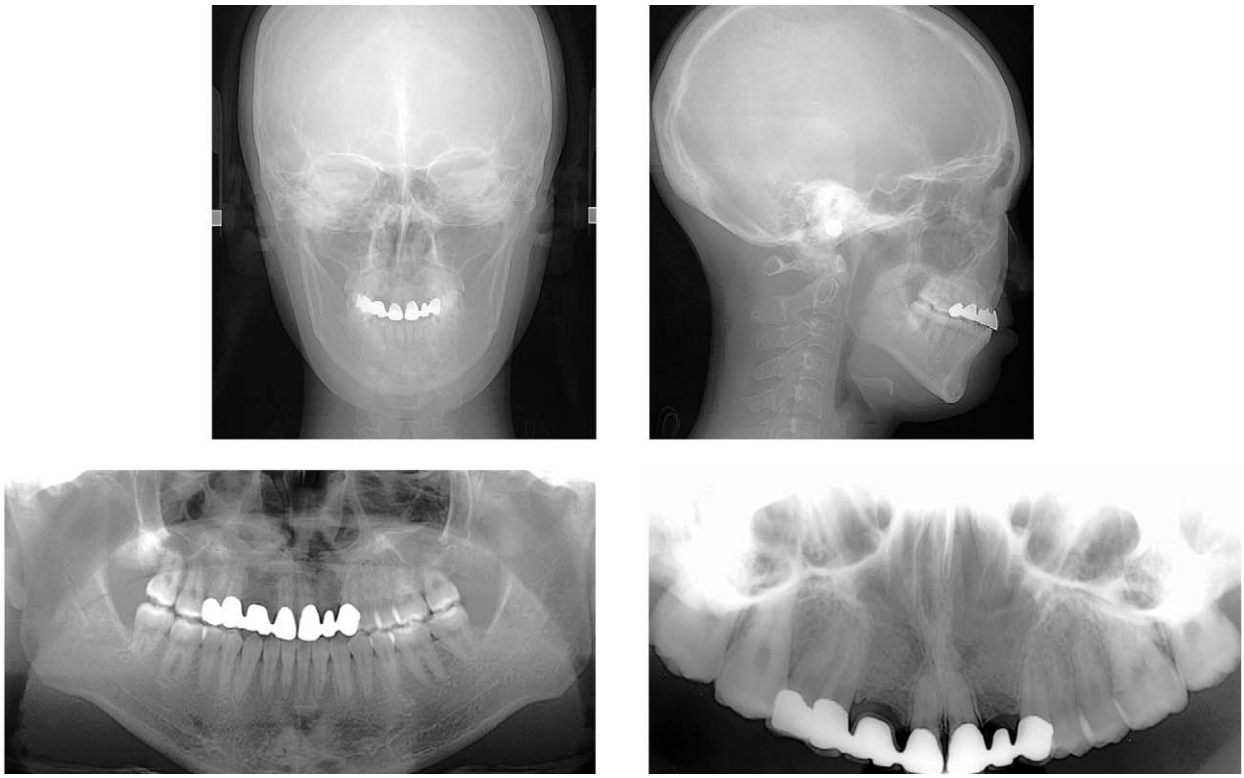

Fig 10. Radiographs after secondary bone graft and prosthetic treatment.

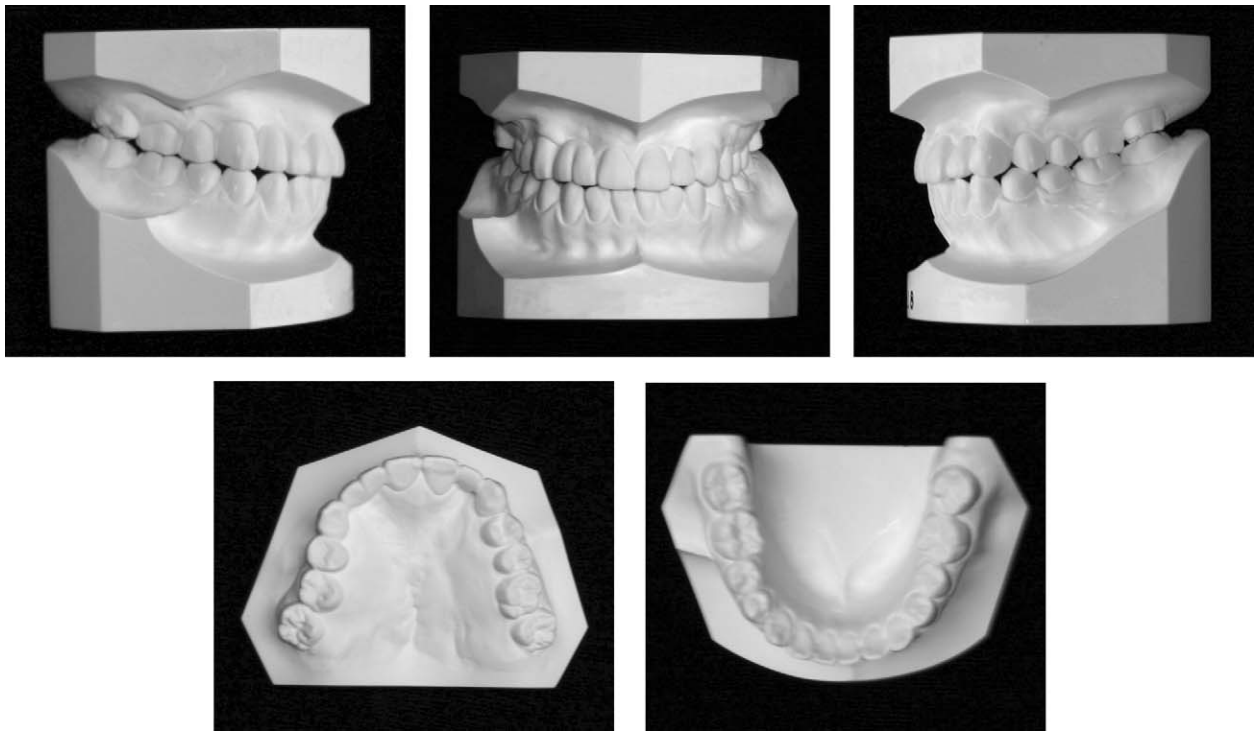

Fig 11. Dental casts after secondary bone graft and prosthetic treatment.

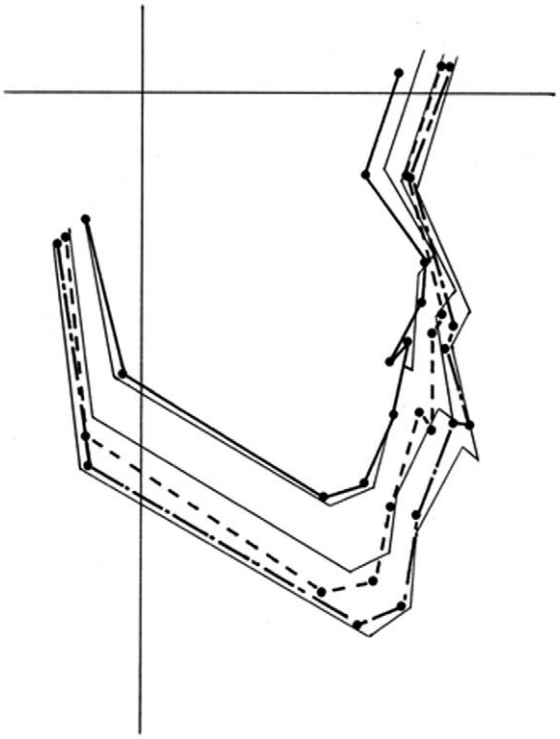

Fig 12. Superimposed profilograms. Pretreatment at 3 years 2 months of age (*solid line with dots*), after first phase of treatment at 9 year 10 months of age (*line with short dashes and dots*), after prosthetic treatment at 18 year 5 months of age (*line with long and short dashes and dots*). Japanese female norms[12] at 5 years 2 months of age, 10 years 3 months of age, and 17 years 7 months of age denoted by solid lines without symbols.

76.2°, and 78.9° at the corresponding stages, respectively). SNA angles were greater than the Japanese norm[11] after both the first phase of treatment and the prosthetic treatment. Superimposed profilograms shows that the direction of mandibular growth was forward and downward, and the amount of growth was less than the Japanese norm[12] (Fig 12).

Skeletal characteristics of the patient's mother

As mentioned earlier, the patient's mother also had VDW (bilateral cleft lip and palate and lower lip pits). She was not treated orthodontically but received prosthetic treatment for the missing maxillary lateral incisors at 27 years 3 months of age (Fig 13). An anterior and lateral crossbite remained even after treatment. As shown in the superimposed profilograms of mother and daughter (Fig 14), the mother had a shorter cranial base and a larger mandible, and strongly tended toward a skeletal Class III malocclusion.

Fig 13. Intraoral photographs of patient's mother at 27 years 3 months of age.

Pretreatment characteristics of 4 other VDW patients

To investigate whether there are common skeletal characteristics in VDW patients, the sizes of the cranial base, the maxilla, and the mandible of 4 other patients before orthodontic treatment are shown in Table III. The characteristics of our patient after the first phase of treatment (9 years 10 months of age) and her mother are also shown. Each value is represented as a Z score: (value – Japanese norm)/SD.[13] Patients 1 and 2 were boys with bilateral cleft lip and palate; patients 3 and 4 were girls with cleft palate and right cleft lip and palate, respectively. All patients had lower lip pits. Four of the 5 patients had shorter anterior cranial bases (SN), and 3 of the 5 showed shorter posterior cranial bases (S-Ba). The sizes of the maxilla (ANS-PNS), the mandibular ramus (Ar-Go), and the mandibular body (Go-Pog) varied among the patients, and there were no common characteristics in the maxilla or the mandible.

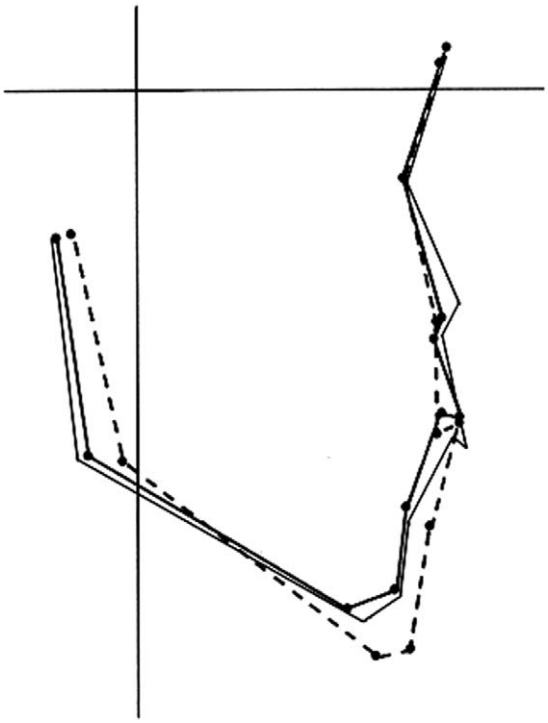

Fig 14. Superimposed profilograms of patient at 18 years 5 months of age (*solid line with dots*) and her untreated mother (*line with dashes and dots*) at 27 years 3 months of age. Japanese female norm[12] at 17 years 7 months of age denoted by solid line without symbols.

The number and position of the congenitally missing teeth are summarized in Table III. All six patients, including our patient and her mother, had congenitally missing teeth, all of which were maxillary lateral incisors or second premolars.

DISCUSSION

VDW is a monogenic congenital disease characterized by cleft lip or palate and lower lip pit.[1] A previous study reported that maxillary length and height are shorter in VDW patients than in nonsyndromic cleft lip and palate patients.[10] In this study, most patients had shorter cranial bases, but the lengths of the maxilla and the mandible varied (Table III). There was wide variation in maxillary and mandibular characteristics, probably due to the type of cleft, the effects of surgical repair, and intrinsic individual growth patterns. Common skeletal characteristics or growth patterns in the maxilla or mandible were not seen in the VDW patients we considered.

In our patient, SNB angle was within 1 SD of the Japanese norm,[11] after both the first phase and prosthetic treatment (Table II). In contrast, her mother, who had the same type of cleft, had a shorter cranial base and showed greater mandibular growth (Fig 13). Our patient received orthodontic treatment starting at 3 years of age, and her anterior crossbite was corrected by the early intervention. This, together with the chincup therapy during the retention period, would have contributed to the smaller amount of mandibular growth compared with that in her mother. Furthermore, a change in tongue position after the maxillary expansion might have resulted in the favorable maxillary and mandibular growth in this patient.

A secondary bone graft to the alveolar clefts was done at 16 years of age. This could have been performed at the stage of permanent canine eruption to stabilize the maxillary arch and promote canine eruption. During active treatment, the maxillary arch was expanded labially and laterally to arrange with the growing mandible. Since such expansion was considered to be easier in the maxillary arch still having alveolar cleft, the bone graft was carried out after the orthodontic treatment. If the secondary bone graft had been performed at earlier stage, she might have been treated orthognathically.

As a treatment alternative, orthognathic surgery was considered to improve her occlusion and profile. However, orthognathic surgery tends to impair skeletal growth when performed during the growing phase. We speculated that the conservative treatment of expanding the maxillary arch was valuable to facilitate normal skeletal growth in this patient.

It has been reported that the percentage of congenitally missing teeth is 27.3% among all Japanese patients with nonsyndromic cleft lip or palate.[14] Schneider[15] reported that 9 of 11 members in a family with VDW had hypodontia, and that many of the missing teeth were maxillary and mandibular second premolars. In contrast, Rizos and Spyropoulos[7] summarized previous studies and case reports on VDW and reported that congenitally missing teeth were not commonly seen. All 6 patients in this study had congenitally missing teeth—maxillary lateral incisors or second premolars (Table III)—supporting the high prevalence reported by Schneider.[15]

Genetic counseling is useful for providing important information to determine the diagnosis and treatment plan. Careful examination of the symptoms and the family record is always necessary for this counseling, especially for patients with VDW who have only minor features.

CONCLUSIONS

The orthodontic treatment of a girl with VDW has been described. She received early intervention, beginning at 3 years of age, and achieved a desirable occlusion. The characteristics of her mother and 4 other VDW patients showed a wide variation in the sizes of their maxillae and mandibles, suggesting that a common skeletal pattern is generally not seen. Interestingly, all patients had congenitally missing teeth, all of which were maxillary lateral incisors or second premolars.

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