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A longitudinal evaluation of craniofacial growth in a patient with Kabuki make-up syndrome: a case report

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SUMMARY The purpose of this investigation was to evaluate the craniofacial growth of a patient diagnosed with Kabuki make-up syndrome (KMS). Craniofacial growth was assessed by analysing lateral cephalometric radiographs with an interval of 12–15 months. They were taken from 6 years 9 months to 14 years 2 months.

Angular and linear measurement analyses of the craniofacial complex showed a hypoplastic maxilla and a constricted maxillary basal arch width. The mandibular size was relatively large and had started to increase from 13 years 4 months. This resulted in a prognathic face caused by forward growth of the mandible and insufficient growth of the maxilla. The skeletal pattern was Class III. Open bite morphology with a steep mandibular plane (SN–MP), a relatively short ramus, and a large gonial angle were also observed.

In this subject, the facial dysmorphism found in the maxilla and mandible may have been influenced by several factors. Connective tissue disorder, macroglossia, lower tongue posture, and tongue thrust swallowing have been identified as possible aetiological factors that may determine dysmorphism in the craniofacial complex in this KMS patient.

Introduction

Kabuki make-up syndrome (KMS) is a multiple congenital anomaly syndrome characterized by a face resembling the make-up of actors in Kabuki, a traditional stage performance in Japan. Several authors (Braun and Schmid, 1984; PeBenito and Ferretti 1989; Gillis *et al*., 1990; Carcione *et al*., 1991; Philip *et al*., 1992; Schrander-Stumpel *et al*., 1994; Galan-Gomez *et al*., 1995; Ilyina *et al*., 1995) have reported the occurrence of KMS in other races. KMS is suggestive of an autosomal dominant disorder of an obscure aetiology (Niikawa *et al*., 1988; Halal *et al*., 1989; Mulvihill and Kaiser-Kupfer, 1989; Tsukahara *et al*., 1997). Five cardinal clinical manifestations are essential to identify this syndrome:

(1) facial peculiarities characterized by eversion of the lower lateral eyelid, arched eyebrows, with sparse or dispersed lateral one-third, a depressed nasal tip and prominent ears;
(2) skeletal anomalies;
(3) dermatoglyphic abnormalities;
(4) mild to moderate mental retardation;
(5) postnatal growth deficiency.

In addition, a variety of somatic abnormalities have been recognized to be associated with this syndrome, such as craniofacial and visceral anomalies (Ohdo *et al*., 1985; Iwama *et al*., 1987; Matsumura *et al*., 1992), precocious puberty (Kuroki *et al*., 1987; Franceschini *et al*., 1993), and anorectal anomalies (Matsumura *et al*., 1992). Previous studies reported that KMS subjects exhibited morphological abnormalities including short and incurved fifth fingers, mainly from brachymesophalangy V, abnormal dentition (Lerone *et al*., 1997), and other minor abnormalities, such as incomplete development of the frontal and/or maxillary sinuses, and under-development of the mastoid processes. Moreover, patients with KMS have also exhibited cleft lip and palate (Ohdo *et al*., 1985; Niikawa *et al*., 1988; Handa *et al*., 1991; Burke and Jones, 1995),

and high-arched palate (Niikawa *et al*., 1981, 1988; Gillis *et al*., 1990). Growth deficiency in height is one of the most frequent irregularities observed in approximately 81 per cent of subjects (Niikawa *et al*., 1988).

As described above, many studies have reported on the occurrence of several abnormalities in KMS. However, longitudinal evaluation of craniofacial growth in a KMS patient has not previously been investigated. The present evaluation was carried out to gain further information on craniofacial growth by means of a 7 year 5 months longitudinal cephalometric radiographic analysis in a subject with KMS.

Subject and methods

Clinical data

A 6-year 9-month-old Japanese girl was referred to the dental hospital of Nagasaki University with an account of severe malocclusion. Pregnancy and delivery were uneventful. No therapeutic agents were taken by the mother that might have complicated the pregnancy. There was no history of hereditary disorder on either side of the family and chromosoma analysis showed normal female karyotype. Intelligence quotient (IQ) test showed mild to moderate mental retardation.

The patient exhibited many clinical features of KMS as summarized in Table 1.

A concave facial profile is shown in Figure 1. The intra-oral findings were as follows:

(1) macroglossia, with tongue thrust swallowing;
(2) high-arched palate, hypertrophic adenoid tissue and abnormal frenulum.

At age 6 years 9 months, the terminal plane was of a mesial step type. After an evaluated period of 7 years 5 months, the terminal plane changed from a mesial step type to an Angle Class III malocclusion with an anterior open bite. The patient had anterior and lateral crossbites with only the first molars in occlusion (Figure 2). A constricted maxillary basal arch width was diagnosed. Panoramic radiography revealed a crown and root shape deformation, and partial anodontia of the permanent dentition (Figure 3).

Table 1 Clinical features of Kabuki make-up syndrome shown by this patient.

Features	62 subjects (%)*	This patient
Craniofacial abnormalities		
Characteristic face	100	+
Lower palpebral eversion	98	+
Short nasal septum	93	–
Arched eyebrows	88	+
Prominent ear	85	+
Depressed nasal tip	79	+
Abnormal dentition	78	+
Spaced arch	67	+
High-arched palate	63	+
Epicanthus	61	–
Lower posterior hair line	53	+
Strabismus	49	+
Pre-auricular dimple	39	+
Micrognathia	36	–
Skeletal abnormalities		
Short finger (V)	89	+
Short middle phalanx (V)	80	+
Scoliosis	49	–
Hip dislocation	33	–
Foot deformity	21	+
Spina bifida oculta	16	+
Dermatoglyphic abnormalities		
Prescence of fingertip pads	78	+
Increase of hypothenar loops	70	+
Increase of ulnar loops	63	+
Occasional abnormalities		
Cardiovascular abnormalities	32	+

*Niikawa *et al.* (1988).

Before taking the serial cephalometric radiographs, the parents of the patient were informed of radiographic measurements along with possible risks and benefits of the serial cephalometric radiographs. After informed consent was obtained, lateral cephalometric radiographs were taken approximately once a year.

Cephalometric analysis

The craniofacial growth of the patient from 6 years 9 months to 14 years 2 months was analysed by means of lateral cephalometric radiographs. The analysis was performed with an interval of 12–15 months. The analysis of

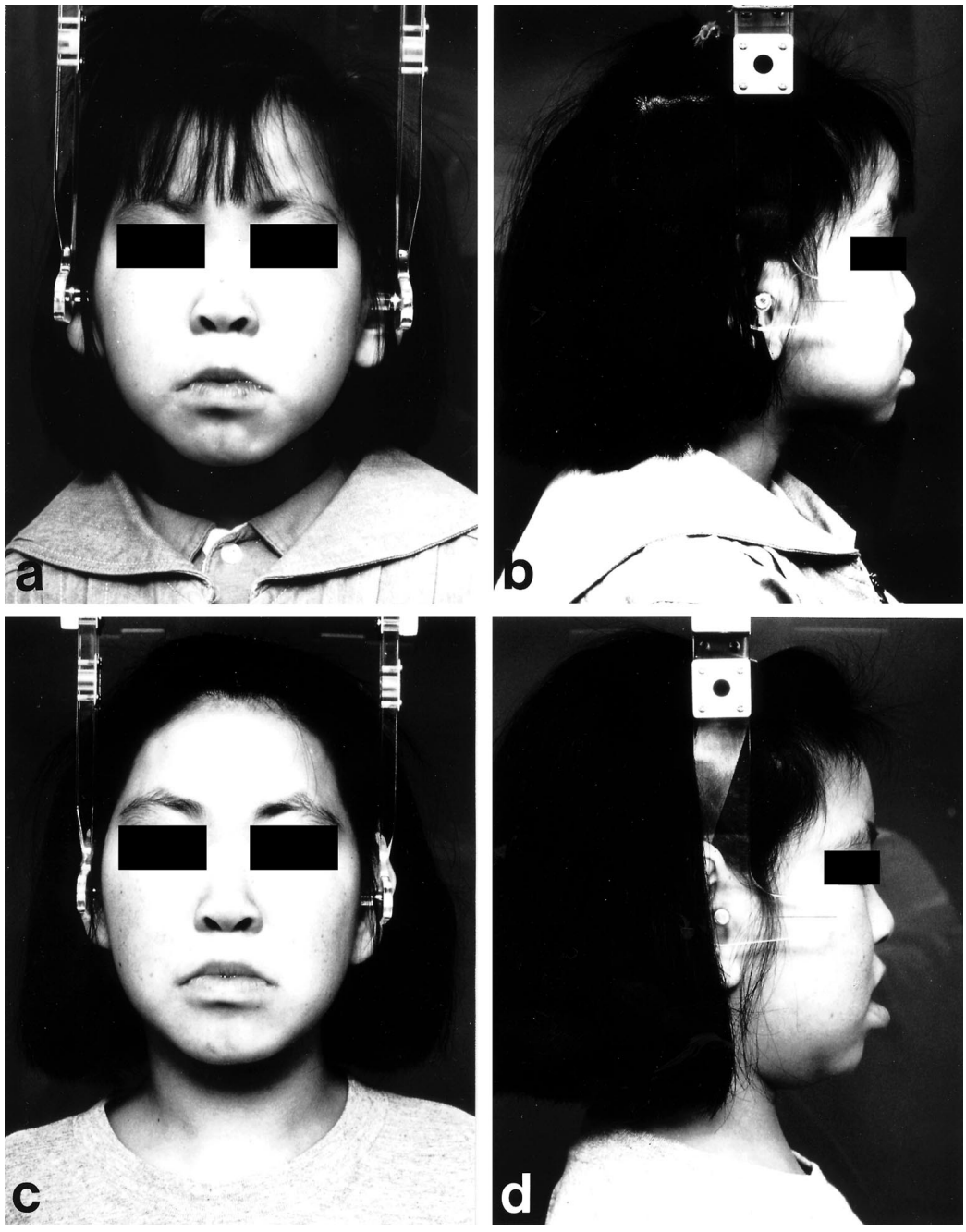

Figure 1 Facial appearance at 6 years 9 months (a,b); 14 years 2 months (c,d), diagnosed as Kabuki make-up syndrome (KMS), showing a concave facial profile.

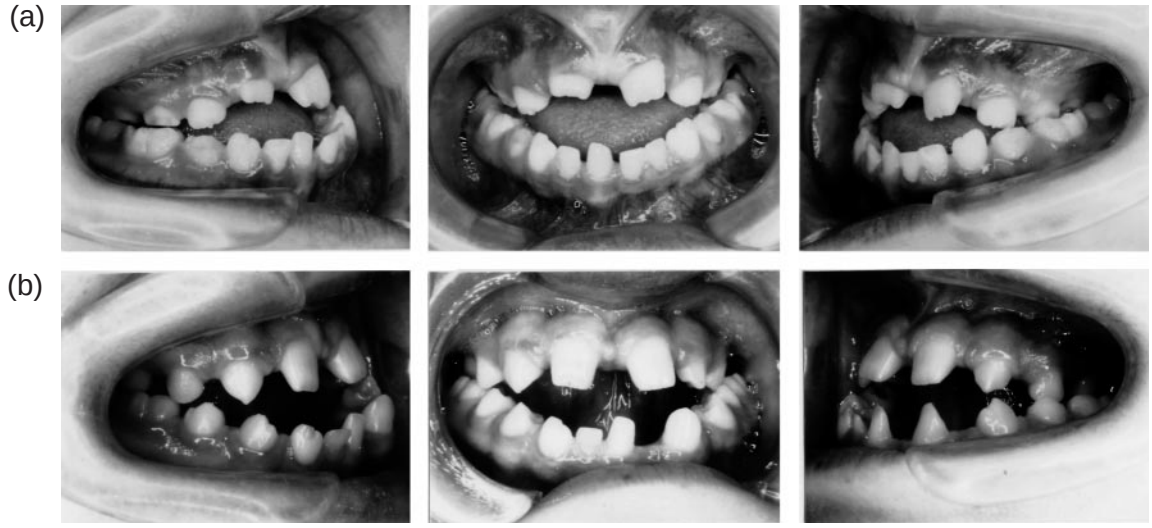

Figure 2 Intra-oral views showing an Angle Class III malocclusion, anterior open bite, anterior and lateral crossbite, from (a) 6 years 9 months to (b) 14 years 2 months.

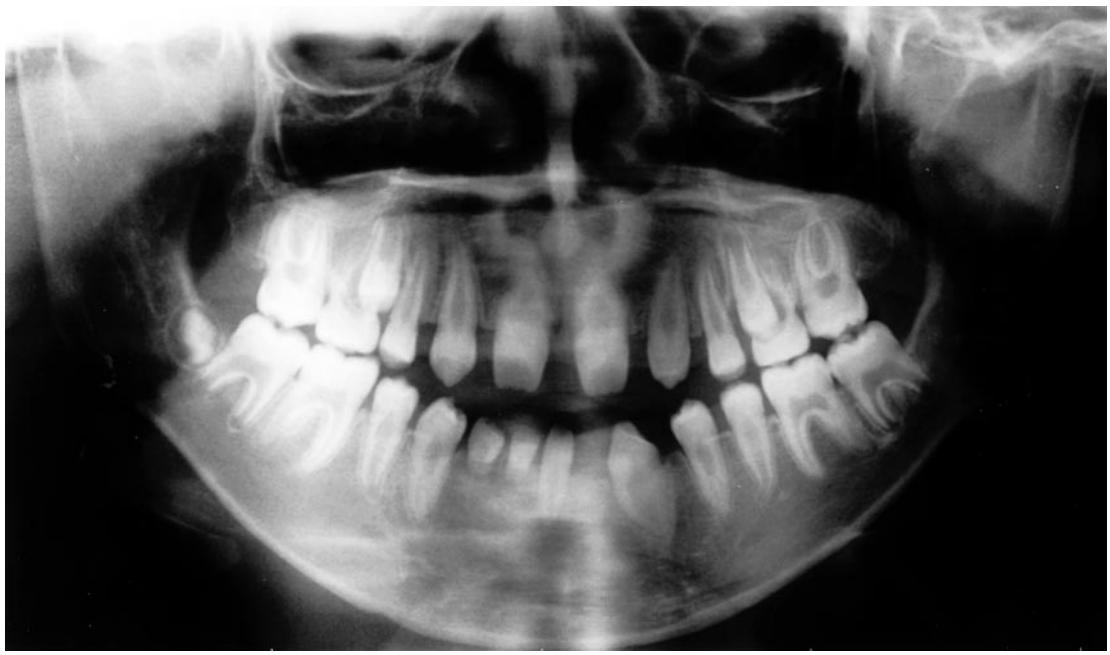

Figure 3 Panoramic radiograph at age 13 years 4 months, showing partial anodontia, and crown and root shape deformities.

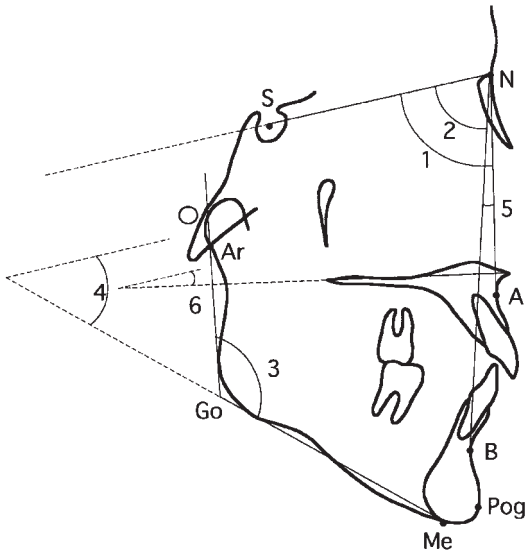

Figure 4 Angular measurements: 1. SNA: sella (S), nasion (N), A point (A); 2. SNB: sella (S), nasion (N) to B point (B); 3. CdGoMe: condylion (Cd), gonion (Go) to menton (Me); 4. SN–MP: mandibular plane to sella–nasion; 5. ANB: A point (A), nasion (N) to B point (B).

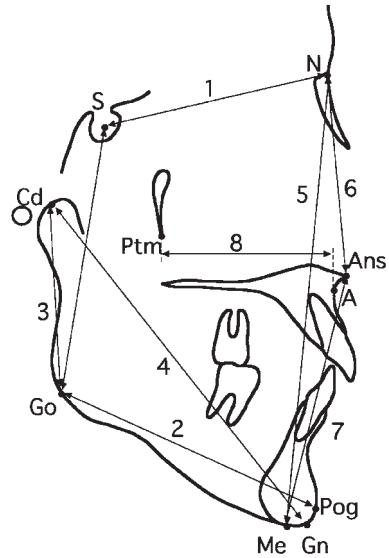

Figure 5 Linear measurements: 1. S–N: sella (S) to nasion (N); 2. Pog–Go: pogonion (Pog) to gonion (Go); 3. Cd–Go: condylion (Cd) to gonion (Go); 4. Cd–Gn: condylion (Cd) to gnathion (Gn); 5. AFH: nasion (N) to menton (Me); 6. UFH: nasion (N) to anterior nasal spine (ANS); 7. LFH: anterior nasal spine (ANS) to menton (Me); 8. A'–Ptm': A' point to Ptm' point.

craniofacial growth was based on the linear and angular measurements of each film (Figures 4 and 5). The values of all cephalometric measurements at age 6 years 9 months to 14 years 2 months are given in Table 2. Cephalometric superimposition was carried out to map the direction of craniofacial growth (Figure 6). All the values demonstrated some deviations compared with the Japanese standards of craniofacial morphology Iizuka and Ishikawa (1957).

Spatial maxillary relationships

The SNA values appeared to be relatively smaller compared with normal Japanese standards of craniofacial morphology. Within the evaluation period, SNA increased from 69.3 to 74.0 degrees resulting in a 4.7 degrees increase in growth. The growth increase was found to be greatest between 6 years 9 months and 7 years 9 months with a value of 2.2 degrees. The A'–Ptm' linear measurement was also smaller.

Spatial mandibular relationships

The anteroposterior position of the mandible represented by SNB angle increased from 71.5 to 77.5 degrees showing an increase in growth of 6.0 degrees. The greatest SNB growth increment was 2.0 degrees, between the ages of 8 years 11 months and 10 years 2 months.

Concerning the mandibular size, the effective length (Cd–Gn) and corpus (Pog–Go) of the mandible appeared to be normal up to 12 years and 3 months, but started to over increase from age 13 years 4 months up to the present. The incremental growth was 25.0 mm and 16.5 mm, respectively. The greatest increase in growth was observed after 11 years 3 months.

The ramus length (Cd–Go) was shorter as compared with normal Japanese standards (Iizuka and Ishikawa, 1957). The ramus growth was 11.0 mm and the gonial angle (Cd–Go–Me) was large. A steep mandibular plane angle (SN–MP) significantly increased from 13 years 4 months to the present.

Table 2 Cephalometric measurements of this patient at 6 years 3 months to 14 years 2 months.

	Age							
Structure	6 y 9 m	7 y 9 m	8 y 11 m	10 y 2 m	11 y 3 m	12 y 3 m	13 y 4 m	14 y 2 m
Cranial base								
S–N (mm)	(62.8 ± 2.4) 60.0	(62.8 ± 2.4) 60.0	(62.8 ± 2.4) 60.0	(65.7 ± 3.1) 61.0	(65.7 ± 3.1) 61.0	(65.7 ± 3.1) 62.5	(65.7 ± 3.1) 62.5	(67.2 ± 3.1) 65.0
Spatial maxillary relationship								
SNA (degree)	(81.4 ± 2.8) 69.3	(81.4 ± 2.8) 71.5	(81.4 ± 2.8) 71.5	(81.4 ± 3.3) 71.5	(81.4 ± 3.3) 72.5	(80.5 ± 3.4) 72.5	(80.5 ± 3.4) 73.0	(80.5 ± 3.4) 74.0
A'–Ptm' (mm)	(43.3 ± 1.8) 39.0	(43.3 ± 1.8) 40.0	(43.3 ± 1.8) 40.0	(43.3 ± 1.8) 40.0	(45.5 ± 2.1) 40.5	(46.3 ± 1.8) 40.5	(46.3 ± 1.8) 41.0	(46.3 ± 1.8) 42.0
Spatial mandibular relationship								
SNB (degree)	(76.4 ± 2.1) 71.5	(76.4 ± 2.1) 73.0	(76.4 ± 2.1) 74.0	(76.2 ± 1.7) 76.0	(76.2 ± 1.7) 77.0	(76.2 ± 1.7) 77.0	(76.2 ± 1.7) 77.0	(76.2 ± 1.7) 77.5
Pog–Go (mm)	(65.6 ± 3.9) 65.0	(65.6 ± 3.9) 66.0	(65.6 ± 3.9) 69.0	(65.6 ± 3.9) 72.0	(65.6 ± 3.9) 73.0	(74.9 ± 3.2) 77.0	(74.9 ± 3.2) 80.0	(74.9 ± 3.2) 81.5
Cd–Go (mm)	(46.8 ± 3.2) 42.0	(46.8 ± 3.2) 43.5	(46.8 ± 3.2) 43.5	(51.9 ± 3.9) 43.5	(51.9 ± 3.9) 45.0	(57.5 ± 3.6) 46.0	(57.5 ± 3.6) 52.0	(57.5 ± 3.6) 53.0
Cd–Gn (mm)	(98.4 ± 5.1) 100.0	(98.4 ± 5.1) 102.0	(98.4 ± 5.1) 103.0	(107 ± 5.4) 108.0	(107 ± 5.4) 110.0	(114 ± 4.3) 115.0	(114 ± 4.3) 120.0	(114 ± 4.3) 125.0
SN–MP (degree)	(31.1 ± 5.1) 42.5	(31.1 ± 5.1) 40.0	(31.1 ± 5.1) 41.0	(31.5 ± 5.1) 40.0	(31.5 ± 5.1) 40.0	(32.4 ± 4.5) 40.0	(32.4 ± 4.5) 38.0	(32.4 ± 4.5) 53.5
Intermaxillary relationship								
ANB (degree)	(4.97 ± 2.6) –2.2	(4.97 ± 2.6) –1.5	(4.97 ± 2.6) –2.5	(5.14 ± 2.6) –4.5	(5.14 ± 2.6) –4.5	(5.14 ± 2.6) –4.5	(5.14 ± 2.6) –3.5	(5.14 ± 2.6) –3.5
Vertical relationship								
AFH (mm)	(106 ± 4.6) 111.0	(106 ± 4.6) 115.0	(106 ± 4.6) 115.0	(114 ± 4.9) 120.0	(114 ± 4.9) 123.0	(121 ± 4.8) 126.5	(121 ± 4.8) 130.0	(121 ± 4.8) 132.0
UFH (mm)	(47.0 ± 2.5) 45.0	(47.0 ± 2.5) 47.0	(47.0 ± 2.5) 47.0	(51.5 ± 2.8) 51.0	(51.5 ± 2.8) 52.0	(53.3 ± 2.8) 52.0	(53.3 ± 2.8) 53.0	(53.3 ± 2.8) 53.0
LFH (mm)	(62.1 ± 2.9) 66.0	(62.1 ± 2.9) 68.0	(62.1 ± 2.9) 68.0	(65.5 ± 3.8) 69.0	(65.5 ± 3.8) 71.0	(70.4 ± 3.8) 74.5	(70.4 ± 3.8) 77.0	(70.4 ± 3.8) 79.0

Mean measurements ± S.D.; figures between parentheses from Iizuka and Ishikawa (1957).

Intermaxillary relationships

The ANB increased slightly from 6 years 9 months to 7 years 9 months, and then decreased significantly during subsequent years. ANB changed from –2.2 to –3.5 degrees. At the beginning of the observation, a negative ANB indicated a Skeletal III relationship that exacerbated from age 10 years 2 months.

Vertical facial relationships

Total anterior facial height (AFH) and lower facial height (LFH) increased from 6 years 9 months up to the present. AFH and LFH showed an increase of 21.0 mm and 13.0 mm, respectively. Upper facial height (UFH) showed no significant change during this period.

Discussion

Facial dysmorphism is a frequent craniofacial abnormality recognized in many patients exhibiting this syndrome. A short nasal septum, high-arched palate, cleft lip/palate, micrognathia are the most common dysmorphic phenotype expressed in KMS cases (Niikawa *et al*., 1988; Philip *et al*., 1992; Burke and Jones, 1995). In the subject investigated, facial dysmorphism appears to be highly expressed in the region of the middle and lower facial thirds during all evaluated periods. From 6 years 9 months to 14 years 2 months, the SNA angle increased from 69.3 to 74.0 degrees. The anteroposterior incremental increase in maxillary growth was 4.7 degrees. The greatest increase in growth was found between the ages of 6 years 9 months

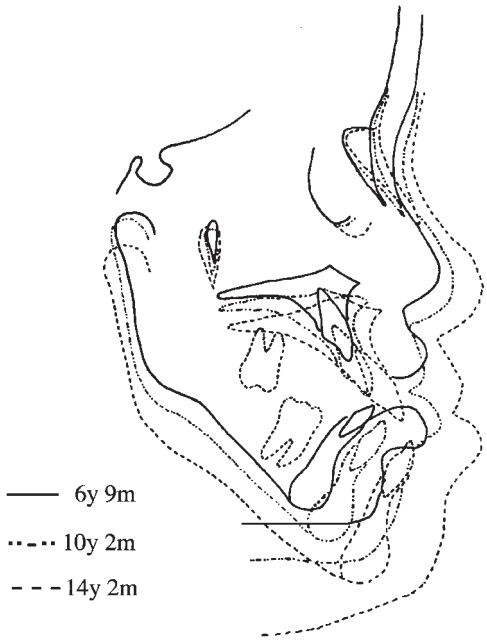

Figure 6 Cephalometric radiographs superimposed on cranial base. Continuous line: age 6 years 9 months. Dash and dots: age 10 years 2 months. Broken line: age 14 years 2 months. The maxilla was retrognathic anteroposteriorly. The mandible grew in a downward and forward direction. The final size and shape of the mandible was relatively large, the aberrant increase in growth started at 13 years 2 months of age.

and 7 years 9 months of age with a value of 2.2 degrees. According to the findings described above, there was remarkable deficiency in the anteroposterior position of the maxilla. A constricted maxillary arch width and bilateral posterior crossbite may be caused by a deficiency in lateral development of the maxilla.

Many aetiological factors might contribute to the anteroposterior/transverse deficiency of maxillary arch in this KMS patient. However, it was not possible to determine which factor directly interferes in the dysmorphism of maxillary structure. In reviewing the literature, connective tissue disorder has been reported to be correlated with KMS patients (Philip *et al*., 1992; Burke and Jones, 1995). Short stature, short finger V, and short middle phalanx V are the disorders strictly related to the development of the cartilaginous structure. Its growth of the nasomaxillary complex occurs concomitantly by the remodelling process and sutural growth (Enlow, 1990), it is possible that a connective tissue disorder may be one of the aetiological factors that plays an important role in growth deficiency, by affecting nasomaxillary growth in KMS.

The lowered tongue posture diagnosed in this patient, is another factor that may also explain the transverse growth deficiency of the maxillary arch. Disturbances in any of these factors may cause irreversible effects on the craniofacial morphology.

The direction of skeletal facial growth and mandibular configuration are affected by the resultant force created by tongue posture and function (Pedrazzi, 1997). In this case, longitudinal mandibular growth, mandibular length (Cd–Gn) and corpus (Cd–Go) were within normal range up to age 12 years 3 months. However, from age 13 years 4 months, mandibular growth started to increase and continues to the present.

Accompanying maxillo-mandibular growth, the low results in tongue posture, such as a high-arched palate, a broadened lower arch, crossbite occlusion in the molar area, and open bite morphology. Thus, there is a high probability that the increase in mandibuler effective length may be associated with low tongue posture and anomalies in the swallowing pattern. Tongue thrust was also observed in this subject. In Turner and Beckwith–Wiedmann Syndromes, associated craniofacial and dentomaxillary abnormalities have also been observed, which could be caused by tongue dysfunction (Friede and Figueroa, 1985; Takeyama *et al*., 1990). An enlarged tongue diagnosed in this patient may be associated with mandibular prognathism, but this effect is not true in all cases (Siebert, 1985).

Some consideration has to be given to individual growth potential regarding mandibular prognathism. In this subject, an accentuated open bite morphology with a steep mandibular plane (SN–MP), a relatively short ramus and a large gonial angle were observed. Open bite morphology has also been reported in other cases of KMS (Philip *et al*., 1992).

In all stages of this evaluation, ANB was negative and increased from age 10 years 2 months (Table 2). The results of serial

cephalometric analyses showed an accentuated increase in the skeletal maxillo-mandibular discrepancy, aggravated mainly by forward transitional growth of the mandible and deficiency of maxillary growth.

Serial cephalometric analyses also provided knowledge of incremental growth of the craniofacial structure in KMS, thus assisting with future treatment planning.

For the oral rehabilitation of this patient, orthognathic surgery (osteotomy) will probably be necessary in the future to correct the maxillomandibular skeletal discrepancy. Camouflage of the skeletal jaw discrepancy by orthodontic tooth movement and growth modification were excluded as a treatment option because, at her age (14 years 2 months), the remaining amount of growth is insufficient to allow any correction of the skeletal problem. Cardiovascular anomaly (Ohdo *et al*., 1985; Niikawa *et al*., 1988; Philip *et al*., 1992; Schrander-Stumpel *et al*., 1994; Hughes and Davies, 1994; Galan-Gomez *et al*., 1995), which is one of the most common internal systemic diseases associated with this syndrome and which is also present in this patient, must be considered as a risk factor during treatment planning. Analysing all the information obtained by serial cephalometic films, an adequate treatment planning was obtained and presurgical orthodontic treatment has commenced.

Whilst the data from one single case is not sufficient to establish the craniofacial growth pattern in KMS patients, the additional knowledge obtained in this investigation provides a valuable insight concerning KMS craniofacial growth. This leads to a better understanding of its abnormalities and playing an important role in clinical diagnosis, planning and orthodontic treatment.

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