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Case Report

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Orthodontic Treatment of a Kabuki Syndrome Patient

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Abstract

Kabuki syndrome (KS) is a rare disorder characterized by somatic and psychological disturbances including special face morphology, skeletal anomalies, and other systemic disorders. Because of the diverse clinical manifestation, the management of a patient with KS may involve several medical and dental specialists, including orthodontics. The aim of the article is to present successful orthodontic treatment performed in a 14-year-old boy diagnosed with the KS. Dental relations and smile aesthetics were normalized after orthodontic treatment; however, problems with patient compliance and cooperation and an increased risk of root resorption may influence treatment outcomes. Interdisciplinary cooperation between medical and dental specialists is essential in patients with KS.

Keywords

dental anomalies, Kabuki syndrome, orthodontic treatment, rare disease, root resorption

Introduction

Kabuki syndrome (KS, OMIM 147920) is a rare congenital disease, which may affect members of any ethnic group. The prevalence ranges from 1:32 000 (Japan) to 1:86 000 (Australia and New Zealand) of live births (Niikawa et al., 1988; White et al., 2004). There is no epidemiological data for the Caucasian race. The etiology of KS is not fully understood. Two genes, *KMT2D* (MLL2) and *KDM6A*, with mutations have been identified and considered to be associated with the phenotypic expression of KS. However, not all patients with clinical manifestations of KS have been diagnosed with such gene mutation indicating that other gene mutations may play a role in the expression of KS. Therefore, the etiology in about 30% of the cases with KS is still unknown, and negative results for *KMT2D* and *KDM6A* mutations do not exclude the presence of the syndrome. The inheritance pattern of KS is autosomal dominant (Zarate et al., 2012; Kim et al., 2013).

Kabuki syndrome was first described in 1985 independently by 2 Japanese scientists: Norio Niikawa and Yoshi Kuroki; hence, multiple names of the syndrome are still in use: Niikawa-Kuroki syndrome or Kabuki make-up syndrome. Later on KS has been also described by other authors (Petzold et al., 2003; Atar et al., 2006; dos Santos et al., 2006; Lung and Rennie 2006; Szczepanik et al., 2006; Suarez Guerrero et al., 2012).

Clinical diagnosis of KS is generally based on the assessment of the characteristic dysmorphic features, coexisting congenital disorders, and psychomotor development delays. Such manifestations are assessed on 0 to 10 scale which facilitates clinical diagnosis of the syndrome (Makrythanasis et al., 2013). The most common symptoms include: (1) special face morphology, (2) postnatal growth retardation, (3) skeletal anomalies, (4) persistence of fetal fingertips, and (5) intellectual deficiency. Additionally, patients can suffer from other systemic disorders, such as heart defects, genitourinary defects, skeletal abnormalities, gastrointestinal anomalies, ophthalmologic problems, feeding disorders, infant hypotonia, joint laxity, microcephaly, frequent respiratory tract infections, and frequent ear infections (Matsune et al., 2001; dos Santos et al., 2006; Teixeira et al., 2009; do Prado Sobral et al., 2013). The facial features of the patients resemble the stage make-up worn by the actors of the traditional Japanese Kabuki theater, hence an alternative name of the syndrome: the Kabuki make-up syndrome. Patients with KS have elongated, almond-shaped palpebral fissures with eversion of the lateral third of

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the lower eyelid, arched eyebrows with sparseness in the lateral third, big, dysplastic auricles, and a wide, depressed nasal tip. The most frequently reported oral manifestations include cleft lip and/or palate, malocclusion, and abnormal number and structure of teeth (Petzold et al., 2003; Teixeira et al., 2009; Suarez Guerrero et al., 2012; Kim et al., 2013), which may affect quality of life for the KS patients (Table 1).

To the best of our knowledge, orthodontic management of a patient with KS has not been described so far in the literature. Therefore, the aim of the article is to describe craniofacial and dentoskeletal abnormalities in a 14-year-old boy with the KS and to present his orthodontic treatment.

Case Description

Anamnesis/Past History of the Disease

A 14-year-old boy diagnosed with KS was referred by a dental practitioner for an orthodontic consultation due to dental crowding.

Early Childhood

The anamnesis revealed that the boy was born on time after an uneventful pregnancy (G3P3). The birth weight was 4.300 gram and the body length was 59 cm. The Apgar score was 9 in the first and the fifth minutes. Feeding problems and episodes of cyanosis occurred from the first days of the neonatal period as a result of congenital heart defect, that is, aortic coarctation, which was operated soon after the diagnosis. The psychomotor development was delayed. The child started to sit unassisted around the age of 12 months and started to walk at the age of 18 months. The mother reported symptoms of sensory hypersensitivity, for example, objections to walking barefoot on the sand or a negative reaction to a loud conversation. The patient was under neurologic care from the age of 5, due to strong headaches associated with vomiting.

Late Childhood

At the age of 12, as the headaches intensified, the patient was referred to the Clinic of Neurology and Epileptology in Warsaw, Poland. The computed tomography angiography revealed cerebral structures without focal lesions, nondilated, symmetrical ventricular system, narrow posterior communicating arteries, and an additional pericallosal artery. The electroencephalography performed during spontaneous sleep showed symmetrical morphological features of sleep. The bioelectric activity was according to the patient's age. The frontal and central leads recorded numerous single sharp waves and spikes with the amplitude of up to 140μV. Moreover, numerous groups of vertex sharp waves and K complexes were also recorded. A cytogenetic blood testing showed a normal male karyotype (46 XY), therefore karyotyping figures were not obtained. The 22q11.2 microdeletion was also excluded (GTG banding and FISH techniques). Kabuki syndrome was diagnosed based on the characteristic phenotype and coexisting congenital disorders. The family history did not reveal any family history of congenital disorders. A psychologist assessed the degree of intellectual disability as mild. At present, the patient is under supervision by various specialists including an ophthalmologist, a neurologist, an endocrinologist, and a nephrologist. From the age of 12, growth hormone therapy was initiated due to his height deficiency. At the age of 14, the patient's height was 157 cm, which was between 10th and 25th percentile of heights for the Polish population (mean = 166 cm).

Orthodontic Diagnosis

The patient was previously treated orthodontically with removable appliances, but no significant clinical improvement was observed. Therefore, the patient was referred to the Orthodontic Unit at the Institute of Mother and Child in Warsaw, Poland, which specializes in treating patients with craniofacial deformities.

Clinical Examination

The extraoral examination revealed the following features, which are typical for KS:

- short stature,
- hypertelorism,
- almond-shaped, elongated palpebral fissures,
- eyebrows with sparseness in the lateral third,
- large, cupped ears,
- short columella,
- distorted facial symmetry, that is, asymmetrical palpebral fissures and auricles,
- hypotonia of the orbicularis oris muscle—an attempt to close the mouth completely resulted in excessive tension of the mentalis muscles (Figure 1A, B, and C), and
- skeletal disorders: scoliosis, flat foot, brachydactyly of the 4th and 5th finger in the left hand and brachydactyly of the 5th finger in the right hand. Persistent fetal fingertip pads in both hands.

The intraoral examination showed (Figure 1D, E, and F; Table 1):

- presence of all permanent teeth except for the third molars,
- upper incisors with flat, screwdriver-like crowns,
- Angle Class II and canine Class III relations,
- normal overjet and overbite,
- posterior crossbite on the left side,
- moderate crowding in the upper arch and severe crowding in the lower arch,
- distinct cusps on the lower canines and additional palatal cusps on the upper canines,
- acceptable oral hygiene and no periodontal pathology, except for mild gingivitis on the buccal sides of the canines.

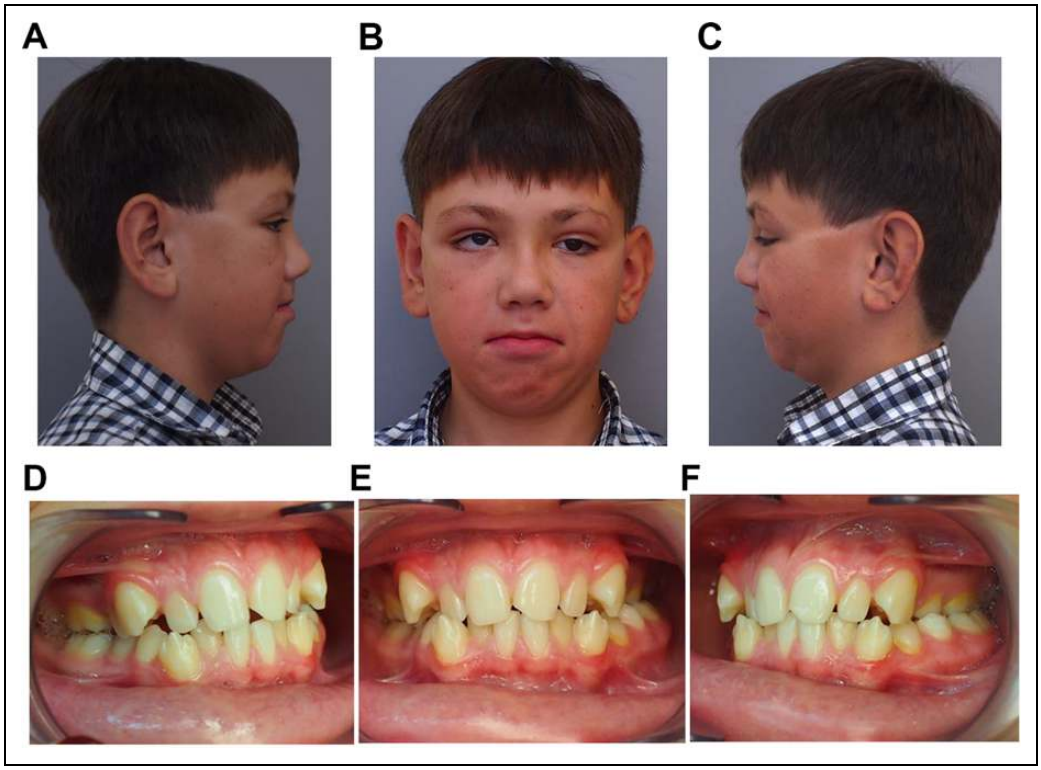

Figure 1. Before orthodontic treatment: (A, B, C) extraoral photographs; (D, E, F) intraoral photographs.

Table 1. Oral Manifestation Symptoms in the Kabuki Syndrome Based on Literature From 2008 to 2016.

Oral Anomalies	Cogulu et al., 2008, 1 Case	Spano et al., 2008, 5 Cases	Rocha et al., 2008, 1 Case	Teixeira et al., 2009, 9 Cases	Suarez Guerrero et al., 2012, 2 Cases	Tuna et al., 2012, 1 Case	do Prado Sobral et al., 2013, 16 Cases	Presented Case
Abnormal tooth shape	1/1		1/1				6/16	+
Conical teeth		2/5						+
Hypodontia		4/5		6/9		1/1	7/16	
Oligodontia	1/1			1/9				
Supernumerary teeth			1/1					
Taurodontic teeth	1/1		1/1				5/16	+
Screw driver-shaped incisors		1/5					11/16	+
Enamel hypoplasia		4/5					14/16	
Widely spaced teeth	1/1				1/2			+
Retrognathia		1/5				1/1		+
Micrognathia						1/1		+
Malocclusions		5/5	1/1			1/1	16/16	+
Cleft palate/lip	1/1			1/9	1/2		2/16	
High-arched palate		5/5	1/1		1/2	1/1	12/16	+
Root abnormalities	1/1						7/16	+
Root resorption							2/16	+

Radiological Examination

The panoramic radiograph, taken at the age of 7, revealed the presence of all permanent teeth including third molars. A panoramic radiograph taken at the age of 14 showed short roots of the maxillary and mandibular incisors and shadowing of the molar pulp chambers, which were probably the result of hard-tissue deposits (Figure 2B).

A lateral head radiograph was taken before the start of the orthodontic treatment (Figure 3A). Cephalometric analysis (Table 2) revealed retrognatic maxilla and mandible. The lower

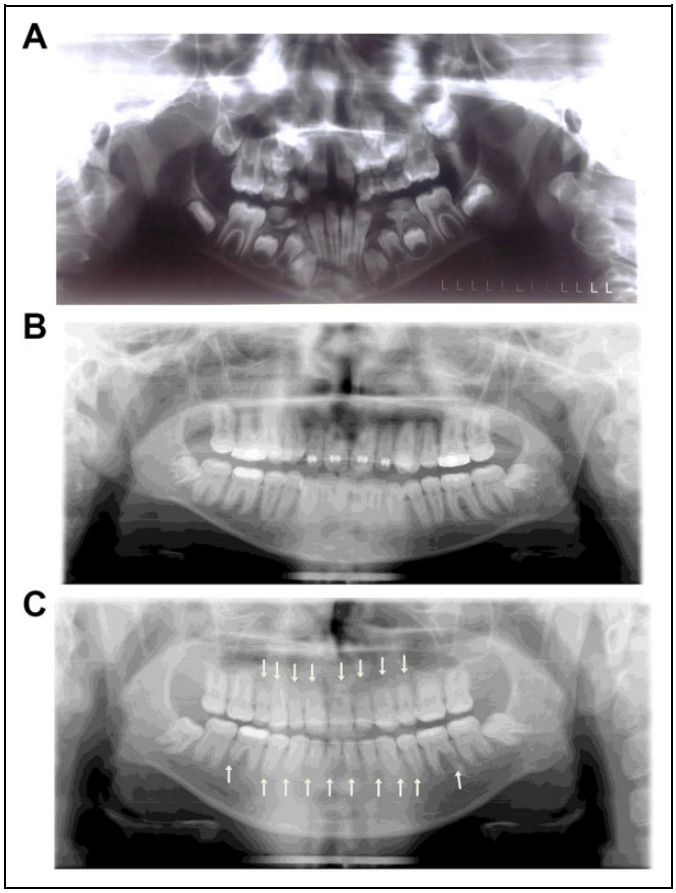

Figure 2. Panoramic radiographs: (A) taken at the age of 7 showed normal appearance of teeth; (B) taken before the orthodontic treatment at the age of 14 showed short roots and wide chambers of all incisors, large pulp chambers of molars and premolars with deposits of hard tissues in the form of a denticle; (C) taken 6 months after debonding of orthodontic appliances showed shortening of roots, except for the upper molars and the lower second molars.

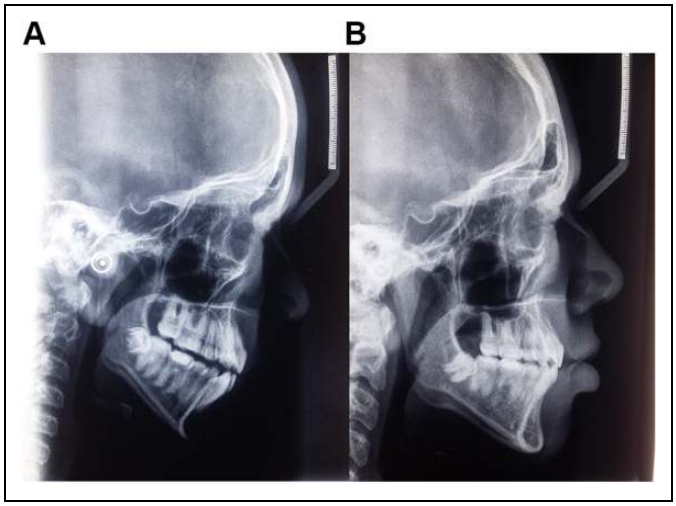

Figure 3. Lateral head radiograph: (A) before the orthodontic treatment, (B) after orthodontic treatment.

Table 2. Pretreatment (T1) and Posttreatment (T1) Cephalometric Analysis KS Patient.

Measurement	Pretreatment	Posttreatment	Mean (SD)
SNA	76°	76°	82° (3.5)
SNB	76°	77°	80° (3.5)
ANB	0°	−1°	2° (2.5)
S-N/ANS-PNS	5°	6°	8° (3.0)
S-N/Go-Gn	37°	38°	33° (2.5)
ANS-PNS/Go-Gn	33°	34°	25° (6.0)
1-ANS-PNS	112°	105°	110° (6.0)
1-Go-Gn	92°	89°	94° (7.0)
1-A-Pg (mm)	5	4	2 (2.0)
Overjet (mm)	2	2	3.5 (2.5)
Overbite (mm)	1.5	1	2 (2.5)
Interincisal angle 1/1	126°	132°	132° (6.0)

Abbreviations: KS, Kabuki syndrome; SD, standard deviation.

anterior face height and the mandibular angle were increased. The inclination of incisors was normal and the lower incisors were protruded. The overjet and overbite were normal.

Orthodontic Treatment

Because of the severity of crowding, especially in the lower arch, the treatment plan included extractions of all first premolars, and bonding of upper and lower fixed appliances. The patient was reluctant to start orthodontic treatment and seemed withdrawn; however, he also expressed a need to improve his smile aesthetics. Due to the patient's fear to start orthodontic treatment, it was decided firstly to bond a partial fixed appliance in the upper arch to correct the lateral crossbite and then to gradually to add the necessary appliances according to the patient's acceptance. After 4 months, the posterior crossbite on the left side was corrected. The patient did not report any discomfort, such as severe migraines, and he was willing to complete the orthodontic treatment with extractions of 4 premolars as it was initially planned. Fixed orthodontic appliances were bonded in the upper and the lower arches. The total treatment duration was 36 months including 25 appointments to activate the appliances. After orthodontic treatment, the upper and lower teeth were aligned and normal dental relations were obtained; however, occlusal contacts were not obtained at the upper left second premolar and the upper left first molar (Figure 4). Fixed retainers were bonded in the anterior segments of the upper and the lower dental arches and a Hawley-type retention plate was given for a night-time use. The panoramic radiograph taken at the end of the orthodontic treatment showed some root resorption in all teeth except for the upper first and second maxillary molars and the second mandibular molars (Figure 2C). The lateral head radiograph was taken after the treatment and the cephalometric analysis showed slightly more forward position and posterior rotation of the mandible. The incisors were more retroclined after the treatment and the protrusion of the lower incisors was decreased. The overbite was slightly reduced and the

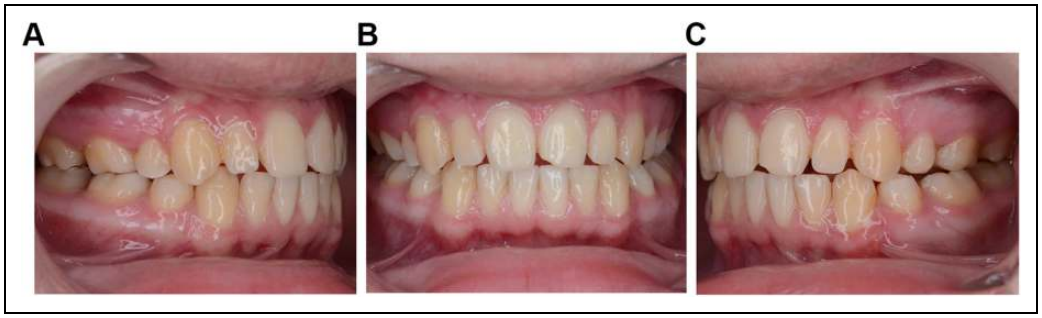

Figure 4. (A, B, C) Intraoral photographs: 6 months after debonding of the fixed appliances.

interincisal angle was increased. Clinical examination 6 months after debonding showed good stability of the treatment result.

Discussion

This is the first report in the literature, which described the orthodontic treatment performed in a growing patient diagnosed with KS. Due to the rarity of KS, it is very difficult to collect large numbers of patients with KS, who could be orthodontically diagnosed and treated.

Four hundred patients diagnosed with KS were described in the literature until 2012 (Teixeira et al., 2009; Bokinni 2012). Very few publications described the occlusal anomalies present in patients with KS. Teixeira et al. (2009) described orofacial anomalies in 9 patients with KS and compared their clinical findings with other cases with KS described in the literature from 1981 to 2006. Hypoplasia of the maxilla, a high palate, small dental arches, presence of malocclusions, dental anomalies related to the time of eruption, deviations in tooth number, and morphology were reported. Orthodontic treatment was not reported. Other clinical and radiologic features like flat, screwdriver-like crowns of maxillary incisors, short incisor roots, enlarged pulp chambers, hard-tissue deposits in wide pulp chambers, and presence of taurodontic teeth were also reported (Petzold et al., 2003; Lung and Rennie, 2006; Rocha et al., 2008; do Prado Sobral et al., 2013).

Occlusal anomalies most commonly associated with the KS include the presence of crossbites, open bites, micrognathia, retrognathia, Angle Class III malocclusion, and spacings (Matsune et al., 2001; Petzold et al., 2003; Rocha et al., 2008; do Prado Sobral et al., 2013). The study by do Prado Sobral et al. (2013), which was performed in a relatively large group of 16 patients with KS, has shown that the symptoms of dental and craniofacial anomalies were highly variable. The authors concluded that it is difficult to describe the most common dentofacial characteristic of patients with KS.

The patient described in the present report had some of the previously reported and typical KS dental anomalies including screwdriver-shaped maxillary incisors, short incisor roots, large pulp chambers, and hard-tissue deposits in the pulp chambers (Petzold et al., 2003). Also, some of the clinical and radiological findings including the presence of lateral crossbite, crowding and the presence of a middle face hypoplasia, were also reported by Matsune et al. (2001).

It may not be possible to perform orthodontic correction in all patients with KS due to the intellectual deficiency associated with the condition and the potentially limited cooperation with treatment. However, possible therapeutic procedures in patients with KS may not differ from normal orthodontic patients (do Prado Sobral et al., 2013). In the reported case, even though the orthodontic treatment was carried out over a long period of time, it was well accepted by the patient. Mild orthodontic forces were applied and periods between activations were somewhat longer than usual (25 appointments over 36 months). During the initial stages of orthodontic treatment, the patient maintained good oral hygiene and no problems related to presence of fixed appliances were observed. The oral hygiene deteriorated toward the end of the treatment.

Radiologic examination performed before the end of active treatment revealed root resorption, except for the upper molars and the lower second molars. Risk of root resorption in patients with KS was previously mentioned only by Petzold et al. (2003), who reported short roots in 3 of the 4 patients with KS. Authors described apical root resorption in 2 other patients and in 1 patient a loss of the upper central incisor at the age of 11 due to complete root resorption without any history of orthodontic treatment or tooth injury. A histopathological analysis of the lost incisor did not reveal any enamel or dentin anomalies (Petzold et al., 2003). Teixeira et al. (2009) reported hypodontia as a main dental finding in the patients with KS hypodontia. Root resorption was evident on radiographs presented in the article; however, the authors did not describe its presence. A genetic predisposition for root resorption in patients with KS should not be precluded.

Conclusions

Patients with KS have a need for orthodontic treatment due to the presence of dental and occlusal deviations from normal. It is possible to successfully perform orthodontic treatment involving extractions of premolars in patients with KS to normalize the occlusion and to improve smile aesthetics. Patients with KS may be more prone to root resorption, and therefore orthodontic mechanics and monitoring of root resorption should be implemented accordingly.

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Declaration of Conflicting Interests

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