

Oral Manifestations and Dental Treatment of Patients with Klinefelter Syndrome: Report of Two Cases

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ABSTRACT

Purpose: The aim of this study is to present the oral manifestations and dental treatment of two patients with Klinefelter syndrome. Both patients were referred to the Dental Department-Special Unit for the Disabled of a General Hospital.

Cases Presentation: The first patient was a 13 years old male with karyotype 47XXY with fair oral hygiene. A large spacing between the upper central incisors, an impacted canine and orthodontic problems were observed. Cooperation with the patient was difficult. Abfraction of many teeth was present and fluoride was applied topically. Oral hygiene instructions were given and he was referred to an orthodontist.

The second patient was a 26 years old male with karyotype of 49XXXXY. Due to the poor level of cooperation, dental care was performed under general anesthesia. The patient had poor oral hygiene, periodontitis, multiple caries, many missing teeth and taurodontism. Scaling, extractions, fillings and topical application of fluoride were performed.

Conclusion: Studies on dental treatment of patients with Klinefelter syndrome are limited. The extra X chromosomes appear to impact on craniofacial growth, on dental tissues and on intellectual ability. The method of providing dental care depends on the medical history, the level of cooperation and the patient needs.

Keywords: Craniofacial and oral characteristics; Dental treatment; Klinefelter syndrome; Oral manifestations; 47XXY karyotype; 49XXXXY karyotype

Introduction

The term Klinefelter syndrome refers to a group of chromosomal disorders with at least one additional X chromosome in the normal male karyotype 46XY [1,2]. The karyotype analysis determines the definite diagnosis [2]. However, many cases remain undiagnosed due to significant variation in phenotype, as well as insufficient professional awareness of the syndrome. Early diagnosis and hormone therapy can improve a person's quality of life and prevent serious consequences [3,4]. Different dental manifestations such as taurodontism, congenital absence of permanent teeth, shovel incisors, occlusal anomalies and increased permanent tooth size have been reported.

Klinefelter syndrome with karyotype 47XXY constitutes 80% of all cases and is one of the most common aneuploidies of sex chromosomes, with a frequency of one in 500-2,000 live births of males [5]. The extra

X chromosome can originate from a) maternal non-separation of the X chromosomes during the first (in most cases) or second reductive division, b) non-separation during mitosis or c) paternal non-separation of X and Y chromosome during the first reduction division, while the mother's age seems to be associated with an increased risk of non-separation during the reduction [4-6].

Males with a 47XXY karyotype show elevated levels of gonadotropins (FSH and LH) and estradiol and decreased testosterone levels. They present testicular hypoplasia, azoospermia, reduced secondary hair growth, gynecomastia in 56% -88%, tall stature (average height 179-188 cm) and long upper and lower limbs [2,5,7]. They also have an increased risk of developing breast cancer and mediastinal tumors; about 20 times more than normal males [5,8-10]. They are more likely to develop osteoporosis, type I and type II diabetes, or autoimmune diseases such as Sjogren's syndrome and lupus systemic,

while rarely they may present congenital heart disease, such as Fallot tetralogy and large vessel displacement [9,11-16].

Klinefelter subjects can have from normal IQ to moderate mental retardation (IQ 89 to 102). In general, there is a decrease in IQ by 15-16 points with the presence of each additional chromosome X [2,17,18]. They have speech delay (51%), delayed emotional development (32%) and difficulty in school adjustment (44%). In addition, they are more likely to have autism spectrum disorders, hyperactivity, psychosis, personality disorders, depression, and bipolar disorder (1.4 to four times more common than in the general population) [2,17-19].

The extra X chromosome appears to affect normal craniofacial growth and the thickness of the tooth enamel [20,21]. In terms of oral characteristics, affected people may have a reduced skull dome and base angle of the skull, and an increase in mandibular body and angle and reduced mandibular ramus length. They may also show maxilla protrusion and more commonly mandibular prognathism, increased transverse diameter of the palate and cleft palate. The prognathic mandible is due to the shape of the skullbase [5,18,22]. Congenital defects of permanent teeth, enamel hypoplasia and taurodontism can be observed, characterized by increased size of the teeth crowns with the pulp cavity extending sharply to the apex mainly in premolars and molars. The incisors' crowns can have a "shovel" shape. There is usually an increased prevalence of carious lesions and a predisposition to periodontal inflammation. Medication taken by these individuals (eg sedatives) can reduce saliva flow and thus increase the susceptibility to caries, while hormonal disorders are a contributing factor for periodontal disease. Orthodontic problems can also be observed, such as the inclination of the molars towards Angle III and increased rates of anterior open bite [5,23-26].

Klinefelter syndrome with karyotype 49XXXXY or Fraccaro syndrome [27] has a frequency of 1 in 85,000-100,000 male births [28]. The extra X chromosomes are in 100% of cases of maternal origin and a possible cause of the syndrome is the maternal non-separation of the first X chromosomes second reducing division, independent of the age of the mother [29].

Patients with Fraccaro syndrome have genital hypoplasia, gynecomastia, multiple orthopedic problems, susceptibility to infections, and often congenital heart disease and brain dysplasia. They also show hypergonadotropic hypogonadism and hypothyroidism or diabetes mellitus. They also have severe mental retardation (IQ 20 to 60), speech problems and psychomotor retardation. In general, they are timid and friendly, with occasional outbursts of anger and have difficulty in changing habits [2,18,28,30,31].

Oral and facial features may include slight microcephaly, short neck, hypertelorism, flat nasal bridge, ear shape disorders, and mandibular protrusion. The manifestations regarding the teeth concern taurodontism, thin tooth enamel, congenital defects of permanent teeth and multiple caries [28,32-35].

The aim of this study is to present the oral manifestations and dental treatment of two patients with Klinefelter syndrome, one with karyotype 47XXY managed at the dental office, and the second with karyotype 49XXXXY under general anesthesia.

Patients Information

Case 1

A 13 years old individual with a karyotype of 47XXY, diagnosed after chromosomal analysis a year before was referred to our hospital. His mother was 38 years old at the time of birth, the pregnancy lasted 37 weeks and was delivered by caesarean section. The patient had azoospermia and gynecomastia. He also had a reversal of the lymphocyte type and a mild regurgitation of the mitral valve. He was recently diagnosed with autism spectrum disorders, while his IQ was normal. His behavior included great introversion and low self-esteem. He was taking testosterone intramuscularly, an antipsychotic, an antidepressant and an anxiolytic.

After taking the medical history, a panoramic x-ray was taken and a clinical examination at the dental office was performed. Intraoral

examination revealed the following:

Large-sized upper central incisors, short mandibular frenulum and gum recession at the lower right central incisor were observed respectively (Figure 1)

The upper left canine was impacted

The upper left deciduous canine was retained and crossbite between the left upper and lower canines was observed (Figure 2)

Open bite was present in the area of the upper right canine and the lower right canine and premolars

Torus palatinus and commissural lip pits were observed, while the patient's tongue was bulky.

The patient's oral hygiene was good. Cooperation during the clinical examination was quite difficult. The treatment plan comprised scaling and topical application of fluoride. The mother was given oral hygiene instructions. Finally, the patient was referred to an orthodontist and re-examination was recommended at regular intervals.



Figure 1: Large upper central incisors, short attachment of the inferior labial frenulum and gum recession of the lower central right incisor respectively.



Figure 2: Retention of the deciduous upper left canine and crossbite between the left canines.

Case 2

A 26 years old patient with Klinefelter syndrome having karyotype 49XXXXY (Fraccaro syndrome) was referred to our clinic. He presented hypergonadotropic hypogonadism, gynecomastia, and severe mental and psychomotor retardation. He had multiple orthopedic problems, such as scoliosis and obesity (body weight 110kg, height 182cm). His medical history included a mild regurgitation of the pulmonary and mitral valves. He had undergone three surgeries due to orthopedic problems and had metal prostheses on his lower limbs, while he was not receiving any medication.

We were informed that the patient had received dental therapy at the age of nine under general anesthesia and at the age of 23 with nitrous oxide sedation at a University Pediatric Dental Clinic. After initial assessment, due to the poor level of cooperation, it was decided to perform his dental treatment under general anesthesia. A panoramic x-ray was taken, and the presence of the two impacted upper canines was observed. Nevertheless, the diagnostic value of the panoramic was not significant, because during taking the x-ray, the patient neither

cooperated nor remained still. Considering the anatomical features of the patient, a nasopharyngeal intubation was performed to facilitate dental management. The patient had poor oral health and periodontitis (Figure 3). Thirteen teeth were missing, eight teeth had carious lesions, and there were three fillings and two stainless steel crowns while the lower central incisors had third degree mobility. A large two-lobe torus palatinus was observed (Figure 4). The dental treatment performed was: a) ultrasonic and manual scaling, b) four extractions (first upper right premolar, upper left third molar and two lower central incisors), c) two amalgam restorations (occlusal surface of the upper right 3rd molar and cervical surface of the upper left 2nd premolar), d) topical application of fluoride and e) two fillings with flow composite resin (cervical surface of the lower canines). All four extracted teeth had extensive carious lesions extending to the pulp chamber. Due to the morphology of the roots, any endodontic treatment was deemed impossible.

The patient was admitted to a hospital ward to be monitored for any postoperative complications of general anesthesia and was discharged the next day. The patient's parents were given oral hygiene instructions and re-examination was recommended at regular intervals.



Figure 3: Poor oral hygiene and periodontitis.



Figure 4: Large two lobe torus palatinus.

Discussion

This study concerns the presentation of the oral manifestations and the dental treatment of a patient with karyotype 47XXY at the dental office and a patient with karyotype 49XXXXY under general anesthesia. Literature review revealed some case reports on the oral characteristics of this syndrome and a limited number of reports of dental treatment of patients.

The different variants of Klinefelter syndrome are associated with varying degrees of severity of mental and psychomotor retardation, depending on the number of extra X chromosomes. This was in line with the situation of our patients, in terms of different mental retardation and level of cooperation [2,18,28,30,31].

The patient with a 47XXY karyotype exhibited many of the clinical features of Klinefelter syndrome. Also, signs recorded frequently in males with this karyotype were observed in this patient's oral cavity, like the large size of the upper central areas and orthodontic problems. Despite medication containing antipsychotics, antidepressants and anxiolytics, no decreased saliva flow was observed, nor did the patient report a dry mouth. On the panoramic xray, it was observed that the upper left canine was impacted. Literature reports the case of a 24-year-

old patient with a 47XXY karyotype who had impacted teeth [36]. In another case of a seven-year-old patient with Klinefelter's syndrome and mild mental retardation, taurodontia in the maxillary molars, multiple caries and congenitally missing of four permanent teeth were observed [37]. No taurodontism was observed in our patient. No carious lesions were found and his oral hygiene was good.

Our second patient with a karyotype 49 XXXXY, despite the fact that he was very friendly, due to his severe mental and psychomotor retardation, he had a very low level of cooperation. The reduced level of patient cooperation is generally associated with poorer oral hygiene and more dental problems [38-43].

In cases where the patient is unable to cooperate, due to mental and/or psychomotor retardation, the dental treatment under local anesthesia is not considered safe and effective and the administration of general anesthesia is appropriate [44-48].

This was evident in our second patient, who had a much lower level of oral hygiene and an increased number of dental problems compared to the first patient. The patient presented with dental features that are observed in individuals with karyotype XXXXY. He had many missing teeth. However, it could not be concluded if there were any congenitally missing teeth or if teeth had been extracted. The patient had multiple caries lesions, as well as taurodontism. Four extractions of teeth with extensive carious lesions (extending to the pulp) were performed. Due to the morphology of the teeth roots, endodontic treatment was deemed impossible.

In a Greek study, the case of a patient with a 49XXXX karyotype and mental retardation was reported; due to the poor level of cooperation he received dental treatment under general anesthesia. This patient was treated twice at the age of 8 and 12 and teeth with severe carious lesions were extracted. The patient had multiple caries and congenital malformations [49]. In another case report with a corresponding karyotype and mental retardation, who was receiving dental treatment from the age of six to the age of 20, the patient showed multiple caries, taurodontia in both the deciduous and permanent dentition and congenitally missing permanent teeth. However, the level of cooperation was satisfactory and the dental treatment was performed at the dental office with the "say-show-do" technique. In another patient with three additional X chromosomes, taurodontism in deciduous and permanent molars, delayed sperm development of permanent teeth and anterior cross bite were reported [34]. Finally, there is a case where the dentist during the examination of a young boy aged 9 years (before adolescence) noticed in his radiograph multiple missing permanent teeth and taurodontism in the first permanent molars and in the second deciduous molars. The dentist also observed the body type of the patient who had large lower limbs relative to his torso and long fingers on the upper limbs. The dentist recommended a chromosomal analysis due to the frequent association of taurodontism with abnormalities on the X chromosome. Patient chromosomal analysis revealed 47 XXY karyotype [50]. It is of crucial importance to evaluate such patients and regular follow-up is recommended.

Conclusions

The number of studies concerning the oral characteristics and dental treatment of patients with Klinefelter syndrome is limited and this patient population is often neglected. The extra X chromosomes appear to impact on the craniofacial development and dental tissues with the phenotypic variety of patients being large. The dentist may be the first to notice the special features in the dentition of a child or young teenager and can lead to the investigation of the coexistence of other problems associated with abnormalities on the X chromosome. Individuals with rare genetic diseases have a lower chance of accessing oral health care services.

In order to decide the method to be followed for the provision of dental treatment, a careful evaluation of the medical history and the level of cooperation should be performed, depending directly on the patient's mental state and his therapeutic needs. A systematic protocol is needed to create a complete, properly sequenced treatment plan.

Klinefelter syndrome is an under diagnosed chromosomal disorder with important challenges for health and medical management. A multidisciplinary and stepwise approach should be adopted. Identifying and improving the factors associated with access to dental care for individuals with rare genetic diseases, like Klinefelter syndrome, may improve the oral health of this population impacting positively on quality of life.

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