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Orofacial features of Treacher Collins syndrome

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Abstract

Treacher Collins syndrome (TCS) is a rare autosomal dominant disorder of craniofacial development. Major features include midface hypoplasia, micrognathia, microtia, conductive hearing loss, and cleft palate. The present study is on the orofacial features of 7 Brazilian patients with sporadic TCS aged 4 to 38 years. All patients presented the typical down-slanting palpebral fissures, colobomas, zygomatic and mandibular hypoplasia, partial absence of the lower eyelid cilia, and abnormalities of the ears. Malocclusion was present in all patients, and an anterior open bite was found in 3 patients. None of the patients had a cleft palate.

Key words: *Treacher Collins syndrome, orofacial features, genetic disease.*

Introduction

Treacher Collins syndrome (TCS) or mandibulofacial dysostosis (OMIM 154500) is an autosomal dominant disorder with high penetrance and variable expressivity (1). The essential features of this syndrome were described by Treacher Collins in the year 1900 (2), but the first extensive description of the condition was produced by Franceschetti and Klein in 1949, who used the term mandibulofacial dysostosis (1). The frequency of TCS is 1 in 50,000 live births (2), and approximately 60% of the autosomal dominant occurrences arise as de novo mutation (3). Genetically, the treacle gene (TCOF1) is mutated. It is found on chromosome 5q31.3-32 and encodes a serine/alanine rich nucleolar phosphoprotein responsible for the craniofacial development (4). Other modes of inheritance such as autosomal recessive transmission and a role for gonadal mosaicism and chromosomal rearrangement in the causation of this syndrome have also been proposed (5).

TCS is characterized by downward slanting palpebral fissures and hypoplasia of the zygomatic arches (6). Other craniofacial alterations of the syndrome are mandibular hypoplasia, coloboma, total or partial absence of lower eyelashes, accessory skin tags or blind pits between the tragus and the mandibular angle, external ear malformations, hearing loss, and malformations of the heart, kidneys, vertebral column and extremities. The oral manifestations are characterized by cleft palate, shortened soft palate, malocclusion, anterior open bite, and enamel hypoplasia (7). The aim of this study is to describe the orofacial features of 7 patients affected by TCS.

Case Reports

We selected a sample of 7 cases from the Stomatology Clinic, Dental School, State University of Montes Claros, and from the Department of Oral Diagnosis, Dental School, University of Alfenas from 2002 to 2006. Minimal criteria for propositi to be included in the casuistic were the presence of hypoplasia of the zygomatic arches and downward slanting palpebral fissures (6). The protocol for evaluation of the patients included identification data; prenatal, perinatal, and family history. Clinical evaluation included general examination with particular concern to oralfacial features. Skull and facial X-rays and hematological exams were also performed. Informed consent was taken from the patients or from the legal guardians of the children. This study was approved by Ethics Committee of Dental School, University of Alfenas. Six patients were females and 1 was male, and the mean age was 21.1 years (range from 4 to 38 years). The mean maternal age was 24.3 years, and the mean paternal age was 26.7 years. There was no history of exposure neither to known teratogenic agents nor maternal diseases. In any pregnancy and case perinatal complications were related. All cases were isolated with negative family history for related features. No parental consanguinity was observed. Hematological studies were normal in all patients. All patients demonstrated an age-appropriate mental and speech development.

The main orofacial findings of the presented cases are listed in (Table 1) (Fig.1-3) show pictures of the representative abnormalities found in the patients of this study. All patients showed downward slating palpebral fissures, zygomatic (malar) hypoplasia, lower eyelid coloboma, partial absence of the eyelashes, lower implantation and deformities of the external ear, and mandibular hypoplasia. In relation to external ear anomalies, 4 out of 7 ears presented microtia. Absence of communication between internal and external accoustic meatus leading to hearing loss was detected in 4 (57.14%) out of 7 patients, extension of the hair-line onto the cheek (facial implantation of the hair) was presented in 6 (85.71%), and narrowed frontal bone was detected in 5 (71.43%). In relation to intraoral anomalies, all patients demonstrated malocclusion, 3 out of 7 presented open bite, and 1 patient showed shortened of the soft palate. Cleft palate was not observed in any patient.

Fig. 1. Frontal facial aspects clinical of the patients 3 and 7. These pictures are showing the antimongoloid slants of the palpebral fissures, mandibular and zygomatic hypoplasia, coloboma of the lower lid, and absence of lower eyelid cilia.

Table 1. The main clinical orofacial findings of our cases.

Clinical findings	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Downward slanting palpebral fissures	+	+	+	+	+	+	+
Coloboma	+	+	+	+	+	+	+
Partial absence of eyelashes	+	+	+	+	+	+	+
Zygomatic (malar) hypoplasia	+	+	+	+	+	+	+
Retrusive mandible	+	+	+	+	+	+	+
Lower implantation of the external ear	+	+	+	+	+	+	+
External ear deformity	+	+	+	+	+	+	+
Absence of communication between internal and external acoustic meatus	+	+	-	-	+	+	-
Narrowed palate	+	+	+	+	-	-	+
Anterior open bite	+	+	+	-	-	-	-
Shortened soft palate	+	-	-	-	-	-	-
Facial implantation of the hair	+	+	+	+	-	+	+
Narrowed frontal bone	+	+	+	+	-	+	-

(+) presence, and (-) absence.

Fig. 2. Clinical features of deformities of the ear often leading to conductive hearing loss (patients 1, 3 and 4). The intraoral exam showed accentuated anterior open bite with malocclusion (patients 1 and 3).

Fig. 3. This figure is showing the patient number 2 with audiological rehabilitation. This picture is also showing the patient 7 after the facial plastic surgery.

Discussion

TCS has been well documented as an autosomal dominant genetic disorder (1). The pleiotropic effects of autosomal dominant mutant genes have been observed in a large number of craniofacial syndromes, such as Apert syndrome (craniosynostosis, maxillary hipoplasia, syndactyly-symphalangism, acne, brachymelia), velocardio-facial syndrome (platybasia, cleft palate, heart anomalies, learning disabilities, ocular anomalies) and Robinow syndrome (hypertelorism, platybasia, brachymelia, and short phallus to name a few). In these syndromes, as in the majority of craniofacial multiple anomaly syndromes, there are both craniofacial and extracranial anomalies (8).

TCS is a well-recognized condition characterized by variable involvement of the craniofacial structures derived from the first and second branchial arches (1). Clinically, it ranges from hypoplasia of the zygomatic arches and antimongoloid slant of the palpebral fissures, which are considered the minimal diagnostic features, to a more complex phenotype with skeletal, cardiac, and renal manifestations (8). The pathogenetic mechanisms involved have been controversial and no definitive causal agent could be found so far. It has been postulated that the TCS represents a defect of blastogenesis that could be attributed to interferences in cephalic neural crest cell histodifferentiation (1); however, the multisystemic involvement in some cases does not sustain only a localized damage.

Teber et al. (2004) (6) defined the downward slanting palpebral fissures and the hypoplasia of the zygomatic archs as the minimal features for the diagnosis of TCS. In this series, besides those minimal diagnostic features, the main signs found in all affected patients were mandibular hypoplasia, lower eyelid coloboma, partial absence of the eyelashes, and deformities and lower implantation of the ears. The absence of communication between the internal and external acoustic meatus leading to hearing impairment was only found in patients with microtia, suggesting that microtia in TCS is related to inner ear defects. In fact, microtia has been reported to be as high as 85%, with one third of patients presenting with stenosis or complete atresia (8). Other ear abnormalities reported in patients with TCS that could contribute with hearing loss include bilateral abnormalities of the pinnae, external auditory canal, tympanic membrane, and middle ear space (9). Systemic anomalies represented by cardiovascular, renal and cervical vertebrae defects, in our sample, were not observed, however, the real incidence of these anomalies in TCS patients is not well known.

Malocclusion and anterior open bite is expected in all patients with TCS due to the zygomatic and mandibular hypoplasia. Effects on the temporomandibular joints (TMJs) and the muscles of mastication are also frequently observed (10). The extension of open bite is attributed to the severity of mandibular retrognathia (11). Anterior facial height was within normal standards, but the total facial height was excessive (8). The angle between the S-N plane and the palatal plane is obtuse, confirming the counterclockwise rotation of the occlusal plane (10). There is an estimated 35% incidence of cleft palate and an additional 30% to 40% incidence of congenital velopharyngeal incompetence in TCS patients (12). Interestingly, clefts were not observed in this series. Of greatest concern is the frequent occurrence of obstructive apnea among patients with TCS (13). Sher et al. (1986) (9) documented obstructive apnea in 25 percent of the TCS sample population. Deglutition may be adversely affected because of the inability of the pharynx to handle large pieces of food. Though there is a tendency for patients with TCS to prefer soft, easy to chew foods, clinicians might incorrectly connect this preference to the anterior skeletal open-bite characteristic of this syndrome. While this malocclusion may be in part contributory, the compromise of the upper airway is more likely to be the cause (8).

Early diagnosis of TCS allows prompt and appropriate treatment of aesthetic and functional deficiencies in these patients. If this can be done early, it is possible to take advantage of anticipated growth during normal skeletal maturation and to obtain better therapeutic results (5). An experienced multidisciplinary team of orthodontists and maxillofacial surgeons is necessary for good results since the method of choice in the treatment of TCS is distraction osteogenesis associated with preoperative and postoperative orthodontic treatment leading to a better quality of life (14-16). In fact, ameliorating the outward signs gives these patients the opportunity to have an improved social life (17).

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