CASE REPORT

Treacher Collins syndrome

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ABSTRACT

Treacher Collins syndrome (TCS) is a rare autosomal dominant disorder of craniofacial development. It is a congenital malformation of first and second branchial arch which may affect the size and shape of the ears, eyelids, cheek bones, and jaws. The extent of facial deformity varies from one affected individual to another. A case of 20-year-old boy having TCS is briefly described in this article.

Key words: Autosomal dominance, first arch derivative, genetic disease, orofacial features, Treacher Collins syndrome

INTRODUCTION

Treacher Collins syndrome (TCS, OMIM number 154500)[1-3] is an autosomal dominant disorder of craniofacial morphogenesis with high penetrance and variable expressivity.[1] The essential features of this syndrome were described by Treacher Collins, a British ophthalmologist, in the year 1900, but the first extensive description of the condition was given by Franceschetti and Klein in 1949 in which they coined the term Mandibulofacial Dysostosis.[1] It is estimated that the frequency of TCS is 1 in 50,000 live births.[2] Approximately 60% of the autosomal dominant occurrences arise as de novo mutation.[4] 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.[1,2]

Symptoms of this disorder vary greatly, ranging from almost unnoticeable to severe.[5] It is most noticeably characterized by abnormalities of the head and face. These include down slanting eyes with notched lower lids,[2,6] sunken cheekbones[7,8] and jawbones, pointed nasal prominence,[9,10] broad mouth[8] and high arched palate.[9,11] They also show malformation of the auricular pinnae[11] and conducting hearing loss[11,12] and preauricular hair extension.[11] A minority of those affected with TCS may have cleft lip and/or palate.[12]

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CASE REPORT

A 20-year-old boy reported to the institute with a chief complaint of multiple carious and malaligned teeth. When the patient was examined, he revealed downward slanting of eyes, depressed zygomatic arches, sunken cheek bones, deformed external ears, coloboma of lower eyelids with deficient eyelashes medial to it, tongue-shaped extension of hairs on cheek, retruded chin giving bird-like appearance [Figures 1 and 2]. Significant hearing loss was not observed nor did he show any signs of mental retardation. Intraoral examination revealed crowding of upper and lower anterior teeth, caries with 11, 14, 15, 21, 25, 26, 27, 36, 46 and 47. The patient also had high arched palate, anterior open bite and bifid uvula [Figures 3 and 4]. Family history revealed that patient's father also suffered from same condition but in milder form.

Radiographic examination revealed underdeveloped condylar and coronoid processes, hypoplastic zygomatic arches, bilateral prominent antegonial notch on mandibular angle and short rami with resultant crowding of teeth [Figures 5 and 6]. A noncontrast high-resolution (0.6) CT scan report of skull and face clearly demonstrated maxillofacial deformity with more prominent mandibular hypoplasia. However, the cranial vault and skull base appeared normal. It also revealed bilateral hypoplasia of external pinnae, marked hypoplasia/aplasia of bony external auditory canals, hypoplasia of middle ear cavity on either side with absence of ear ossicles [Figure 7]. No paranasal sinus pathology was evident.

Based on clinical and radiographical findings he was diagnosed with TCS.

DISCUSSION

TCS is a severe congenital disorder of craniofacial development of the head and neck region.[2] It is characterized by numerous

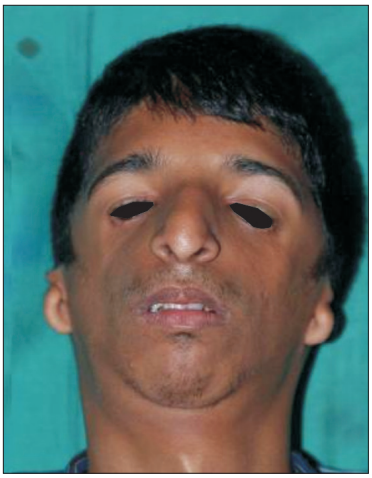

Figure 1: Antimongoloid features, coloboma of eyes, sunken cheekbones

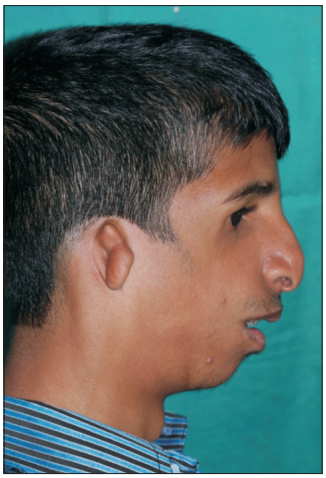

Figure 2: Fish facies (retruded chin), preauricular hair displacement, malformation of external ear

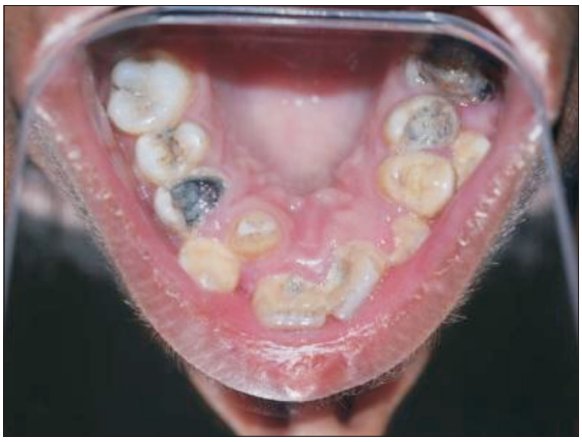

Figure 3: High arched palate

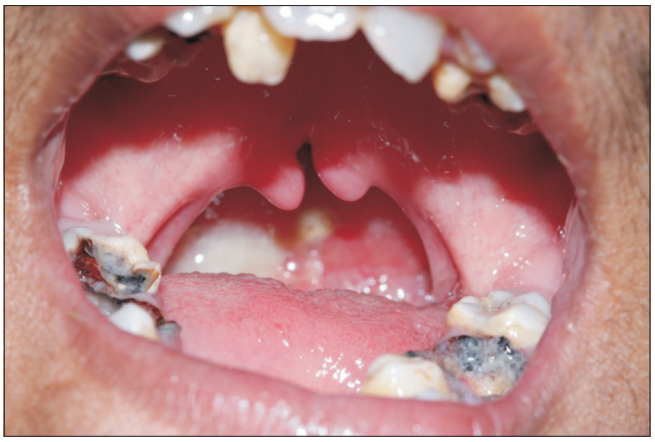

Figure 4: Bifid uvula, crowding of teeth

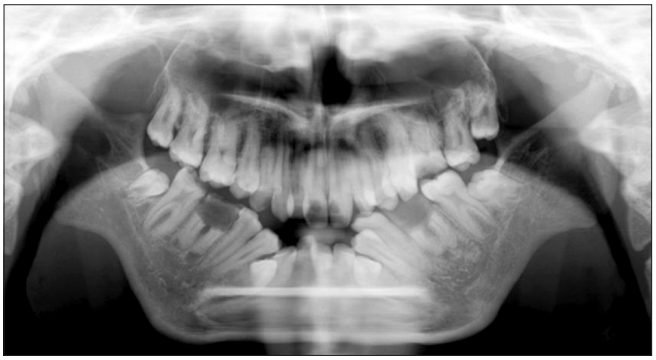

Figure 5: Bilateral antegonial notches, short rami

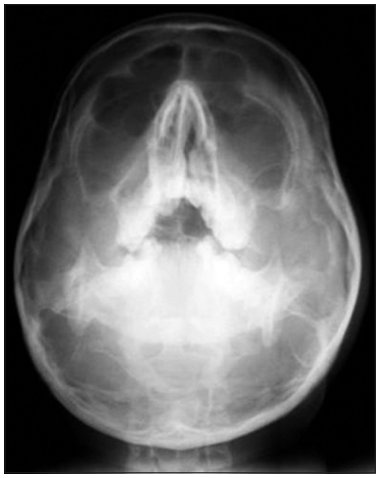

Figure 6: Underdeveloped condylar and coronoid processes, hypoplastic zygomatic arches

bilateral symmetrical developmental anomalies derived from first and second branchial arches.[8,13] It is also called as Franschetti-Klein Syndrom or Mandibulofacial dysostosis. This was describe for the first time by Thompson (1846);[7,8,14] however, the syndrome is named after Edward Treacher Collins, the English surgeon and ophthalmologist who described two cases in 1900.[6] Franceschetti and Klein in 1949 published an extensive review of the condition in which they expanded the phenotype, employing the designation "Mandibulo-Facial Dysostosis".[12] TCS occurs with an estimated incidence of 1/50 000 live births.[2]

TCS exhibits autosomal dominant inheritance with variable penetrance.[2] It is caused by a mutation of the TCOF1gene

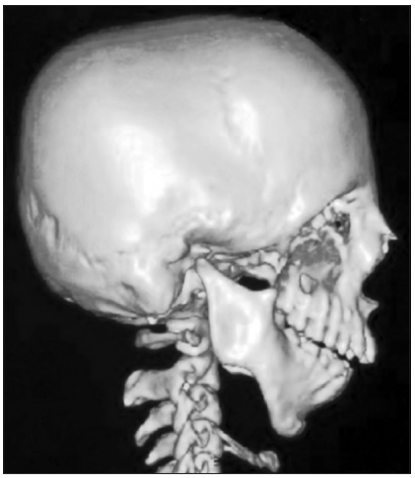

Figure 7: 3D CT (3 dimensional computed tomography) scan showing mandibular hypoplasia involving condylar andcoronoid processes

which exhibit linkage to the human chromosome 5q32 locus. The mutation may be inherited from the parents (40%). Individuals who have the TCOF1 mutation have a 50% chance of passing it on to their children. TCS shows high penetrance and extreme variation in expressivity of phenotype. It is common for mildly affected TCS patients to be diagnosed retrospectively after the birth of a more severely affected child.[2] This similar feature was seen in this current case. Intriguingly, however, 60% of the cases do not appear to have a previous family history and are thought to arise as the result of a de novo mutation. TCOF1 is found to encode a low complexity, serine/alanine-rich, nucleolar phosphoprotein-termed Treacle.[2,3] It helps in neuroepithelial survival and neural crest cell proliferation that is central to normal craniofacial development. Mutations in TCOF1gene leads to high degree of neuroepithelial apoptosis and consequent loss of neural crest cells. General cranioskeletal hypoplasia occurs due to generation of insufficient neural crest cells.[2,10,15]

Clinical features include hypoplasia of the facial bones, particularly the mandible (78% of cases) and zygomatic complex (81%), considered as an extremely common feature of TCS. In severe cases, the zygomatic arches may be completely absent (Poswillo, 1975).[2] Hypoplasia of the facial bones may manifest dental malocclusion, with resultant anterior open bite. The teeth may be widely spaced, malpositioned or reduced in number. In a large proportion of cases, the palate is high arched and sometime shows cleft (28%). However, this patient has unique presentation of bifid uvula which is as yet unreported in referred literature. Ophthalmic abnormalities include downward slanting of the palpebral fissures (89%) with colobomata or notching of the lower eyelids (69%) and a paucity of lid lashes medial to the defect (69%) which was seen in current case.[2] Other clinical features of TCS include alterations in the shape, size and position of the external ears, which are frequently associated with atresia of the external auditory canals and anomalies of the middle ear ossicles.[2,11]

Franceschetti has classified TCS into five categories- i.e., complete, incomplete, unilateral, abortive and atypical form.[6,10,16]

Radiographic analysis of the middle ears of TCS patients has revealed irregular or absent auditory ossicles with fusion between rudiments of the malleus and incus, partial absence of the stapes and oval window, or even complete absence of the middle ear and epitympanic space. Consequently, bilateral conductive hearing loss is common in TCS patients, whereas mixed or sensorineural hearing loss is rare.[2,11]

A number of conditions exhibit phenotypic overlap with TCS, including Nager and Miller syndrome.[2,12,11] Nager syndrome has similar facial features to TCS, but preaxial limb abnormalities are a consistent feature of Nager syndrome, unlike TCS. Thumbs may be hypoplastic, aplastic, or duplicated and the radius and ulna may be fused. Cases of Nager syndrome are generally sporadic. Miller syndrome also has features in common with TCS, with the additional diagnostic feature of ectropion or out-turning of the lower lids. The cleft lip, with or without cleft palate, is more common than in TCS. The limb anomalies are postaxial, most commonly with absence or incomplete development of the fifth digital ray of all four limbs.[2,12]

This present case has shown almost all the features describe above for TCS except the complete development of cleft palate and hearing loss. According to the Franceschetti's classification of this syndrome, present case was showing complete form of the syndrome. Present case also has shown the positive family history suggesting familial mutation transfer in TCOF1gene which is seen in 40% of cases.

CONCLUSIONS

TCS is an autosomal dominant condition caused by the mutation in TCOF1 gene. This gene can be detected by prenatal testing in embryos. Thus prenatal diagnosis and genetic counseling helps parents to make intelligent decisions regarding the pregnancy which will reduce the incidence of TCS.

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