CASE REPORT

Treacher Collins Syndrome: A Case Report and Review of Literature

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Abstract

Introduction: Treacher Collins syndrome (TCS) is a rare autosomal dominant disorder of craniofacial morphogenesis. The congenital malformation is restricted to first and second branchial arches which affects the mandible, maxillozygomatic complex, ears, and eyelids. Many cases also manifest with dental anomalies resultant of the craniofacial abnormality. The severity of the facial deformity varies with affected individuals based on the variability of penetrance. This paper reports a case of a 31-year-old male with TCS.

Case description: A 31-year-old male patient reported to the institution with a chief complaint of forwardly placed upper front teeth since 15 years. He also reported difficulty in speech, loosened anterior teeth since 5 years, and mild pain on gums while having food and during speech. The patient also gave a history of surgical correction for the "widened" mouth at the age of 2 years and has been on medications for recurrent ear infections.

Management: Treatment consists of surgical management of anomalous facial structures. Preoperative planning and evaluation should begin as early as possible. A staged treatment and multidisciplinary craniofacial team is required to coordinate cranio-orofacial, dental, ocular, and pediatric care beginning in the early neonatal life throughout childhood.

Conclusion: Prenatal diagnosis and genetic counseling are mandatory to help parents to make decisions regarding pregnancy. These patients require care from birth through adulthood. Proper treatment planning, counseling, and surgical management are essential for optimizing patient outcomes.

Keywords: Autosomal dominance, Craniofacial complex, Hypoplasia, Treacher Collins syndrome.

Oral and Maxillofacial Pathology Journal (2019): 10.5005/jp-journals-10037-1164

Introduction

Treacher Collins syndrome (OMIM number 154500) is an autosomal dominant disorder of craniofacial development. It has an incidence of 1 in every 50,000 live births.[1] This condition was first presented by Thomson in 1846 and later described by George Andreas Berry (1889) as a congenital neonatal deformity with colobomata of lower eyelids.[2] Edward Treacher Collins (1900), an ophthalmologist, after whom the disorder has derived its name, illustrated the essential components of the syndrome.[3] This condition is also known as mandibulofacial dysostosis (MFD) and Franceschetti–Zwahlen–Klein (Franceschetti and Klein).[4]

Treacher Collins syndrome affects the entire craniofacial complex, and the symptoms of the disorder vary from unnoticeable features to severe deformities. Characteristic abnormalities include hypoplasia to the absence of the facial bones, predominantly maxilla, zygomatic complex, and mandible.[5] Dental malocclusion is an associated feature in occurrence with the hypoplasia leading to anterior open bite, spacing, or hypodontia. A large fraction of cases presented with high arch/cleft palate.

Alterations in the size, shape, and position of the external ears are common manifestations and are associated with anomalies of middle ear ossicles and atresia of external auditory canals. Ophthalmic abnormalities include downward slanting of the palpebral fissures with colobomas of the lower eyelids. Other clinical features of TCS may include microcephaly, mental retardation, and psychomotor delay.[6]

Though patients have normal intelligence, they often face social challenges because of their physical appearance. These patients require counseling and multidisciplinary team approach to remove the social stigma. Early prenatal diagnosis is essential to prevent the occurrence of the syndrome.

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How to cite this article: Thomas P, Krishnapillai R, *et al.* Treacher Collins Syndrome: A Case Report and Review of Literature. Oral Maxillofac Patho J 2019;10(2):90–94.

Source of support: Nil

Conflict of interest: None

Case Description

A 31-year-old male patient reported to the institution with a chief complaint of forwardly placed upper front teeth since 15 years. He also reported difficulty in speech, loosened anterior teeth since 5 years, and mild pain on gums while having food and during speech. The patient also gave a history of surgical correction for the "widened" mouth at the age of 2 years and has been on medications for recurrent ear infections.

On general physical examination, the patient was poorly built but with normal intelligence. The patient had mild hearing loss. Extraoral examination depicted square-shaped skull with asymmetry. His eyes portrayed downward slanting, strabismus, and coloboma with sparse cilia of lower eyelids. The ears were positioned below the zygomatic arch extending to the lower border of mandible. The patient also exhibited a convex facial profile, a prominent broad nose with narrow nostrils, hypoplasia of the malar-zygomatic complex with "sunk-in" appearance,

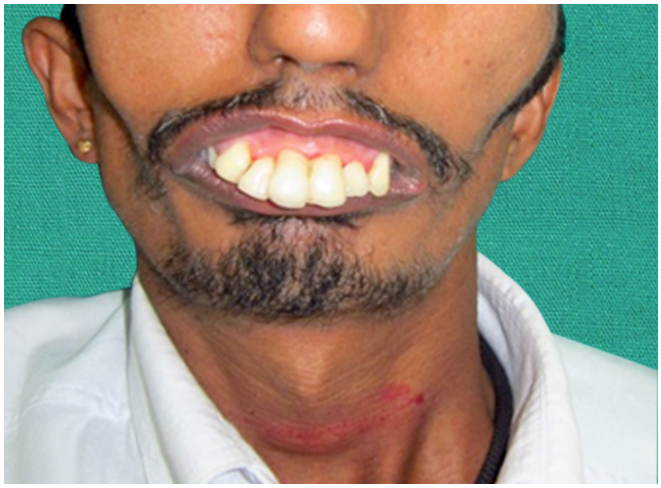

Fig. 1: Craniofacial hypoplasia, mandibular retrognathia, and proclined anteriors

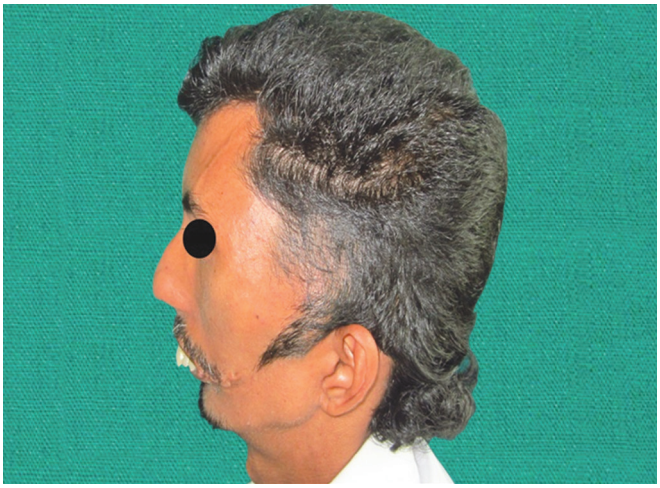

Fig. 2: Preauricular hair displacement

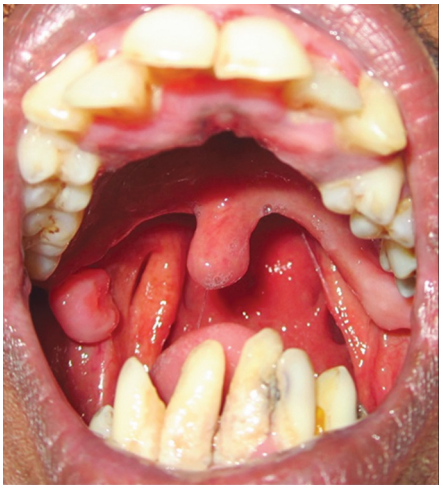

Fig. 3: Intraoral findings: palatopharyngeal incompetence, high arched palate, and malocclusion

hypoplasia and retrognathia of mandible, and protrusion of maxillary dentition leading to incompetency of lips. Deep mentolabial sulcus and flattening of the occipitoparietal region were also noticed (Fig. 1).

Noninflammatory alopecia in the left parietal scalp and preauricular hair displacement with bilateral atypical tongue-shaped processes of the hairline (hairlick) were seen extending toward the cheek. Scar formation associated with the surgical correction for macrostomia was seen on the left corner of the mouth (Fig. 2). The patient also expressed mouth-breathing habit.

Intraoral examination revealed high arched palate with palatopharyngeal incompetence, malocclusion with deep bite, and proclined maxillary anteriors (Fig. 3). Generalized periodontitis, gingival recession, periodontal pocket formation, grade II and grade III mobility of upper and lower anteriors, and multiple carious teeth (16, 24, 27, 28, 32, 34, 35, 46, 47) were also apparent.

The clinical findings were supplemented with radiographic evidences. Cephalogram evaluation demonstrated hypoplasia of mandible and zygomatic bone, severe protrusion of premaxillary segment, steep mandibular inclination, and enlarged paranasal sinuses. Orthopantomogram revealed prominent antegonial notch, reduced ramus height and width, bilateral coronoid aplasia, and impacted 48 (Fig. 4).

Discussion

Treacher Collins syndrome or MFD is a rare congenital/genetic disorder of craniofacial dysmorphism characterized by numerous

Figs 4A and B: (A) Cephalogram: hypoplasia of mandible and zygomatic bone, prognathic premaxillary segment and steep mandibular inclination; (B) Orthopantomogram—prominent antegonial notch, reduced ramus height and width, bilateral coronoid aplasia, and impacted 48

developmental anomalies restricted to the head and neck. Treacher Collins syndrome exhibits autosomal dominant pattern with variable penetrance and expressivity of phenotype.[7] Gene and transcript mapping has identified TCOF1 to be the major gene mutated in TCS, encoding a low complexity protein, "Treacle" (Tcof1/treacle).[8] Treacle, serine/alanine-rich, nucleolar phosphoprotein, is involved in ribosomal DNA gene transcription (ribosome biogenesis pathway) through its interaction with upstream binding factor (UBF) which helps in neural crest cell proliferation that is central to normal craniofacial development. Mutations in the TCOF1 gene reduce the amount of treacle and also direct neuroepithelial apoptosis with consequent loss/depletion of neural crest cells in pharyngeal arches 1 and 2, thereby resulting in cranioskeletal hypoplasia.[7,9,10] Treacher Collins syndrome is thought to be genetically homogeneous and the linkage has been mapped to the human chromosome 5q32 locus. One hundred and thirty other distinct mutations have also been identified. Mutations in RNA polymerase I subunit D (POLR1D) located on 13q12.2 and RNA polymerase I subunit C (POLR1C) located on 6p21.1 produce the autosomal-dominant and autosomal-recessive form of TCS, respectively.[11]

Forty percent of the cases are associated with previous family history and those affected have a 50% chance of passing it on to their next generation.[12] The remaining 60% of the cases are thought to arise as a de novo mutation.[13] Our case did not report with a familial history of the syndrome.

Clinical and Radiographic Overview

The syndrome is restricted to craniofacial complex affecting the skull, eyes, ears, nasal structures, facial bones, and orodental tissues (Table 1). The clinical presentation is usually bilaterally symmetrical and evident at birth. Our case, though bilaterally present, hypoplasia was more pronounced to the left side of the face.
Franceschetti has classified TCS into the following categories:[14,15]

- Complete: classic major features
- Incomplete: less severe ear, eye, zygoma, and mandibular abnormalities
- Unilateral: affecting one side
- Abortive: only the lower lid pseudocoloboma and zygoma hypoplasia
- Atypical form: combined with other abnormalities not usually part of the typical syndrome.

Radiographic findings can be interpreted on a computed tomography (CT) scan, orthopantomogram, or occipitomental radiograph. The classic features include hypoplasia or aplasia of the malar—zygomatic arch, mandibular hypoplasia and retrognathia, facial convexity, and dental abnormalities. Malar hypoplasia can be confirmed by intraorbital measurements by CT that are at the mean, with zygomatic measurements less than normal.[16]

Da Silva Dalben et al. in his study observed associated dental anomalies in 60% of individuals with TCS. Anomalies identified included tooth agenesis of predominantly mandibular 2nd premolar (33.3%), enamel opacities (20%), and ectopic eruption of maxillary first molars (13.3%).[17]

Other radiographic findings include middle ears irregularity or the absence of auditory ossicles with the fusion of malleus and incus rudiments, partial absence of stapes, or complete absence of middle ear space.[18] Bilateral conductive hearing loss is common in TCS, whereas mixed or sensorineural hearing loss is rare.[7,19] The present case has been reported with a mild bilateral hearing loss.

Table 1: Clinical features of TCS[15,27,28]

I. Ophthalmic
- Antimongoloid slant of the palpebral fissures
- Coloboma (notching) and hypoplasia of the lower lids and lateral canthus
- Sparse, partially absent or totally absent lower eyelid cilia (particularly medial third)

Minor features
- Vision loss, amblyopia, refractive errors, anisometropia, strabismus, hypertelorism
- Congenital cataracts and occasional microphthalmia/anophthalmia
- Lacrimal duct atresia, absence of puncta, narrowed tear ducts (dacrostenosis)

II. Orbits
- Skeletal dysmorphism
- Hypoplastic lateral aspects

III. Otological abnormalities
- External ear anomalies—alteration in size, shape, and position [small, malformed ears (microtia) or rotated ears]
- External auditory canal atresia
- Middle ear cavity ossicular deformities
- Conductive hearing loss upto 60 dB due to hypoplasia of the external auditory canals

IV. Facial bone malformation
- Bilaterally symmetrical convex facial profile
- Hypoplasia of the malar bones and zygomatic complex (cardinal feature)

V. Maxilla and mandible
- Characteristically hypoplastic
- Distalization of mandible
- Variable effects on tempromandibular joint (TMJ)
- A steep occlusal plane

VI. Nose/mouth
- Respiratory compromise
- Maxillary hypoplasia (nasal passage constriction)
- Mandibular micrognathia and retropositioned tongue (oropharyngeal and hypopharyngeal spaces obstruction)
- Prominent nose with nasal deformity
- Microstomia
- Cleft palate with or without cleft lip
- High-arched palate

VII. Dental abnormalities
- Malocclusion
- Tooth agenesis
- Enamel opacities
- Widely spaced teeth and skeletal open bite
- "Bird-like facies"
- Ectopic eruption of maxillary first molars

VIII. Other minor manifestations
- Preauricular hair displacement—hair growth extends in front of ear to lateral cheekbones
- Airway abnormalities, tracheostoma, unilateral or bilateral choanal stenosis or atresia

Contd...

Contd...

- Absence of parotid glands
- Cervical spine malformation, cryptorchidism, extremity malformation, renal anomalies, congenital heart disease
- Delayed motor or speech development

This case has shown almost all features described for TCS but with moderate degree of phenotypic expression. According to the Franceschetti's classification, the present case can be categorized to the incomplete form of the syndrome.

Differential Diagnosis (Table 2)

Numerous other conditions exhibit phenotypic overlap with TCS: Nager and Miller syndrome, oculoauriculovertebral dysostosis, first branchial arch syndrome, and Pierre Robin syndrome.[20,21] Nager syndrome has similar facial features but present with preaxial limb abnormalities unlike TCS. Miller syndrome exhibits ectropion, an additional diagnostic clue to the common features of MFD. The cleft lip, with or without cleft palate, is more common compared to TCS.

Diagnostic Aids

Prenatal diagnosis. Prenatal screening ultrasound can be used to detect TCS, though adequate view of facial structures can be obtained only after 30 weeks.[22] 3D sonographic imaging has been used to identify down-slanting palpebral fissures, micrognathia, and low set ears/microtia.[23] Amniocentesis may be performed to identify the mutation detect in TCOF1 (14–18 weeks IUL).[24]

Diagnostic tests include radiographs and CT images to detect craniofacial abnormalities. Audiological evaluation for audio impairment and DNA sequencing for the detection of TCOF1 defects can be employed to asses TCS.

Management (Table 3)

Treatment consists of surgical management of anomalous facial structures. Preoperative planning and evaluation should begin as early as possible. A staged treatment and multidisciplinary craniofacial team is required to coordinate cranio-oro-facial, dental, ocular, and pediatric care beginning from the early neonatal life throughout childhood. Airway obstructions are common in these patients due to hypoplastic midface and narrow nasal cavity. Mandibular distraction represents an alternative to tracheostomy for airway obstruction. Airway assessment is the prime requisite, followed by oropharyngeal restoration and midface reconstruction.[25] Zhang et al. proposed a staged reconstruction protocol comprising "(a) upper-facial reconstruction with specially designed outer calvarial table, (b) mandibular lengthening by distraction osteogenesis and orthognathic surgery for correction of 'bird-like' facial appearance and anterior open bite, and (c) lipofilling for residual depressive deformities."[26]

Conclusion

Treacher Collins syndrome patients typically undergo, over several years, multiple major reconstructive surgeries that are rarely fully corrective. Prenatal diagnosis and genetic counseling are

Table 2: Differential diagnosis of TCS[20,21]

Nager syndrome—generally sporadic in nature
• Mandible—more hypoplastic
• Downward slanting of palpebrae
• Cleft palate
• Scalp hair extending to cheek
• Rare lower lid colobomas
• Pre-axial limb abnormalities (hypoplastic/aplastic/duplicated thumbs, fused radius and ulna)
Miller syndrome
• Postaxial limb anomalies with absence/incomplete development of 5th digital ray of all four limbs
• Ectropion/out-turning of lower eyelids
• Cleft lip with or without palate
1st branchial arch syndrome
• Macrostomia
• Hemignathia
• Tragus abnormalities
Pierre Robin syndrome
• Retrognathia
• Glossoptosis
• Cleft palate
Oculo-auriculo-vertebral dysostosis
• Facial assymetry
• Flattened maxillary, temporal, malar bones
• Aplasia of condyle
• Ramus agenesis + macrostomia + lateral facial cleft + malocclusion
• Unilateral coloboma of upper eyelid
• Malformation of external ear
• Severe mental retardation

Table 3: Treatment plan and management of TCS

Management of TCS
Airway obstruction
• Distraction osteogenesis enables neonatal mandible advancement—relieves airway obstruction
• Airway stable—mandibular distraction delayed until early childhood
Retrognathic mandible
• Mandibular lengthening performed at 2–3 years or later
• Bone reconstruction (autogenous tissues) should precede soft tissue correction
• Before facial growth is complete—Chin augmentation + mandibular distraction
• Definitive orthognathic surgery—delayed until 16–18 years
• Bilateral sagittal ramus/maxillary segmental/Le Fort I osteotomy
Nose/eyes/ear-late childhood
• High-bridged nose—classical rhinoplasty
• Coloboma of the lower eyelid—Z-plasty
• Prosthetic auricular reconstruction and bone-assisted hearing aid (BAHA) placement
Cleft palate
• Palatoplasty—as early as the first year of life
• Speech therapy—evaluation by otolaryngologist
Dental correction
• Orthodontic and dental treatment—undertaken once definitive skeletal correction is finalized

mandatory to help parents to make decisions regarding pregnancy. These patients require care from birth through adulthood. Proper treatment planning, counseling, and surgical management are essential for optimizing patient outcomes.

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