

## TREACHER COLLINS SYNDROME: CASE REPORT AND REVIEW OF LITERATURE

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## ABSTRACT

Treacher-Collins syndrome (TCS) is a rare congenital, craniofacial disorder that is inherited as an autosomal dominant pattern. The present case report describes TCS in a Caucasian girl aged 8 years with full tetrad of cardinal features in addition to mental retardation, deafness and dumbness since birth. The management of the child while delivering the treatment requires patience, skill and knowledge about the condition, which are essential for a Pedodontist and treatment that has to be tailored to the specific needs of each individual and preferably done by a multidisciplinary management team.

**KEY WORDS:** Treacher-Collins, Syndrome, Congenital, Autosomal dominant, Craniofacial

## INTRODUCTION

Treacher Collins syndrome (TCS) is named after Edward Treacher Collins (1862–1932), an English surgeon and ophthalmologist who described its essential traits in 1900<sup>1</sup>. Treacher Collins syndrome (TCS) is characterized by hypoplasia of the zygomatic bones and mandible, external ear abnormalities, coloboma (notching) of the lower eyelid, absence of the lower eyelid cilia and preauricular hair displacement. About 40-50% of individuals have conductive hearing loss attributed most commonly to malformation (including ankylosis, hypoplasia, or absence) of the ossicles and hypoplasia of the middle ear cavities. Other less common abnormalities include cleft palate with or without cleft lip and unilateral or bilateral choanal stenosis or atresia<sup>1</sup>.

## Incidence

Incidence is estimated to range from 1 in 40,000 to 1 in 70,000 of live births.

## Etiology

One known cause of this syndrome is a mutation in the **TCOF1 gene**, at **chromosome 5q32-q33**.<sup>21</sup> The protein coded by this gene is called treacle and has been hypothesized to assist in protein sorting during particular stages in embryonic development. Recently investigators are pondering the teratogenic role of hypervitaminosis-A as a cause of TCS.

## Case report

A Caucasian girl patient aged 8 was referred to the Department of Pedodontics and Preventive Dentistry, with a chief complaint of pain in the right lower back region of the jaw since one week. Her pre and post-natal histories were not relevant. Her health history revealed Deafness and Dumbness since birth and the family history revealed consanguinity of the parents and patient is the youngest of the 3 children with the other two siblings being normal.

## Clinical findings

Extraoral examination revealed (**Fig.s1 to 3**) asymmetrical face with a flattened broad nasal bridge, bird-like profile, hypoplastic mandible with deviation onto left side during speech with prominent 'clicking sound' on opening and closing of jaw, bilateral pre-auricular tags, malformed pinna (microtia) on the left side. Intra-oral examination (**Fig.s 4 and 5**) revealed poor oral hygiene with halitosis, erythematous gingiva, deep dental caries involving all primary molars and upper canines and Angle's class-I molar occlusion with lower anterior crowding.

## Investigations: (Fig.6 and Fig.7)

Orthopantomograph showed underdeveloped left condyle and mandibular retrognathia was seen in Lateral cephalogram

**Differential Diagnosis**

Goldenhar syndrome, Treacher-Collins syndrome

**Treatment**

The patient was co-operative, but required repeated instructions since she was physically challenged (deaf and dumb). The mode of communication was through signs and gestures. **(Fig.8)** Short and multiple appointments were used so as to instill a positive attitude towards the dental treatment which is very essential for the future treatment procedures. Supragingival scaling was done followed by the extraction of retained and grossly decayed primary molars under local anesthesia. Maxillary canines were restored with GIC. The parents were counseled about the importance of oral hygiene procedures and periodic dental check-ups and the child was enrolled in a school meant for children with special health care needs to train her in occupational and functional skills with the consent of parents.

**Discussion**

Significant clinical variability is common in TCS, while some individuals may be so mildly affected as to go undiagnosed, others can have severe facial involvement and life-threatening airway compromise.<sup>10</sup>

**Genetic counseling:** TCS is inherited as an autosomal dominant trait. About 60% of probands with TCS have the disorder as the result of a de novo gene mutation. Each child of an individual with TCS has a 50% chance of inheriting the mutation.

**Diagnosis:**Diagnosis of Treacher Collins syndrome (TCS) relies upon clinical and radiographic findings with genetic testing as a confirmatory diagnosis.

**Gene testing:**Before the identification of the TCOF1 gene, diagnosis of TCS was possible only by linked polymorphic markers and clinical evaluation.<sup>2</sup> TCOF1 is the only gene currently known to be associated with TCS. Direct sequencing of the coding and flanking intronic regions of TCOF1 detects mutations in about 90%-95% of individuals.<sup>3</sup>

**Major clinical features**

1. Hypoplasia of the zygomatic bones and mandible resulting in the following:<sup>4</sup>
2. Midface hypoplasia (89%)
3. Micrognathia and retrognathia (78%),
4. External ear abnormalities (77%) including absent or small, and malformed ears (microtia) or rotated ears

5. Lower eyelid abnormalities including the following: Coloboma (notching) (69%), Sparse, partially absent, or totally absent cilia (lashes) (53%)
6. Family history consistent with autosomal dominant inheritance (40%)

**Minor clinical features**

1. Conductive hearing loss (40%-50%)
2. Ophthalmologic defects like Vision loss (37%), Amblyopia (33%), Refractive errors (58%), Anisometropia (17%), Strabismus (37%)
3. Cleft palate with or without cleft lip (28%)
4. Preauricular hair displacement (26%)
5. Airway abnormalities
6. Delayed motor or speech development.

**Dental Anomalies**

Da Silva Dalben et al (2006)<sup>5</sup> found dental anomalies in 60% of individuals with TCS, with one to eight anomalies per individual. Anomalies identified included tooth agenesis (33.3%), enamel opacities (20 %), and ectopic eruption of the maxillary first molars (13.3%)

**Distinguishing radiographic features**

Hypoplasia or aplasia (discontinuity) of the zygomatic arch can be detected by occipitontal radiographs. These radiographs include an occipitontal projection of the skull (Water's view) and orthopantomograph to identify mandibular hypoplasia or other abnormalities. Malar hypoplasia confirmed by intraorbital measurements by CT that are at the mean, with zygomatic measurements less than normal<sup>6</sup>

**Prenatal Testing:** Technological advances in sonography have facilitated accurate in-utero prenatal diagnosis of TCS.<sup>7</sup> Diagnosis of TCS is also possible by analysis of DNA extracted from fetal cells obtained by amniocentesis usually performed at about 15-18 weeks' gestation or chorionic villus sampling (CVS) at about ten to 12 weeks' gestation.

**Differential Diagnosis;** Features of Treacher Collins syndrome (TCS) are also associated with Goldenhar syndrome, Nager syndrome, Miller syndrome, Pierre Robin sequence, and nonsyndromic mandibular hypoplasia.

**Management** In infants, evaluation should include assessment of the following: the airway, palate for clefts, swallowing function, hearing and ophthal-



Fig.1



Fig.2



Fig.3

Fig.1, 2, 3- clinical findings



Fig.4



Fig.5

Fig.s 4, 5- intra-oral findings



Fig.6. Lateral View of the skull

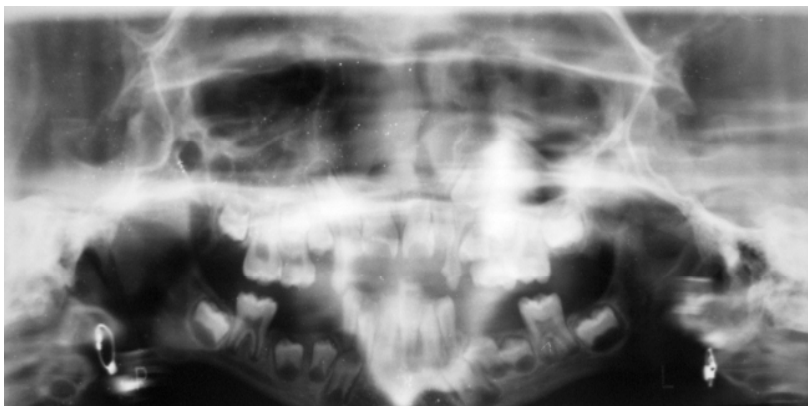


Fig.-7. OPG radiograph of the patient.



Fig.8. Behavior management

mologic evaluation. During the first six months of life, a craniofacial CT scan (axial and coronal slices) is indicated to document the anatomy of the head and neck and the external auditory canal, middle ear, and inner ear. Assessment for dental anomalies should be made when teeth have erupted.

**Treatment of Manifestations:** Treatment should be tailored to the specific needs of each individual and preferably done by a multidisciplinary craniofacial management team that includes a Pedodontist. Management of the airway in neonates generally includes special positioning of the infant or tracheostomy. Gastrostomy may be needed to assure adequate caloric intake while protecting the airway.<sup>8</sup> Bone conduction amplification, speech therapy, and educational intervention are indicated for treatment of hearing loss. The bone-anchored hearing aid (BAHA) is an alternative for individuals with ear anomalies.<sup>9</sup> Craniofacial reconstruction is often necessary. Generally, bone reconstruction precedes soft tissue corrections. Reconstruction can prevent the progression of facial asymmetry and orthognathic procedures are typically indicated before age 16 years. Misaligned teeth often require orthodontic treatment. Nasal reconstruction, if needed, should follow orthognathic surgeries.

**Prevention of TCS craniofacial anomalies;** The onset and pathogenesis of TCS can be prevented in vivo by blocking p53 function which has been successfully carried out in animal models. A major surprise arising from these experiments was that the pharmacological and genetic inhibition of p53 that was so successful in inhibiting neuroepithelial apoptosis occurred without altering or restoring ribosome biogenesis.<sup>10</sup>

## CONCLUSION

The major challenges facing the TCS clinical and research community in terms of improving the prognosis of affected or at risk individuals reside in three key areas; detection, repair and prevention. With recent advances one could even envision the therapeutic application of stem cells in-utero to treat some of the debilitating malformations associated with TCS. The numerous limitations in detection and repair of TCS leave prevention as the most promising alternative therapeutic avenue. Ultimately, the long-term goal should be to identify a natural compound that could be administered before and during pregnancy, such as folic acid, that will provide measurable protection for the embryo from apoptosis without detrimental side effects during the 3 to 12-week period when the embryo is most susceptible to the development of craniofacial and other anomalies.

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