

A Case Report of Treacher Collins Syndrome; an Unusual Case

Dr.Premita Devi Nandeibam¹, Dr.Abhinav Kumar², Dr.ParagNarayanaKisave³,Dr.Shalini Yurembam⁴, Dr.Bharati Lisam⁵.

Post-graduate student^{1,2,3}, Department of Oral Medicine and Radiology¹, Department of Oral Maxillofacial Surgery^{2,3}, Bachelor of Dental Surgery^{4,5}, Rajasthan University of Health and Sciences, Rajasthan, Ashiana Amarbagh Flat no.S1-1144, Kudi Bhagatsani, Pali Road, Jodhpur-342001, Rajasthan, India,

Abstract

Treacher Collins syndrome (TCS) also known as Mandibulo facial dysostosis or Treacher Collins-Franceschetti syndrome, is an a typical autosomal dominant disorder of craniofacial development affecting the development of structures derived from the first and second brachial arches during early embryonic development. It is conspicuous at birth and it is caused by a mutation in the *TCOF1* (Treacle ribosome biogenesis factor 1) gene on chromosome 5. Prevalence of TCS is 1:50,000. Half of cases arise as the sporadic mutation and the rest are familial. Here we present a case report of TCS with their extraoral and intraoral findings, their radiographic findings and treatment plan. We have also discussed about etymological factors, clinical features, differential diagnosis and multidisciplinary approach.

Keywords - Treacher Collins syndrome, brachial arches, *TCOF1*, prevalence, chromosome 5, sporadic mutation, multidisciplinary approach.

I. INTRODUCTION

Treacher Collins syndrome is eponymously named after Treacher Collins [1,2] who described the essential components of the condition in 1900. Early descriptions were given by Berry [3] in (1889) and the first extensive review of the condition was given by Franceschetti and Klien [4] in 1949 who used the term mandibulofacial dysostosis to describe the clinical features. From the structures affected and from studies in mice exposed to teratogenic cis- or trans-retinoic acid, it has been inferred that the disease emanates from interference in the development of the first and second branchial arches [5,6,7]. This disease may present different features such as antimongoloid palpebral fissures, malar hypoplasia, mandibular hypoplasia, malformation of auricular pinna, coloboma of the lower eyelids, conductive deafness, and cleft palate are among the most frequent clinical presentations [8,9,10]. High arch or palate constitutes 30% and because of hypoplasia of the mandible and a steep mandibular angle results in an Angle Class II

anterior open-bite malocclusion [11]. These clinical features are usually bilateral and symmetrical [12].

A. A case report

A 11 years old girl came to department of Oral Medicine and Radiology, Vyas Dental College and Hospital, Jodhpur, Rajasthan with the chief complaint of bleeding gums from 15-20 days back. She gave history of bleeding which occurs on its own without any stimuli and relieves after few minutes without taking medication. There was no history of pain. In past medical history, she had undergone reconstructive surgery of frontal bone since 8 years back and under syrup valproin medication from 6 years back as she got seizures after the surgery.



Fig: (A) 11 yrs old girl facial profile

On **extraoral** examination, the head was dolicocephalic with slightly bossing frontal bone which was palpable and soft in consistency, sparseness of hair was noticed, convex facial profile appeared, micromegathia and hypoplastic mandible was seen. The eyes were antimongoloid slant of the palpebral fissures which presented sad face appearance, there was increased distance between the orbits (hypertelorism), the external nose was constricted and nasal septum deviated toward right side of face which gave bird face appearance, coloboma of the eyelid, sparseness of eyelashes was present and decrease epicanthial fold. The zygoma was underdeveloped, hypoplasia of malar bone, incompetent lip and everted ear with hair growth

extension toward preauricular region. There was hypomobility and stiffness of upper and lower limbs rather than webbing.



(B)



(C)



(D)

Fig: (B) Coloboma present in the right eye. (C) and (D) upper and lower limbs which shows stiffness.

Intraorally, malocclusion due to the hypoplastic mandible and high and narrow arched palate, micrognathia with microstomia, microglossia with linear fissured tongue over posterior 1/3rd, attached uvula on right palatoglossal arch, lingually erupted teeth irt 12, 22, 32, labially erupted tooth irt 41, retained root stump irt 55, buccal pit irt 36, decayed tooth irt 83, grossly decayed tooth irt 84.



(E)



(F)

Fig:- (E) & (F) shows malocclusion, uvula which attached to the right palatoglossal arch and retained root stump 55.



Fig:- (G) Narrow constricted maxillary and mandibular arches, hypoplastic condyles, decrease the size of maxillary sinus and multiple fixative plates on left and right supraorbital margins.

On radiographic findings, Orthopantomograph showed hypoplasia of the condyle with accentuation of antegonial notches was noticed, narrow maxillary and mandibular arches and multiple fixative plates were present on left and right supraorbital margins. Treacher Collins syndrome was made based on the history and records, clinical features and radiographic examination.

According to the chief complaint, needed treatment includes scaling, extraction of root stump, restoration of various carious teeth, artificial

prosthesis for mastication till the eruption of the permanent teeth and advice to use chlorhexidine mouth wash.

II. DISCUSSION

Treacher Collins syndrome is an uncommon congenital disorder which lead to multiple craniofacial developmental anomalies like antimongoloid slant of palpebral fissures, hypoplasia of mandible, underdevelopment of zygoma, sparseness of hair and eyelashes, constricted nose, abnormalities of external ear and ossicles, hypoplasia of the middle ear cavities, Coloboma, hypertelorism, hair growth extending toward preauricular region, microstomia, high narrow constricted palate, retrorathic mandible, malocclusion with anterior openbite and retained multiple teeth [13]. An abnormally large mouth gives a “fish-mouth” appearance [14]. According to Arvystas and Shprintzen (1991), paranasal sinus are smaller in size or completely absent. It is present at birth and bilaterally. It can be associated with cleft palate with or without cleft lip and unilateral or bilateral choanal stenosis or atresia, conductive deafness. According to Dixon (1996), etiology is an autosomal dominant gene, with incomplete penetrance and variable expressivity [15].

Author Renju R et al, revealed five clinical forms of TCS based on the clinical features have been identified by Franceschetti and Klein [7]. They are the complete form (having all known features), an incomplete form (presenting with less severe ear, eye, zygoma, and mandibular abnormalities), the abortive form (only the lower lid pseudo coloboma and zygoma hypoplasia are present), the unilateral form (anomalies limited to only one side of the face) and the atypical form (combined with other abnormalities not usually part of this syndrome). In this case, the patient presented complete form of the TCS.

According to Trainor et al, facial bones especially the mandible occurs in 78% of cases and zygomatic process (81%), cleft (28%) and in severe cases, the zygomatic arches may be completely absent (Poswillo, 1975). Downward slanting of the palpebral fissures (89%) with notching of the lower eyelids (69%) and a paucity of lid lashes medial to the defect (69%). TCS may affect the the external ears in shape, size and position which are frequently associated with atresia of the external auditory canals and anomalies of the middle ear ossicles. Radiographic findings 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 [16,17]. Therefore, bilateral conductive hearing loss is common in TCS patients, whereas mixed or sensorineural hearing loss is rare [18].

According to Shetty SB et al, the chance of giving birth to a second child with TCS is negligible for unaffected parents with one child with TCS and adults with TCS have a 50% chance of passing the condition to the offspring. When a parent with TCS passes on the genes, the children may be affected in varying degrees. The degree may be the same as the parent, milder or more severe. There are two possible ways that TCS develops. First, TCS can develop as a new mutation. This indicates that both parents pass on normal genes to their child. The second way that TCS develops is by inheriting it from one of the parents [fig.1]. The only gene currently known to be associated with TCS is TCOF1 which is mapped to chromosome 5 q31.3-q33.3, encoding a serine/alanine-rich protein, called ‘treacle’. Prevalence among sex and races are equal. Its phenotypical expression probably results from bilateral congenital malformation involving the first and second brachial arches [13].

Neural crest cells migrate over extensive distances to the periphery of the face giving rise to most of the cartilage, bone, connective and peripheral tissues in the head. Most disorders of craniofacial development are thought to be caused by defects in the formation, proliferation, migration and/or differentiation of cranial neural crest cells and TCS is no exception. Hence, abnormal neural crest migration, ectopic cell death and inappropriate differentiation have all been hypothesized as underlying causes of TCS. Therefore, focuses on recent advances in our understanding of the basic etiology, pathogenesis and emerging prospects for prevention are required [13,19].

Diagnosis of TCS depends on clinical and radiographic findings. Investigation which help in diagnosis of TCS are as follows:-

Orthopantomograph, lateral cephalogram, CT, DNA diagnosis (Direct sequencing of the coding and flanking intronic regions of TCOF1 defects mutations in about 90 to 95% of patients). Audiological evaluation for hearing impairment [13], Hb%, TLC, DLC, Platelets count.

Early diagnosis of TCS requires, it will promote in intervention which will improve aesthetic and functional deficiencies [fig.2]. Prenatal diagnosis for pregnancies includes; Two-dimensional and preferably three-dimensional sonography: polyhydramnios, demonstration of characteristic facies of TCS, like downward slanting palpebral fissures, micrognathia, abnormal appearance of the nose with narrow nostrils, cleft lip/palate, low set dysplastic ears and abnormal fetal swallowing. Amniocentesis or CVS: to detect TCOF1, the disease causing allele of an affected individual must be identified before prenatal testing can be performed the presence of a TCOF1 mutation detected by prenatal diagnosis does not predict the specific malformation or severity of the disease [13]. Differential diagnosis includes; acrofacial dysostosis (Nager and Miller syndromes) and oculoauricular over

tebral spectrum (hemifacialmicrosomia and Goldenhar syndrome) [3,13].

In acrofacialdysostoses, limb abnormalities occur in a patient whose facial gestalt resembles that of Treacher Collins syndrome (Treacher Collins syndrome itself is not associated with anomalies of the limbs).most cases of Nagar and Miller syndromes are sporadic, both autosomal dominant and autosomal recessive transmission have been reported [20].Nager syndrome may simulate facial features of TCS. In addition, thumbs may be hypoplastic, aplastic, or duplicated and the radius and ulna may be

fused. Miller syndrome also appears as TCS, with the additional diagnostic feature of ectropion or out-turning of the lower lids.Cleft lip with or without cleft palate is more prevalent in this syndrome than in TCS. Hemifacialmicrosomia primarily affects development of the ear,mouth, mandible and usually only one side ofCleft lip with or without cleft palate is more prevalent in this syndrome than in TCS. Hemifacialmicrosomia primarily affects development of the ear,mouth, mandible and usually only one side of the face. It varies from mild to severe form. Goldenhar syndrome shows vertebral abnormalities, epibulbar dermoids, and facial

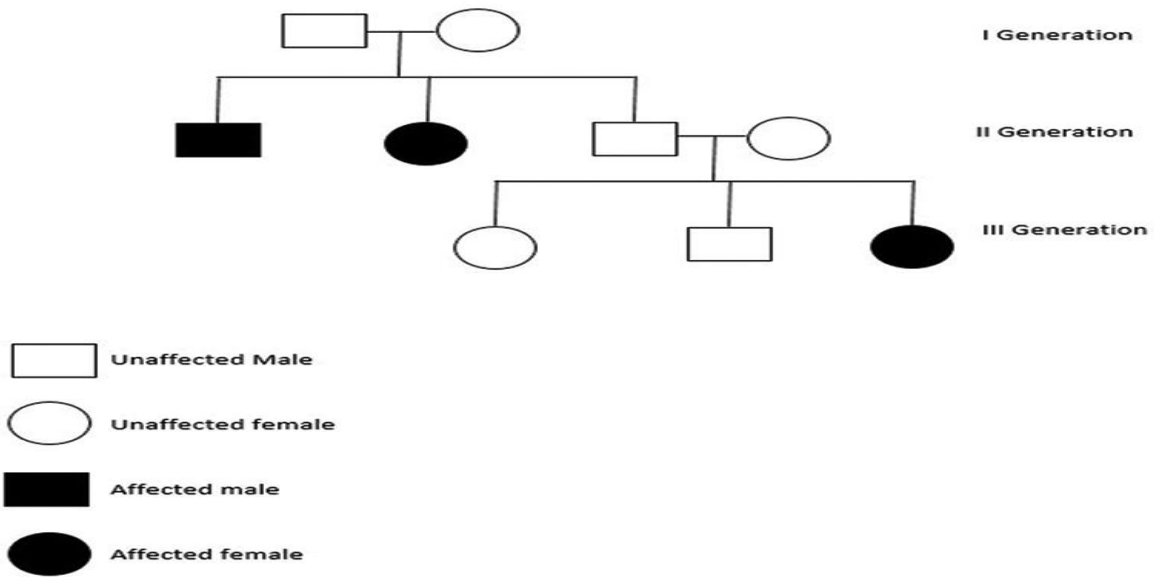


Figure 1: Pedigree chart of the patient going up to three generations

deformities. Since this case had all the features of TCS and no additional features like hypoplastic thumb, fusion of radius and ulna, ectropion of lower lids, cleft lip, vertebral anomalies, etc., we preferred the diagnosis of TCS [3].

First of all TCS is an incurable complex congenital disorder. The treatment includes; 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 if hearing loss is reported during the first six months of life.Dental anomalies should be examined after the eruption of teeth. Treatment should be aimed

to the specific needs of each individual and preferably done by a multidisciplinary craniofacial management team that typically comprises a clinical geneticist, plastic surgeon, head and neck surgeon, otolaryngologist, oral surgeon, orthodontist, audiologist, speech pathologist, and psychologist[21]. Preoperative planning and evaluation should begin as early as possible [22].

Genetic counselling should provide available for parents affected with the syndrome or for parents with a child showing features of TCS.It should be explained to the parents that the probability that a second child shows the same phenotype is negligible [23].

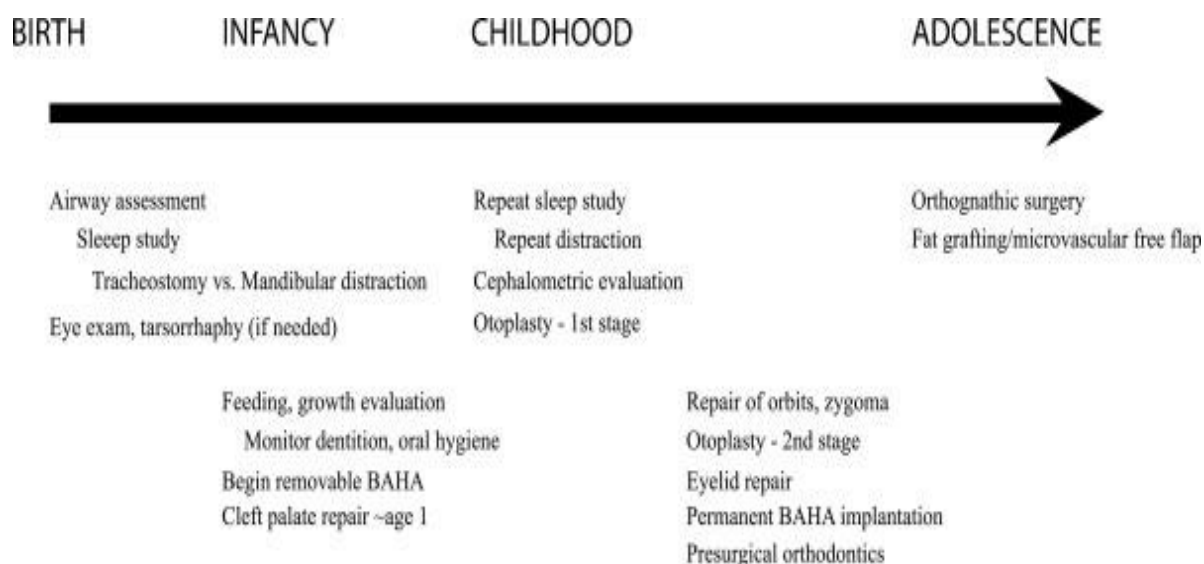


Fig.2:- A treatment timeline is presented for surgical considerations and staging throughout the patient's childhood [22]

III. CONCLUSION

Detection of TCS is crucial and their features can be different from one person to another. Multidisciplinary approach is required in order to meet the individual patients require, considering the growth patterns, function and psychological benefit (to build up self-esteem, thereby enabling to lead a normal life). We should consult a craniofacial surgeons, pediatrician, ENT, surgeon, ophthalmologist, geneticists and anaesthetists. After obtaining their consent we should complete our treatment. We should try to diagnose as early as possible. And last but not least, many more research is required especially in the field of surgical treatment in order to fulfil the patient needs and aesthetic.

REFERENCES

- [1] Dixon M.J. Treacher Collins syndrome. *Journal of Medical Genetics* 1995;32:806-808.
- [2] Treacher Collins E. Cases with symmetrical congenital notches in the outer part of each lid and defective development of the malar bones. *Transactions Ophthalmological Societies United Kingdom* 1900;20:190-92.
- [3] Kumar T, Puri G, Konidena A, Arora N. Treacher Collins syndrome: A case report and review of literature. *Journal of Indian Academy of Oral Medicine & Radiology* 2015; 27(3):488-491
- [4] Franceschetti A, Klein D. Mandibulo-facial dysostosis: new hereditary syndrome. *Acta Ophthalmologica* 1949;27:143-224.
- [5] Gorlin R.J, Cohen M.M Jr, Levin L.S. *Syndromes of the Head and Neck*. 3rd ed. New York: Oxford University Press 1990; 649-52.
- [6] Posnick J.C, Ruiz R.L. Treacher Collins syndrome: Current evaluation, treatment, and future directions. *The Cleft Palate-Craniofacial Journal* 2000;37:434.
- [7] Renju R, Varma B.R, Kumar S.J, Kumaran P. Mandibulofacial dysostosis (Treacher Collins syndrome): A case report and review of literature. *Journal of Contemporary Clinical Dentistry*. 2014 Oct-Dec; 5(4): 532-534.
- [8] Andrade E.C, Júnior V.S, Didoni A.L, Freitas P.Z, Carneiro A.F, Yoshimoto F.R. Treacher Collins syndrome with choanal atresia: A case report and review of disease features. *Brazilian Journal Otorhinolaryngology* 2005;71:107-10.
- [9] Rovin S, Dachi S.F, Borenstein D.B, Cotter W.B. Mandibulofacial dysostosis, a familial study of five generations. *Journal of Pediatrics* 1964;65:215-21.
- [10] Frazer L.E, Elmore J, Nadler H.L. Mandibulo-facial dysostosis (Treacher Collins syndrome). *American Journal of Diseases of Children* 1967;113:406-10.
- [11] White SC, Pharoah MJ. *Oral Radiology: Principles and Interpretation* 6th edition; p-567
- [12] Kay E.D, Kay C.N. Dymorphogenesis of the mandible, zygoma, and middle ear ossicles in hemifacial microsomia and mandibulofacial dysostosis. *American Journal of Medical Genetics* 1989; 32:27-31.
- [13] Shetty SB, Thomas A, Pidamale R. Treacher Collins Syndrome: A Case Report and a Brief Review on Diagnostic Aids. *International Journal of Clinical Pediatric Dentistry* 2011;4(3):235-239.
- [14] Madiyal A, Babu SG, Bhat S, Madi M, Kamath J. Diagnosis and treatment of Treacher Collins syndrome: Report of a rare case with literature review. *Journal of Research in Dental Sciences* 2018;8(4):179-82.
- [15] Ortega ADOL, Zwir L.M.L.F, Ciamponi A.L, Guimaraes A.S, Alonso L.G. Radiological Findings and Dynamic Aspects of Stomatognathic Structures in Treacher Collins Syndrome: Clinical Case Report. *The Cleft Palate-Craniofacial Journal* 2007; 44(6):678-82.
- [16] Trainor P.A, Dixon J, Dixon M.J. Treacher Collins syndrome: etiology, pathogenesis and prevention. *European Journal of Human Genetics* 2009;17:275-83.
- [17] Stovin JJ, Lyon Jr JA, Clemmens RL. Mandibulofacial dysostosis. *Radiology* 1960; 74: 225- 231.
- [18] Phelps PD, Poswillo D, Lloyd GA. The ear deformities in mandibulofacial dysostosis (Treacher Collins syndrome). *Clinical Otolaryngology* 1981; 6: 15- 28.
- [19] Trainor PA. Craniofacial birth defects. The role of neural crest cells in the etiology and pathogenesis of Treacher Collins syndrome and the potential for prevention. *American Journal of Medical Genetics A* 2010;152A(12):2984-94.
- [20] Dixon MJ. Treacher Collins syndrome. *Journal of Medical Genetics* 1995;32(10):806-8.
- [21] Katsanis SH, Jabs EW. Treacher Collins Syndrome. *Gene reviews* 2004.
- [22] Chang CC, Steinbacher DM. Treacher Collins Syndrome. *Seminars in Plastic Surgery* 2002;26(2):83-90.
- [23] Kasat V, Baldawa R. Treacher Collins syndrome - A case report and review of literature. *Journal of Clinical and Experimental Dentistry* 2011;3:395-9.