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Treacher-Collins Syndrome: Case Reports with Familial Occurance

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Case Study
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ABSTRACT

Treacher-Collins syndrome is an autosomal dominant congenital disorder characterised by a range of features involving the underdevelopment of zygomatic complex, cheekbones, jaws, palate, and mouth. Others may present with malformation of the eyes including a downward slant of the opening between upper and lower eyelids and anomalies of the external and middle ear. Individuals diagnosed with TCS are considered at high risk for OSA due to micrognathia. This article presents a case report of two sisters who exhibited similar but varying presentations in terms of severity and aberrations.

Keywords: Franceschetti-Klein Syndrome, Obstructive Sleep Apnoea, Treacher Collins Syndrome.

Introduction

Treacher-Collins syndrome (TCS) also known as mandibulofacial dysostosis and Franceschetti-Zwahlen-Klein syndrome is a rare congenital disorder of craniofacial development.[1] It is an autosomal dominant disorder of facial development affecting approximately 1 in 50 000 live births. It occurs due to the mutation in the TCOF 1 gene which encodes a nucleolar phosphoprotein known as Treacle Tcof1/Treacle is an important spatiotemporal regulator of ribosome biogenesis. Haploinsufficiency of Tcof1/Treacle results in deficient ribosome biogenesis, which is incapable of meeting the proliferative needs of the neuroepithelium. Craniofacial abnormalities tend to involve underdevelopment of the zygomatic complex, cheekbones, jaws, palate, and mouth, leading to breathing and feeding difficulties.[2]

Case Report-I

A 17-year-old female reported to the department with the chief complaint of pain in right lower back tooth region for the last 1 day. On general physical examination, she appeared to be poorly nourished for her age. Although her height was normal, she had an asthenic build with abnormal facial features. The shape of hands and nails was normal and the patient had a normal gait. Pallor was observed on eye examination. The patient gave a history of breathlessness, Snoring, the habit of mouth breathing, and impaired hearing from the left ear

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as she wore a hearing aid for 3 years of her age. She also reported episodes of hypotension with increased sweating. Late onset of menstruation with a history of irregular periods. She was also taking Vit-D supplements as she has been diagnosed with Vitamin-D deficiency (13.4 nmol/l) 2 years back.

Extraoral examination revealed bilateral facial abnormalities like downward slanting of eyes, coloboma of the lower eyelid with deficient eyelashes, parrot's beak shape nose, crumpled external ears with impaired hearing, and bilaterally depressed zygomatic arches with sunken cheekbones. Retruded chin elucidated the convex profile of the patient. Skeletally, a solitary deformity of a bend in the left shoulder was also seen (**Figure-1**). Intraoral examination revealed Angles class I type 1 and type 2 malocclusion with incompetent lips, high arched palate, constricted maxillary arch, and crowding of maxillary and mandibular anterior teeth with open bite.

Figure 1: Profile picture of case -1.

On radiographic examination, OPG revealed impacted 13, periapical radiolucency in 46, and chest x-ray revealed dorsiflexion of the spine towards the right side. The lateral skull radiograph confirmed the open bite, retruded mandible, and deep anti-gonial notch (**Figure 2**). The chest radiograph revealed dorsiflexion of the spine towards the right side (**Figure 3**).

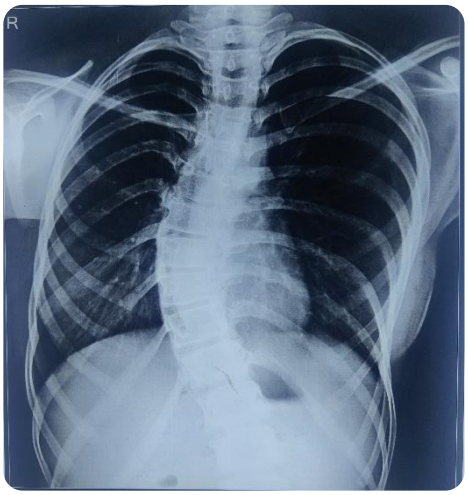

Figure 2: Chest X-Ray Reveals – Dorsiflexion of Spine towards Right Side.

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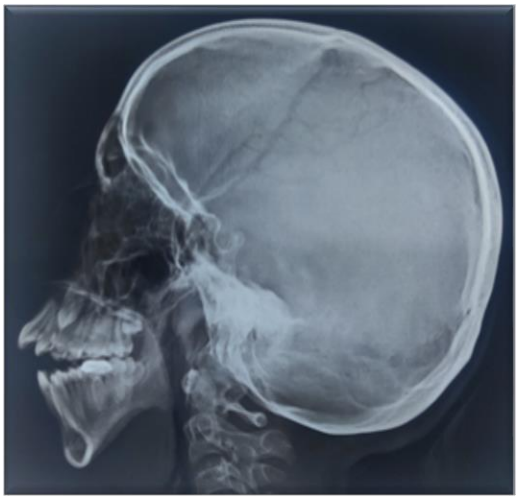

Figure 3: Lateral skull radiograph of case 1

Lab investigations revealed normal T3, T4, TSH, PTH and serum calcium but increased serum phosphorus levels(5.17mg/dl).

Case Report-II

Her younger sister who was 11 years old came with the complaint of extra teeth in the mouth. She also showed the same morphological features like Bilateral facial abnormalities with downward slanting of eyes, depressed zygomatic arches, convex profile due to retruded chin, and bird's beak-shaped nose. The external ear was crumpled but no signs of hearing impairment were present (**Figure-4**). She did not give any history of waking up at night, snoring and breathlessness. Intraoral examination revealed crowding in maxillary and mandibular anterior teeth, high arched palate, open bite, palatally placed and mesially rotated12, crossbite in relation to 21, partially erupting 22 in the buccal vestibule and rotated, buccally erupted 33 and 43 and constricted maxillary arch (**Figure-5**). On taking familial history her father had the same facial features including a history of snoring.

Figure 4: Bilateral facial abnormalities.

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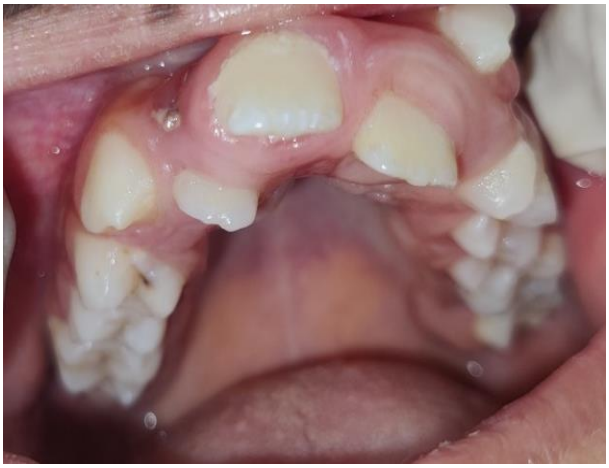

Figure 5: Crowding in maxillary and mandibular anterior teeth & high arched palate.

On radiographic examination, OPG revealed an impacted left maxillary lateral incisor. However, no other significant finding was seen apart from that. The lateral skull conformed to the retrognathic mandible and open bite (**Figure 6**).

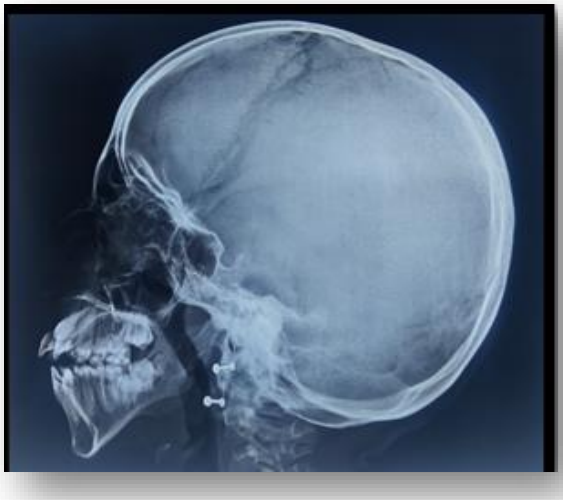

Figure 6: Lateral skull showing open bite and retruded mandible.

Lab investigations revealed Decreased T4 levels (6.10 µg/dl) while T3 and TSH were normal, Decreased Vit-D levels (14.48nmol/l), Increased serum phosphorous (5.63 mg/dl), and Decreased PTH levels (7.5pg/ml).

Diagnosis of TCS was made on the basis of phenotypic and radiographic findings for both cases. The preliminary radiographic investigation like OPG and lateral skull view showed multiple impacted permanent teeth, a retrognathic mandible, and a prominent ante-gonial notch.

Discussion

TCS is a complex genetic disorder of craniofacial deformities involving the maxilla, mandible, and malar bone along with external ear abnormalities. TCS is caused by mutation of the TCOF1, POLR1B, POLR1C or POLR1D

genes mode of inheritance is generally autosomal dominant, with very few cases of autosomal recessive mutations observed. Males and females are equally affected with an estimated prevalence of 1 in 10,000-50,000 individuals in the general population.[3]

More than 60% of TCS cases arise as de novo mutation with no family history however in 40%, the mutation may be inherited from the parents.[4] The present cases show positive family history suggesting familial mutation transfer in the TCOF1 gene, which is seen in 40% of cases.

Franceshetti and Klein identified five clinical forms of TCS based on the clinical features. This included 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).[5] Our cases presented the complete form of this syndrome with bilateral facial abnormality like downward slanting of eyes, coloboma of the lower eyelid with deficient eyelashes, depressed zygomatic arches with sunken cheekbone, crumpled external ear with impaired hearing, retruded chin, convex profile, and High-arched palate.

A study by Harriet. A. et. al showed that all participants had breathing disturbances while sleeping suggesting a high prevalence of Obstructive sleep apnoea in TCS.[6] Similarly, a history of snoring and episodes of breathlessness were also reported by our patient thus a detailed questionnaire-based evaluation was done with; STOP (snoring, tiredness, observed apnoea, high blood pressure), STOP-BANG, Epworth sleepiness scale, Berlin questionnaire all pointing towards high risk for OSA. Although a study by R. G. Plomp et. al. concluded Brouillette score and Epworth sleepiness scale are of minimal usefulness in TCS. Thus, we confirmed our diagnosis of OSA based on the CT finding which was the narrowing of oropharyngeal space due to soft tissue thickening. Another study by Plomp et. al showed airway obstruction in 10 out of 11 patients with endoscopic evaluation at a different level from nose to trachea.[7] Besides endoscopy and CT evaluation Polysomnography in an attended setting has been used as the standard for the diagnosis of OSA.[6,7]

Due to clinical similarities, it is difficult to distinguish between the oculo-auriculo-vertebral spectrum (known as Goldenhar syndrome), Miller and Nager syndrome, and mandibulofacial dysostosis with microcephaly. Nager syndrome includes features of TCA combined with predominantly radial limb defects like absence or hypoplastic thumbs and hypoplasia radius with radioulnar synostosis. Whereas in miller syndrome absence or incomplete development of the 5th digital ray of all four limbs, and, frequently, forearm abnormalities. The cleft lip, with or without a cleft palate is more common in both cases than in TCS.[8]

The management of TCS involves a multi-disciplinary approach with airway assessment as the first priority, followed by oropharyngeal repair, and midface reconstruction.

Conclusion

Not all the cases of TCS have a classical presentation, hence each needs to be assessed individually. OSA in TCS patients is an emerging problem in childhood and adulthood, thus all TCS patients should always be screened for OSA, repeated regularly throughout childhood as the size of the airway and soft tissue changes as the child develops. When confirmed, a properly planned treatment helps restore the patient's function and form.

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