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Case report

Treacher Collins syndrome: A case report and review of ophthalmic features

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ABSTRACT

Treacher Collins syndrome is a congenital disorder with bilaterally symmetric anomalies of the structures developing from the first and second branchial arches. The ocular and orbital features are an obligatory component for the diagnosis. We presented a case of typical, complete syndrome and also reviewed the varied ophthalmological manifestations of the disease in the literature. Antimongoloid slanting of palpebral fissures and lower lid colobomas are constant features of the syndrome. However, varied ocular and lacrimal drainage anomalies are also associated. TCS is a syndrome with multiple ocular and orbital features, a knowledge of which will help in the diagnosis of incomplete forms of the syndrome.

1. Introduction

Treacher Collins syndrome (TCS), also known as Treacher Collins–Franceschetti syndrome,[1] is a rare autosomaldominant congenital disorder characterized by multiple craniofacial deformities.[2] There are bilaterally symmetric anomalies of the structures within the first and second branchial arches. The essential features of this syndrome were described by Treacher Collins, a British ophthalmologist, in the year 1900. It is a rare congenital anomaly occurring in one in 50,000 births.[3]

TCS exhibits autosomal dominant inheritance with variable penetrance. It is the result of mutations in the TCS gene (TCOF1) at chromosome 5q32; 60% of cases being spontaneous and 40% familial.[4] These mutations in the TCOF1 gene reduce the amount of treacle, a nucleolar protein that is produced in cells and this results in development of a disorder with abnormal craniofacial development.[5]

Franceschetti and Klein[6] described the syndrome in 1949, in which they coined the term mandibulofacial dysostosis. The clinical features of TCS are bilaterally symmetrical and include: (1) abnormalities of the external ears, atresia of external auditory canals, and malformation of the middle ear ossicles, which result in bilateral conductive hearing loss[7]; (2) lateral downward sloping of the palpebral fissures (antimongoloid slant), frequently with coloboma of the lower eyelids and a paucity of lid lashes medial to the defect; (3) hypoplasia of the mandible and zygomatic complex; and (4) cleft palate.[8,9] The patients are thus characterized by hypoplastic facial bones (mandibular and zygomatic), ear and eye anomalies, cleft palate, airway and dental anomalies.[10–13]

The literature has scarce information about the ophthalmological features of TCS. We report a case of the syndrome in a neonate, and also review the ophthalmological features of the syndrome.

2. Case Report

A 28-day-old male child was brought to the ophthalmology outpatient department with a complaint of redness in both eyes for the past 10 days. It was not associated with any discharge from either of the eyes.

The patient was the first child of a 22-year-old woman who delivered at the same hospital at term. There was a history of delayed crying at birth. He was born of a nonconsanguinous marriage and the pedigree analysis revealed no other affected member in the family. The developmental milestones were age appropriate except for hearing deficit as he did not turn his head to sound. He was breast feeding with no difficulty in swallowing.

The child was 37 cm long with a body weight of 3 kg. The skull was normal except for an open anterior fontanelle. The facial characteristics were bilaterally symmetrical but abnormal. There were multiple facial dysmorphic features including downward-slanting eyes, malar hypoplasia, mandibular hypoplasia

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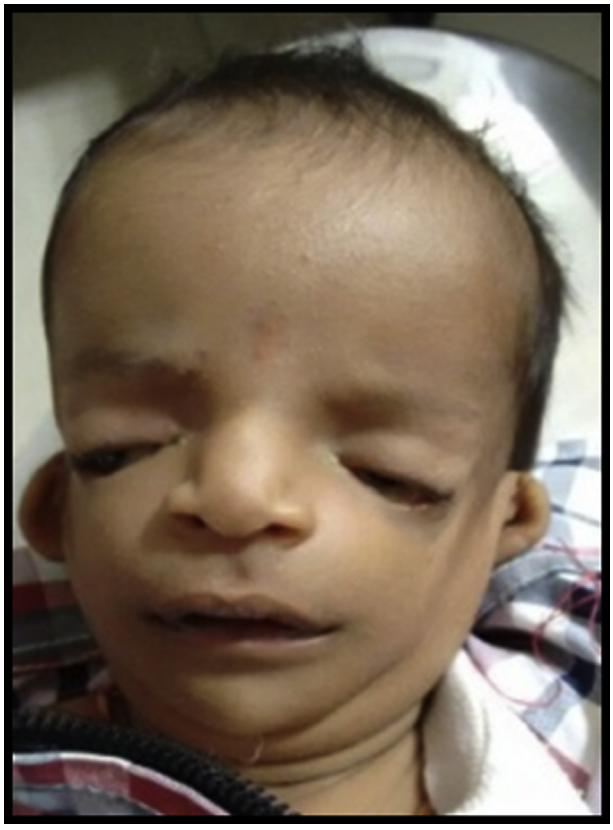

Figure 1. Facial dysmorphism with downslanting palpebral apertures, malar, and mandibular hypoplasia (micrognathia).

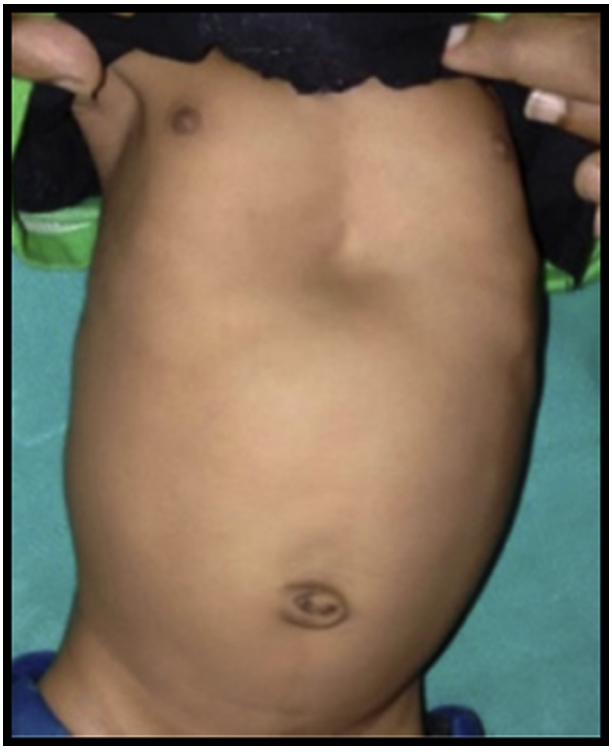

Figure 3. Pectus carinatum and chest indrawing.

(micrognathia), a large fishlike mouth (macrostomia) with a high arched palate (Figure 1). The tongue was retropositioned but the child had no difficulty in feeding and swallowing. The child had malformed and crumpled bilateral pinnae. The right ear had external auditory canal stenosis and left ear had external auditory canal atresia (Figure 2). He also had pectus carinatum and chest indrawing (Figure 3). Auscultation revealed vesicular breath sounds with prolonged expiration. The abdomen was scaphoid, and there was no other abnormality in the limbs, back, and genitals.

The ophthalmological examination revealed antimongoloid slant of the palpebral fissures. The child had bilateral lower lid coloboma (lateral one third) with absence of eyelashes in the entire extent of the lower lids (Figure 4). The inferior conjunctiva was congested in both eyes with superficial haze of the inferior cornea (exposure keratopathy). The cornea of the right eye also had a 1 mm $\times$ 1 mm nebulomacular opacity at the 6 o'clock position. The

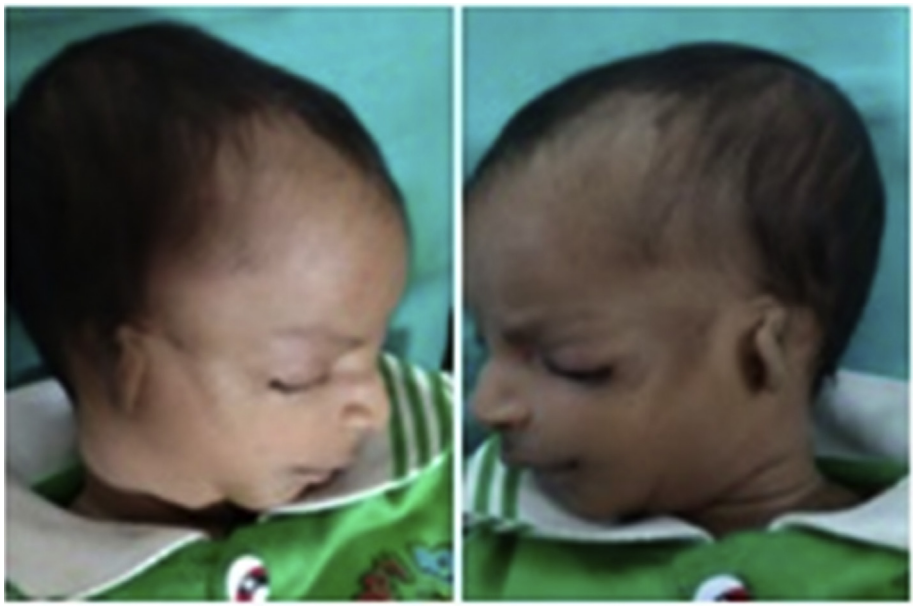

Figure 2. Lateral view of face demonstrating malformed and crumpled bilateral pinna, and retruded mandible.

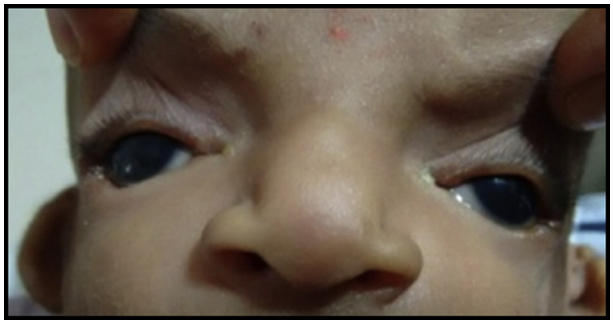

Figure 4. Antimongoloid slant of palpebral aperture with bilateral shallow lower lid coloboma (temporal) and lack of eyelashes in the entire extent of the lower lid.

pupils were normal in size with normal reaction to light. The fundus examination was also normal.

The neonatal infant was diagnosed with TCS with bilateral lower lid coloboma with exposure keratopathy.[5]

The child was prescribed a topical antibiotic and a topical lubricant. He responded dramatically, with both conjunctival congestion and corneal haze disappearing at 3 days follow-up.

3. Discussion

TCS is an autosomal dominant disorder of craniofacial development. As the tissues affected in TCS arise during early embryonic development from the first and second branchial arches, it is proposed that the condition may arise from abnormal neural crest cell migration, improper cellular differentiation during development, or an abnormality of the extracellular matrix.[14–16]

In 1963, Axelsson et al[17] named the following features as obligatory for the diagnosis of TCS: (1) antimongoloid palpebral fissures[11]; (2) anomaly of the lower lid: coloboma of the outer third, or deficient lashes, or both; (3) hypoplasia of the malar bones; and (4) hypoplasia of the mandible. Our case had all these features.

Franceschetti and Klein[6] described five clinical forms: complete form, incomplete form, abortive form, unilateral form and atypical form. Our patient had the complete form of TCS with all known features of the disease. As the patient had no affected family member, he may be considered a case of *de novo* mutation. Therefore, it is unlikely that the siblings would be affected.

We reviewed the literature for the different ophthalmological presentations of the syndrome. The findings are summarized below.

3.1. Orbital features of TCS

TCS is characterised by hypoplasia and retrusion of the malar region, obliteration of the frontonasal angle, and a receding chin. Protrusion of the nose and maxilla may produce an enophthalmic appearance.[6,18] The inferior lateral angle of the orbit is defective and the superolateral part of the orbit is displaced caudally, giving the orbit an egg-shaped appearance.[18,19] The orbital contents appear displaced into the deficiency created by the malar hypoplasia. Orbital hypoplasia, lipodermoids, and limbal dermoids have also been reported.[20–22]

3.2. Ocular features of TCS

Hertle et al[13] described the ocular findings in 24 patients with TCS. All patients had some eye abnormality such as amblyopia, anisometropia, refractive errors, strabismus and vision loss.[13,23] Vision loss was present in 37% of patients, amblyopia in 33% of patients, significant refractive errors in 58% of patients, anisometropia in 17% of patients, and strabismus in 37% of patients. Strabismus has been reported in several forms, including esotropia, exotropia, Duane's syndrome, and cranial nerve palsy. Cataract, ectopic pupil, uveal coloboma, and occasional microphthalmos, and even anophthalmos, have also been reported.[20,21,24] Holla et al[25] reported a case with microcornea with retinal detachment in a case of TCS.[25]

Thus, several ocular abnormalities are seen. Vision may still be normal in TCS because the retina does not develop from the affected branchial arches and many patients retain good vision in at least one eye.[13]

3.3. Eyelid and adnexal anomalies of TCS

Hertle et al[13] also described lid and adnexal abnormalities in 96% of TCS patients. Significant reported abnormalities included canthal dystopia, dacryostenosis, blepharoptosis, lateral lower lid true coloboma, and pseudocolobomas.[13,26,19] True colobomas are full-thickness absence of tissue of the lids, while pseudocolobomas have hypoplastic subcutaneous tissue and muscle. This may be associated with absence of the lateral canthal tendon, which requires reconstruction.[27,28]

Downward slanting of the palpebral fissures has been reported in 89% of cases of TCS, notching of the lower eyelids in 69% of cases, and a paucity of lid lashes medial to the defect in 69% of cases.[12,13]

Lacrimal duct atresia and distichiasis have also been reported.[20,21,29] Inferior punctal atresia accompanying inferior canalicular atresia was identified in all seven patients in a study of associated lacrimal anomalies by Bartley.[30] One patient had coexistent bilateral nasolacrimal duct obstruction and needed dacryocystorhinostomy surgery.

Various other skeletal and facial anomalies have been reported. The presence of an abnormally shaped skull is not distinctive for TCS, but brachycephaly with bitemporal narrowing is sometimes observed.[11]

Every patient with TCS is different and management depends on the primary complaints. Breathing problems may arise at birth as a consequence of micrognathia and tongue obstruction of the hypopharynx. These have to be treated as a priority and emergency surgery in the form of tracheostomy may be required to achieve an adequate airway.

Further management of the hard and soft tissue defects usually needs multiple operations. Depending on severity, eyelid coloboma is corrected in the earliest years of life. Others may prefer to perform only neonatal tarsorrhaphy to protect corneal exposure, and delay other periorbital correction. This is because the extent of the lower lid skin deficit can be best assessed after skeletal correction, which is zygoma and orbit reconstruction. Depending on the extent of the deformity, orbicularis transposition, skin grafting, Z-plasty, and/or canthopexy can be performed for correction of lid coloboma.[31] A careful ocular assessment and timely management of refractive errors, strabismus, amblyopia, and lacrimal anomalies is also needed.

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