Int J Biol Med Res. 2014; 5(2): 4112-4115

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

CASE REPORT

Treacher Collins Syndrome In The Newborn

Dr. Girish Gopal[a] , Dr. Divya Durga[b], Dr. S. Prashanth[c]

[a]*Senior Resident, Department of Pediatrics, Mysore Medical College and Research Institute, Mysore -570001, Karnataka.*
[b]*Post graduate student, Department of Pediatrics, Mysore Medical College and Research Institute, Mysore -570001, Karnataka.*
[c]*Assistant Professor, Department of Pediatrics, Mysore Medical College and Research Institute, Mysore -570001, Karnataka.*

ARTICLE INFO

Keywords:
Autosomal dominant
Branchial arch
Congenital malformation
Craniofacial development
Treacher Collins Syndrome.

ABSTRACT

Treacher Collins Syndrome (TCS) is a rare autosomal dominant disorder of craniofacial development. It is a congenital malformation involving the structures derived from the first and second branchial arches, characterized by hypoplasia of the facial bones (mandible, maxilla and zygoma) and abnormality in the shape and size of the ears and eyelids. The extent of facial deformity varies from one affected individual to another. We report a newborn with Treacher Collins Syndrome.

1. Introduction

Treacher Collins Syndrome is a rare autosomal dominant disorder of craniofacial morphogenesis with high penetrance and variable expressivity [1-3]; affecting the development of structures derived from the first and second branchial arches during early embryonic period. The estimated incidence of TCS ranges from 1:40000 to 1:70000 live births. Hypoplasia of the facial bones may be the first indicator of this disorder [4]. The presence of characteristic anomalies involving the facial bones, eyelids and ears led us to the diagnosis.

Case report

A four hour old male baby was referred to the outborn NICU of our institution, with the complaints of the baby not having cried immediately after birth. This baby was the third born to a non consanguineously married couple. The first child of the couple was a female child who was deaf mute and the second child was also a female and had died three days after birth, the exact cause of which was not known. During this pregnancy the mother was registered and immunized. She underwent regular antenatal check ups but only one obstetric scan was done in her last trimester of pregnancy which was told to be normal (dating and anomaly scans were not done). The baby was delivered at term through vaginal route in a government hospital at Kollegal. There was no history of premature rupture of membranes, meconium stained amniotic fluid or prolonged labour. The baby did not cry immediately after birth, was resuscitated and referred to us for further management. On examination, baby's general condition was not satisfactory. Baby was hemodynamically unstable (had signs of compensated shock) with tachypnoea and increased work of breathing; spO2 was maintained with 8-10lts of hood box oxygen. Baby was euglycemic, hypothermic with acrocyanosis and had poor cry and activity. There was microcephaly, anterior fontanelle was around 1.5cm * 1.5cm at level, hair column extended anterior to the left pinna (Fig 1). Baby had hypertelorism, antimongoloid slant with coloboma at the lateral aspect of the lower eyelids and absent eyelashes (Fig 2 and 3). There was beaking of the nose, long philtrum, malar hypoplasia with temporal hollowing (Fig 3). Both ears were malformed. Right pinna was atretic with absent external auditory canal; left pinna was low set, malformed with hypoplastic external auditory canal (Fig 1 and 4). There was short neck with micro and retrognathia (Fig 4), complete cleft palate and glossoptosis causing airway compromise (Fig 5). Upper limbs, lower limbs, spine and external genitalia were normal. Systemic examination revealed a short systolic murmur in the left paracardiac region; Moro's and other newborn reflexes (sucking, rooting etc.) were depressed. The characteristic facial features led us to a diagnosis of Treacher Collins Syndrome with hypoxic ischemic encephalopathy. On investigation, baby's septic screen was negative, chest X-ray and 2D echocardiography were normal. Baby was nursed in the prone position (due to the abnormal oro facial

* Corresponding Author : **Dr. Girish Gopal**
Senior Resident, Department of Pediatrics,
Mysore Medical College and Research Institute,
Irwin Road, Mysore – 570001, Karnataka.
girishgpl@gmail.com, Mob No. +919739799850.

anatomy resulting in glossoptosis and airway compromise) and was treated for hypoxic encephalopathy as per the unit protocol. Parents were counseled regarding the congenital problems associated with the baby, prognosis, need for further audiometric, dental and plastic surgical evaluation and also the options to prevent its recurrence in subsequent pregnancies.

Figure 1 : Showing (i) Hair column extending anterior to left pinna (ii) Beaked nose (iii) Malformed, low set pinna and hypoplastic external auditory canal

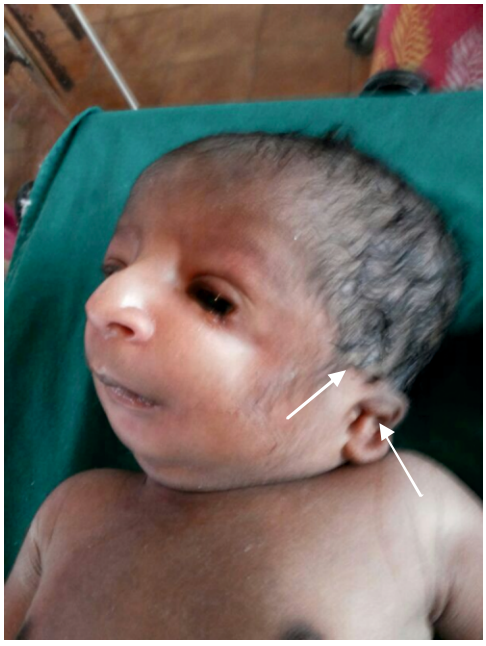

Figure 2 : Showing (i) Coloboma and notching of both lower eyelids (ii) absent eyelashes of both the lower eyelids.

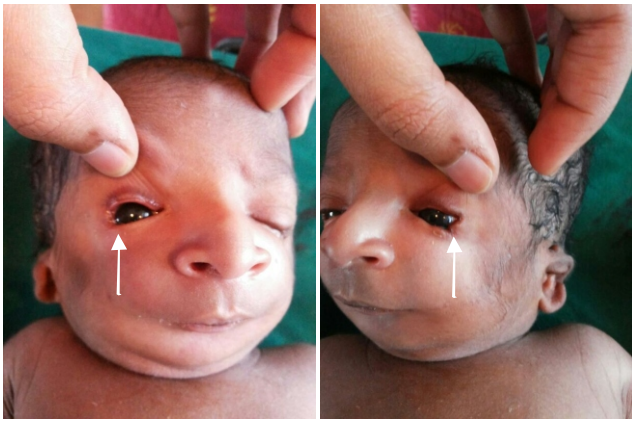

Figure 3 : Showing (i) Antimongoloid slant of palpebral fissures (ii) long philtrum, microstomia (iii) coloboma, notching of the lower eyelids, absent eyelashes, temporal hollowing and malar hypoplasia

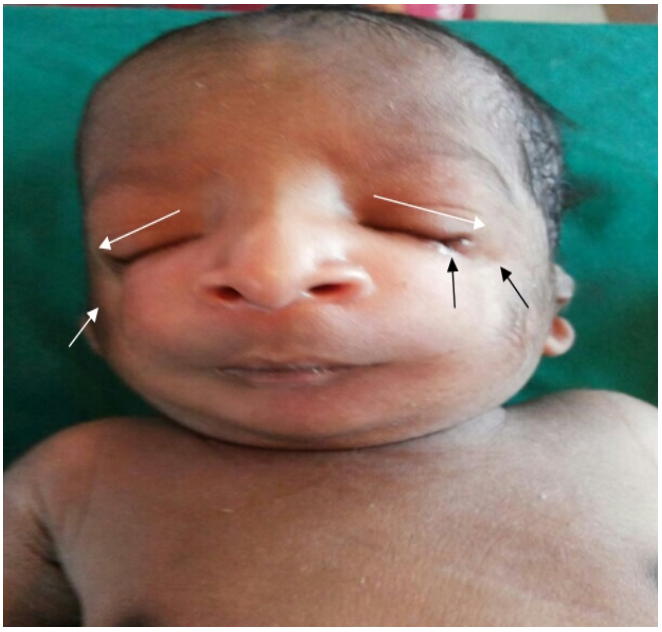

Figure 4 : Showing (i) Atretic right pinna and absent external auditory canal (ii) Temporal hollowing and malar hypoplasia more evident (iii) Micro and retrognathia with short neck.

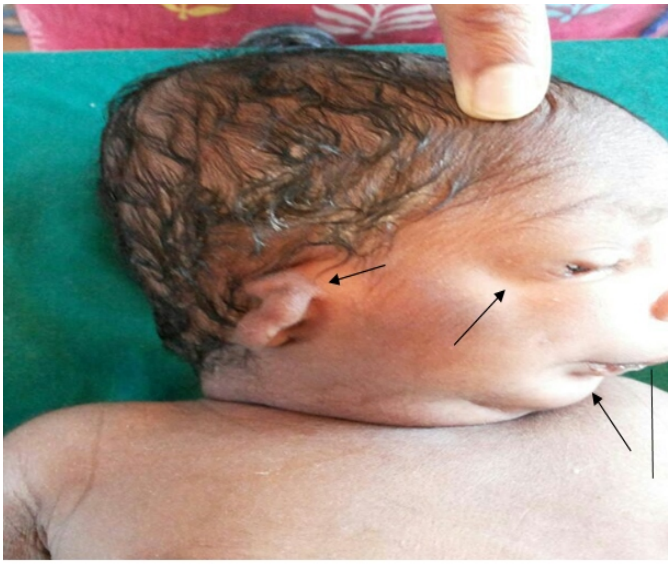

Figure 5 : Showing (i) High arched and complete cleft palate (ii) Glossoptosis

Discussion

Treacher Collins Syndrome (TCS, OMIM 154500) is a severe congenital disorder of craniofacial development of the head and neck region [1,5]. It is characterized by numerous bilateral symetrical developmental anomalies derived from the first and second branchial arches [1,6,7]. It is also called as Franceschetti – Klein syndrome or Mandibulofacial dysostosis. This was described for the first time by Thompson in 1846; however, the syndrome is named after Edward Treacher Collins, the English ophthalmologist who described two cases in 1900 [8]. Franceschetti and Klein in 1949 published an extensive review of this condition in which they expanded the phenotype, employing the designation "Mandibulofacial Dysostosis" [1,9].

TCS exhibits autosomal dominant inheritance with incomplete penetrance and variable expressivity [3,5]. It affects both genders equally [4]. While 40% of the cases have a previous family history, the remaining 60% appear to arise as a result of a de novo mutation [10]. Several hypotheses were proposed to explain the pathogenesis of TCS including abnormal patterns of neural crest cell migration, abnormal domains of cell death, improper cellular differentiation during development or abnormalities of the extracellular matrix. Mann and Kilner, assumed the etiology to be an inhibitory process occurring towards the end of the seventh week of embryonic life and affected the facial bones derived from the first visceral arch. John Mckenzie suggested that the cause of the abnormality was a defect in the stapedial artery which causes maldevelopment in its own field as well as in the region of the first visceral arch [10,11]. Recently genetic, physical and transcript mapping techniques have identified the gene mutated in TCS which is designated as TCOF1 and mapped to chromosome 5q32-33.2 locus, which encodes a low complexity serine/alanine rich nucleolar phosphoprotein termed Treacle [5,11]. Mutation in the TCOF1 gene leads to high degree of neuroepithelial apoptosis and consequent loss of neural crest cells. Cranioskeletal hypoplasia occurs due to generation of insufficient neural crest cells [1,5,12]. Individuals who have the TCOF1 mutation have a 50% chance of passing it on to their children. TCS shows high penetrance and extreme variation in the expressivity of the phenotype [1].

Clinical features – It varies greatly ranging from almost unnoticeable to severe deformities. It is most noticeably characterized by abnormalities of the head and face. Atypical hair growth in the form of tongue shaped processes of the hair line extending towards the cheeks in the preauricular region may be seen [10]. Ocular manifestations include hypertelorism, antimongoloid slant of the palpebral fissures (89%), partial absence of eyelid cilia (69%), colobomata and hypoplasia of the lower eyelids and lateral canthi (69%) may also be seen. Abnormalities of the ear include alterations in the shape, size and position of the external ears, which are frequently associated with atresia of the external auditory canals and anomalies of the middle ear ossicles, resulting in conductive hearing loss. Facial bone malformations are the most characteristic and include hypoplasia of the malar, maxilla, mandible and inferolateral aspect of the bony orbital margins [1,4]. These children may also have respiratory compromise due to (i) maxillary hypoplasia which results in choanal stenosis/atresia and tends to constrict the nasal passages (ii) presence of mandibular micrognathia and a retropositioned tongue obstructing the oropharyngeal and hypopharngeal spaces [4]. There may be beaking of the nose resulting in a bird head appearance. Variable degrees of cleft palate (28%) with or without cleft lip, microstomia, high arched palate, malocclusion/malaligned teeth may also be seen [1]. Very rarely sleep apnoea and sudden infant death syndrome have been described in these patients [2,4,13]. based on the spectrum of clinical features Franceschetti and Klein described five clinical forms namely (i) complete form (ii) incomplete form (iii) abortive form (iv) unilateral form and (v) atypical form [10] .

Work up – includes radiograph of the skull and facial bones with CT scan for evaluation of the extent and severity of the craniofacial malformation. Audiological evaluation for hearing impairment; genetic evaluation for detecting the mutation in TCOF1 gene which is present in about 90-95% of the cases may be done [1].

Diagnostic methods – The classical facial features described above in the absence of skeletal abnormalities of the upper/lower limbs would support the diagnosis of TCS.

Differential diagnosis – Include Nager syndrome and Miller syndrome. Both these syndromes have facial abnormalities similar to TCS, but Nager syndrome is associated with preaxial limb abnormalities like hypoplastic/aplastic thumb and/or radius. Miller syndrome has post axial limb abnormalities like absence of the 5th digit in all 4 limbs [5,9].

Management – The current approach for TCS's clinical deformities seeks functional and esthetical correction as well as psychosocial support. Multidisciplinary approach involving

pediatricians, otorhinolarngologists, craniofacial surgeons, ophthalmologists, speech therapists, psychologists and pediatric dentists is the most appropriate way to manage these patients [4]. Treatment involves the use of hearing aids and multiple reconstructive surgeries based on the severity to correct the facial malformations.

Antenatal diagnosis – Good quality two dimensional/three dimensional sonography may reveal polyhydramnios, abnormal fetal swallowing and the classical facial features of TCS as early as 15 weeks of gestation [14]. Amniocentesis and/or chorionic villus sampling may detect mutations in the TCOF1 gene as early as 8-12 weeks of gestation.

Prognosis – The longevity of survival in patients with TCS is comparable with that of the normal population. However, individuals with severe form of TCS usually, over a period of time, undergo multiple major reconstructive surgeries that are rarely fully corrective. As the great majority of these patients are of normal intelligence, early recognition of deafness and its correction using hearing aids and/or surgery is of great importance to enable them to lead a near normal life [10].

Prevention – It is mainly important to prevent its occurrence in the offspring of affected parents (40% chance of transmitting it). Genetic counseling, good quality antenatal sonography with amniocentesis and/or chorionic villus sampling will help in prevention of the occurrence of TCS in the offspring of affected parents.

Conclusion

TCS in an autosomal dominant disorder of craniofacial development with unusual clinical features associated with abnormalities of structures derived from the first and second branchial arches due to mutation in the TCOF1 gene. Management of TCS needs a multidisciplinary approach and the treatment plan is made to meet the individual patient's need, considering the growth patterns, function and psychological development. Prenatal diagnosis and genetic counseling helps parents make intelligent decisions regarding the pregnancy which will reduce the incidence of TCS.

References

[1] Prachi Shete, Tupkare JV, Tabita Benjamin, Aarti Singh. Treacher Collins Syndrome. J Oral Maxillofac Pathol 2011;15(3):348-351.

[2] Martelli – Junior H, Coletta RD, Miranda RT, Barrros LM, Swerts MS, Bonan PR. Orofacial features of Treacher Collins Syndrome. Med Oral Patol Oral Cir Bucal 2009;14:e344-348.

[3] Dean. L. Mittmann, Orlando. G. Rodman. Mandibulofacial Dysostosis (Treacher Collins Syndrome) : A Case Report. Journal of National Medical Association 1992;84(12):1051-1054.

[4] Sowmya B Shetty, Ann Thomas, Raghavendrea Pidamale. Treacher Collins Syndrome : A Case Report and a Brief Review on Diagnostic Aids. International Journal of Clinical Pediatric Dentistry 2011;4(3):235-239.

[5] Trainor PA, Dixon J, Dixon MJ. Treacher Collins Syndrome : Etiology, pathogenesis and prevention. Eur J Hum Genet 2009;17:275-283.

[6] Anil S, Beena VT, Ankathil R, Remani P, Vijaykumar T. Mandibulofacial Dysostosis : A Case Report. Aust Dent J 1995;40:39-42.

[7] Madhan R, Nair S. Prosthetic Management of a Patient with Treacher Collins Syndrome. Ind J Dent Res 2006;17:78-81.

[8] Arvystas M, Sprintzen R. Craniofacial morphology in Treacher Collins Syndrome. Cleft Palate Craniofac J 1991;28:226-231.

[9] Alexander, Sherry P. Treacher Collins Syndrome. J Ind Acad Oral Med Radiol 2010;22:49-52.

[10] Vikrant Kasat, Rahul Baldawa. Treacher Collins Syndrome – a case report and review of literature. J Clin Exp Dent 2011;3:e395-399.

[11] John Mckenzie, John Craige. Mandibulofacial Dysostosis (Treacher Collins Syndrome). Arch Dis Child 1955;391-395.

[12] Hertle RW, Ziylan S, Katowitz J. Ophthalmic features and visual progress in the Treacher Collins Syndrome. Br J Ophthalmol 1993;77:642-645.

[13] Marszatek B, Wojcicki P, Kobus K, Trzeciak WH. Clinical features, treatment and genetic background of Treacher Collins Syndrome. J Appl Genet 2002;43(2):223-233.

[14] Rolf . G. Behrents, James . A. McNamara, James . K. Avery. Prenatal Mandibulofacial Dysostosis (Treacher Collins Syndrome). Cleft Palate Journal 1977;14(1):13-34.