Treacher Collins Syndrome : A Report on Two Cases

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Introduction

Treacher Collins syndrome is an autosomal dominant inherited malformation of structures derived from the first and the second branchial arches [1]. It is characterized by malar hypoplasia with down slanting palpebral fissure, defects of the lower lid and malformation of external ear [2]. We report two cases of this syndrome, briefly highlighting aspects of molecular genetics involved in its occurrence.

Case Report-1

2 year old male infant, first in the sibling order, born to non consanguineous parents after an uneventful gestational period was noticed to have deformed pinna on both sides, cleft in the soft palate and receding chin. Child was brought to the out-patient department by parents for seeking counselling as regards chances of occurrence of the same defect in future children.

Examination revealed male child weighing 9 kg with multiple congenital anomalies, namely, downward slanting palpebral fissure and scant lower lid eyelashes. There was malar and mandibular hypoplasia with cleft in the soft palate and macrostomia. Developmental mile stones were mildly delayed. Computerised tomography (CT) scan showed absence of external auditory canal on the left side with non visualization of mastoids bilaterally. Otological and orthodontic evaluation revealed conductive hearing loss and malocclusion of teeth respectively. Echocardiographic and ophthalmological examinations were within normal limits.

Case Report-2

This child was a 4 year old male, product of nonconsanguineous marriage, referred to Base Hospital, Delhi Cantt, to explore the possibility of cosmetic surgery from a peripheral hospital. Child had strikingly similar appearance and clinical signs as described in the first case barring minor variations in that he did not have malocclusion of teeth and mastoids were visible on CT scan examination.

Discussion

Treacher Collins syndrome, is also called Franceschetti-Klein syndrome or mandibulofacial dysostosis. This was for the first time described by Thompson in 1846, however, syndrome has been associated with

Treacher Collins who described two cases in 1900 [2].

The facial appearance in this syndrome is characterized by palpebral fissure sloping downward towards the outer canthi (89%), coloboma of the lower eyelids (69%), sunken cheek bones, blind fistula opening between the angles of the mouth and ears, deformed pinnas (77%), atypical hair growth extending towards the cheek and large mouth (26%) [2,3]. Other abnormalities are mandibular and malar hypoplasia (78 & 81%) with or without cleft in the zygomatic bone, external canal defect (36%) and conductive deafness (40%). Partial or total absence of lower eyelashes (53%), clefted soft palate (28%), visual loss (37%) are other known associations. Occasionally, the syndrome also has abnormalities like choanal atresia. Rare features are macrostomia, coloboma of the upper eyelids, refractive errors, squint, congenital heart defects, cryptorchidism and absence of parotid glands [2].

In our cases, commonly described abnormalities viz antimongoloid slant, malar and mandibular hypoplasia, partial absence of lower eyelashes, malformation of auricles, external ear canal defect, conductive deafness and cleft of the soft palate were present. In the first case other occasionally described anomalies, in the form of macrostomia, malocclusion of teeth and non-visualization of mastoids were present.

This syndrome is autosomal dominant in pattern of inheritance with variable expression. It involves structures derived from the first and second branchial arch and has an incidence of 1:10000 newborns [3]. Approximately 66% of the cases represent presumed fresh mutations. Mutation in a gene of unknown function referred to as 'treacle', which maps to 5q 32-33.1 is responsible, at least for some cases of Treacher Collins Syndrome. In case of a large family, linkage analysis has suggested that the gene is linked to marker in the region of 5q 32-33.2 and, hence, linkage analysis can be used to identify affected individuals even in the absence of clinical and radiological evidence of Treacher Collins syndrome [2].

But for one isolated report in the literature describing association of this syndrome with dermatomyosi-

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Fig. 1: Photograph showing antimongoloid slant, absence of lower lid eyelashes, deformed ears both sides, macrosomia, maloccluded teeth, malar and mandibular hypoplasia

tis, no other autoimmune disorder associated with Treacher Collins syndrome has been reported. For occurrence of this association, no genetic or physiological explanation could be offered, as in Treacher Collins the affected gene has been mapped to 5th chromosome, while dermatomyositis is related to HLA B8 and DR3, coded on the sixth chromosome [1].

The function of the encoded protein of the implicated gene "treacle" has yet not been established. However, appropriate kinase activity in branchial arches I and II which coincides with peak expression of Treacher Collins syndrome gene product, treacle has been detected [4].

Experiments on mouse carried out with a view to investigate molecular pathogenesis of Treacher Collins syndrome have shown that the defect arises due to a massive increase in the level of apoptosis in the perfusion neural folds which are the site of highest level of 'treacle' gene expression.

Study further demonstrates that Treacher Collins syndrome arises from haploinsufficiency of a protein that plays a crucial role in craniofacial development and indicates that the correct dosage of treacle is essential for survival of cephalic neural crest cells [5].

Fig. 2: Photograph showing antimongoloid slant, absence of lower lid eyelashes, deformed ears both sides, malar and mandibular hypoplasia

References

1. Larcenas-Linnemann DE, Berron-Perez R, Ortega-Martell JA, Onuma-Takane, Huicochea-Grobet Z. Treacher Collins syndrome and co-existing dermatomyositis. *Ann Allergy Asthma Immunol* 1998;80(1):50-4.
2. Lyon K, Jones MD. Treacher Collins syndrome. In :Smith's recognizable patterns of human malformation. 5th ed. WB Saunders Co 1997;250-1.
3. Johnsen D, Tinanoff N. Syndromes with Oral Manifestations. In : Behrman RE, Kliegman RM, Jenson HB, editors. *Nelson text book of Paediatrics*. 16th ed, Philadelphia : WB Saunders Co 2000;1113.
4. Jones NC, Farlie PG, Minichiello J, Newgreen DF. Detection of an appropriate kinase activity in branchial arches I and II that coincides with peak expression of the Treacher Collins syndrome gene product, treacle. *Hum Mol Genet* 1999; 8(12):2239-45.
5. Dixon J, Brakebusch C, Frassler R, Dixon MJ. Increased levels of apoptosis in the perfusion neural folds underlie the craniofacial disorder, Treacher Collins syndrome. *Hum Mol Genet* 2000;12;9(10):1473-80.