Brief Communication

Treacher Collins Syndrome; Anesthetic considerations and Molecular Findings

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Abstract

Treacher Collins Syndrome (TCS) is a rare disease with mandibulofacial dysostosis. The deformities accompanied by this syndrome could cause especial challenges for anesthesiologist. On the other hand Treacher protein is well recognized in the pathogenesis of this syndrome. In this report we want to present a successful management of a patient with Treacher Collins syndrome and also describe new advances in the molecular aspect of this disease.

Keywords: Treacher Collins Syndrome, Mandibulofacial Dysostosis, Anesthesia, Treacher Protein

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Introduction

Rare genetic disorders are great challenges for Treacher Collins Syndrome (TCS, OMIM number 154500) is named after Edward Treacher Collins, an ophthalmologist from London who described this disorder in 1900 (1, 2). In 1949, Franceschetti and Klein described more features and coined the term mandibulofacial dysostosis. It is an autosomal dominant disorder of craniofacial morphogenesis with high penetrance and variable expressivity. It has the frequency of 1 in 50 000 live births and about 60%-90% of them are *de novo* mutations in treacle gene (TCOF1) (1, 2). Up to 130 mutations are reported for this gene and most of them are deletions (1). Treacle protein is essential for proper development of cranial neural crest cells (CNCC) (2). Other mutations are found like POLR1C and POLR1D in which the pattern would be autosomal recessive. TCOF1 is located in chromosome 5q31.3-32 and encodes a serine/alanine rich nucleolar phosphoprotein (treacle protein) which is responsible for the craniofacial development, proliferation, and differentiation of neural crest cells by affecting ribosomes (3, 4). This gene is responsible for 80% of the cases. POLR1C and POLR1D encode subunits of RNA polymerases I and III which are also essential for ribosome biogenesis.

This syndrome contains a congenital malformation of the 1st and 2nd branchial arches (5). The craniofacial abnormalities involve underdevelopment of zygomatic arch, mandible, hard palate and oral cavity (3). These deformities could result in choanal stenosis or dysphagia. These patients also have ocular abnormalities including antimongoloid slanting of the palpebral fissures, and abnormalities if external and middle ear structures resulting in hearing loss. Microcephaly and behavior abnormalities also reported in several cases. These

abnormalities could involve: Hypoplastic malars, mandibular hypoplasia, micrognathia, pharyngeal hypoplasia, cleft palate, obstructive sleep apnea, choanal stenosis or atresia, tooth agenesis, conductive hearing loss, microtia, preauricular Tags, eyelid coloboma (6), strabismus, dacrostenosis, microphthalmia, macrostomia, High arch palate, psychomotor delay (2). In spite of heterogeneity of clinical presentations there has not been any explanation for it. The variety of epigenetic factors, gene modifiers and the role of non-mutated genes are proposed (1). The diagnosis is made by thorough clinical evaluation, detailed history and identification of characteristic physical findings. In some cases X-Rays could be helpful.

There is not any clinical therapy for this syndrome. Therefore, early intervention is important to ensure that affected child could reach his/her potential. These interventions include speech therapy, special social support and genetic counseling. Surgery might be indicated in patients with cleft palate, zygomatic or orbital reconstruction, external and inner ear reconstruction.

Brief Report

A 24-year- old boy (153 cm; 45 kg) with TCS was scheduled due to revision of strabismus under general anesthesia. He did not have any past medical or surgical history except characteristic facial appearance of TCS (Fig 1). Thyromental distance was 35 mm and open mouth was one finger. The Mallampati score of four was detected. Preoperative laboratory tests were all within normal limits and no abnormal findings were shown on chest radiograph or electrocardiograph. In the operating room, his vital signs were within normal limits and standard monitoring was applied. Due to anticipated difficult airway, oral flexible fiber optic was performed by administering premedication with Amp Atropine 0.5 mg IV and Amp Fentanyl 50 µgr IV. Spray As You Go (SAYGO) technic was performed for analgesia of airway tract. The trachea was successfully intubated with an ID 6.0 mm armored endotracheal tube.

Discussion

All of the proteins in a cell are synthetized by ribosomes, which in term are constructed by transcription of ribosomal RNA (rRNA) by RNA polymerase I and III. This is called ribosome biogenesis. Ribosome biogenesis is a metabolically expensive and complex task for the cell therefore this process is highly regulated by, and integrated with, cell growth, proliferation and differentiation (8). By accepting its great importance, it is surprising that ribosomopathies like Treacher Collins Syndrome exhibit specific clinical phenotype including craniofacial, axial, or limb skeleton as well as hematopoiesis or organogenesis (8).

Watt *et al*. described a zebra fish model for treacher Collins syndrome and proposed the mechanism of the three genes involved in this syndrome (8). They discovered that POLR1C and POLR1D are spatiotemporally and dynamically expressed specially in craniofacial development. In addition, these genes cause disruptions in biogenesis of ribosome resulting in Tp53-dependent neuroepithelial cell death and deficiency of migrating neural crest cells. Their model also showed that genetic inhibition of Tp53 could suppress this phenomenon and there for could be a gate for the treatment of this syndrome (8).

There has not been any correlation between phenotype and genotype although Teber et al. proposed a lower frequency of conductive hearing loss in patients with mutations of the 3′ part of the open reading frame of TCOF1, which do not confirmed by Vincent et al (4, 9). On the other hand, patients with mutations in POLR1D seemed to have a milder phenotype.(9) Vincent et al. reviewed 146 patients with this syndrome and found that 4% of them were affected with this syndrome but do not have ant mutation in these three genes therefore there could be more genes involved in this syndrome yet to be found (9).

As mentioned above these patients may require anesthesia in different stages of their life. The most important anesthetic consideration for these patients is airway management. It is particularly important due to smaller oropharynx, limited mouth opening, mandibular hypoplasia and hypo plastic larynx.

Anesthesiologist should consider effect of age on the condition of anatomy. This is mentioned in literature that the difficulty with intubation could be increased by advanced age (6). different methods of airway management is proposed including: Direct Laryngoscopy, Fiber optic Bronchoscopy, light wands, blind nasal intubation, Supra Glottic Airway Devices, video laryngoscopy, retrograde intubation and tracheostomy. Shin et al. reported airway management with I-Gel (6). Tsujimoto et al. used McGRATH MAC which turned Cormack-Lehane classification grade four ,with Macintosh blade no. 3, to one (10). Goel et al. described difficulties encountered when using Intubating LMA or light wand due to anterior placement of glottis and posteriorly protruded tongue (11). They also recommended a modified direct laryngoscopy when to additional technics is readily available. It includes (a) maintaining spontaneous breathing with deeper plane of anesthesia (b) Forward lift of both angles of mandible to conquer retrognathia and (c) a good backward upward and rightward pressure (BURP) by a professional assistant (11). Lin et al, described a case in which ventilation could not be adequate with LMA and they had the patient ventilated through endoscopic mask and perform nasal fiber optic intubation. They also had difficulty in extubating the patient which they overcome by Cook airway catheter exchanger and at last they decided to perform tracheostomy (12).

Another view indicated that most of the cases are caused by TCOF1 gene that could be detected by prenatal testing in embryos. Therefore prenatal diagnosis and genetic counseling could help parents to make intelligent decisions and reducing the incidence of TCS (13).

The last efforts of Sakai et al. have considerably interesting results (14). They ameliorate the features of these syndromes by using antioxidant supplementation in mouse models that could be a gate to treatment of this genetic abnormality in humans**.**

Conclusion

Treacher Collins Syndrome could be a challenge for anesthesiologists due to anticipated difficult airway management. Many approaches have been described with successful outcomes. Hence the gold standard would be awake flexible fiberoptic bronchoscopy and intubation. Also new findings in genetic aspect of this syndrome could be a path for definite treatment of TCS and prevent dysostosis in emberyonic period.

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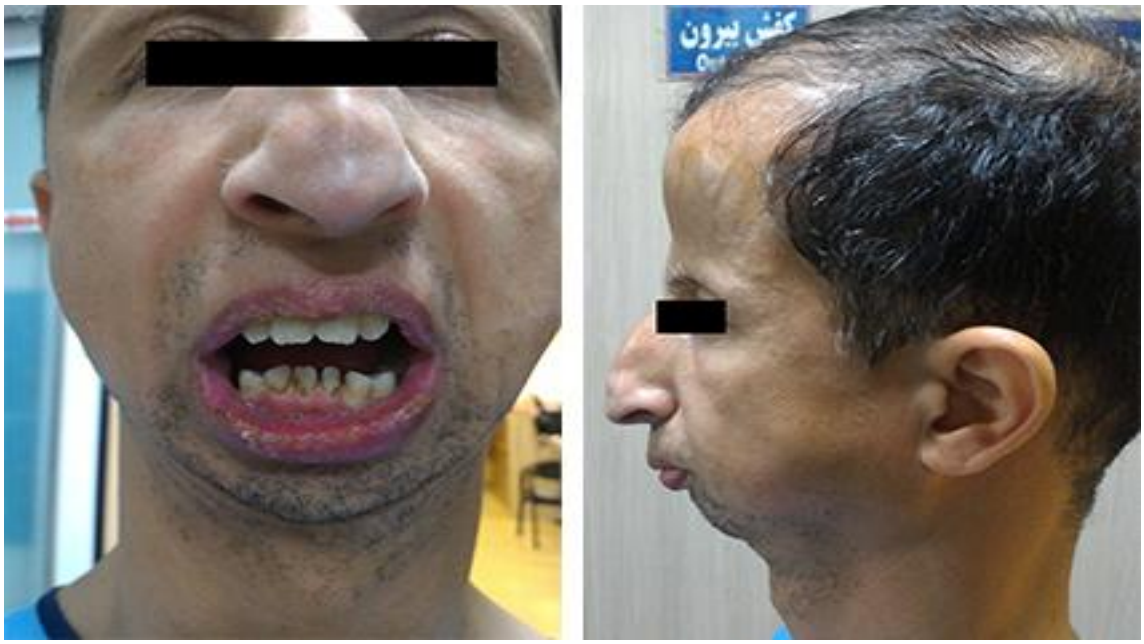

Figure 1. The patient was asked to perform full open mouth (a), Lateral View (b).

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Conflicts of Interest

The authors declare that there are no conflicts of interest.

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