

Treacher-Collins syndrome

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Treacher-Collins syndrome is genetic disease that alters the development of bones and other tissues in the face. Signs and symptoms of this syndrome, vary from almost unnoticeable face changes to severe facial and ear deformities, cleft palate and restricted airway. The syndrome is named after Edward Treacher Collins, an English surgeon and ophthalmologist who described its essential traits in 1900.

Treacher-Collins syndrome can be passed down through families or most of the time do not affect another member of the family. Mutations in *TCOF1* and *POLR1D* cause the autosomal dominant form of Treacher Collins, and mutations in *POLR1C* cause the autosomal recessive form [1]. The integration of molecular biology, cell biology, mouse genetics and experimental embryology has recently provided novel insights into the molecular pathogenesis of TCS.

When an affected child is born, it is important to investigate the parents to determine whether the affected gene is present, because the parent could have a mild form of the disease that has not been diagnosed. The diagnosis of Treacher Collins syndrome relies upon clinical and radiographic findings. Prenatal diagnosis cannot be guaranteed. Mutations in the main genes responsible for TCS can be detected with chorionic villus sampling or amniocentesis. Rare mutations may not be detected by these methods. Ultrasonography can be used to detect craniofacial abnormalities later in pregnancy, but may not detect milder cases. The *TCOF1* gene is located on the long arm (q) of chromosome 5, a region which is designated 5q32. *TCOF1* encodes a protein known as treacle [1]. De Peratta et al find a positive correlation between the expression of CNBP and *TCOF1* in mesenchymal cells from both control and TCS subject. Based on that, they suggest CNBP as a additional target for new alternative therapeutic treatments to reduce craniofacial effects not only in TCS but also in other neurocristopathies [2].

Deficient ribosome biogenesis which occur in this syndrome is insufficient to meet the proliferation and growth needs of cells during development of the embryo. It is assumed that the changes occur from 19-28 day of early intrauterine development due to destruction of the trigeminal neuron cells (of unknown origin) and is associated with generalized lack of mesenchymal tissue, leading to underdevelopment of the upper jaw and lower jaw. Because TCS is highly variable, researchers speculate that additional genetic and possibly environmental factors may also play a role in the variable severity of the disorder (guide for TCS).

One possibility for improving the surgical outcome might be the incorporation of stem cells in therapeutic treatment of craniofacial abnormalities. There is enormous potential in the application of stem cells in engineering tissues, such as bone and cartilage, that constitute the head and facial tissues so severely disrupted in TCS. However, at present, there is no universal recommendation for the in utero correction of prenatally diagnosed craniofacial anomalies and the decision to pursue fetal surgical intervention carries with it the potential for dual mortality

(mother and fetus). Thus, fetal surgery at present remains experimental and controversial [3].

All described changes in Treacher-Collins syndrome can be divided in three groups: otological, ophthalmic and dental findings. Otological findings are Conductive hearing loss (ranging from mild to severe) usually due to malformations of structures within the middle ear, absent, abnormally small or underdeveloped external ears, malformed external ears (hypoplasia of ear shells, low position of the ear shells (earlobes), presence of skin extensions and blind fistula in the area before the ear shells), the absence of the outer ear canal (atresia), stenosis of the external auditory canal and often deafness.

A child with TCS may have sleep apnea [4], conductive hearing loss, which may require a resource to provide child hearing aids. Some individuals can be affected severely, and they may develop life-threatening breathing problems known as infantile apnea. When infant with Treacher-Collins Syndrome is scheduled for mandibular surgery under general endotracheal anesthesia, the fiber optic intubation method through a laryngeal mask airway, described by Ellis et al can be successfully used in small infants with Treacher Collins Syndrome [5,6].

Ophthalmic findings associated with TCS include: antimongoloid palpebral position, narrowed tear ducts (dacryostenosis), notching (coloboma) of the lower eyelid, downward angle of the upper and lower eyelids (downward slanting palpebral fissures, partial or complete absence of the lower eyelashes in the inner corner of the eye, drooping eyelids, vision loss. Dental findings developed among 60% of individuals with TCS. More often seen are: missing teeth (tooth agenesis), discoloration of the teeth (enamel opacities), widely-spaced teeth, skeletal open bite, bite distal (distalisation of the mandible), "profile of a bird", abnormal eruption of certain teeth (ectopic eruption of maxillary first molars) and malocclusion (improper positioning of the teeth and jaw) and hypoplasia of the mandible jaw with a unique concavity on the lower edge of the mandible, which can be seen well in cephalometric radiograph. Less frequently included findings, associated with TCS are: Congenital heart defect, Abnormal scalp hair pattern (front of the ears and extending toward the cheeks), an abnormally wide mouth (macrostomia occur in 15% of cases), notching of the upper eyelid, hypoplasia or absence of zygomatic bones, widely spaced eyes, nasal deformity, cleft palate and highly arched roof of the

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mouth (high Gothic palate accompanied by a cleft palate in 30% of cases).

The Orthodontic treatment is focuses on the expansion of the upper jaw with mobile devices. If the cleft palate is present, the design of the orthodontic appliance is specially adapted. In the presence of the permanent dentition application of fixed orthodontic appliance is indicated, in order to establish satisfactory intercuspation and establish proper leveling of the jaws arches. Angle Class II skeletal relationship of the jaws is retained because of the underdevelopment of the lower jaw.

Better performance in school is ensured by treatment of hearing loss. The children with Treacher-Collins syndrome have to be followed by a plastic surgeon because they may need a series of operations to correct birth defects. Receding chin and other changes in face structure can be corrected by plastic surgery [7-9].

Because Treacher Collins syndrome affects multiple body systems, experienced, multidisciplinary team care is extremely important in achieving the best outcomes for physical and psychosocial needs associated with this syndrome, including surgical repair, airway management, feeding and breathing support, orthodontic needs, speech language therapeutic follow-up [10], management of vision and hearing problems and long-term follow-up care.

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