

TREACHER COLLINS SYNDROME

SÍNDROME DE TREACHER COLLINS

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ABSTRACT

Justification: Treacher Collins Syndrome is a very rare autosomal dominant genetic condition, resulting from mutations in the TCOF1 (main), POLR1B, POLR1C, or POLR1D genes, which are also responsible for the musculoskeletal formation of the face, resulting in serious symmetrical musculoskeletal impairments in the orocraniofacial region from the fetal period (which can be observed in morphological ultrasounds, chorionic villus sampling and/or amniocentesis), continuing after birth in clinical examinations. Since it can occur through autosomal genetic inheritance with different mutations or due to random factors, Treacher Collins Syndrome is classified into types 1, 2, or 3 to characterise these occurrences.

Objective: general, is to disseminate information about Treacher Collins syndrome to dentistry and physiotherapy professionals; specific objectives include identifying the main signs and symptoms of the syndrome and discussing the primary paediatric dental, clinical, surgical, and physiotherapeutic treatments. **Methodology:** exploratory-explanatory research, through a systematic search in the SciELO (Scientific Electronic Library Online) database and in the Virtual Health Library, using the descriptors "Treacher Collins Syndrome", "Mandibulofacial Dysostosis" in Portuguese, Spanish, French, Italian, Russian and English, in an open period, and based on the team's experience in rare orofacial syndromes. **Conclusion:** Treacher Collins Syndrome currently has no cure; however, some specialised dental and medical surgeries, both functional and restorative aesthetic, significantly improve chewing, swallowing, breathing, appearance, etc., and consequently, the patient's quality of life. Pre- and post-operative physiotherapy will facilitate the success of these procedures.

Keywords: Treacher Collins syndrome; Mandibulofacial dysostosis;

Rare diseases; Franceschetti-Zwahlen-Klein syndrome; Orofacial syndromes; Chromosome 5q32-q33.1.

RESUMO

Justificativa: A Síndrome de Treacher Collins é uma condição raríssima de característica genética, autossômica dominante, ocorrendo mutações nos genes TCOF1 (principal), POLR1B, POLR1C ou POLR1D, que também são responsáveis pela formação musculoesquelética da face, resultando em sérios comprometimentos musculoesqueléticos simétricos na região orocraneofacial desde o período fetal (que pode ser observado em ultrassonografias morfológicas, biópsia do vilo corial e/ou amniocentese), prosseguindo após o nascimento em exames clínicos. Como pode ocorrer por herança genética de genes diferentes mutações ou por fatores aleatórios, surge a classificação da Síndrome de Treacher Collins tipos 1, 2 ou 3 para caracterizar essas ocorrências. **Objetivo:** geral, disseminar informações da Síndrome Treacher Collins aos profissionais de odontologia e fisioterapia e, específicos são: indicar os principais sinais e sintomas da Síndrome Treacher Collins; discutir os principais tratamentos odontopediátricos, clínicos, cirúrgicos e fisioterapêuticos. **Metodologia:** pesquisa exploratória-explicativa, com busca sistemática na base de dados SciELO (Scientific Electronic Library Online) e na Biblioteca Virtual em Saúde, através dos descritores “Síndrome de Treacher Collins”, “Disostose mandibulofacial” em português, espanhol, francês, italiano, russo e inglês, em período aberto, e com base na experiência da equipe em síndromes orofaciais raras. **Conclusão:** A Síndrome de Treacher Collins não possui cura no atual momento, todavia, algumas cirurgias odontomédicas, tanto funcionais, quanto estética reparadora, melhoram significativamente a mastigação, deglutição, respiração, aparência,

etc., e, consequentemente, a qualidade de vida do paciente e, a fisioterapia no pré e pós-operatório facilitará o sucesso desses procedimentos.

Palavras-chave: Síndrome de Treacher Collins; Disostose mandibulofacial; Doenças raras; Síndrome de Franceschetti-Zwahlen-Klein; Síndromes orofaciais; Cromossomo 5q32-q33.1.

1. INTRODUCTION

Treacher Collins syndrome (TCS), also known as mandibulofacial dysostosis (ICD11: Q75.4), Berry syndrome, Franceschetti-Zwahlen-Klein syndrome, was described in 1900 by the English ophthalmologist and surgeon Edward Treacher Collins. This is a very rare genetic disorder, autosomal dominant, occurring due to mutations in the TCOF1 (main), POLR1B, POLR1C or POLR1D genes, which are also responsible for the musculoskeletal formation of the face, resulting in serious bilateral symmetrical musculoskeletal impairments in the orocraniofacial region from the fetal period (which can be observed in morphological ultrasounds, chorionic villus sampling and/or amniocentesis), continuing after birth in clinical examinations. Since it can occur through autosomal genetic inheritance with different mutations or due to random factors, Treacher Collins Syndrome is classified into types 1, 2, or 3 to characterise these occurrences.

In approximately 90% of cases, Treacher Collins Syndrome results from mutations in the TCOF1 gene, which encodes the treacle phosphoprotein^[1], through mutations on chromosome 5q32-q33.1, in the premature termination codon in the distal portion^[2,3]. In these cases, apoptosis of neural crest cells increases and their proliferation decreases, resulting in craniofacial disorders^[1].

The World Health Organisation (WHO) defines a rare disease as one that affects 65 people per 100.000—that is, 1.3 per 2.000 people^[4]. The estimated incidence of children born with a diagnosis of Treacher Collins syndrome is approximately 1 in 80.000^[5].

Treacher Collins syndrome does not differentiate by ethnicity, gender, or region and presents a wide variation in phenotype, therefore with different presentations among individuals ranging from simpler cases, with almost imperceptible phenotype, to more severe cases that require surgical interventions from the neonatal period to adulthood.

General signs and symptoms may vary depending on the condition, with some of the following occurring in more severe cases: total or partial hearing loss, agenesis or congenital anomalies of the external auricles, basocranial anomalies, sleep apnea, choanal atresia (rare occurrence), lacrimal duct atresia, absence of parotid glands (rare), blepharoptosis, coloboma or pseudocoloboma of the lower eyelid, nasal septum deviation, oropharyngeal dysphagia, dyspnoea, hypertelorism, hypoplasia of the lower eyelids, recurrent infections, orbital malformation, lower ciliary madarosis, hypoplasia of the zygomatic bones, convex facial profile, choanal stenosis or atresia may occur, preauricular hairs invading the zygomatic region, pronounced nasal prominence, conductive hearing loss, preauricular hairs invading the zygomatic region, pronounced nasal prominence, conductive hearing loss, among others.

Signs and symptoms of paediatric dental significance may also vary depending on the clinical presentation and can include: agenesis (in some cases), dental crowding, absence of the mandibular ramus and condyle (in some cases), temporomandibular joint (TMJ)

ankylosis, oropharyngeal dysphagia, temporomandibular joint, dysfunction, ectopic tooth eruption, glossoptosis, enamel hypoplasia, mandibular hypoplasia or absence, zygomatic arch hypoplasia, posteriorly positioned tongue, Class II or III malocclusion, unstable occlusion, macrostomia, bilateral micrognathia, anterior open bite, crossbite, dry labial mucosa, high-arched (ogival) palate, convex facial profile, cleft lip and/or palate, retrognathia, mouth breathing, and xerostomia, among others.

In light of the foregoing, the general objective of this article is to disseminate information about Treacher Collins syndrome to professionals in fields such as dentistry and physical therapy; the specific objectives are to outline the main signs and symptoms of Treacher Collins syndrome and to discuss the primary paediatric dental, clinical, surgical, and physical therapy treatments.

2. METHODOLOGY

This is an exploratory-explanatory study, with a systematic search in the SciELO (Scientific Electronic Library Online) database and the Virtual Health Library, using the descriptors "Treacher Collins Syndrome" and "Mandibulofacial Dysostosis" in Portuguese, Spanish, French, Italian, Russian, and English, during an open period, and based on the team's experience with rare orofacial syndromes.

3. RESULTS AND DISCUSSION

Treacher Collins syndrome can be diagnosed via 3D morphological ultrasound, chorionic villus sampling, and/or amniocentesis. In the case of newborns, it can be clinically confirmed, and by testing the TCOF1, POLR1B, POLR1C or POLR1D genes (which can be extended to the parents). Some tests may be necessary to assess the affected

areas and type of impairment, for example, panoramic radiography, computed tomography, magnetic resonance imaging, audiometry and other hearing tests, cephalometry, among others, to evaluate the affected structures for specialised referrals.

The differential diagnosis should rule out nonsyndromic congenital mandibular hypoplasia, Apert syndrome, Crouzon syndrome, Goldenhar syndrome, Miller syndrome, Nager syndrome, and Pierre Robin syndrome, among others.

Treacher Collins syndrome presents a highly variable clinical picture, even among members of the same family, which, combined with the high rate of mutations, can lead to diagnostic failure^[6].

In neonatal management, initial priorities should focus on the airways, nutrition, and growth. Patients may exhibit continuous apnoea, requiring oxygen saturation monitoring, among other procedures. A formal sleep study can document the severity and type of apnoea. A targeted assessment is also necessary to determine the cause of the airway obstruction, as multiple sites may be involved, such as the nasopharynx (choanal atresia), oropharynx/hypopharynx (glossoptosis/micrognathia), or laryngopharynx (laryngomalacia). The intervention is based on severity and location. In mild cases without significant anatomical constriction, conservative management (suction or nasopharyngeal airway) and positioning (lateral/prone) may be sufficient. If the obstruction is more severe, early tongue-lip advancement or mandibular advancement may be necessary. In the most severe cases, intubation or tracheostomy may be necessary^[7].

Even though the signs and symptoms are well characterised, there is a significant amount of individual variability that has not yet been genetically established. Each person with Treacher Collins syndrome has different functional, aesthetic, and psychological needs and desires. Therefore, even if patients receive a general schedule of the operation and a detailed description of the available assistance, an individualised approach is always necessary^[8].

Dyspnoea may be present, compromising other important systems of the patient, including oropharyngeal dysphagia; in some cases, masticatory and respiratory exercises may help. However, in more complex cases, a tracheostomy and/or the placement of a gastric or nasogastric tube may be required, often resulting in a dependency on this equipment.

Patients may present with chronic upper airway obstruction, which impairs eating and sleeping, and increases the number of hospitalisations. Micrognathia, abnormal tongue posture, pharyngeal hypoplasia, and narrowing of the larynx and trachea are frequently observed, resulting in respiratory obstruction and obstructive sleep apnoea syndrome^[2]. Transpalatal, transseptal, and endonasal correction surgeries^[9], among others, are generally recommended by otolaryngologists.

Depending on the degree of ocular exposure, early tarsorrhaphy may be necessary to prevent corneal scarring, ulceration, and blindness. Parenteral nutrition should be started as soon as possible to support growth and development. Parents should be instructed on feeding techniques and aspiration prevention. In cases presenting with overt or submucous cleft palate, specialised feeders may also be required. Once the child is stable, feeding, breathing

without significant obstruction, and has adequate corneal protection, the remaining dysmorphology can be treated using a coordinated, staged approach^[7].

A subsequent approach to correcting clinical deformities in Treacher Collins Syndrome aims at functional correction, aesthetic correction, and the need for psychosocial support, with the joint participation of a multidisciplinary team composed of otolaryngologists, craniofacial surgeons, ophthalmologists, speech therapists, psychologists, and dental surgeons to achieve this goal. In addition to anatomical and physiological anomalies, patients with Treacher Collins syndrome suffer social stigma due to severe facial deformities^[2].

In dentistry, due to dystrophy, some muscles of orofacial importance may be compromised, causing dysarthria, masticatory dysfunction, and dysphagia, requiring intervention by the dental surgeon. Another factor is the intubations that occur in the patient, requiring the hospital dentist to perform some interventions related to the patient's oral health^[10].

Paediatric dentistry must involve teaching masticatory exercises; monitoring and intervening in cases of delayed primary tooth eruption; treating mouth breathing; periodically optimising the oral environment; providing guidance to caregivers on proper oral hygiene and necessary adaptations; treating common infections; periodically applying fluoride varnish; managing postoperative pain and infections associated with orofacial surgeries; and addressing other dental needs related to the signs and symptoms common to Treacher Collins syndrome. Visits to the dentist should be more frequent for monitoring oral health.

Given the accumulation of biofilm in areas of dental crowding, it is crucial to provide guidance to parents and caregivers; since the patient may find it difficult or impossible to perform oral hygiene, the paediatric dentist often needs to recommend adaptations, such as modified toothbrushes or dental floss to make this task possible^[11].

However, even simple dental restorative procedures can be challenging in these patients due to associated medical comorbidities, such as congenital heart disease, narrowed oropharyngeal airways, hearing loss, and anxiety regarding treatment ^[12].

Virtual surgical planning is a reliable, precise, and safe surgical tool for midfacial and orthognathic reconstruction in late-presenting Treacher Collins syndrome. Both aesthetic and functional results are highly encouraging, as demonstrated by cephalometric improvements following surgery. Virtual Surgical Planning allows for the consideration of various surgical options for all parts of mesofacial reconstruction in multiple stages, enabling the early identification of challenges, including choosing ideal procedures before surgery, designing anatomically individualised mesofacial bone grafts, and precisely planning orthognathic surgery in a late presentation of Treacher Collins Syndrome^[13].

Counter-clockwise craniofacial distraction osteogenesis aims to correct facial skeletal deformity and expand the upper airway volume by rotating the subcranial complex as a block around the nasofrontal junction. This surgical technique provides significant increases in nasopharyngeal and oropharyngeal airway volumes,

with successful decannulation in the majority of patients who underwent the procedure^[14].

Many patients present with anomalous internal structures and ossicles that do not function correctly, resulting in conductive hearing loss in the majority of cases. Many centres advocate completing definitive ear reconstruction before implanting a bone-anchored hearing aid (BAHA); However, hearing delay can cause significant delays in language and socialisation in children with Treacher Collins syndrome. For this reason, many patients use removable BAHA headbands (Softbands) that allow for early auditory rehabilitation^[7]. In cases of ear deformity (microtia) or total absence of the ear (anotia), the number of surgeries increases significantly, imposing a social burden on the individual and their family members, likely impacting their quality of life^[15]. In these and other situations, the support of a speech therapist is very important, both for adaptations and for speech and hearing training, etc., complemented by physiotherapy services.

A combined orthodontic-orthognathic approach is required to correct the malocclusion, most frequently characterised by short posterior vertical height and anterior open bite. Orthognathic correction frequently requires Le Fort I and bilateral sagittal split osteotomies. Bimaxillary orthognathic surgery in Treacher Collins patients can be performed safely, providing long-term dental and skeletal stability^[16].

Total or partial tarsorrhaphy, advancement mentoplasty ^[17], uvulopalatoplasty, rhinoplasty, autogenous facial grafts, and other complementary functional and corrective aesthetic surgeries are indicated. However, they should take place after more complex

surgeries, such as craniofacial distraction osteogenesis, orthognathic surgery, and airway clearance relief, among others.

When a patient undergoes surgical procedures, the physiotherapist plays an important role in the postoperative period, mainly in adopting activities capable of preventing contractures, such as proper positioning and specific stretches, in order to increase the range of motion of shortened muscles. Increased mobility enables the patient to improve balance and coordination when performing routine activities^[18].

In facial kinesitherapy, the goal is to strengthen the muscles involved in jaw movements, such as protrusion, retraction, lateral movements, as well as mandibular elevation and lowering, thus improving chewing, swallowing, speech, yawning, facial expression, and other functions^[9,19,20].

Regarding the role of respiratory physiotherapy, bronchial hygiene techniques should be employed, such as percussion, compression/decompression, vibrocompression, and postural drainage, with the aim of mobilising secretions. The therapeutic approach in this case aims to promote improvements in thoracic-pulmonary expansion and oxygenation. ^[21]. The importance of respiratory exercises, especially those targeting the upper respiratory tract, is highlighted.

Orofacial physiotherapy using proprioceptive exercises should aim to enable the patient to identify food textures and use the tongue to locate areas within the mouth, thereby preventing accidental biting. In this case, kinesiotherapy aims to strengthen the muscles involved and restore jaw movements, such as protrusion, retraction, lateral

movements, and elevation and lowering of the jaw, thus improving chewing, swallowing, speech, yawning, facial expression, and other functions^[19,20,22].

Low-level laser therapy (LLLT) has provided excellent responses to the signs and symptoms of orofacial pain, mainly concerning its analgesic, anti-hypersensitivity, anti-inflammatory, pre- and post-surgical effects (especially in the surgical wound healing process), among others^[23].

Patients have normal intelligence, but often face social challenges throughout their lives because of their physical appearance^[7]. However, psychological support is necessary for several reasons, including the large number of surgeries required in the most complex cases and the potential for bullying at school, among others.

Social assistance should focus on guaranteeing the patient's rights, in accordance with the laws of the country, providing assistance and guidance to caregivers and relatives, referring patients to specialised institutions for appropriate treatment, combating discrimination, supporting and encouraging social inclusion, developing projects and providing guidance on public policies related to education, health, and accessibility for patients, among other things^[24].

4. CONCLUSION

Treacher Collins Syndrome is a genetic condition that currently has no cure, presenting with symptoms ranging from mild to severe, varying from patient to patient. However, for moderate to severe cases, some dental-medical surgeries, both functional and

restorative aesthetic, significantly improve chewing, swallowing, breathing, sleep, appearance, etc. and consequently, the patient's quality of life, and physiotherapy in the pre and post-operative periods will facilitate the success of these procedures.

In most cases, specialised care is needed during the neonatal period, continuing with surgeries into adulthood, when the facial bones have stopped developing. Throughout this entire process, the patient should receive care from a multidisciplinary team, involving surgeons, paediatric dentists, oral and maxillofacial surgeons, head and neck surgeons, plastic surgeons, otolaryngologists, physical therapists, speech therapists, nutritionists, social workers, psychologists, among others, to ensure quality health.

It should be noted that the procedures discussed here are merely suggestions based on the current state of scientific knowledge regarding Treacher Collins syndrome; professionals must keep pace with emerging advances, as this is an extremely rare syndrome that can present with a wide range of clinical pictures, from mild to complex.

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