UDC 616-039.42+617.52+616-007-053.1
DOI: 10.56871/CmN-W.2023.67.33.013

CLINICAL CASE: TREACHER COLLINS SYNDROME

© Taras S. Dyakov[1], Dmitry G. Penkov[1, 2], Elena S. Ulyanicheva[2]

[1] Pavlov First Saint Petersburg State Medical University. L'va Tolstogo st., 6–8, Saint Petersburg, Russian Federation, 197022
[2] Saint Petersburg Orphanage No. 3. Zagrebskiy 42, Saint Petersburg, Russian Federation, 192288

Contact information:
Dmitry G. Penkov — Associate Professor of the Department of Pediatric Diseases with a Course in Neonatology, Pavlov First Saint Petersburg State Medical University, St. Petersburg Orphanage No. 3, chief medical officer. E-mail: penkov76@bk.ru
ORCID ID: 0000-0002-1927-9684

For citation: Dyakov TS, Penkov DG, Ulyanicheva ES. Clinical case: Treacher Collins syndrome. Children's medicine of the North-West (St. Petersburg). 2023; 11(3): 145-149. DOI: https://doi.org/10.56871/CmN-W.2023.67.33.013

Received: 23.05.2023 **Revised: 10.08.2023** **Accepted: 12.09.2023**

Abstract. Treacher Collins syndrome is a congenital developmental disorder of the craniofacial region associated with an anomaly in the differentiation of the first and second pharyngeal arches. This syndrome is a rare pathology, its frequency of occurrence is 1 per 50,000 cases of live births, but we had the opportunity to observe a patient with this syndrome on the basis of the St. Petersburg Orphanage. *Aim.* To analyze the literature, present a description of the Treacher Collins syndrome and analyze a clinical case in a patient under observation in a children's home (St. Petersburg). *Materials and methods*. International and domestic scientific publications, analysis of clinical cases in the literature, medical documentation of the orphanage. *Results.* In our article, we assess the severity of congenital malformations in a patient at the orphanage, and give a conclusion about the specificity of the severity of his condition for Treacher Collins syndrome.

Key words: *Treacher Collins syndrome; STC; Franceschetti's syndrome; mandibular dysostosis.*

КЛИНИЧЕСКИЙ СЛУЧАЙ: СИНДРОМ ТРИЧЕРА КОЛЛИНЗА

© Тарас Сергеевич Дьяков[1], Дмитрий Григорьевич Пеньков[1, 2], Елена Сергеевна Ульяничева[2]

[1] Первый Санкт-Петербургский государственный медицинский университет им. академика И.П. Павлова. 197022, г. Санкт-Петербург, ул. Льва Толстого, 6–8
[2] СПб ГКУЗ СДР № 3. 192288, г. Санкт-Петербург, Загребский бул., 42

Контактная информация:
Дмитрий Григорьевич Пеньков — доцент кафедры детских болезней с курсом неонатологии ПСПбГМУ им. акад. И.П. Павлова; главный врач СПб ГКУЗ СДР № 3. E-mail: penkov76@bk.ru ORCID ID: 0000-0002-1927-9684

Для цитирования: Дьяков Т.С., Пеньков Д.Г., Ульяничева Е.С. Клинический случай: синдром Тричера Коллинза // Children's medicine of the North-West. 2023. Т. 11. № 3. С. 145–149. DOI: https://doi.org/10.56871/CmN-W.2023.67.33.013

Поступила: 23.05.2023 **Одобрена: 10.08.2023** **Принята к печати: 12.09.2023**

Резюме. Синдром Тричера Коллинза — врожденное нарушение развития черепно-лицевой области, связанное с аномалией дифференцировки первой и второй глоточных дуг. Данный синдром является редкой патологией, частота его встречаемости — 1 на 50 000 случаев живорожденных, но нам представилась возможность наблюдать пациента с данным синдромом на базе Санкт-Петербургского дома ребенка. *Цель.* Провести анализ литературы, представить описание синдрома Тричера Коллинза и разобрать клинический случай у пациента, находящегося под наблюдением в доме ребенка (Санкт-Петербург). *Материалы и методы.* Международные и отечественные научные публикации, разбор клинических случаев в литературе, медицинская документация дома ребенка. *Результаты.* В нашей статье мы даем оценку степени выраженности врожденных пороков развития у пациента дома ребенка и делаем заключение по поводу характерности тяжести его состояния для синдрома Тричера Коллинза.

Ключевые слова: *синдром Тричера Коллинза; СТК; синдром Франческетти; нижнечелюстно-лицевой дизостоз.*

 ISSN 2221-2582

INTRODUCTION

Treacher Collins syndrome (TCS, Franceschetti syndrome or mandibulofacial dysostosis) is a congenital developmental disorder of the craniofacial region. The cause of the syndrome is an anomaly in the differentiation of the first and second pharyngeal arches, which occurs during intrauterine development of the fetus [1, 2]. The disease is characterized by bilateral symmetrical oto-mandibular dysplasia without limb anomalies and leads to a number of head and neck defects [1].

EPIDEMIOLOGY

The incidence of Treacher Collins syndrome has been estimated by various researchers to range from 1 in 25,000 to 1 in 70,000 live births (most often reported as 1 in 50,000) [1–3].

OBJECTIVE

The aim of this study is to analyze the literature, present a description of the Treacher Collins syndrome and review a clinical case in a patient under observation in an orphanage (St. Petersburg).

MATERIALS AND METHODS

International and national scientific publications, analysis of clinical cases in the literature, medical documentation of the orphanage.

DISCUSSION AND RESULTS

Treacher Collins syndrome has an autosomal dominant and, less commonly, autosomal recessive pattern of inheritance, but, despite some well-known familial cases, for the most part (the authors note, 60% or more) the mutation is sporadic [4–6].

TCS is genetically and phenotypically heterogeneous. Based on the mutation of a specific gene, authors distinguish from three to four types of TCS.

1) type 1 — mutation in the *TCOF1* gene;
2) type 2 — mutation in the *POLR1D* gene;
3) type 3 — mutation in the *POLR1C* gene;
4) type 4 — mutation in the *POLR1B* gene.

Up to 93% of all cases of Treacher Collins syndrome are type 1 syndrome. TCS type 1 is associated with mutations in the *TCOF1* gene, which is located on chromosome 5q32-q33.1 [1, 2, 5, 7, 8]. The mode of inheritance is autosomal dominant with 90% penetrance and variable expressivity, including patients within the same family. There are known observations of children with pronounced clinical manifestations of the syndrome in one family, while one of the parents was found to have the same mutation without pronounced clinical manifestations of the disease [1, 4].

Type 2 of Treacher Collins syndrome is caused by a mutation in the *POLR1D* gene on chromosome 13q12; Type 3 — mutation in the *POLR1C* gene on chromosome 6p21 [1, 6, 7].

The first 3 types of Treacher Collins syndrome are noted by the authors of the articles, and the authors in more recent publications distinguish the 4th type of TCS based on the newly identified mutation in the *POLR1B* gene [2].

According to the authors of the researched publications, there is no correlation between the clinical features of patients and the gene in which mutations occur, therefore the classification of the syndrome by type of affected chromosome is conditional [3, 9, 11].

The authors also note a large share of intrafamilial phenotypic variability in this syndrome. For example, in one familial case, the proband suffered from severe craniofacial deformities and conductive hearing loss, while the proband's mother was a carrier of the same gene mutation variant but had mild lesions [8].

CLINICAL MANIFESTATIONS

Treacher Collins syndrome is a condition with high phenotypic variability, both in intrafamilial and in sporadic cases.

People with TCS have characteristic facial dysmorphism with bilateral symmetrical malar hypoplasia (95% of cases) and mandibular hypoplasia (78% of cases), leading to micrognathia and malocclusion.

Abnormalities of the external ear, such as microtia or anotia, external auditory canal atresia, and abnormal development of the auditory ossicles (60% of cases), are often observed, causing conductive hearing loss [7, 9, 10].

Pharyngeal hypoplasia is common, which in turn can contribute to feeding problems and/or difficulty breathing.

Choanal atresia and eyelid coloboma have been described (69% of cases), accompanied by the absent eyelashes. Features include complex disorders in the structure of the temporomandibular joint, which leads to a limited ability to open the mouth of varying degrees of severity [1, 7].

People with TCS may develop hearing loss due to sound waves not passing through the middle ear (conductive hearing loss, 77% of cases). The outer ear may be crumpled or rotated, but the inner ear is usually not affected [1].

The severity of deformities does not increase with age [2, 8]. The syndrome is not a progressive disease.

Mental retardation occurs in 5% of people with TCS [1]. 60% of children have poor speech quality resulting from hearing impairment [11, 12].

As a result of the above, we can make the assumption that the likelihood of developing mental retardation correlates with the pathology of the auditory system, which complicates the development of active speech and leads to problems with mastering the curriculum.

CLINICAL CASE

Patient F., 08.09.2022 (9 months), has been in the orphanage since 6 months 12 days. From the anamnesis vitae, it is known that the mother's pregnancy proceeded against the background: class 2 obesity, stage 2 hypertension, varicose veins of the lower extremities, vaginitis, gestational diabetes mellitus, preeclampsia, chronic kidney disease, uterine scar. The delivery was preterm, operative, at a gestational age of 33 3/7 weeks. At birth, body weight was 1130 g, body length 37 cm. Apgar score was 4/6/7 points.

From the moment of birth, a serious condition due to respiratory failure, circulatory failure, immaturity, intra-amniotic infection, intrauterine growth restriction. He was intubated in the delivery room. From the first days of life to 6 months, he received antibiotics (including from the reserve group), inhaled corticosteroids, was on artificial ventilation, and had blood transfusions due to regularly occurring infections. At 2 months of life, a tracheostomy was performed. At 5 months, percutaneous endoscopic gastrostomy was carried out.

Anamnesis morbi. At birth, the phenotype allowed us to suspect Treacher Collins syndrome, because multiple congenital malformations (CM) were identified: underdevelopment of the zygomatic bones, ptosis of the upper and lower eyelids, abnormally developed low-set ears, flat nasal bone, high-arched palate, incomplete cleft of the upper gum, micrognathia, retrognathia, glossoptosis. Subsequently, the presumptive diagnosis of TCS was confirmed by laboratory tests.

The patient has the following congenital malformations (with noticed frequency of their occurrence within the framework of the TCS):

1) hypoplasia of the bones of the facial part of the skull, including: underdevelopment of the zygomatic bones, flat nasal bone, stenosis of the nasolacrimal duct OU, mandibular hypoplasia, micrognathia, retrognathia, glossoptosis, high-arched palate (in the sources these symptoms are described as very common, they are registered in 91–97% of cases);
2) CM of the organ of vision, including: OU — blepharophimosis, hypertelorism, grade 3 bilateral microtia (reported in sources in 77% of cases);
3) CM of the hearing organ, including: abnormally developed low-set ears (reported in sources in 60% of cases).

This patient also has symptoms classified as rare within the TCS:

- choanal atresia on both sides (up to 25% of cases);
- incomplete hard palate cleft and complete soft palate cleft (up to 33% of cases).

The operations performed on him (gastrostomy and tracheostomy) in the studied sources are also classified as rare:

- gastrostomy (up to 28% of cases);
- tracheostomy (up to 18% of cases).

The above allows us to infer that in most cases, patients with TCS have less pronounced phenotypic manifestations than the presented clinical case.

The boy was extremely premature at the time of birth, but a study of the sources allows us to conclude that this situation is in many ways rare. In the literature we studied, only one clinical case indicated preterm delivery (at 37 weeks of gestation); in most cases, delivery was urgent and spontaneous [6, 10].

At the moment, the child has a physical developmental delay, which is assessed by the centile method as very low, with retarded growth and body weight (corresponding to 6 months of age). There is no underweight.

CONCLUSION

The child has common congenital malformations characteristic of TCS: hypoplasia of the bones of the facial part of the skull, congenital defects of the organ of vision, congenital anomalies of the organ of hearing, which initially made it possible to phenotypically suspect this syndrome, which was later confirmed by laboratory tests.

At the same time, this patient has rare CM: choanal atresia on both sides, incomplete hard palate cleft and complete soft palate cleft. The following operations were performed: tracheostomy and gastrostomy (which are also rare for this syndrome).

The causes of prematurity, physical developmental delay, and the generally more severe condition of our patient compared to other clinical cases of TCS were the mother's pregnancy pathology (uterine scar, chronic infection, preeclampsia, stage 2 hypertension, class 2 obesity, gestational

diabetes mellitus), which led to preterm surgical delivery, as well as intrauterine infection, which complicated the patient's condition and led to an undulating course infectious process for up to 6 months of his life.

INFERENCE

Treacher Collins syndrome is characterized by multiple congenital malformations of the facial part of the skull. The syndrome is transmitted in an autosomal dominant type and is characterized by preserved intelligence.

In the clinical case presented by us, the child has multiple CM, typical of TCS, but the severity of the child's condition is due to prematurity at 33 3/7 weeks of gestation, which is not characteristic of the described syndrome.

Due to the fact that TCS is not a progressive disease, patients often have preserved intelligence, so the child has a relatively favorable clinical prognosis for managing the disease and satisfactory rehabilitation potential using modern medical and surgical treatment methods, as well as methods of habilitation and rehabilitation of children.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent for publication. The authors obtained written consent from the patients' legal representatives for the publication of medical data.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие законных представителей пациентов на публикацию медицинских данных.

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