Treacher-Collins Syndrome: Case Series

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ABSTRACT

Aim The aim of our report is to describe the most common features and some of the associated complications of TCS and to report the involved genetic mutations that lead to this disorder.

Case Report Patients typically present with downslanting palpebral fissures, lower eyelid colobomas, microtia, malar and mandibular hypoplasia which could lead to respiratory distress. Care for these patients requires a multidisciplinary team from birth through adulthood. Proper planning, counseling and surgical techniques are essential for optimizing patient outcomes. Moreover, TCS patients may require additional psychological care to avoid being rejected by society.

Discussion Treacher Collins syndrome (TCS) is one of the rare genetic disorders characterized by symmetrical craniofacial malformation without affecting the growth or neurological development. This autosomal dominant disorder has a variable degree of phenotypic expression.

Conclusion PTreacher Collins syndrome is rare and a complex congenital disorder with a variable degree of craniofacial deformity. It does not associate neurodevelopmental impairment. Patients usually suffer from social distancing and failure to integrate properly with the socitey due to their physical appearance. Taking care of these patients requires a multidisciplinary team and a reconstructive treatment is important for their social and psychological wellbeing.

Keywords Dentistry, Franceschetti-Zwahlen-Klein Syndromegenetic syndrome, Mandibulofacial dysostosis, Syndromes, Treacher Collins syndrome

Introduction

Mandibulofacial dysostosis (Treacher - Collins syndrome or Franceschetti - Zwahlen - Klein Syndrome) is a rare genetic disorder that commonly leads to craniofacial dysmorphism. It is an autosomal dominant disorder with a variable degree of phenotypic expression (1). TCS is generally characterized by external and middle ear anomalies, antimongoloid obliquity of the eyelids, ocular hypertelorism, coloboma of the lower eyelids, absence of eyelashes, hypoplasia of the pinna and outer auditory canal, and hypoplasia of the mandible (2).

The disease was first described by Franceschetti and Zwahlen as a congenital deformation of the jaw and facial bones. There is no chromosomal anomaly in this disease, but the anomaly is potential at the gene level (3). Some researchers have concluded that this disease is caused by poor blood conduction in the area of the internal carotid artery, up to the stapedial artery. The researchers reported that poor blood conduction inhibits (limits) the normal growth and development of the fetus during the fetal development stage. The degree of this inhibition may also extend to include tissue parts originating from the first and second Branchial arches (4).

More extensive research has been done on this disorder by Poswillo and Roa (5, 6). In severe cases, hypoplasia of the orbit or aplasia of the bone edge of the orbit may be seen. In the majority of cases, the nose is disproportionately large or there may be no nasal bone. Poor bone development often results in malocclusion. Due to hypoplasia of the mandible, compression and crowding may occur in the lower teeth. The prognathic upper jaw causes an open bite in the area of incisors. Although cleft lip was not documented, cleft palate was detected in 1/3 of the cases. Macrostomy is prevalent in these cases, and the patient's appearance resembles a fish in profile (7).

The severity of the disease varies. In some cases, the manifestations are minimal and barely noticeable. In this case, it is difficult to distinguish the affected individuals from healthy ones. In some families, miscarriage and early postnatal deaths are common. However, sometimes such a situation may not occur and the syndrome is transmitted from generation to generation. Due to the syndrome's autosomal dominant transmission, the disorder is definitely seen in the next generation. This does not definitely mean that all the siblings are going to be affected by the disorder. In his research on animal specimens showing similar orofacial syndrome pathogenesis, Postwillo observed that preotic neural crest ectomezenchymal cells migrating to the face and primitive ear were destroyed (5). The researcher has shown that these are the cells that affect the development of the skeleton, mandible and the lower part of the face. There is no apparent cure for this disease. However, a number of surgical interventions are applied for aesthetic and reconstructive purposes.

The rarity of this syndrome alongside with its transmission from generation to generation causing chin and facial defor-

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mities as what we encountered in two siblings and in a single child of a family with no previous history of such a syndrome constitute the subject of our article.

Case Report

Our first two cases were two siblings who applied for dental crowding and pre-surgical orthodontic treatment. The older sibling was a 19-year-old male, and the younger was an 18-year-old female. In the anamnesis, it was understood that the patients who were born with normal delivery had a different appearance from the time of birth, but the family did not seek any treatment for a long time. Family history of the patients, revealed that such cases were also encountered in previous generations. A family tree was prepared based on the information obtained from the patients.

When the family tree was made, it was determined that besides our cases, mothers, grandmothers and fathers of their grandmothers were also affected by this disease. Among the diseased individuals in the family, only the mother and her two children are alive. Our cases represent two of the six siblings in the family who were affected. The other four are healthy. The disease is transmitted from generation to generation by carrying an autosomal dominant character.

Our first case was an 18-year-old woman with a face shape that had the characteristic features of the disease. Palpebral fissures were prominent. Antimongoloid obliqueness and coloboma on the lower eyelids were detected in the eyes of the patient, and the eyelashes were missing. The eyes were hyperteloric and the nose disproportionately large. A mild deformity was detected in the auricle of our case. Ears were relatively low and the patient had hearing difficulties. Very stiff hairs were obvious, starting just in front of the upper edge of the auricle and continuing as a band to the middle of the cheek. The patient had a fish-like appearance when viewed in profile, due to micrognathia in the lower jaw and anterior thrust in the upper jaw (Figure 1).

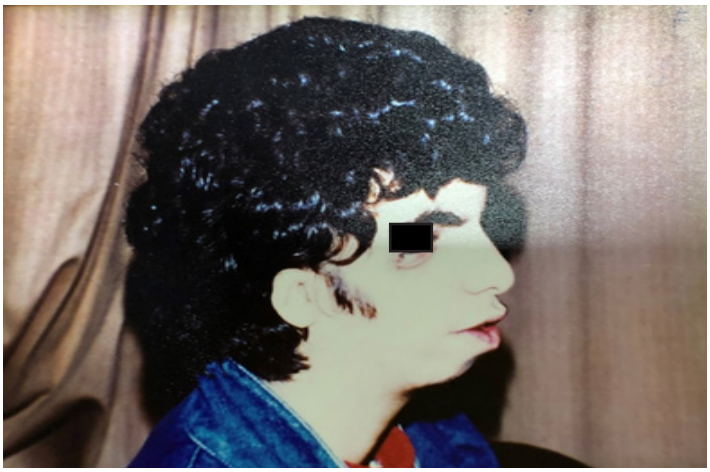

Figure 1: Right profile view of the patient

In the oral examination, although the condition of the teeth was quite good, it was observed that the gums were edematous. This is related to the patient's inability to close his lips and mouth-breathing as a result of the open bite caused by the incompatibility of the jaws. Our patient had a crowding in the lower teeth and remaining root belonging to tooth number 25. During the examination, it was decided to remove this root.

Our second case was a 19-year-old male patient, who had the characteristic features of the disease, but was mildly affected by it. Eyes were hyperteloric and palpebral fissures were prominent. There was no deformity in the ears, but they were relatively low (inferiorly positioned). The patient also had mild hearing impairment. This patient does not have the hair growth seen in his sister. Similar to the first case, due to micrognathia in the lower jaw and prognathia in the upper jaw, there was a fish-like appearance when viewed from a face profile (lateral profile) (Figure 2). Oral examination revealed good oral hygiene. There was no need for orthodontic treatment before surgery for the patient's tooth crowding. No additional pathology was detected in the radiographic examination. Dentally, it was decided to perform endodontic treatment for tooth no. 16, which was diagnosed with deep dentin caries, and extraction of remaining roots of teeth no. 36 and 46.

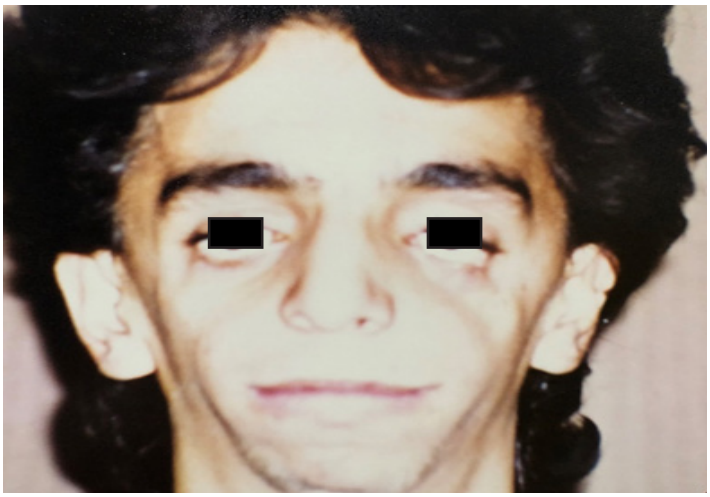

Figure 2: Front view of the patient

Our third case was a 9-year-old female. Our patient showed all the features of this syndrome like the antimongoloid obliqueness, coloboma in the eyelids and no eyelashes in the lower eyelid were observed. In addition, the ear deformity in our patient was advanced and there was a hearing loss of 40%. Our patient, who stated that she had been using a hearing aids since the age of four, also had micrognathia in the lower jaw and the patient's profile was fish-like.

Oral examination showed good oral hygiene. It was observed that she was a mouth breather due to malocclusion and as a result the patient suffered from periodontal problems. There was a crowding in the teeth. Periapical lesions caused by caries in teeth 36-46 were seen in periapical and panoramic radiographs.

Submandibular lymphadenopathies were detected on both sides due to decayed teeth. It is interesting that there were no abnormal features in the family history of our patient. Although the syndrome is known to be autosomal dominant. İt was not previously encountered in our patient's family, and it was encountered for the first time in our case which means that a patient may suffered from a sudden mutation at the gene level. It is also worth mentioning that the other siblings of our patient did not have such an anomaly.

In the medical history taken, it was learned that our patient was born by Caesarean section and was exposed to cord entanglement. The patient was admitted to extract the decayed teeth and to treat the restorable ones under general anesthesia. However, the patient could not tolerate general anesthesia and treatment could not be continued due to tachycardia. Later on the patient applied to our faculty and was advised to have her decayed and unrestorable teeth extracted with local anesthesia, get her periodontal problems solved and undergo the recommended orthodontic treatment required prior to the surgical intervention planned to correct the jaw deformities after the age of 18.

Discussion

Treacher-Collins syndrome is a disease characterized by antimongoloid obliqueness of the eyelids, ocular hypertelorism, coloboma and absence of eyelashes of the lower eyelids, ear anomalies and hypoplasia of the mandible. The face is quite remarkable. All three of our cases have all the features of this syndrome and a bird's face appearance is dominant. There is micrognathia in the lower jaw, anterior thrust and open bite in the upper jaw.

Even though a minimal ear deformity was noticeable in the first case there was no ear deformity in the second case. However, in both cases, the ears were inferiorly positioned. In our third case, the ear deformity was severe and the airway was found to be obstructed. Hearing impairment is an important feature in such cases. All three of our cases have hearing impairment. Especially in our third case, the hearing difficulty was more severe and it was learned that the patient had been using hearing aids since the age of 4. TCS affected patients must have audiological testing and an early hearing abilities check must be carried out by a specialist as soon as possible. Speech therapy, bone conduction amplification and hearing aids are useful means to help aquire new communicational skills. Unfortunately, external ear and auditory canal reconstruction surgeries rarely help in hearing improvement. (8).

The disease has a familial course due to its autosomal dominant transmission (9, 10). There is familial transmission in our first two cases. The syndrome is passed on from generation to generation. On the maternal side of our cases, at least one patient is encountered in each generation. However, in our third case, this syndrome is seen for the first time in the family. The cause of this event is attributed to mutation.

Since it is autosomal dominant, it is likely to be seen in future generations in the family. In the literature, cleft palate was found in 1/3 of the cases (2). In our cases, however, such a situation was not observed. On the other hand, as seen in many cases, the profiles of our patients took on a fish-like appearance. The severity of the disease varies (11). In some cases, the disorder's effect is barely noticeable. Although the features in our cases were the defining characteristics of the disease, the male patient was less affected than his sister. The mothers of the patients are the least affected individuals. In our third case, the characteristic face shapes and severe ear deformity were remarkable.

Miscarriage and early postnatal deaths are common in some families (12). It was learned that there was no miscarriage or early postnatal death in the family of our first two cases, therefore the disease was passed on from generation to generation. The disease does not necessarily affect all individuals in a generation. As seen in our cases, only two of the six siblings were affected. It was stated that there was no miscarriage or early postnatal death in the family of our last case, and that such an anomaly was encountered for the first time. There is no mental retardation in Treacher - Collins syndrome, but the affected persons are usually shy due to their physical characteristics (4). It was obvious that our patients were shy because of their physical features and were in need for psychological counseling as soon as possible.

Conclusion

Treacher Collins syndrome is rare and a complex congenital disorder with a variable degree of craniofacial deformity. It does not associate neurodevelopmental impairment. Patients usually suffer from social distancing and failure to integrate properly with the socitey due to their physical appearance. Taking care of these patients requires a multidisciplinary team and a reconstructive treatment is important for their social and psychological well-being.

Declarations

Author Contributions: *Conception/Design of Study- M.Y.K., O.E.B., M.A., T.S., R.S.; Data Acquisition- M.Y.K., O.E.B., M.A., T.S., R.S.; Data Analysis/Interpretation- M.Y.K., O.E.B., M.A., T.S., R.S.; Drafting Manuscript- M.Y.K., O.E.B., M.A., T.S., R.S.; Critical Revision of Manuscript- M.Y.K., O.E.B., M.A., T.S., R.S.; Final Approval and Accountability- M.Y.K., O.E.B., M.A., T.S., R.S.; Material and Technical Support- M.Y.K., O.E.B., M.A., T.S., R.S.; Supervision- M.Y.K., O.E.B., M.A., T.S., R.S.*

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