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Treacher Collins Syndrome associated with foot deformity and genital anomalies

Ayak deformitesi ve genital anomali ile birliktelik gösteren Treacher Collins Sendromu

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Treacher Collins syndrome (TCS) is a rare syndrome also known as mandibulofacial dysostosis. It mainly affects facial morphology and therefore, most reports have focused on the facial features of this syndrome. This is the first report of a newborn with typical features of TCS having micropenis, cryptorchidism and metatarsus adductus deformity.

Key words: ***Metatarsus adductus deformity, micropenis, Treacher Collins syndrome***

Treacher Collins sendromu, mandibulofasiyal disostozis olarak bilinen nadir bir sendromdur. Sendrom başlıca yüz morfolojisini etkiler. Treacher Collins ile ilgili yayınların çoğu sendromun fasiyal özelliklerine odaklanmıştır. Bu yazıda mikropenis, kriptoorşidizm ve metatarsus adduktus deformitesine sahip Treacher Collins sendromlu bir yenidoğan sunulmuştur.

Anahtar sözcükler: ***Metatarsus adduktus deformitesi, mikropenis, Treacher Collins sendromu***

Treacher Collins syndrome is an autosomal dominant genetic disorder and affects mainly the head and face. The incidence is estimated to range from 1 in 40 000 to in 70 000 live births. The patients with TCS have usually characteristic bilateral facial anomalies (1). This article reports a case of Treacher Collins syndrome with the presence of genital anomalies and foot abnormality that has not been previously described clinically in this disorder.

Case Report

Sixteen hours old, full term male newborn was referred to our clinic because of a distinctive facial appearance. He was the first child born to a 23-year-old woman. Both parents were normal, and there was no family history of congenital defects, especially facial anomaly. The parents were first cousins. The antenatal period of the mother and delivery had been uneventful. The baby was delivered by spontaneous vaginal way. On physical examination, he weighed 2300 g (< 5%), he was 44 cm in height (< 5%) and his head circumference was 34.5 cm at birth (25%). He was considered to be small for gestational age. He had a triangular face, and long and thin hairs. There were hypertelorism (interpupillary distance was 5 cm, >97%) and proptosis. His palpebral fissures were downslanted. Malar region was hypoplasic. There were sparse eyelashes. His ears were dysplastic, small (2 cm, < 3%), and low-set. External auditory canals were atretic, therefore ear membranes could not be seen. He had also micrognathia (Fig. 1, 2).

Apart from his facial defects, he had cryptorchidism on the left, micropenis (penile length was 0.5 cm, < 10 %, normal age matched penile length 2.5-5 cm) and metatarsus adductus deformity in both feet (Fig. 3). All the other system examinations were normal. Chromosomal analysis revealed no abnormality.

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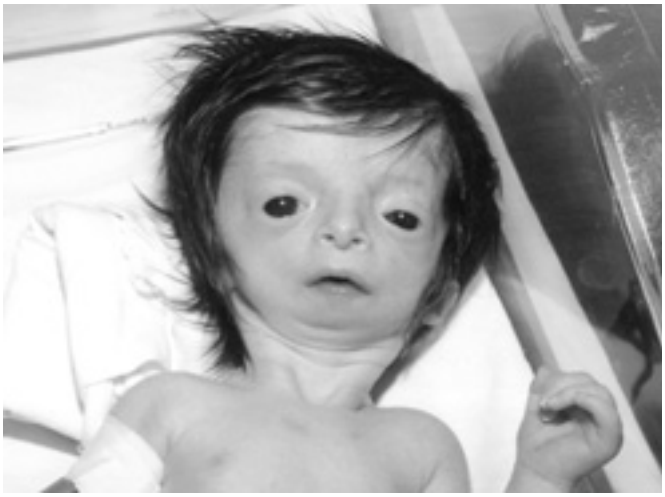

Figure 1. Typical facial appearance of Treacher Collins syndrome from the front.

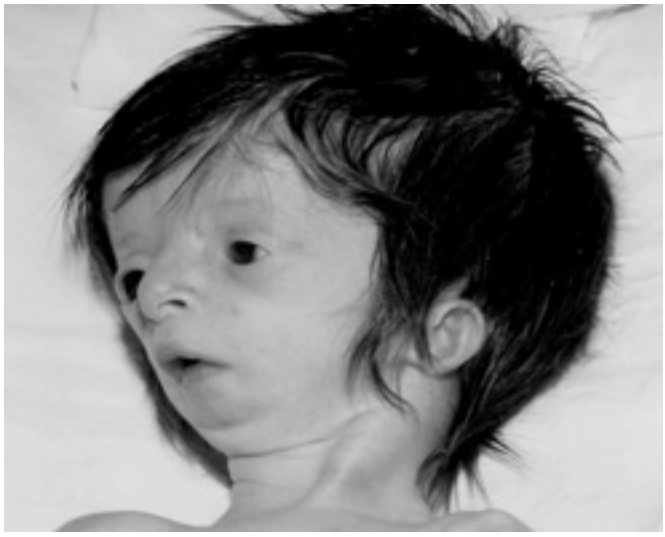

Figure 2. Typical facial appearance of Treacher Collins syndrome from the site.

The patient was investigated for additional anomalies. Abdominal and transfontanel ultrasonography, and echocardiography were normal. Cranial MRI was performed for evaluation of the additional brain anomalies, however no abnormality was found. Bilateral unpneumatized mastoid bones and stenotic external auditory canals were observed on temporal CT (Fig. 4).

The patient was discharged at 10 days of age and came to control 2 weeks later. The parents said that he did not have any problem and his physical examination revealed no abnormality. During this two weeks period, he did not gain weight. Parents were educated about feeding and he was given a control appointment 1 month later. Since the patient did not show up at the appointment we called the parents who said that the patient was unexpectedly found dead at his bed after feeding.

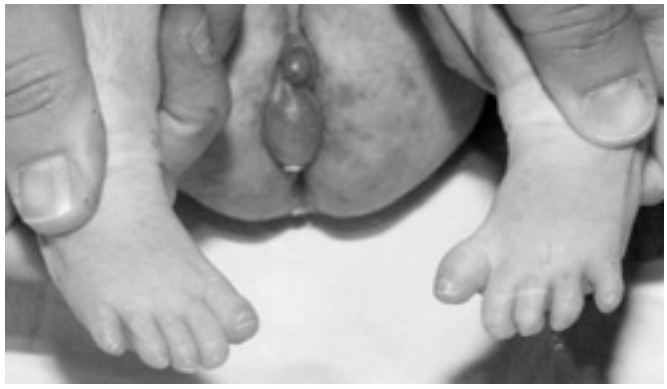

Figure 3. Micropenis and metatarsus adductus deformity in both feet.

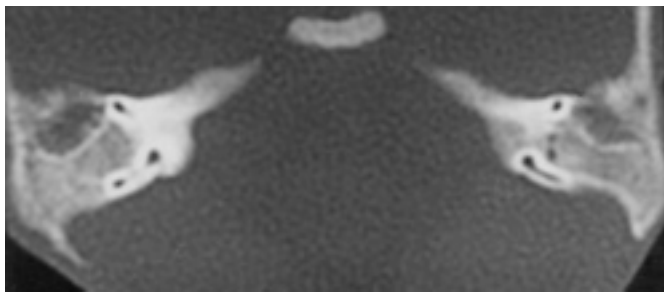

Figure 4. Bilateral unpneumatized mastoid bones on temporal CT.

Discussion

Treacher Collins syndrome is rare. The main features are symmetrical facial abnormalities consisting of malformed ears, malar hypoplasia, coloboma of the lateral part of the lower lid, mandibular hypoplasia, cleft palate and conductive hearing loss. In cases with full expression of the syndrome, TCS can be diagnosed easily on the basis of the clinical appearance. However, there are a few syndromes with similar clinical manifestations such as Nager syndrome, Goldenhar's syndrome, Miller's syndrome (digit and limb abnormalities, and acrofacial dysostosis), and Hutterite mandibulofacial dysostosis. Especially, Nager syndrome should be distinguished because genital anomalies and foot abnormalities may accompany in these patients. The thumbs are hypoplastic or absent, the radius and ulna may be fused or there may be absence or hypoplasia of the radius and/or one or more metacarpals in this syndrome. Lower lid colobomas are rarer, cleft palate is more frequent, and the mandible is more severely retarted in growth than TCS (2). Since no limb abnormality was found in our patient, we considered that a diagnosis of Nager syndrome is unlikely.

TCS is caused by haploinsufficiency of the TCOF1 gene. TCOF1 gene affects facial development. The TCS locus has been mapped to chromosome 5q31.3-32. The TCOF1 gene contains 26 exons and encodes a 1411 amino acid protein named treacle. In the TCOF1 gene 51

mutations have been identified. Most of these mutations are insertions or deletions, which result in an introduction of a premature termination codon into the reading frame. About 40% of the cases have a previous family history. 60% of cases possibly arise as a result of *de novo* mutations (3). All Treacher Collins patients and their families should be evaluated to determine if the disease has been caused by inheritance of a family trait or as a result of a spontaneous gene mutation (4, 5). Unfortunately, genetic evaluation and careful prenatal screening of these patients have been accomplished extremely rare. Linkage analysis can be used to identify affected individuals even in the absence of clinical and radiological evidence of TCS. Marres et al (1) reported that the diagnosis of TCS could be made in 13 persons after clinical examination. In addition to the 13 persons with TCS, gene linkage studies showed positive linkage to chromosome 5q32-33.2 in three persons with clinical nonpenetrance. Since linkage analysis can not be performed in our city, we could not perform gene analysis in both patient and his parents. There was not any facial abnormality in family history, however it is known that if only minor stigmata are present as in some cases, diagnosis becomes more difficult. In this situation, diagnosis is determined by gene analysis.

The most common abnormalities recognizable radiologically are zygomatic arch and mandibular hypoplasia in the TCS. These findings are useful to confirm the diagnosis in some cases if only minor stigmata are present. Jahrsdoerfer et al (6) reported that there were three radiographic findings noted on CT scanning that made the TCS group unique and separated them from nonsyndromic patients with microtia and aural atresia. First, there was absence of mastoid pneumatization. In no patient with this syndrome was the mastoid bone found to be pneumatized. Second, there was ossicular dysjunction. The third finding was a commonly seen bony cleft in the lateral aspect of the temporal bone just anterior to the mastoid. In our case, temporal CT demonstrated bilateral unpneumatized mastoid bones and stenotic external auditory canals. There was no ossicular dysjunction and no bony cleft.

The complications of this syndrome include respiratory difficulties (upper airway obstruction, obstructive sleep apnea) due to midface and mandibular hypoplasia and feeding difficulties in the newborn period. Breathing problems can occur at birth and during sleep when the base of the tongue obstructs the small hypopharynx (7). In our case, infant was unexpectedly found dead in his crib at home of apparent clinical stability before death. It was learnt that he was stabile clinically before death. Although autopsy report would be very useful to diagnose the reason of the death, autopsy could not be performed. Death was considered most likely due to airway obstruction related to mandibular hypoplasia.

Treacher Collins syndrome mainly is characterized by facial abnormalities. The cases reported in the literature who had typical facial abnormality together with the other abnormalities were rare. Robb et al (8) reported a case with tracheo-oesophagial fistula, rectovaginal fistula and anal atresia. Hansen et al (9) reported a severely affected case with arhinia and uveal colobomas together with almost absent ears. In one case, a patient with TCS and dermatomyositis was reported (10). Bruni et al (11) used genotyping with flanking DNA markers to ascertain Treacher Collins Franceschetti syndrome (TCOF1) in a subject affected by tetralogy of Fallot and cryptorchidism. They found cardiac malformation and cryptorchidism unrelated with TCS in this patient. Since genetic evaluation was not available, we could not evaluate the relation of anomalies present in our patient with TCS.

This article reports a case of Treacher Collins syndrome with the presence of genital anomalies and foot abnormality, which are possibly coincidental symptoms, however have not been previously described clinically in this syndrome.

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