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Case Report

A Novel *TCOF1* Variant of Treacher Collins Syndrome

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Abstract

We report a newborn patient who was consulted for her dysmorphic facial features. She was born at 37 gestational weeks as 2970 gr (25 p-50 p) through vaginal route. Her birth height was 50 cm (50 p) and head circumference was 33.3 cm (<3p). She cried immediately after birth but she had dyspnea and feeding difficulties that were caused by cleft palate. We examined the patient at postnatal fourth day. She was the second child of non-consanguineous parents. Her mother had a history of spontaneous abortus before her. The parents did not have any diseases also there is no history of similar illness in the family.

Keywords: Treacher collins syndrome; Child; *TCOF1* gene

Introduction

On head-to toe examination, there were down slanted palpebral fissures, broad nasal bridge, hypertelorism, microcephaly, depressed nasal bridge, malar hypoplasia, micrognathia, microtia and cleft palate. On systemic examination, there was pectus deformity and cardiac murmur heard (Figure 1 A-D). On cranial magnetic resonance imaging, abnormal maxillofacial appearance, micrognathia, cleft palate, hypoplasia of external and middle ear, normal brain parenchyma was detected. Echocardiography performed for cardiac murmur revealed atrial septal defect. A heterozygous c. 2952+1G>A variant was found in the *TCOF1* gene (NM_000356.4). As far as we know this splice site variant has not been stated previously. We did not determine this mutation in both parents of the proband. Therefore, it was interpreted de-novo mutation.

Case Presentation

During the long-term follow-up of the patient, recurrent lung infections were observed. At electatic changes were observed in the right lung on thorax CT. On the other hand, she was evaluated by an otolaryngologist due to microtia and it was decided to use a hearing aid. Cleft palate repair surgery was performed in two stages. Currently it continues to be followed with a multidisciplinary approach. TCS is a well described MFD that is inherited autosomal dominantly with an estimated prevalence of 1 in 50,000 live births [1]. Although TCS is also caused by the *PLOR1D*, *POLR1C* and *POLR1B* genes mutations the *TCOF1* mutation is responsible for the majority of TCS cases. Most of these mutations are truncate mutations that mostly cause premature stop codon [2]. Deletions of 5bp in exon were responsible for 17% of TCS cases [3].

Patients with TCS, have characteristic craniofacial features, hearing loss and radiological findings. Characteristic facial features include a bilaterally symmetrical convex facial profile, prominent nose, down slanting palpebral fissures, and microretrognathia. Down-slanting palpebral fissures are seen due to zygomatic arc hypoplasia. An absence of ears, small, malformed and rotated ears is detected external ear anomalies. Along with this, atresia or stenosis of the external auditory canal is also observed. Lower eye lid coloboma is among the most common anomalies. Our patient also had craniofacial features such as downslantig palpebral fissures, malar hypoplasia, cleft palate and mandibular hypoplasia, similar to the literature. In addition our patient also had microtia and external auditory canal atresia. While microcephaly and cardiac malformation were described less frequently in the literature our case had microcephaly and atrial septal defect. Immune deficiency which has not been defined in the literature before was also detected in our patient [1].

In conclusion, we report a penitent who has immune deficiency and a novel variant of *TCOF1*. TCS is a clinically variable disease segregation of parents is necessary. Although the diagnosis is made with common findings, it is necessary to investigate the patient in terms of rarer findings that may accompany.

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Figure 1A-1B: Patient with TCS at birth, characteristic facial features (down-slanting palpebral fissures, broad nasal bridge, microretrognathia, microtia). **C-D**. Patient at 16 months, dysmorphic facial features (down-slanting palpebral fissures, hypertelorism, broad nasal bridge, short philtrum, microretrognathia, bilateral microtia).