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Identification of the audiological and temporal bone radiology manifestations of SOFT syndrome: a case report

Sema Satici[1,2*], Ahsen Kartal[1,2], Elif Dilara Topcuoglu[3] and Zahra Polat[1]

Abstract

Background SOFT syndrome is characterized by prenatal onset growth retardation, brachydactyly, onychodysplasia, postpubertal onset hypotrichosis, normal psychomotor development, and facial dysmorphism including dolichocephaly, elongated triangular face, prominent forehead and nose, and abnormal ear structure. This syndrome has been described in 31 patients worldwide.

Case presentation In this case report, the audiological and temporal bone radiological results of a 4-year- and 5-month-old patient with SOFT syndrome are presented. Bilateral internal acoustic canals (IAC) are dilated with lobulated contour.

Conclusions This case report is the first in the literature as it reports audiological and temporal bone radiology observations in SOFT syndrome. It is thought that regular and detailed audiological and temporal bone radiology evaluations performed in patients with different SOFT syndrome will be a reference for determining the characteristic audiological and temporal bone radiological findings related to this syndrome.

Keywords SOFT syndrome, POC1A gene, Hearing loss

Background

Short stature-onychodysplasia-facial dysmorphism-hypotrichosis (SOFT) syndrome is a rare genetic disorder. SOFT syndrome (MIM no. 614813) is characterized by prenatal onset growth retardation, brachydactyly, onychodysplasia, postpubertal onset hypotrichosis, normal psychomotor development, and facial dysmorphism including dolichocephaly, elongated triangular face, prominent forehead and nose, and abnormal ear structure [1, 2]. The cause of this syndrome is the mutations of the POC1A, and it is an autosomal recessive trait [3].

SOFT syndrome was first described in 2012 by Shalev et al. in eight patients from two different Arab families [4]. The prevalence of SOFT syndrome has not yet been determined. However, Mericq et al. (2022) report that this syndrome has been described in 31 patients worldwide [5].

Since it is a newly defined syndrome, studies investigating its phenotypic and genotypic features are proliferating. However, no studies in the literature performed audiological and temporal bone radiology evaluations in patients with the SOFT syndrome. This study reported the audiological evaluation results of a patient with SOFT syndrome to the Audiology Clinic.

*Correspondence:
Sema Satici
sema.satici@sbu.edu.tr
[1] Audiology Department, Hamidiye Faculty of Health Sciences, University of Health Sciences, Istanbul, Türkiye
[2] Audiology and Speech Disorders Program, Institute of Health Science, Marmara University Istanbul, Istanbul, Türkiye
[3] Department of Radiology, Umraniye Training and Research Hospital, University of Health Sciences, Istanbul, Türkiye

Case presentation

Case history and family history

At 4 years and 5 months, the patient who had undergone an adenoidectomy operation due to a long-standing middle ear infection and had a ventilation tube placed in his right ear by otolaryngology was referred for an audiological evaluation.

Prenatal history revealed skeletal development, growth retardation, and short stature during the 25th weeks were not normal. The prenatal follow-ups of the mother were usual. Risk factors, such as medications and exposure to radiation, were not reported during pregnancy. The mother and father are first-degree relatives.

A male patient with a gestational age of 37 weeks was born by cesarean section. He had a neonatal intensive care unit history of 25 days due to respiratory distress and feeding problems.

The patient had skeletal dysplasia, short stature, brachydactyly, pectus carinatum, and a triangular facial appearance. The parents and siblings had normal phenotypes. Molecular genetic analysis was performed on the patient at the Genetic Diseases Diagnostic Centre at 2 years old. Homozygous intronic splice donor variant (c.103 + 1 G > T) in the POC1A gene (NM_001161580) was detected in the patient, and a diagnosis of SOFT syndrome was established.

The family did not provide any newborn hearing screening result. As a part of the audiological evaluation, acoustic immitansmetry, play audiometry, and distortion product otoacoustic emission (DPOAE) were performed on the patient.

The *immitancemetric* evaluation was performed with an Inventis Flute Plus (Inventis, Padova, Italy) immitansmetry using a 226-Hz probe tone. Tympanometry measurement results were analyzed in accordance with Jerger's tympanogram classification. Play audiometry air conduction hearing thresholds were evaluated with GN Otometrics Madsen Astera2 (GN Otometrics, Denmark) clinical audiometer using Telephonics TDH-39 (Telephonics, Farmingdale, NY, USA) on-ear headphones; we evaluated the bone conduction hearing thresholds using the Radioear B-71 (Radioear Corporation, New Eagle, PA, USA) bone vibratory. After hearing thresholds were determined, pure-tone averages were calculated between 500 and 4000 Hz. The pure-tone audiometry results were classified with Clark's classification of hearing loss.

Temporal bone computed tomography

In terms of an advanced diagnosis, temporal bone computed tomography (CT) imaging with a slice thickness of 0.625 mm was performed. The temporal bone CT revealed narrowed external auditory canals and normal middle ear morphology. On the left tympanic cavity, stapes footplate and round window niche were found to be obliterated with soft tissue density. Bilateral IAC dilated with lobulated contour. On the right temporal bone, IAC diameter was 2 mm at the fundus level, 6.5 mm at the middle portion, and 5.8 mm at the porus level. On the left temporal bone, IAC diameter was 2.2 mm at the fundus level, 6.5 mm at the middle portion, and 6.1 mm at the porus level. The cochlea was found to have normal structural features with 2.5 turn and normal modiolus. It is also found that the vestibule and semicircular canals were having normal morphological radiologic appearance. CT images are given in Figs. 1 and 2. Both external acoustic canals were narrow on temporal bone CT. At CT, a minimum diameter of right and left EAC was 2.3 mm and 1.6 mm, respectively. The tympanostomy tube was visible on the right tympanic membrane (Fig. 3).

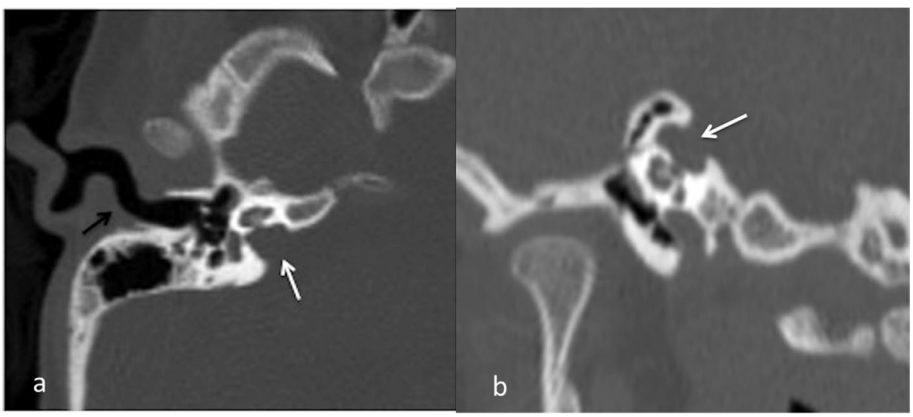

Fig. 1 Axial (**a**) and coronal (**b**) oblique reformatted CT image shows right IAC (white arrows) and right EAC (black arrow)

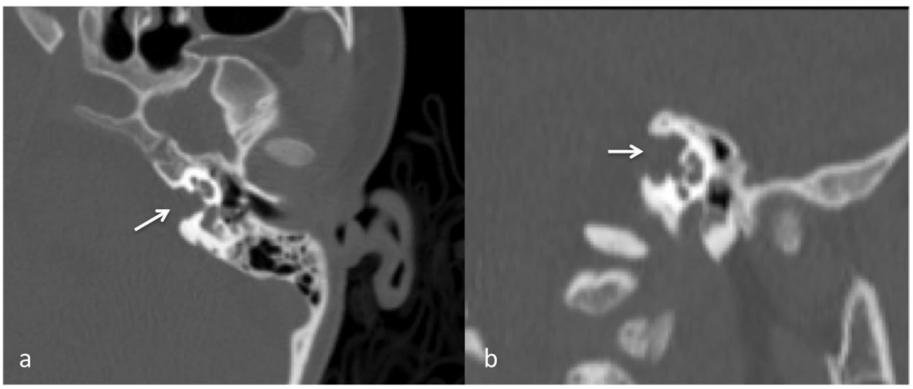

Fig. 2 Axial (**a**) and coronal (**b**) oblique reformatted CT image shows left IAC (white arrows)

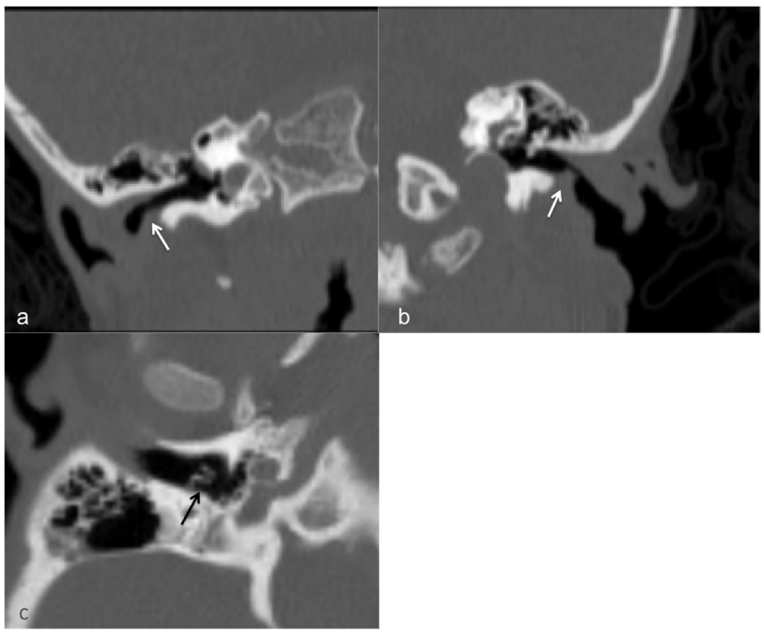

Fig. 3 Coronal oblique reformatted CT image reveals narrowing of right (**a**) and left (**b**) EAC (white arrows). Tympanostomy tube (black arrow) on right tympanic membrane is seen on axial CT image

Audiological assessment

The first audiological assessment was made in University of Health Sciences Umraniye Training and Research Hospital before the patient was discharged from the otorhinolaryngology service. Tympanometric examination using a 226-Hz probe tone revealed a type B tympanogram in the left ear, and the right ear could not be tested. Acoustic immitansmetric examination was not performed on the right ear as it was recently operated on. Additionally, the patient was evaluated with play audiometry. Bilateral moderate conductive hearing loss (Fig. 4A) was found as the result. Masked air and bone conduction thresholds could not be performed as the patient did not cooperate during masking. In this session, DPOAE was not performed due to middle ear pathological findings.

A follow-up appointment was given for 2 months after the first audiological evaluation. Acoustic immitansmetry and pure-tone audiometry were performed in this control session. Tympanometric examination using a 226-Hz probe tone observed a type B tympanogram in the left ear. In the right ear, a tympanogram was obtained with a peak in the positive pressure area (96 daPa). According to the tympanometry result, the

ventilation tube in the right ear was open. According to the pure-tone audiometry, average normal hearing in the left ear was observed, and a conductive component was seen. In the right ear, moderately severe mixed hearing loss (Fig. 4B) was obtained. After the operation, the patient was started on a drug treatment. The left ear air conduction hearing thresholds were within normal limits showing that this treatment resulted in positive progress in the left ear. The patient was referred to the otorhinolaryngology clinic after the audiological evaluation. In this session, emission could not be recorded in the right ear, and DPOAE was not performed due to middle ear pathological finding in the left ear.

An additional follow-up appointment was given for 3 months after the second audiological evaluation. Acoustic immitansmetry, DPOAE, and pure-tone audiometry were performed this session. Type B findings in the left ear were determined using a 226-Hz probe tone. In the right ear, a tympanogram was obtained with a peak in the positive pressure area (99 daPa). According to the tympanometry result, the ventilation tube was still open in the right ear. As a result of play audiometry, normal hearing in the left ear was observed, and there was also a conductive component. In the right ear, moderate mixed hearing loss (Fig. 4C) was obtained. In this session, emission could not be recorded in the right ear, and DPOAE was not performed due to middle ear pathological finding in the left ear (Fig. 4 and Table 1).

Language assessment

The Preschool Language Scale-4 (PLS-4) Screening Test was used for language assessment. The receptive and expressive language age of the patient was compatible with the chronological age.

Discussion

It has been shown that pathogenic variants in the POC1A gene can cause SOFT syndrome, and short stature, facial dysmorphism with hypotrichosis, and facial dysmorphism characterize this syndrome. Li et al. (2021) reported a large pinna in a case with SOFT syndrome [3]. In contrast, Barraza-García et al. (2016) reported that their cases had relatively small pinna [6]. Because of the scarcity of studies on SOFT syndrome in the literature, no pinna size characterizing this syndrome has been defined. In the present case, the patient has short stature, a triangular facial appearance, and brachydactyly in line with other studies. We observed that the pinna size was compatible with the head size. However, it was reported by the ENT doctor that the external auditory canal was narrow on both sides. This observation was confirmed using CT imaging. The ventilation tube could not be placed due to narrowness of the left ear canal.

This case with SOFT syndrome has a history of otitis media. It is not known whether this condition developed because of the syndrome. The case had received medical treatment due to their history of otitis media. The tympanometric evaluation performed on the patient revealed that the left ear benefited from the medical treatment, and the ventilation tube in the right ear was open. Taking the mixed type of hearing loss in the right ear and the syndrome into consideration, a radiological assessment was used to evaluate middle and inner ear malformations in the final audiological evaluation.

On radiological assessment, the patient has normal cochlea and vestibular structures. On both sides, IACs

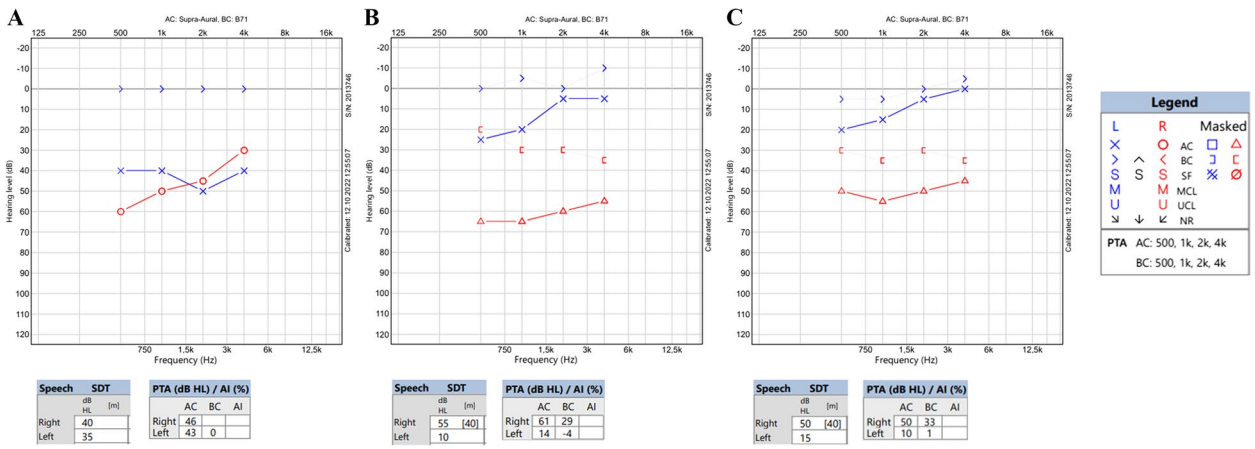

Fig. 4 Pure-tone audiometry results. **A** Initial audiological evaluation. **B** Audiological evaluation results after 2 months. **C** Audiological evaluation results after 5 months

Table 1 The results of the evaluation of the tympanometry and otoacoustic emission test

Sessions	Tests	Right ear	Left ear
Initial evaluation	**Tympanometry**	NT	Type B
	DPOAE	NT	NT
After 2 months	**Tympanometry**	Atypical	Type B
	DPOAE	Not observed	NT
After 5 months	**Tympanometry**	Atypical	Type B
	DPOAE	Not observed	NT

NT Not tested

were dilated and have lobulated contour. Sakashita et al. demonstrated that in their autopsy, specimens of patients with 1 month to 72 years of age have normal diameter of IACs at the fundus, and a middle portion and porus of the canal ranged between 3.7 and 5.6 mm, 3.2 and 6.5 mm, and 2.9 and 6.4 mm, respectively [7]. The 4-year-old patient described in this study presented with an IAC diameter 2 mm at the fundus, 6.5 mm at the middle portion, and 5.8 mm at the porus level of the canal on the right side and 2.2 mm, 6.5 mm, and 6.1 mm on the left side, respectively. Both IACs of our patient were enlarged on the middle portion and narrowed at the fundus level.

The relationship between dilated IAC and audiological findings is not clear. Studies demonstrate that dilated IAC is associated with sensorineural hearing loss [8–10]. However, most have inner ear malformations accompanying dilated IAC. As this case presented and found alone dilated IAC, it is difficult to comment on whether this situation affects the existing hearing loss. It is thought that the hearing loss in the right ear may be related to the dilated IAC.

The patient described in this study has normal middle ear morphology on both sides. The soft tissue density at the left stapes footplate may have caused conductive hearing loss by preventing the normal function of the oval window.

Conclusions

This case report is the first in the literature as it reports audiological and temporal bone radiology observations in SOFT syndrome. It is thought that the regular and detailed audiological and temporal bone radiology evaluations performed in patients with different SOFT syndrome will be a reference for determining the characteristic of audiological findings related to this syndrome.

Abbreviations

IAC	Internal acoustic canal
DPOAE	Distortion product otoacoustic emission
CT	Computed tomography
PLS-4	The Preschool Language Scale-4
ENT	Ear-nose-throat
PTA	Pure-tone average
SDT	Speech detection threshold

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Authors' contributions

All authors read and approved the final manuscript. Manuscript preparation, SS, AK, and EDT. Manuscript revision, ZP. Concept and design, SS and AK.

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Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent for publication of the child's clinical details and/or clinical images was obtained from the patient family.

Competing interests

The authors declare that they have no competing interests.

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