B-ENT, 2019, **15**, 209-215

Does cholesteatoma matrix removal impair hearing in patients with low-grade labyrinthine fistulas?

M.K. Balci[1], E. Eren[1], K. Önal[1], S. Arslanoğlu[1]

[1]Department of Otorhinolaryngology and Head & Neck Surgery, Katip Çelebi University Atatürk Training and Research Hospital, İzmir, Turkey.

Key-words. Bone conduction; cholesteatoma; fascia; labyrinthine fistula; mastoidectomy

Abstract. *Objective*: To evaluate the functional outcomes of labyrinthine fistula treatment when the cholesteatoma matrix is totally removed and the defect is sealed with temporalis fascia during the same procedure.
Materials and methods: Records of 188 patients who underwent middle ear surgery for chronic otitis media with cholesteatoma between June 2008-June 2014 in a tertiary referral center were retrospectively reviewed. Incidence of labyrinthine fistula, preoperative findings, types of surgery, intraoperative findings and postoperative functional outcomes were analyzed.
Results: Incidence of labyrinth fistula was 17% (n=32). Lateral semicircular canal (LSSC) was the most frequent site for the fistula (90.6%). Thirty-two patients (10 females, 22 males) suffered this complication. Twenty-one patients underwent Canal Wall Down (CWD) Mastoidectomy without tympanoplasty and 11 patients underwent CWD Mastoidectomy + myringo-stapediopexy. Cholesteatoma matrix was removed and the defect was sealed with temporalis fascia (without using any other sealing material) in all cases. Bone conduction (BC) hearing level improved or remained unchanged in 24 patients; whereas eight patients out of 32 (25%) had a decrease in BC levels. In five (15.6%) of these patients, the impairment was more than 10 dB. None of the patients suffered total hearing loss preoperatively or postoperatively
Conclusions: Removing the cholesteatoma matrix from the fistula site and covering the defect with temporalis fascia is a safe procedure in cases with labyrinthine fistulas. Temporalis fascia is a safe, economical and 'easy to harvest' sealing material that can be used alone especially for Type I and II fistulas.

Introduction

A fistula between the labyrinth and the middle ear is one of the most common complications of chronic otitis media with cholesteatoma. All types of temporal bone erosion -including the bony labyrinth- were reported to be significantly more frequent in complicated chronic otitis media patients with cholesteatoma.[1] The incidence of this complication is about 10% in the literature and there is no definite agreement on the treatment.[2] Some surgeons choose to remove the cholesteatoma matrix totally from the fistula and to repair the defect with a sealing material; whereas others preserve the matrix over the fistula site. The effects of these procedures on hearing and vestibular functions are major subjects searched in the literature. Latest reports on this topic suggest removing cholesteatoma tissue completely and repairing the defect with a sealing material.[3-5] Leaving the cholesteatoma matrix over the fistula and a close follow up for recurrent disease is another approach, which can help to avoid a possible perilymphatic leak and labyrinthitis.[6] Both techniques seem to preserve cochlear and vestibular functions, but the need for a safer procedure still leads the authors to search for alternative approaches. Kobayashi et al. presented a novel technique, which involved the occlusion of the canal after the removal of cholesteatoma matrix, whereas Yamauchi et al. proposed the underwater endoscopic ear surgery technique, which provided a clear operative field without the need of a suction and helped to protect the inner ear from unexpected aeration.[7,8]

In the light of these findings; every report, evaluating the outcomes of a previously described

Conflict of Interest: The authors declare that they have no conflict of interest.
Funding: This article did not require or receive any financial support.
This study was presented as a poster presentation at the 9th Turkish Congress of Otology, Neuro-otology and Cochlear Implantation, December 2017, Antalya, Turkey.

Balci.indd 209 16/09/19 17:06

method or proposing a novel approach, adds to the knowledge about the treatment of this disease. In the current study, we evaluated the outcomes of the following procedure, which has been our treatment of choice for labyrinthine fistula for the last decade: total removal of cholesteatoma matrix from the fistula site and repair of the defect with temporalis fascia -without using any other sealing material. We aimed to assess if the matrix removal and sealing procedure would cause an impairment in hearing levels of the patient.

Materials and methods

Patients

Records of 188 patients, who underwent middle ear surgery for chronic otitis media with cholesteatoma between June 2008-June 2014 in a tertiary referral center were retrospectively searched. The study was conducted in concordance with international ethical standards and the World Health Organization Declaration of Helsinki and informed consent forms were collected from all participating patients. Thirty-two patients (32 ears) diagnosed with labyrinthine fistula (17%) were included in the study. The diagnosis was confirmed during the surgery in all cases. Preoperatively, all patients underwent oto-microscopic examination, fistula test, and computed tomography (CT) of the temporal bone. Air conduction (AC), bone conduction (BC), air-bone gap (ABG) and pure tone average (PTA) levels were assessed with pure tone audiometry. Fistula tests were performed with a pneumatic otoscope and were accepted positive if nystagmus was detected. Patients' demographic data, preoperative and postoperative examination findings, hearing results, types of surgeries, intraoperative findings, locations and grades of fistulas, and accompanying complications were analyzed. According to the intraoperative classification of Dornhoffer and Milewski; fistulas were classified as: Type I (n=5, perilymphatic membrane covered with bone; i.e., a blue line only), Type IIa (n=12, perilymphatic membrane exposed but intact), Type IIb (n = 15, perilymphatic membrane exposed with perilymph leak).[9] A Type III fistula (perilymphatic membrane eroded onto organs) was not detected in any patient.

Surgical technique

All operations were performed by two senior surgeons (K.O., S.A.). Eleven patients underwent CWD Mastoidectomy with myringostapediopexy (the cartilage graft was placed over the intact stapes). The remaining patients underwent CWD mastoidectomy without tympanoplasty-with obliteration of the eustachian tube. A retroauricular approach was used in all cases and conchal cartilage was used as a graft. After the elevation of the tympanomeatal flap, a transcortical attico-antrotomy was performed. The middle ear environment, ossicles, the extent of cholesteatoma and accompanying complications (dehiscence in the fallopian canal, erosion in the bony plate of tegmen, sigmoid sinus pathologies) were evaluated. Diseased ossicles were removed and the external ear canal wall was drilled. The removal of cholesteatoma matrix from the fistula site was planned as the last step of the procedure. In a sterile environment, the cholesteatoma matrix was gently removed without an aspirator or suction in the field. A semi-wet temporalis fascia graft was placed immediately over the fistula. Before removing the cholesteatoma matrix, intravenous steroids (prednisolone, 500mg) were administered as recommended by Dornhoffer and Milewski.[9] Sealing materials such as fibrin glue or bone paste were not used in any case. Antibiotic and steroid (prednisolone) impregnated spongel pieces were placed over the graft. Intravenous steroids (prednisolone, 1mg/kg) and large spectrum antibiotics (ceftriaxone, 4x1 gr) were given on the next three postoperative days in order to prevent labyrinthitis or possible intracranial complications.

Follow up

The mastoid dressing was applied for two days. Antibiotic and steroid drops were applied to the spongel pieces in the cavity during the first week. Follow-up examinations were performed at three, six, and 12 months after the surgery. After the study was designed, patients were called for a control visit and PTA tests and oto-microscopic examinations were repeated. For the patients who did not respond the call, charts were reviewed.

Outcome measures

Functional results were evaluated with BC thresholds and change in BC levels. The change in postoperative BC (DBC) was calculated as ''postoperative mean BC level'' minus ''pre-operative mean BC level''. With regards to previous reports, cases with an improvement or no alteration in BC levels were considered success;

whereas cases with a loss of more than 10 dB were considered failure.[4] PTA and ABG levels were also assessed but were not used to measure success. Hearing levels were measured at 500, 1,000, 2,000 and 4,000 Hz in order to calculate the averages.

Statistical analysis

For data collection and statistical analysis, Excel 2010 (Microsoft, Redmond, WA, USA) was used.

Results

The incidence of labyrinthine fistula was 17%. Thirty-two patients (ten females, 22 males) suffered this complication. The mean patient age was 37.1 years (range: 17-56 years).

Preoperatively: the hearing loss was present in 32 (100%) patients, otorrhea in 24 (75%) patients, and vertigo and/or dizziness in 20 (62.5%) patients. The fistula test was positive in 15 (46.8%) patients. Twenty-three (71.8%) patients had erosions in the bony labyrinth which were detected by CT scans. These cases were accepted 'positive' for CT scan findings. All Type IIb fistulas (n=15) were diagnosed preoperatively according to CT scan findings. There wasn't a sign of fistula in five of 12 Type IIa patients and in four of five Type I patients in CT scans.

The cholesteatoma was present in epitympanum in 23 cases (71.8%), mastoid antrum in 28 (87.5%) cases, posterior mesotympanum in 19 cases (59.3%), and mastoid air cell system in 28 cases (87.5%). Twenty patients underwent CWD mastoidectomy without tympanoplasty – with obliteration of the eustachian tube, one patient underwent Revision CWD mastoidectomy without tympanoplasty and 11 patients underwent CWD mastoidectomy + myringostapediopexy (the cartilage graft was placed over the intact stapes). In these cases, the ossicles were not present or were heavily eroded. Therefore; they could not be used for an ossiculoplasty. The main indication for the CWD mastoidectomy procedures was extensive cholesteatoma, without any healthy mucosa in the middle ear or the mastoid cavity.

All fistulas were detected on the lateral semicircular canal (LSSC) except for three: two Type IIb fistulas on the posterior semicircular canal (PSSC) and one Type IIa fistula on the promontory. A dehiscence on the facial nerve bony canal was detected in nine patients (28%). In seven cases the dehiscence was on the tympanic segment, in one case on geniculate ganglion region and in one case both tympanic and mastoid segments were involved. None of the patients suffered facial paralysis preoperatively or postoperatively. Two patients, who had Type IIb fistulas, suffered from dizziness in the early postoperative period but the symptoms vanished within two weeks. A dehiscence of the tegmen was detected in 11 (34%) cases and defects were repaired with conchal cartilage if the diameter of the defect was greater than one cm.

All cases were followed up for at least 12 months. The maximum follow-up was seven years.

Table 1

Preoperative and postoperative functional results.

	Mean PTA level	*Mean BC level*	*Mean ABG level*
Preoperative	54.5 (±18.8)dB	20.8 (±14.7)dB	37 (±10.2)dB
Postoperative	55.6 (±17.9)dB	21.8 (±15.2)dB	35,5 (±9.1)dB
Change	-1.1 (±13.2)dB	-1,0 (±10.4) dB	1,5 (±10.8)dB

PTA, pure tone average; BC, bone conduction; ABG, air bone gap

Table 2

Changes in BC (Bone Conduction) levels and success rates according to fistula type

		Success rate (%)*	*Mean change in BC*
	I (n=5)	100 (5/5)	5,6 (±2,5)dB
Fistula Type	IIa (n=12)	83 (10/12)	2,8 (±7,6)dB
	IIb (n=15)	60 (9/15)	-3,8 (±9,8)dB

*Bone conduction average improved or remained unchanged. BC, bone conduction

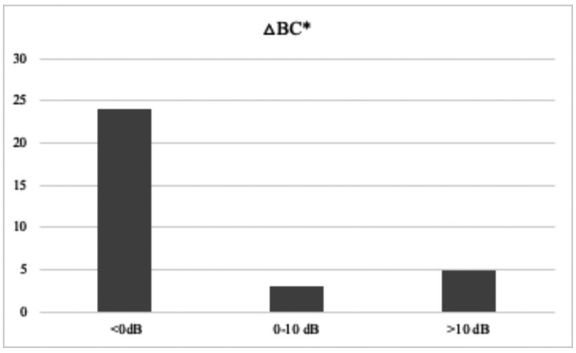

Figure 1

Cases showing a change in postoperative bone conduction (BC) levels in 10-dB bins (n=32). *-BC: 'Postoperative mean BC level' minus 'Preoperative mean BC level'

Preoperative and postoperative functional results are shown in Table 1. The mean postoperative audiometry time was 15.2 months (min.12, max.30 months). The BC (Bone Conduction) hearing level improved or remained unchanged in 24 patients; whereas eight patients out of 32 (25%) had a decrease in BC levels and in five (15.6%) of these patients the impairment was more than 10 dB. The overall success rate was 75%. Changes in BC levels and success rates according to the fistula type are presented in Table 2. In type I fistula group five (100%) patients, in type IIa fistula group 10 (83.3%) patients, and in type IIb fistula group nine (60%) patients had an improved or unchanged hearing. Changes in BC levels grouped in 10-dB bins are displayed in Figure 1. None of the patients suffered total hearing loss preoperatively or postoperatively and no major postoperative complications were observed.

Discussion

LSSC was the most common site of the fistula (90.6%) and almost all studies in the literature report similar findings.[2-4] The incidence of labyrinthine fistula was 17%, which is slightly higher than the incidence reported by Copeland et al's meta-analysis of 13.696 mastoidectomies.[2] Our tertiary health center is a referral center in our region and complicated cases -such as cases with labyrinthine fistulas- are frequently referred from neighbor cities and institutions. This issue could be the main reason for the higher incidence. The authors reported the incidence of labyrinthine fistula as 7% and the incidence of superior SSC and posterior SSC fistulas as 6% and 2%, respectively.[2] In the current study, two (6%) fistulas were located on posterior SSC; however, no fistula was detected on superior SSC. A type IIa fistula was detected on

Table 3

Preoperative findings, surgical treatments and success rates in the recent studies

	Incidence of fistula	*Labyrinth related symptoms (vertigo and/or dizziness)*	*Positive fistula test*	*Positive CT scan findings*	*Surgical technique*	*Success rate (hearing improved or unchanged)*
Quaranta 2009[3] (n=46)	12.7%	43%	Not-performed	43%	Matrix removal + BD and FG	
Soda-Merhy 2000[5] (n=27)	7.5%	78%	55%	93%	Matrix removal + TF/P/M and BD	86%
Grewal 2003[13] (n=50)	11.4%	32%	36%	Not mentioned	Matrix removal + TF/P and BD	
Ueda 2009[12] (n=31)	6.0%	74%	65%	Not mentioned	Matrix removal + BD and TF	89%
Copeland et al.'s review[2] 2003 (n=1018)	7%	64%	50%	57%	Matrix removed + sealed	84%
Chen. 2010*[18] (n=22)	6.5%	59%	54%	100%	Canal occlusion	90%
Gocea 2011[15] (n=31)	7%	Not mentioned	Not mentioned	Not-performed for all cases	Matrix removal + BD/C/Periost	85%
Current Study (n=32)	17%	62%	46%	71%	Matrix removal + TF	75%

*Only cases with high-grade fistulas were included in this study. CT computed tomography; BD, bone dust; FG, fibrin glue; TF, temporalis fascia; P, perichondrium; C, cartilage.

the promontorium, which brings a higher risk of sensorineural hearing loss. Copeland et al. proposed that the promontory fistula should be managed exclusively with the matrix in situ technique to increase the chances of hearing preservation.[2] In the current study, the matrix at this area was also removed and a temporalis fascia was placed, and the BC level of the patient remained unchanged.

The clinical examination and CT images are essential for the diagnosis of the fistula, but the diagnosis was mostly confirmed during the surgery. The CT scan is considered the gold standard diagnostic method for labyrinthine fistula. In our series, nine patients did not have a sign of fistula in CT scan images and the sensitivity of the CT scan was 71%. Excluding type I fistulas, the sensitivity of the CT scan was 81% (22/27), which emphasizes the value of this diagnostic tool, especially for high-grade fistulas. The fistula test also does not seem to be specific and sensitive to the disease, as only 46% of the patients had a positive fistula test. In Copeland et al.'s review, 50% of cases had a positive fistula test and the sensitivity of the CT scan was 57%.[2] Preoperative findings reported in recent studies are presented in Table 3. We experienced that in cases with intense preoperative ear discharge and extensive cholesteatoma; the semicircular canal site should be the last place to remove the cholesteatoma matrix during the surgery. This helps the surgeon to avoid excessive manipulation and complications if a fistula is present.

There are different opinions in the literature about the treatment of cholesteatoma matrix on the fistula site. Leaving the matrix on the fistula site or total removal of the cholesteatoma tissue are the two main approaches. Copeland et al.'s report revealed similar outcomes for both of these techniques: 84% of patients managed with complete matrix removal had an unchanged or increased hearing; whereas 83% of cases managed by maintaining matrix in situ over the fistula were noted to have unchanged or improved postoperative hearing.[2] Sheehy et al. proposed performing the canal wall up technique in two steps, with the removal of the matrix over the fistula during the second stage.[10] Sanna et al. also recommended leaving the matrix over the fistula in all cases in which a canal wall down mastoidectomy is performed.[11] Albu et al's study, in which 97 patients with semicircular canal fistulas were included, the matrix was removed and the fistula was sealed with bone dust mixed with fibrin glue in 62 patients, whereas the canal was drilled and occluded in 35 patients.[4] The authors reported a total success rate of 89% and concluded that low-grade fistulas could be successfully treated with matrix removal and sealing. Ueda et al. completely removed the cholesteatoma matrix in the first stage in 31 patients and they repaired the defect with bone dust and/or temporalis fascia.[12] The authors observed that 26% of patients had improved hearing, and 63% of patients had no change in hearing levels. Authors who advocate the removal of cholesteatoma matrix reported that proteolytic enzymes secreted by the cholesteatoma matrix (acid phosphatase, collagenase, TNF-a) would continue bone erosion if the matrix is left in place.[13,14] In the current study, the cholesteatoma matrix was removed in all patients and the fistula site was covered with temporalis muscle fascia immediately. No other soft tissues or sealing materials were used, and a success rate of 75% was observed. The surgical techniques and success rates reported in recent studies are presented in Table 3. The studies mentioned above and the comprehensive review of Copeland revealed that both treatment methods can lead to successful outcomes, and the decision to perform a technique depends mainly on the experience of the surgeon. However, patient-related factors can also play a major role in the choice of treatment. Patients who could not be followed up regularly in the postoperative period are not suitable candidates for staged surgeries. The patient's general condition and the ipsilateral and contralateral hearing thresholds should also be evaluated before the surgery.[12]

In the current study, the main indications for a CWD mastoidectomy were extensive cholesteatoma and the absence of any healthy mucosa in the middle ear or mastoid cavity. Another reason for preferring a CWD procedure is that most of our cases were referred from rural areas with low socio-economical standards. A regular follow up with appropriate imaging modalities can be difficult in these cases. Therefore, a single staged CWD procedure was considered a safer procedure for these patients.

In the literature, there is no definite agreement about the postoperative medical treatment of labyrinthine fistulas. Dornhoffer recommended the use of corticosteroids (prednisolone, 500 mg, IV) during the surgery and on the following three days.[9] The authors concluded that the concomitant use of corticosteroids appeared to improve the

postoperative outcome in those cases with type III fistulas and type IIb fistulas. Gocea et al also administered 500 mg of methylprednisolone 15 min before removing the cholesteatoma matrix over the fistula.[15] The authors used additional intravenous injections of 250 mg of prednisolone on the two following days after surgery. They reported that 22 (84%) out of 26 patients treated intra-operatively with steroids had preservation or improvement of bone conduction after a single-staged matrix removal. Hearing preservation or improvement were also recorded in 80% of the group treated with steroids plus antibiotics. Kobayashi et al. also favored the use of antibiotics in order to prevent labyrinthitis and to preserve hearing.[16] In the current study, we used intravenous steroids (prednisolone, 1mg/kg) and large spectrum antibiotics (ceftriaxone, 4x1 gr) on the next three postoperative days in order to prevent labyrinthitis and possible intracranial complications. Although there is no scientific proof that antibiotics help to preserve hearing; we believe postoperative broad-spectrum antibiotherapy may play a major role in preventing infectious complications in these complicated chronic otitis media cases.

The causes of the decrease in the BC thresholds after the surgery are searched by Kitahara et al. and the authors reported that the deterioration of the inner ear function was the possible reason.[17] A mild or severe serous labyrinthitis can occur when the endosteum is opened and can lead to deterioration. In the current study, 40% (6/15) of type IIb fistula cases had an impairment in BC levels. The BC levels have a tendency to fall when the fistula depth is greater, regardless of the sealing material. In these cases, semicircular canal occlusion procedures can be an alternative.[7]

Copeland et al.'s review revealed that 29% of labyrinthine fistula patients also had involvement of the facial nerve.[2] In the current study, nine cases out of 32 (28%) had a dehiscence on the facial nerve bony canal. Accompanying complications and/or bony defects are likely to be present in cases with labyrinthine fistula and should also be kept in mind preoperatively.

The main limitation of our study is that objective vestibular tests were not performed to evaluate the vestibular functions of the patients preoperatively and postoperatively. These tests could provide valuable information about the effect of the procedure on vestibular functions.

Conclusion

In the current report, the incidence of labyrinth fistula was found to be 17%, and the lateral SSC was the main location (90.6%). To our knowledge, our study is one of the few case series in which the labyrinthine fistula is repaired with only temporalis fascia, without using any other sealing material or soft tissues. Removing the cholesteatoma matrix from the fistula area and covering the defect with temporalis fascia is considered a safe procedure in these cases. Among other sealing materials such as perichondrium, bone pate, bone dust and fibrin glue; temporalis fascia is also a safe, economical, and 'easy to harvest' material that can be used alone especially for Type I and II fistulas.

References

1. Yorgancilar E, Akkus Z, Gun R, Yildirim M, Bakir S, Kinis V, Meric F, Topcu I. Temporal bone erosion in patients with chronic suppurative otitis media. *B-ENT*. 2013;9(1):17-22.
2. Copeland BJ, Buchman CA. Management of labyrinthine fistulae in chronic ear surgery. *Am J Otolaryngol*. 2003; 24(1):51-60.
3. Quaranta N, Liuzzi C, Zizzi S, Dicorato A, Quaranta A. Surgical treatment of labyrinthine fistula in cholesteatoma surgery. *Otolaryngol Head Neck Surg*. 2009;140(3):406-411.
4. Albu S, Amadori M, Babighian G. Predictors of Hearing preservation in the management of labyrinthine fistulas positioned on the semicircular canals. *Ann Otol Rhinol Laryngol*. 2013;122(8):529-534.
5. Soda-Merhy A, Betancourt-Suárez MA. Surgical treatment of labyrinthine fistula caused by cholesteatoma. *Otolaryngol Head Neck Surg*. 2000;122(5):739-742.
6. Freeman, P. Fistula of the lateral semicircular canal. *Clin Otolaryngol Allied Sci*. 1978;3(3):315-321.
7. Kobayashi, T, Sato, T, Toshima, M, Ishidoya, M, Suetake, M, Takasaka, T. Treatment of labyrinthine fistula with interruption of the semicircular canals. *Arch Otolaryngol Head Neck Surg*. 1995;121(4):469-475.
8. Yamauchi D, Yamazaki M, Ohta J, Kadowaki S, Nomura K, Hidaka H, Oshima T, Kawase T, Katori Y. Closure technique for labyrinthine fistula by ''underwater'' endoscopic ear surgery. *Laryngoscope*. 2014;124(11):2616-2618.
9. Dornhoffer JL, Milewski C. Management of the open labyrinth. *Otolaryngol Head Neck Surg*. 1995;112(3):410-414.
10. Sheehy JL, Brackmann DE. Cholesteatoma surgery: management of the labyrinthine fistula: a report of 97 cases. *Laryngoscope*. 1979;89(1):78-87.
11. Sanna M, Zini C, Bacciu S, Scandellari R, Delogu P, Jemmi G. Management of the labyrinthine fistula in cholesteatoma surgery. *ORL J Otorhinolaryngol Relat Spec*. 1984;46(3):165-172.

12. Ueda Y, Kurita T, Matsuda Y, Ito S, Nakashima T. Surgical treatment of labyrinthine fistula in patients with cholesteatoma. *J Laryngol Otol Suppl*. 2009;(31):64-67.
13. Grewal DS, Hathiram BT, Dwivedi A, Kumar L, Sheth K, Srivastava S. Labyrinthine fistula: a complication of chronic suppurative otitis media. *J Laryngol Otol*. 2003; 117(5):353-357.
14. Sastry KV, Sharma SC, Mann SBS, Ganguly NK, Panda NK. Aural cholesteatoma: role of tumor necrosis factoralpha in bone destruction. *Am J Otol.* 1999;20:158-161.
15. Gocea A, Martinez-Vidal B, Panuschka C, Epprecht P, Caballero M, Bernal-Sprekelsen M. Preserving bone conduction in patients with labyrinthine fistula. *Eur Arch Otorhinolaryngol.* 2012;269(4):1085-1089.
16. Kobayashi T, Sakurai T, Okitsu T, Yuasa R, Kawase T, Kusakari J, Takasaka T. Labyrinthine fistula caused by cholesteatoma. Improved bone conduction by treatment. *Am J Otol.*1989;10:5-10.
17. Kitahara T, Kamakura T, Ohta Y, Morihana T, Horii A, Uno A, Imai T, Mishiro Y, ınohara H. Chronic otitis media with cholesteatoma with canal fistula and bone conduction threshold after tympanoplasty with mastoidectomy. *Otol Neurotol*. 2014;35(6):981-988.
18. Chen Z, Dongzhen, Wu Y, Shi H, Zhou H, Wang J, Miyoshi A, Yin S. Surgical treatment of labyrinthine fistula caused by cholesteatoma with semicircular canal occlusion. *Acta Otolaryngol*. 2010;130(1):75-78.

Erdem Eren, Assoc.Prof.Dr.
Department of Otorhinolaryngology and Head & Neck Surgery, Katip *Çelebi* University Atatürk Training and Research Hospital.
Basın Sitesi Mh. Karabağlar,
35170 İzmir, Turkey.
Phone: +90 232 244 44 44
Fax: +90 232 243 15 30
E-mail: erd2eren@yahoo.com

Balci.indd 215 16/09/19 17:06