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Original article

Clinical findings and surgical results of middle ear cholesteatoma behind an intact tympanic membrane in adults

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Summary. *Background and aim:* Cholesteatoma usually arises in the middle ear by the formation of a retraction pocket or a tympanic membrane perforation. In some cases, cholesteatoma presents behind an intact tympanic membrane (ITMC) and the underlying mechanism of its development is controversial. The aim of this study was to describe clinical features, pathogenesis and surgical results in a series of adult patients affected by ITMC. *Methods:* We analyzed retrospectively 27 adult patients (age > 18 years) diagnosed with ITMC who underwent surgery between 1994 and 2013. We investigated the demographic data, presenting symptoms, otoscopic findings, disease location, surgical technique, postoperative complications and outcomes. *Results:* Diagnosis was made on the basis of a white mass seen through the tympanic membrane in 24 cases and on explorative surgery in the remaining 3 patients. In 16 cases cholesteatoma was related to an acquired cause, while in 11 ears a congenital origin was supposed. Hearing loss was the chief complaint and it was present in 19 (70.3%) subjects. Cholesteatoma was managed by purely endaural or retroauricular transcanal tympanoplasty in 12 cases, by planned staged canal wall up mastoidectomy in 10 cases (37%), by canal wall down mastoidectomy in 3 cases, and by modified Bondy technique in 2 cases. A recurrent cholesteatoma was observed in one ear; one patient experienced a postoperative profound sensorineural hearing loss. *Conclusions:* ITMC in adults may have both congenital and acquired origin. It may grow silently over many years and develops into a massive size before being detected. Each patient's management should be tailored to clinical findings. (www.actabiomedica.it)

Key words: cholesteatoma, intact tympanic membrane, mastoidectomy, tympanoplasty, hearing

Introduction

The term "cholesteatoma" identifies a growth of skin cells, characterized by erosive and expansive properties, but not malignant in nature. Cholesteatoma can occur in different sites of the temporal bone, being the middle ear and the petrous apex the most common locations. The otoscopic classification proposed by Tos (1) and successively modified by Mills and Padgham (2), distinguishes two main types of cholesteatoma: those arising in a retraction pocket of the tympanic membrane (TM) and those arising behind an intact TM. The first type is more frequent and usually occur because of Eustachian tube dysfunction: when the Eustachian tube work poorly, a negative pressure develops into the middle ear and pulls medially a part of the tympanic membrane, creating a retraction pocket; over time, this pocket fills with old skin cells, can become infected and enlarges until the formation of a cholesteatoma. In acquired cholesteatoma, otoscopy may show a retraction pocket or a tympanic perforation, often with purulent drainage.

In a minority of cases cholesteatoma occurs behind an intact tympanic membrane. The underlying mechanism of development of intact tympanic membrane cholesteatoma (ITMC) is controversial. Although none of the proposed theories provide compelling support for one theory over another, the congenital theory is the most credited in the literature; it postulates that ITMC may originate from rests of epidermoid cells incorporated into the middle ear during embryonic development (3). To be classified as congenital, cholesteatoma must respect the criteria proposed by Derlacki and Clemis (4) and successively modified by Levenson et al. (5): an intact eardrum; no history of tympanic membrane perforation, otorrhea or previous ear surgery. Congenital cholesteatoma is usually diagnosed during childhood and the majority of cases are located in the antero-superior part of the middle ear. It has been reported that, in adults, ITMC may be established differently from that entity in children (6). Although a congenital origin is possible, a variety of other mechanisms of development have been described (7). To the best of our knowledge, in the literature there are few studies that have specifically analyzed ITMC in adults. In this study, we retrospectively reviewed our experience with ITMC in adults focusing on clinical features, possible pathogenesis, anatomical and functional results.

Materials and methods

Our otological database was used to search out all adults patients diagnosed with ITMC who underwent surgery at the Department of Otolaryngology of the University of Parma between January 1994 and December 2011. The study complies with the declaration of Helsinki and a written informed consent was obtained from all patients. Cholesteatoma was diagnosed otoscopically and confirmed by high resolution computed tomography (HRCT) of the temporal bone in all cases. Inclusion criteria were as follows: adult age (≥ 18 years), intact tympanic membrane, fresh cholesteatoma. Exclusion criteria were as follows: pediatric age (<18 years), otoscopic evidence of retraction pocket or tympanic membrane perforation, recurrent cholesteatoma. ITMC was considered congenital in presence of a whitish mass behind an intact tympanic in a patient with no history of tympanic membrane perforation, otorrhea, trauma or previous ear surgery. Medical reports were analyzed by demographic data, presenting symptoms, otoscopic features, disease location and extension, surgical technique and outcomes.

The extent of the disease was defined by the number of sites involved with cholesteatoma, according to Saleh and Mills classification (8). Based on intraoperative involvement of the attic, antrum, mastoid, mesotympanum, Eustachian tube, labyrinth, and middle cranial fossa, cholesteatoma was classified as Stage I (1 site), Stage II (2 sites), Stage III (3 sites), Stage IV (4 sites), and Stage V (5 or more sites). Recurrent cholesteatoma, postoperative complications, and hearing levels were the main outcomes measured. Hearing results were evaluated according to guidelines set forth by the Committee on Hearing and Equilibrium of the American Academy of Otolaryngology and Neck Surgery for the evaluation of results of treatment of conductive hearing loss (9). Pure-tone average (PTA) was calculated as the mean of 500, 1000, 2000, and 3000 Hz thresholds. The air-bone gap was reported as the four-tone PTA for air-conduction and bone-conduction values determined at the same time. Hearing results were determined at the last follow-up.

Results

A total of 27 patients were identified and included in this study. Relevant clinical data are reported in Table 1. There were 15 males and 12 females. The right ear was involved in 55.5% of cases. The patients ranged in age from 18 to 66 years (mean age 38.5 years). Eleven patients satisfied the criteria of Derlacki and Clemis and were considered as congenital cholesteatomas. In 10 cases there was a history of recurrent episodes of otorrhea without otoscopic evidence of retraction pocket or tympanic perforation at the time of our observation; no previous ear surgery was reported in these patients. In 4 subjects there was a history of previous middle ear surgery for non-cholesteatomatous chronic otitis media (Figure 1); in these patients, ITMC was supposed to be iatrogenic. In the remaining 2 cases, a cranial trauma was considered as the cause of the presence of the skin into the middle ear. Hearing loss was

Table 1. Relevant patient demographic data, cholesteatoma etiology, type of surgery and postoperative complications

Patient	Age/Sex	Cholesteatoma etiology	Surgical technique	Postoperative complications
1	22/M	Congenital	Tympanoplasty	None
2	31/F	Congenital	Staged CWUM	None
3	33/M	Congenital	Staged CWUM	RC requiring CWDM
4	59/M	Congenital	Tympanoplasty	None
5	48/M	Congenital	Staged CWUM	None
6	26/F	Congenital	Tympanoplasty	None
7	18/M	Congenital	Tympanoplasty	None
8	40/M	Congenital	Staged CWUM	None
9	31//F	Congenital	Tympanoplasty	None
10	52/F	Congenital	Tympanoplasty	None
11	49/M	Congenital	Staged CWUM	None
12	27/F	Resolved COM	Tympanoplasty	None
13	37/M	Resolved COM	Tympanoplasty	None
14	26/M	Resolved COM	Staged CWUM	None
15	21/F	Resolved COM	Staged CWUM	None
16	33/M	Resolved COM	Tympanoplasty	None
17	19/F	Resolved COM	Staged CWUM	None
18	18/M	Resolved COM	Tympanoplasty	None
19	56/F	Resolved COM	Staged CWUM	None
20	50/M	Resolved COM	CWDM	None
21	40/M	Resolved COM	Staged CWUM	None
22	61//F	Iatrogenic	Tympanoplasty	None
23	56/F	Iatrogenic	CWDM	None
23	39/M	Iatrogenic	MBT	None
25	66/F	Iatrogenic	Tympanoplasty	None
26	37/M	Post-traumatic	MBT	None
27	47/F	Post-traumatic	CWDM	Profound SNHL

COM: chronic otitis media; CWUM: canal wall up mastoidectomy; CWDM: canal wall down mastoidectomy; MBT: modified Bondy technique; RC: recurrent cholesteatoma; SNHL: sensorineural hearing loss.

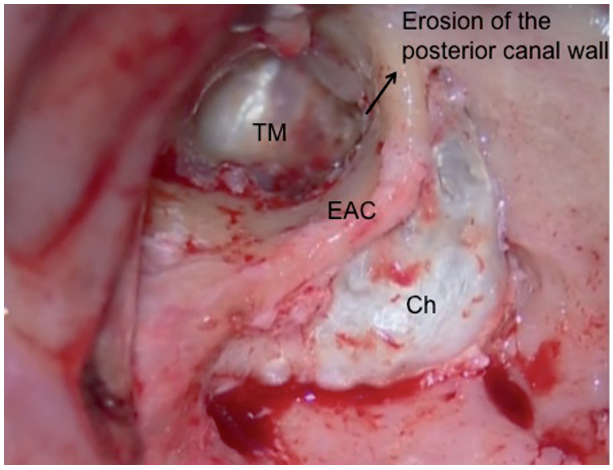

Figure 1. Intraoperative view of an intact tympanic membrane cholesteatoma developed after tympanomastoidectomy for chronic otitis media. TM: tympanic membrane; EAC: external auditory canal; Ch: cholesteatoma

the chief complaint and it was present in 19 (70.3%) ears. Six patients (22.2%) were asymptomatic and were incidentally found to have an ITMC on a ENT visit for non-otologic complaints. Other symptoms were tinnitus (13 cases), otalgia (5 cases), ear fullness (3 cases), dizziness (2 cases), and facial paresis (1 case). Diagnosis was made on the basis of a white mass seen through the tympanic membrane in 24 patients; in the remaining 3 cases diagnosis was suspected on the basis of HRCT of the temporal bone and confirmed on explorative surgery. Based on morphologic examination at surgery, cholesteatoma presented as a cystic lesion of varying size in 23 cases, while in the remaining 4 patients cholesteatoma developed as flat keratinizing epithelium in direct contact with granulation tissue. In 15 patients, cholesteatoma was confined to the middle ear, in 5 there was also attic involvement, and in 7 there

was extension to the mastoid cells. A labyrinthine fistula was present in two ears; in one case the disease eroded the fallopian canal and in another patient there was a bony defect of the middle cranial fossa. The ossicular chain was found intact in 7 patients; the most frequently eroded ossicle was incus (70.3%), followed by stapes (48.1%) and, then, malleus (14.8%). Cholesteatoma staging according to Saleh and Mills (8) classification is reported in Table 2. Twelve ITMCs (44.4%) were removed by purely endaural or retroauricular transcanal tympanoplasty. A planned staged canal wall up mastoidectomy was done in 10 cases (37%). In order to prevent secondary retraction pockets after surgery, all defects of the postero-superior canal wall using bone patè, as previously described (10). Three subjects underwent canal wall down mastoidectomy, while two a modified Bondy technique (11). In order to decrease the chance of residual disease, in all cases we used Mesna, a mucolytic agent capable to break disulfide bonds (12) and to make the cholesteatoma removal easier (13-14). The mean length of follow-up was 7.2 years (range 3-15 years). Recurrent cholesteatoma was observed in only one case (treated with a canal wall up mastoidectomy) and required conversion to canal wall down mastoidectomy. The mean preoperative to postoperative four-tone air-bone change is reported in Table 3. One patient with a cholesteatoma infiltrating the labyrinth experienced a postoperative profound sensorineural hearing loss.

Table 3. Pre- and post-operative hearing results

Type of surgery	Number of cases	Mean preoperative ABG	Mean follow-up	Mean postoperative ABG
Tympanoplasty	12	25 dB	6.5 years	15 dB
CWUM	10	35 dB	7 years	15 dB
CWDM	3	35 dB	8 years	30 dB
MBT	2	12.5 dB	4 years	12.5 dB

ABG: air-bone gap; CWUM: canal wall up mastoidectomy; CWDM: canal wall down mastoidectomy; MBT: modified Bondy technique.

Discussion

Cholesteatoma is a benign keratinizing hyperproliferative epithelial lesion that can affect middle ear and inner ear structures with possible hearing loss, vestibular disfunction, facial paralysis, and even intracranial complications (15). In most cases, cholesteatoma is otoscopically characterized by the presence of tympanic abnormalities, such as retraction

Table 2. Cholesteatoma stadiation (8): correlation with disease etiology and type of surgery

Cholestaetoma stadiation	Cholesteatoma etiology	Surgical technique
Stage 1 (4 cases)	3 congenital 1 resolved COM	4 tympanoplasties
Stage 2 (10 cases)	3 congenital 4 resolved COM 3 iatrogenic	8 tympanoplasties 1 CWUM 1 MBT
Stage 3 (8 cases)	4 congenital 3 resolved COM 1 iatrogenic	6 CWUM 2 CWDM
Stage 4 (4 cases)	1 congenital 1 resolved COM 1 iatrogenic 1 post-traumatic	3 CWUM 1 MBT
Stage 5 (1 case)	1 post-traumatic	1 CWDM

COM: chronic otitis media; CWUM: canal wall up mastoidectomy; CWDM: canal wall down mastoidectomy; MBT: modified Bondy technique.

pockets and perforations; under these circumstances, cholesteatoma is classified as acquired and related to a dysfunction of the Eustachian tube. In a minority of cases cholesteatoma occurs behind an intact tympanic membrane. Several pathogenic mechanisms may contribute to ITMC formation. It is widely assumed that in children ITMC arises after failure of the epibranchial placode to involute (16). Although a congenital origin has been proposed in several studies (17-19), in adults, ITMC may be established differently from that entity in children (6). It has been demonstrated that squamous epithelium can enter the middle ear from the edge of a tympanic perforation with subsequent healing of the tympanic membrane leaving a keratin cyst deep to eardrum (7). Similarly, an histopathological study provided evidence that ITMC can be established from a resolved retraction pocket of the tympanic membrane (6). Another known cause of ITMC is accidental implantation of squamous epithelium during otologic surgery; iatrogenic cholesteatoma has been reported to occur after ventilation tube insertion (20), intact canal wall mastoidectomy (21), canal wall reconstruction tympano-mastoidectomy (22).

A rare cause of migration of skin from external ear canal into the middle ear is represented by cranial trauma. The presence of fracture lines in temporal bone may promote migration of epithelium years after trauma (23).

Finally, Sade et al. (24) proposed that squamous metaplasia, some with keratinization, can occur in the middle ear in response to otitis media.

Although there is no possibility to determine with absolute certainty whether or not an ITMC is congenital or acquired, an accurate medical history, combined with clinical and radiologic features, allows the identification of the underlying mechanism with a good margin of confidence.

In the present study, the congenital origin (11 patients) and the entrance of skin into the middle ear through a resolved retraction pocket or perforation of the tympanic membrane (10 patients) account for the majority of cases (77.7%) of ITMC treated in our Department; iatrogenic (4 patients) and post-traumatic (2 patients) cholesteatomas are less common. The diagnosis of ITMC was usually made by means of otoscopy revealing a retrotympanic white mass; HRCT of the temporal bone can be useful to confirm the diagnosis. In addition, neuroradiological study is mandatory to evaluate the extension of the lesion in order to choice the most appropriate surgical technique. Although transfer technologies have been proposed to treat or prevent middle ear disease (25), surgical treatment is our only tool to avoid cholesteatoma-related complications. Cholesteatomas confined to the middle ear can be removed through a tympanotomy approach, while lesions extended to the mastoid or to the attic require a mastoidectomy. It is interesting to note that the most challenging cases are the post-traumatic ones. Entrapment of the epithelium in the fracture line, traumatic implantation of the eardrum epidermis, and entrapment of the external auditory canal medial to a stenosis are the most common mechanism by which a post-traumatic cholesteatoma might develop (26). Unfortunately, these lesions often grow for many years asymptomatically and develop into a massive size before causing symptoms. In our 2 patients, a massive post-traumatic cholesteatoma was diagnosed 10 and 13 years after the trauma, respectively; in both cases an extensive surgery was needed. Furthermore, the only postoperative complication experienced was a profound sensorineural hearing loss occurred in a patient with a large post-traumatic cholesteatoma infiltrating the labyrinth.

In conclusion, ITMC may be congenital as well as acquired. Ingrowth of meatal epidermis, metaplasia, cranial trauma, and inadvertent introduction of squamous epithelium into the middle ear during otologic surgery are the mechanisms by which an acquired ITMC might develop. Patients with ITMC often present with hearing loss, but asymptomatic cases are not infrequent and may grow silently over many years developing into massive disease before being diagnosed, especially in post-traumatic cholesteatoma. In most cases, ITMC can be treated successfully via a tympanoplasty, but in a minority of cases a more extensive surgery may be required.

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