Cholesteatomas in Children: Update

Tal Marom and Sharon Ovnat Tamir

Introduction

Cholesteatomas, more accurately coined as as *keratomas*, are epidermal inclusion cysts of the middle ear cleft, the mastoid or the external auditory canal (when the "inclusion cyst" opens into the external auditory canal). These cysts contain the desquamated debris (principally keratin) from their keratinizing, squamous epithelial lining. Cruveilhier was the first to describe aural cholesteatoma as a "pearly tumor" of the temporal bone [1]. The term *cholesteatoma*, coined by the German physiologist Müller in 1838, is a misnomer. Cholesteatomas do not contain cholesterol, but rather white-yellow keratin flakes, which grossly resemble cholesterol crystals [2,3]. Similar to other chronic ear disorders, the prevalence of cholesteatoma in children varies among populations. Among children who were followed for 15 years after ventilating tubes insertion (VTI), the cumulative percentage of children who developed cholesteatoma after one VTI procedure was 0.9%, after two VTIs - 2.1%, after three VTIs - 3.8%, and after four or more VTIs - 5.2%[3]. In parallel, development of cholesteatoma was estimated to be present in 6.9% of patients presenting with cleft palate [4].

Pathophysiology

The destructive nature of cholesteatoma is responsible for much of the morbidity associated with chronic otitis media. The propensity of cholesteatomas to erode bone and the lack of effective, non-surgical management add importance to the understanding of this disease. Pediatric cholesteatomas are traditionally categorized either as congenital or acquired (primary or secondary):

***Congenital cholesteatoma*:** children without a history of significant ear disease or perforation of the tympanic membrane are found to have squamous epithelium growth in the middle ear cleft, presumably from inappropriate or incomplete migration of precursor cells during embryologic development (**Figure 1**). Michaels showed that during fetal life a small area in the anterior tympanum in the developing ear often contains a small quantity of keratinizing epithelium. He found evidence of epidermoid formation in 37/68 temporal bones of fetuses at 10-33 weeks' gestation [5]. Congenital cholesteatomas may originate in this region. Although congenital

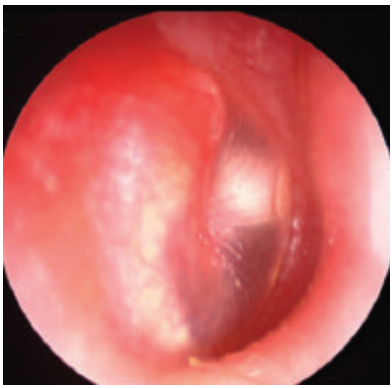

Figure 1. Congenital cholesteatoma in the antero-superior quadrant of the left tympanic membrane.

cholesteatomas generally are seen as pearl-like masses behind an intact tympanic membrane, Koltai presented a convincing case that some congenital cholesteatomas advance to perforate and become chronically infected, taking on the appearance of an acquired cholesteatoma [6].

***Primary acquired cholesteatoma*:** progressive retraction of the tympanic membrane (TM) leads to ingrowth of a debris-filled pocket into the middle ear cleft.

***Secondary acquired cholesteatoma*:** prior infection or perforation allows ingress of squamous epithelium through a defect in the TM.

The pathogenesis of acquired cholesteatoma has been debated for decades[7]. There are four basic theories of the pathogenesis of acquired cholesteatoma:

(1) invagination of the tympanic membrane (retraction pocket cholesteatoma), (2) basal cell hyperplasia, (3) epithelial ingrowth through a perforation (the migration theory), and (4) squamous metaplasia of middle ear epithelium. Additionally, combination of the invagination and the basal cell theories can explain the etiology of retraction pocket cholesteatoma formation.

Cholesteatoma causes damage to the middle ear cavity and its content, the mastoid, and the surrounding structures in various ways. As an expansile mass, it causes bone loss (including ossicular bone) through pressure resorption. In addition, the sub-epithelial layer produces enzymes that destroy bone [8]. The sac can also become colonized with bacteria, acting as an ongoing source of repeated infections. Any or all of these mechanisms can lead to further intra-temporal or intracranial complications, primarily caused by direct extension of infection into nearby structures. Although cholesteatomas in children and adults are similar on the molecular level, the disease process generally behaves more aggressively in the younger age group, a finding that may be the result of anatomic and physiologic differences in the vicinity of the squamous growth.

Clinical Presentation

Except in unusual cases, in which cholesteatomas are clearly visible on examination, no pathognomonic symptoms or signs denote cholesteatoma presence. In many cases, the cholesteatoma remains completely asymptomatic for a long time. A substantial number of patients, and especially children, do not notice the mild and insidious progression of conductive hearing loss associated with progressive tympanic membrane (TM) retraction and ossicular erosion. In a recent retrospective review, more than 50% of children with cholesteatoma presented with chronic otorrhea, recurrent acute otitis media, conductive hearing loss, or some combination of these three findings [8].

When present, more dramatic symptoms such as otalgia, dizziness, or sensorineural hearing loss should prompt an urgent search for other complications of otitis media, and cholesteatoma will often be found lurking in these patients. In any suspected case, complete otomicroscopic examination is mandatory. If such a procedure, which must include removal of any crusts or drainage that obscure the examiner's vision, is not tolerated by the patient, arrangements for appropriate sedation or anesthesia must be made.

Under the microscope or otoscope, cholesteatoma is often suspected when an aural polyp is present, obvious squamous debris seen either behind or through

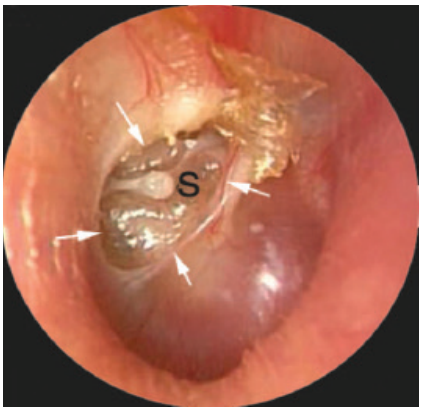

Figure 2. A pocket retraction pocket in the posterior-superior quadrant. The long process of the incus bone is eroded, which left the tympanic membrane adherent to the stapes (S). Note the squamous debris in the attic.

the tympanic membrane, or in the middle ear cavity itself. The otoscopic appearance of an aural cholesteatoma also varies. A typical attic retraction cholesteatoma appears as a defect of variable size adjacent to the posterior-superior portion of the tympanic membrane. The center of the defect contains keratin debris (primary acquired cholesteatoma). In other patients, keratinizing epithelium has migrated through a perforation into the middle ear (secondary acquired cholesteatoma). Cholesteatomas sometimes appear behind or within an intact tympanic membrane- so-called congenital cholesteatoma. An infected cholesteatoma sometimes manifests as an "aural polyp." These "polyps" actually are granulation tissue at the junction between an eroding cholesteatoma and bone (**Figure 2**). The presence of an aural polyp in a chronically infected ear should be considered to be a cholesteatoma until proved otherwise. Occasionally, a cholesteatoma cannot be seen otoscopically, but is discovered during tympanomastoid surgery.

Patients with infected cholesteatoma occasionally are misdiagnosed as having external otitis. Careful follow-up evaluation and thorough canal debridement of a patient with otorrhea are mandatory, because the cholesteatoma may not be evident during an acute flare-up.

Role of Imaging

The final diagnosis of an aural cholesteatoma and its extent are determined by different complementary imaging techniques, and ultimately during surgical exploration. While there are audiometric measures that may suggest the presence of cholesteatoma (e.g. conductive hearing loss, with/without the presence of sensorineural hearing loss in case of inner involvement), these tests are neither specific nor sensitive enough, and may lead to an erroneous judgment on the presence or absence of cholesteatoma.

To date, different imaging modalities are the main stay of diagnosis. High-resolution computed tomography (HRCT) scan of the temporal bone is the mainstay of imaging. HRCT scan is performed in two different and complementary plains: axial and coronal, in 1-2 mm slices. The HRCT permits a good visualization of the bony structures of the middle ear and mastoid (**Figure 3**). Using both plains, the surgeon is able to evaluate the different structures prior to surgery: scutum, tegmen tympani, ossicular chain, lateral semi-circular canal, oval window and round window niches, aditus ad antrum, mastoid, and the tympanic and mastoid segments of the facial nerve, the position of the dura, the sigmoid sinus and the jugular bulb, which assists in planning the surgical approach, as well as the extent of surgery.

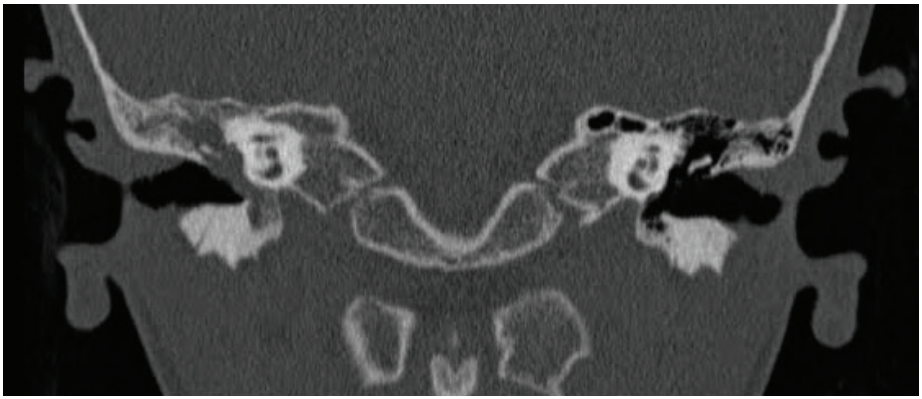

Figure 3. Coronal view of HRCT, demonstrating soft tissue filling the right middle ear cleft and mastoid. The tympanic membrane seems to be intact, and the scutum is not blunted.

Cholesteatoma can be seen as a homogenous soft tissue mass with local bone erosion, middle ear opacification, attic or lateral wall (scutum) erosion, aditus ad antrum widening, dislocation or discontinuity of the ossicular chain, erosion of ossicles, labyrinthine fistula, facial nerve canal (fallopian canal) erosion, tegmen tympani dehiscence, mastoid destruction (automastoidectomy), and sigmoid plate dehiscence. The specificity of HRCT scan regarding cholesteatoma can be low. In a study performed by Lee *et al*., they observed that when using Hounsfield units (HU) (i.e. units that are used to measure tissue density in CT scanning), it was impossible to differentiate cholesteatoma from inflammatory tissue [9].

In order to distinguish more easily cholesteatoma from middle ear mucoid secretions, fibrosis of inflammatory tissue, a second imaging modality includes turbo-spin echo (TSE), also known as non-echo planar imaging (non-EPI) diffusion-weighted (DW) magnetic resonance imaging (MRI). This imaging modality is both sensitive and specific for the detection of cholesteatoma, both prior to surgery and following surgery (for inspection of residual or recurrent cholesteatoma)[10]. The DWI technique is a variation of conventional MR techniques, based on the principles of the Brownian motion of water molecules in tissues: water molecules entrapped in laminated tissues, like that of a cholesteatoma, experience restriction of their free diffusion and produce a characteristic hyperintense signal (**Figure 4**). Therefore, the DW-MRI detects the keratin content of a cholesteatoma, but it is unlikely to reveal a recurrent retraction pocket without keratin or a tiny layer of epithelium without a matrix sac.

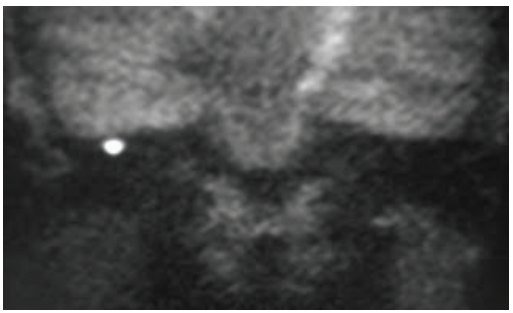

Figure 4. Non-EPI MRI shows cholesteatoma in the right middle ear cleft.

The two main limitations of the non-EPI DW-MRI imaging modality include lesions which are

smaller than 3 mm remain below the current detection limits of standard DW-MRI sequences [11], and the poor visualization of all other structures leading to the need for complementary imaging studies such as T1 and T2 MRI sequences with high spatial resolution in at least two planes in order to allow exact anatomic orientation (these imaging techniques have a long acquisition time hindering their use in the pediatric population). Alternatively, MR data may be fused with CT data if available [12].

Surgical Approaches

In addition to the traditional, well-established surgical techniques for the treatment of cholesteatomas in the pediatric population, newer techniques have been introduced and are gradually gain acceptance. The traditional techniques are based on the usage of a microscope during surgical dissection. These techniques include transcanal tympanoplasty (TT), canal wall up tympanomastoidectomy (CWU) and canal wall-down tympanomastoidectomy (CWD). CWD differs from CWU by the removal of the bony posterior canal wall to the level of the facial ridge. In the pediatric population the maintenance of the posterior canal wall remains a high priority, permitting children to continue their habitual recreational activities (swimming, etc.) When comparing both "canal wall" procedures, the major advantage of the CWU procedure are the preservation of normal anatomic contours in the external auditory canal with less structural destruction which can facilitate wound healing, as well as prevent the lifelong cavity inspection and clearance needed after the CWD procedure. A second advantage is seen in hearing outcomes, which may be superior when compared to CWD. In case of need for a hearing-aid, this surgical procedure permits an easy fitting. The major disadvantage of this procedure includes the frequent need for revision surgery (9%-70%), due to cholesteatoma recurrence or residue in areas which are difficult to visualize[13]. Revision surgery entails the possibility of complications and further discomfort to the child.

Another time honored technique is the CWD procedure. This procedure permits the surgeon a good inspection of the middle ear cavity and mastoid, and especially areas which are of difficult access. The exteriorization of the mastoid cavity into the middle ear permits through visualization of all areas prone to cholesteatoma recurrence, which leads to a lower rate of recidivism when compared to the CWU procedure. These advantages do not come without a price. The patients who undergo the CWD procedure usually have poorer hearing outcomes which are difficult to deal with (difficulty in hearing-aid fitting). The patient's ear cannot be exposed to water due to the likelihood of infections that require frequent cavity cleaning, which is difficult to perform in the pediatric population. When exposed to water a caloric stimulation may result, and some patients find that an enlarged meatus is cosmetically unappealing.

Nowadays, the border between these procedures has become more fluid, permitting the creation of the retrograde mastoidectomy with the advantages of following the disease, but in the main time leaving the smallest possible cavity in a well-aerated mastoid. In addition, in this technique, small cholesteatomas limited to the middle ear are accessed through a tympanoplasty alone, without mastoidectomy.

Another hybrid procedure is the CWD procedure with reconstruction of the posterior canal wall, permitting the conversion of a CWD into a CWU procedure. This procedure has shown to prevent retraction of the eardrum into the mastoid cavity by providing a solid barrier and decreasing air absorption from the mastoid dead space.

More recent, emerging techniques utilize transcanal endoscopes (0° and/or 30° endoscopes), and have shown promising results. This technique is generally referred as the endoscopic transcanal tympanoplasty (ETT), or the "hybrid" technique. The simple TT is the least frequently used primary procedure, due to exposure limitations. The addition of endoscopy to this technique, which permits a hybrid technique (ETT), has revived the usage of the transcanal access and retrograde step-by-step pursuit of cholesteatoma for limited cholesteatomas (in the middle ear cavity and with only minor invasion of the mastoid cavity), permitting safe surgery with through visualization of areas not demonstrated priorly (e.g. sinus tympani, facial recess, supratubal recess, the attic, posterior crus of the stapes). This procedure can be aided by the dissection under microscope becoming a hybrid procedure. We should note that this procedure is relatively recent, patients having a limited follow-up period (when compared to CWU and CWD procedures). More recently, a combination of techniques has been advocated, namely endoscopically-assisted CWU or CWD, with reconstruction of the posterior canal wall. A supplementary surgical procedure which is a synthesis of the latter, entails a retrograde mastoidectomy (an inside-out approach), which aims "tracking the lesion to its end". This creates an atticotomy, attico-antrectomy or attico-antro-mastoidectomy open cavity [14]. The last surgical method is laser assisted surgery. The application of laser technology (erbium yttrium aluminium garnet (Er:YAG) laser, potassium titanyl phosphate (KTP) laser and carbon dioxide (CO_2) laser permits both blood coagulation, for better visualization, as well as irradiation and evaporation of cholesteatoma epithelial remnants, found adjacent to the ossicles, without mechanical or acoustic trauma [15-17].

As reviewed, each of these techniques has its own inherent strengths and weaknesses. The choice of the technique used is based on location and extent of disease at time of surgery, as well as surgeon preference and experience. The use of hybrid techniques is new, permitting only short follow-up periods but permitting new prospective in cholesteatoma surgery.

References

1. Sudhoff H, Linthicum FH. Cholesteatoma behind an intact tympanic membrane: histopathologic evidence for a tympanic membrane origin. Otol Neurotol. 2001;22(4):444-6.
2. Soldati D, Mudry A. Knowledge about cholesteatoma, from the first description to the modern histopathology. Otol Neurotol. 2001;22(6):723-30.
3. Spilsbury K, Miller I, Semmens JB, Lannigan FJ. Factors associated with developing cholesteatoma: a study of 45,980 children with middle ear disease. Laryngoscope. 2010;120(3):625-30.
4. Spilsbury K, Ha JF, Semmens JB, Lannigan F. Cholesteatoma in cleft lip and palate: a population-based follow-up study of children after ventilation tubes. Laryngoscope. 2013;123(8):2024-9.

5. Michaels L. An epidermoid formation in the developing middle ear: possible source of cholesteatoma. J Otolaryngol. 1986;15(3):169-74.
6. Koltai PJ, Nelson M, Castellon RJ, Garabedian EN, Triglia JM, Roman S, et al. The natural history of congenital cholesteatoma. Arch Otolaryngol Head Neck Surg. 2002;128(7):804-9.
7. Kuo CL. Etiopathogenesis of acquired cholesteatoma: Prominent theories and recent advances in biomolecular research. Laryngoscope. 2014.
8. Jung JY, Chole RA. Bone resorption in chronic otitis media: the role of the osteoclast. ORL J Otorhinolaryngol Relat Spec. 2002;64(2):95-107.
9. Lee DH, Kim CS, Park CW, Chung DY. Is preoperative computed tomographic density measurement of soft tissues helpful in the diagnosis of cholesteatoma? Ann Otol Rhinol Laryngol. 2012;121(12):792-7.
10. Koitschev A, Behringer P, Bögner D, Amrhein P, Winkler P, von Kalle T. Does diffusion-weighted MRI (DW-MRI) change treatment strategy in pediatric cholesteatoma? Acta Otolaryngol. 2013;133(5):443-8.
11. Jindal M, Riskalla A, Jiang D, Connor S, O'Connor AF. A systematic review of diffusion-weighted magnetic resonance imaging in the assessment of postoperative cholesteatoma. Otol Neurotol. 2011;32(8):1243-9.
12. Plouin-Gaudon I, Bossard D, Ayari-Khalfallah S, Froehlich P. Fusion of MRIs and CT scans for surgical treatment of cholesteatoma of the middle ear in children. Arch Otolaryngol Head Neck Surg. 2010;136(9):878-83.
13. Tomlin J, Chang D, McCutcheon B, Harris J. Surgical technique and recurrence in cholesteatoma: a meta-analysis. Audiol Neurootol. 2013;18(3):135-42.
14. Nikolopoulos TP, Gerbesiotis P. Surgical management of cholesteatoma: the two main options and the third way--atticotomy/limited mastoidectomy. Int J Pediatr Otorhinolaryngol. 2009;73(9):1222-7.
15. James AL, Papsin BC. Some considerations in congenital cholesteatoma. Curr Opin Otolaryngol Head Neck Surg. 2013;21(5):431-9.
16. Hamilton JW. Systematic preservation of the ossicular chain in cholesteatoma surgery using a fiber-guided laser. Otol Neurotol. 2010;31(7):1104-8.
17. Hamilton JW. Efficacy of the KTP laser in the treatment of middle ear cholesteatoma. Otol Neurotol. 2005;26(2):135-9.