The Natural History of Congenital Cholesteatoma

Peter J. Koltai, MD; Marc Nelson, MD; Roberto J. Castellon, MD; Erea-Noel Garabedian, MD; Jean-Michel Triglia, MD; Stephane Roman, MD; Gilles Roger, MD

Objectives: To describe the natural history of congenital cholesteatoma (CC) and to determine whether such a description provides clues about the origins and endpoints of these lesions.

Design: A retrospective qualitative analysis of intraoperative illustrations of 34 consecutive patients with 35 CCs (1 bilateral).

Setting: Two tertiary care children’s hospitals.

Patients: Thirty-four children with CC, mean age, 5.6 years (range, 2-13 years).

Results: Congenital cholesteatoma originates generally, but not universally, in the anterior superior quadrant. The progression of growth is toward the posterior superior quadrant and attic and then into the mastoid. Contact with the ossicular chain generally results in loss of ossicular continuity and in conductive hearing loss.

Conclusions: Congenital cholesteatoma appears to have a predictable trajectory of growth, starting as a small pearl in the middle ear, eventually growing to involve the ossicles and mastoid, and causing varying degrees of destruction and functional impairment. The clinical picture of a young child with otorrhea, conductive hearing loss, tympanic membrane perforation in a nontraditional location, and a mastoid filled with cholesteatoma may represent the end point in the natural history of CC, despite the fact that this type of lesion is outside the accepted definition of CC.


CONGENITAL cholesteatoma (CC) presents early in life as a white pearly mass behind an intact tympanic membrane, usually in the anterior superior quadrant of the middle ear. As it grows, it typically expands into other areas in a predictable sequence. A classification system for this lesion based on this sequence of growth has been proposed.1

In this article, we present a series of intraoperative illustrations from 35 consecutive CCs to show the sequence of growth. We also describe 2 children with atypical cases of CC suggesting that mastoid invasion and tympanic membrane perforation may be part of the natural history of CC. The clinical course of a third patient is described and used to illustrate a theory of CC origin.

RESULTS

The intraoperative drawings arranged by size and spread of the cholesteatomas provide a visual representation of much of the natural history of CC. Most lesions start out as a matrix-enclosed spherical keratin pearl in the anterior superior quadrant. The pearl grows like a round balloon inflating. Anterior growth is toward the eustachian tube, and an early sign of a growing CC can be otitis media with effusion secondary to obstruction of the eustachian tube by the lesion. Later, negative pressure causes the drum to retract, which puts the CC into relief, making it more discernible on otoscopy.

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Inferior growth, resulting in extension of the CC toward the hypotympanum, is seen with continued spherical enlargement. The matrix rind remains smooth, without fully assuming the irregular topography of the hypotympanic cavity.

Posterior growth is toward the handle of the malleus, and, generally, as it proceeds, the CC follows the contour of the underside of the drum, developing an indentation under the handle of the mal-
PATIENTS AND METHODS

Between July 1, 1989, and June 30, 2000, 34 children were treated for CC at the children’s hospitals of The Cleveland Clinic and Albany Medical Center. The mean ± SD age was 5.6 ± 2.8 years (range, 2-13 years). One of the children had bilateral CCs, resulting in 35 CCs in this series. The medical records from these children were added to a database for a quantitative analysis of outcomes and classifications of CC. In addition, we prepared templates from intraoperative illustrations of the 35 CCs maintained by one of us (P.J.K.). Each drawing was oriented to a right ear template. These were arranged in order of increasing size to simulate the presumed natural growth pattern of CC (Figure 1).

COMMENT

The question of whether CC can cause rupture of the tympanic membrane is an interesting one, because the presence of a perforation places the lesion outside the accepted definition of CC. Nevertheless, it is reasonable to suppose that, with sufficient growth of the CC, tympanic membrane perforation is a possibility, and this supposition is also supported by clinical evidence. We have seen several cases (not included in this analysis because of the aforementioned problems with definition) of young children (ages 3-6 years) presenting with sudden unremitting otorrhea, with little or no history of otitis media. The culture from the drainage usually grows *Pseudomonas aeruginosa*, *Staphylococcus aureus*, or both. The computed tomographic (CT) scan generally shows complete occupation of the mastoid by soft tissue that is causing osteolysis of the mastoid septa. On exploration, tympanic membrane rupture has been observed at various points on the drum other than the pars flaccida or the posterior quadrant. At mastoidectomy, the entire mastoid, from antrum to tip, is host to the cholesteatoma.

The clinical picture of a very young child with otorrhea of several months’ duration, maximum conductive hearing loss, tympanic membrane perforation in a nontraditional location, and a mastoid full of cholesteatoma probably represents the end point in the natural history of CC. In these young children, tympanic membrane perforation and otorrhea always seem to be coincidental with complete occupation of the mastoid with cholesteatoma. This suggests 2 possible, perhaps related, mechanisms of CC growth in the late stages. One is that the volume of cholesteatoma exceeds the capacity of the middle ear and mastoid, resulting in tympanic membrane perforation. The other is that tympanic membrane perforation and subsequent infection accelerate the growth of the CC, resulting in complete filling of the middle ear and mastoid. Acquired cholesteatoma can also present with otorrhea and complete cholesteatoma invasion of the middle ear and mastoid, but tympanic perforation and otorrhea typically occur well before the entire mastoid is involved.

Two cases of unusual presentation and circumstance shed some additional light on the end point of the natural history of CC and provide further evidence that mastoid invasion and tympanic membrane perforation are part of that history. A third case illustrates a theory of origin of CC.

CASE 1

This case occurred in a 4-year-old boy with a well documented history of bilateral recurrent acute otitis media treated with antibiotics, but with no history of tube insertion or previous otorrhea associated with episodes of acute otitis media. He presented initially with a history of left-sided otorrhea, which on culture grew *P aerugi-
nosa. This was treated with systemic antibiotics and antibiotic ear drops. Despite this therapy, the drainage continued and he eventually was referred to us with left-sided mastoiditis. An audiogram showed a 50-dB conductive hearing loss on the left and a 30-dB conductive hearing loss on the right. A tympanogram could not be obtained on the left, and the right side showed a flat type B. A CT scan showed soft tissue opacification of the left middle ear and mastoid, with thinning and destruction of the mastoid septa and cortex (Figure 2). The CT scan also demonstrated similar opacification of the right middle ear and mastoid (Figure 3).

At exploration of the left ear, a large cholesteatoma occupying the middle ear and mastoid was found. There was erosion of the posterior canal wall, with keratin abutting the posterior canal wall skin. There was loss of the stapes superstructure and long process of incus, as well as complete encirclement of the malleus and incus heads. A canal wall down tympanomastoidectomy with a wide meatoplasty was performed.

At the same operation, the right ear was examined with a microscope. A CC occupying the anterior and posterior quadrants of the middle ear was seen through an intact tympanic membrane. A subsequent exploratory tympanotomy and mastoidectomy of the right ear revealed a CC extending from the eustachian tube back underneath the malleus, up into the anterior attic around the heads of the incus and malleus, and into the mastoid. A canal wall up tympanomastoidectomy with incus interposition was performed.

CASE 2

This cholesteatoma was in a 3-year-old boy with no history of otitis media. It had been discovered 4 months previously during surgery for an aural polyp that appeared to originate on the left posterior canal wall. His tympanic membrane was intact, and a myringotomy and tube placement were performed. During the procedure, keratin in the middle ear was biopsied and found to contain cholesteatoma. At referral, he had an indwelling pneumatic equalization tube and what appeared to be a white mass occupying the middle ear behind the tympanic membrane. An audiogram showed a 40-dB conductive hearing loss in the left ear and normal hearing in the right ear. A CT scan showed soft tissue opacification of the left middle ear and mastoid, with thinning and destruction of the mastoid septa and cortex (Figure 4). The CT scan of the right temporal bone showed no abnormalities.

At exploration of the left ear, the tympanic membrane was intact, with an indwelling ventilation tube and a CC behind it. There was a fistula between the skin of the posterior canal and the mastoid through a defect in the posterior canal wall. The mastoid was completely occupied by cholesteatoma. In the middle ear there was loss of the stapes superstructure and long process of incus,
as well as complete encirclement of the malleus and incus heads. A canal wall down tympanomastoidectomy with a wide meatoplasty was performed.

**CASE DISCUSSION**

In the first patient, the location in the left ear rendered the lesion outside the accepted definition of CC. Nevertheless, with the contralateral right ear having a moderate-sized CC that fell well within the definition, it seemed reasonable to conclude that the left-sided lesion, like the right-sided one, originated as a CC. It is not unusual for children to have bilateral CC,2-5 but this case was unusual in demonstrating the continuity of a bilateral late-stage CC in which the tympanic membrane was perforated on one side but not on the other.

In the second patient, the location in the left ear was initially thought to put the lesion outside the accepted definition of CC. However, because the otorrhea was originating from a defect in the posterior canal wall and the tympanic membrane was intact, this lesion was classified as a CC. Similar observations of posterior canal wall destruction have been reported.6,7 Except for the loss of tympanic membrane integrity, the trajectory of destructiveness of the left ears in the first and second patients was similar clinically and on CT imaging. Both demonstrate end-stage lesions of CC, with the second case being slightly less advanced than the first, and both highlight the problems of defining the origin of a cholesteatoma that has spread far enough to destroy the function of the ear. Our intent, with this analysis of late disease, is not to change the definition of CC but to deepen our understanding of the end stages of this disease.

**FOUR THEORIES OF CC ORIGIN**

Like the end stages of CC, its origin continues to be a source of controversy and debate. The competing theories of the pathogenesis of CC fall into 4 broad categories: implantation, invagination, metaplasia, and epidermoid formation.

Friedberg,8 House and Sheehy,9 and Herdman and Wright10 suggested that a possible rare cause of CC is implantation of squamous epithelium in the middle ear during ventilation tube insertion. Northrop et al11 observed viable squamous epithelial cells in the amniotic fluid present in the middle ears of neonates and hypothesized that this was a possible source of CC. However, these authors presented no evidence that these cells could implant to form a CC.
Invagination

Several variations of the invagination theory have been proposed,\textsuperscript{12,13} most based on Ruedi’s\textsuperscript{14} suggestion that otitis media causes an inflammatory injury of the tympanic membrane that invaginates into the middle ear to form a CC. A review of the literature fails to reveal any buttressing histologic or clinical evidence for this postulate. Moreover, Karmody et al\textsuperscript{15} suggest that for plausibility the invagination theory demands in utero inflammation of the tympanic membrane.

The epithelial migration theory is an alternative version of the invagination theory, independent of otitis media, which was proposed by Aimi.\textsuperscript{16} This theory suggests that ectoderm from the embryonic external auditory canal overcomes a hypothetical restrictive mechanism of the tympanic ring and migrates into the middle ear. Although this theory also lacks definitive clinical documentation and requires several hypothetical hurdles for serious consideration, it presents an attractive possible explanation for the 4 cases in Figure 2 (images 32-35) in which CC occurred in the posterior and inferior parts of the middle ear, in proximity to the site of the embryonic tympanic ring. The clinical course of the patient described in Case 3 would appear to support the epithelial migration theory.

CASE 3

A 3-year-old girl with no history of otitis media was referred after her pediatrician noted a white pearly mass behind her right tympanic membrane in the posterior inferior quadrant adjacent to the tympanic ring. An audiogram showed no hearing abnormalities. A CT scan showed dense soft tissue adjacent to the tympanic membrane and posterior tympanic ring, extending some distance into the hypotympanum (Figure 5). At exploratory tympanotomy, a CC was found to adhere to the underside of the drum and the posterior inferior annulus. It dissected free as a single pearl from the tympanic membrane, the annulus, and the hypotympanum. The child healed without incident and has had no recurrence of her lesion. This case illustrates 1 of 4 theories of CC origin discussed herein.

Metaplasia

The metaplasia theory was proposed by Sade et al\textsuperscript{17} and is based on their observation that squamous metaplasia, some with keratinization, can occur in the middle ear in response to otitis media. They postulated that such keratinizing metaplastic change of the mucosa can possibly result in CC. However, Friedberg\textsuperscript{8} has pointed out the discrepancy between the consistent location of CC (in the anterior superior quadrant) and the inconsistent location of middle ear metaplasia. Like the invagination theory, the metaplasia theory appears to require in utero inflammation of the tympanic membrane to be plausible.\textsuperscript{15}

Epidermoid Formation

The epidermoid formation theory of CC is based on Michael’s\textsuperscript{18} observation of a rest of squamous epithelial cells, which occasionally keratinize, in the lateral wall of the embryonic tympanic cavity below the level of the pars flaccida. The rest of the cells, which he termed an epidermoid formation, was noted in more than half of the specimens examined. It was observed as early as the tenth week of gestation and consistently disappeared by 33 weeks of gestation. This observation had also been made by Teed\textsuperscript{19} 50 years earlier and was verified by Wang\textsuperscript{20} and McGill\textsuperscript{21} and their colleagues. McGill et al pointed out in 1991 that confirmation of the epidermoid formation theory would require finding intermediate forms of anterior superior quadrant epithelial cell rests between 33 weeks of gestation, when epidermoid formations involute, and early childhood, when CC typically presents. Seven years later, Karmody et al\textsuperscript{15} described finding such evidence in 2 postmortem investigations: a keratinizing epidermoid formation in the temporal bone of a 3½-month-old boy and a nonkeratinizing epidermoid formation in the temporal bone of a 7½-month-old boy. In addition, Potsic et al\textsuperscript{22} described a 4-month-old girl with bilateral CC confirmed at exploratory tympanotomy.

Although we have no cases that contribute new evidence to support any one theory about the pathogenesis of CC, one observation that must be accounted for by any plausible explanation of the origin of CC is the very young age of the children in whom it was found (mean age, 3.6 years; range, 2-13 years). This is consistent with findings from other large series.\textsuperscript{6,21-24}

In contrast, the mean±SD age of 991 children with acquired cholesteatoma from 4 institutions was 9.7±3.3 years,\textsuperscript{1} significantly older than the children with CC in this series (P<.001). These are separate populations with different diseases, which suggests a relationship between early age and the pathogenesis of CC. Age-related pathogenesis could support either an embryonic origin (the migration and epidermoid formation theories) or an origin related to otitis media during infancy (the invagination and metaplasia theories). However, the observation that only 48.7% among the series\textsuperscript{1} of 991 children with acquired cholesteatoma had a history of otitis me-

Figure 5. Coronal computed tomographic scan of the right (R) temporal bone of a 3-year-old girl with a hypotympanum congenital cholesteatoma (case 3). This ear corresponds to number 34 on the composite Figure 1. L indicates left.
dia (acute otitis media or otitis media with effusion) weakens the argument for a causative role of otitis media. One would have to invoke a hypothetical history of “silent otitis media” in a large number of children to salvage this line of reasoning, which seems inelegant and unnecessarily complicated.

CONCLUSIONS

1. The origin of CC remains uncertain, but a substantial body of evidence suggests that most CC begins as an embryonic epidermoid formation in the anterior mesotympanum that fails to involute.
2. The mass is usually in the anterior superior quadrant, but does not consistently remain there and may variably occupy the middle ear and mastoid and result in ossicular destruction and conductive hearing loss.
3. The progression of growth is from the middle ear, initially into the posterior superior quadrant and attic, and finally into the mastoid.
4. The clinical picture of a young child with otorrhea, conductive hearing loss, tympanic membrane perforation in a nontraditional location, and a mastoid filled with cholesteatoma may represent the end point in the natural history of CC, despite the fact that this type of lesion is outside the accepted definition of CC.

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Corresponding author: Peter J. Koltai, MD, Section of Pediatric Otolaryngology, The Cleveland Clinic Foundation, 9500 Euclid Ave, Desk A71, Cleveland, OH 44195 (e-mail: koltai@ccf.org).

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