

Cholesteatomatous otitis media: histopathological changes

A post mortem study on temporal bones

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Abstract. – The histopathological changes in the temporal bones of 3 deceased donors individuals with concomitant chronic cholesteatomatous otitis media have been studied. The different forms of cholesteatoma are analyzed: the primary congenital, the primary acquired and the secondary acquired. The different clinical relevance and the different therapeutic guidelines are discussed.

Key Words:

Cholesteatoma, Histology, Surgery, Temporal bone, Chronic otitis, Middle ear.

Introduction

Cholesteatoma (synonym: keratoma)¹, is an important concomitant in from one-third to one-half of cases of chronic otitis media. It is a cyst lined by squamous epithelium within the middle ear cavity. The term cholesteatoma is an unfortunate one, because the entity it designates bears no relation to cholesterol granuloma or to a neoplasm. It is usual to separate a congenital or primary form of cholesteatoma, in which a cyst is present behind an intact tympanic membrane, from an acquired form, in which there is a perforation of the tympanic membrane.

Materials and Methods

We have studied the histopathological changes in the temporal bones of 3 deceased individuals with chronic cholesteatomatous otitis media.

These patients were donors and agreed during their life to donate *post mortem* their temporal bones to the House Ear Institute Los Angeles, CA, USA, as a contribution to a better knowledge of temporal bone diseases.

We have removed the temporal bones in our² usual way.

Results and Discussion

Clinical features

A small cholesteatoma may be present with normal hearing and no discharge. Typically, however, there is a foul smelling discharge and hearing loss. On examination of the tympanic membrane there is, in most cases, a perforation of the superior or postero-superior margin.

Gross appearances

The cholesteatoma appears as a pearly gray or yellow cyst-like structure in the middle ear cavity. The wall of the cyst may often be seen as a thin membrane. The congenital (primary) form of cholesteatoma appears as a cyst in the mesotympanum and is not related to the pars flaccida of the tympanic membrane (Figure 1). In the majority of cases it is situated in relation to the upper anterior position of the tympanic membrane in a space bounded by the handle of the *malleus*, the *tensor tympani* muscle and the *processus cochleariformis*. In some cases it has been found to be occluding the eustachian tube³. It is not typically associated with inflammation of the middle ear mucosa⁴.

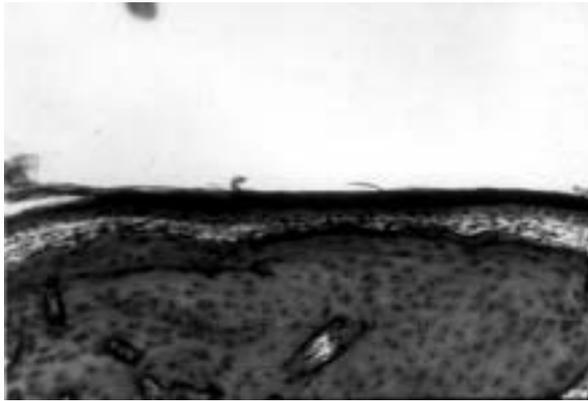


Figure 1. Primary (congenital) cholesteatoma matrix with no evidence of inflammation. Desquamation is visible on left side of picture. $\times 117$

The term congenital cholesteatoma is also applied to a squamous epithelial cyst arising deep in the temporal bone and elsewhere, which causes damage by erosion of the skull⁵. This is quite a different entity from the middle ear cholesteatoma and the description "epidermoid" for the deeper entity is more appropriate (Figure 2).

The much more frequent "acquired" form of cholesteatoma is usually situated in the upper part of the middle ear cleft and discharges through a perforation of the *pars flaccida* of the tympanic membrane. The cholesteatoma may extend through the aditus into the mastoid *antrum* and mastoid air cells.

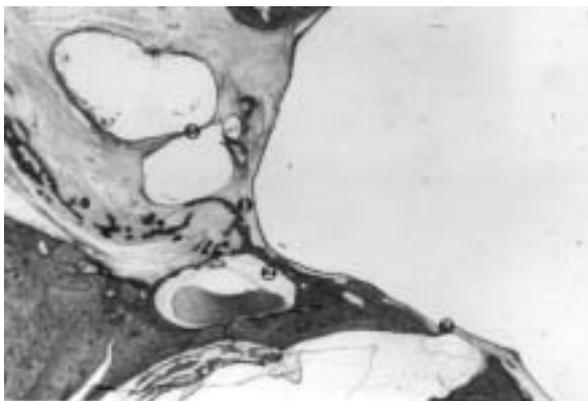


Figure 2. Primary acquired cholesteatoma in the epitympanum above the level of the malleolar ligament and chorda tympani. The matrix is adherent to the pyramidal process (1); fallopian canal (2); fistula in the horizontal canal (3); the anterior epitympanum filled with fibrous tissue surrounding two cysts (4). $\times 15$

Frequently the outline of the cholesteatomatous sac is adapted to that of normal structures such as ossicles. Chronic inflammatory changes are always present. In most cases at least one ossicle is seriously damaged, so interrupting the continuity of the ossicular chain (Figure 3). The scutum, the upper part of the bony ring of the tympanic opening, is eroded in 42% of ears with cholesteatoma⁶.

Microscopic appearances

Under the microscope the pearly material of the cholesteatoma consists of dead, fully differentiated anucleate keratin squames. This is the corneal layer of the squamous cell epithelium. Sometimes biopsy material shows only squames when the so-called *capsule* has not been excised. This capsule, often called the matrix, is composed of fully differentiated, squamous epithelium similar to the epidermis of skin, and resting on connective tissue. There is a basal layer of small cuboidal cells above which is a spinal or malpighian layer composed of five or six rows of cells with intercellular prickles. A thin, granular layer, in which the cells display prominent cytoplasmic keratohyaline granules, separates the malpighian layer from the extensive corneal layer.

The eroded ossicles which are frequently present in cholesteatoma may be invested by the squamous epithelial wall of the endolymphatic sac. There is always, even in these cir-

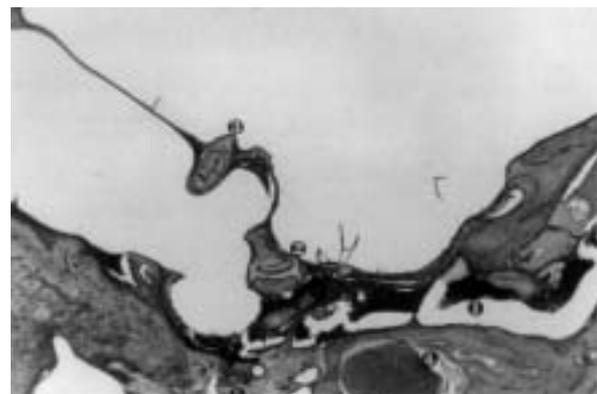


Figure 3. Secondary acquired cholesteatoma below the level of the posterior malleolar ligament and chorda tympani. There is an inflammatory exudate in the middle ear space (1). The atrophic tympanic membrane is retracted to the incostapedial joint (2). The malleus handle (3) and facial nerve (4) are visible. The oval window is filled with fibrous tissue. $\times 15$

cumstances, a layer of granulation tissue in contact with the bone and it seems likely that it is the chronic inflammatory covering, not the squamous epithelium, that produces the erosion.

Retraction pocket

A retraction pocket is an invagination of part of the tympanic membrane into the middle ear cavity as a result of chronic otitis media. It is usually the *pars flaccida* that is so indented. It frequently becomes adherent to the posterior wall of the middle ear in the region of the facial nerve or stapes.

Histological sections of the wall of the retraction pocket show an absence of the normal tympanic membrane connective tissue, which may have been destroyed by inflammation¹.

Migration of squamous epithelium

The outer epithelium of the tympanic membrane and the epithelium of the adjacent ear canal have the property of migrating laterally, as a result of which a foreign body such as an ink dot can be seen to move at a rate of about 0,07 mm each day from the ear drum laterally along the canal⁷. This property, which is also found in other mammals, is unique in the squamous epithelia of the body. Its biological function is clearly that of cleaning the surface of the tympanic membrane of desquamated keratin so that it should not be impeded in sound vibration. It seems likely that migration occurs by displacement of basal epithelial cells laterally away from the central part of the tympanic membrane⁸ (Litton 1968). The phenomenon of migration has been invoked to explain the origin of cholesteatoma from ear drum and external auditory epithelium (see below).

Pathogenesis

4 concepts of the pathogenesis of cholesteatoma have been put forward. It has been suggested that cholesteatoma may arise:

- from invasion of canal and tympanic membrane epithelium into the middle ear
- from invagination of tympanic membrane in the form of a retraction pocket (see above)
- from metaplasia of the epithelia of the middle ear

- from epidermoid cell rests, which have arisen during development in the middle ear epithelium

There is evidence to favor each of these concepts and it is possible that cholesteatoma may arise as a result of each mechanism under different circumstances.

a) Squamous epithelium may grow in from the tympanic membrane or ear canal through a perforation to involve parts of the middle ear, sometimes extensively. Such a migration does frequently occur, but is not usually accompanied by true cholesteatoma⁹, even though there may be progressive invasion of skin from the ear canal to line most of the middle ear and its attic. Migration of squamous epithelium has been induced experimentally in otitis media following inoculation of bacteria¹⁰ and quinine¹¹ into the middle ear of guinea pigs. Ultrastructural examination of cholesteatoma epithelium often reveals the presence of Langerhans cells¹², as does ear canal skin, and this observation has been taken as evidence in favor of the migratory origin of cholesteatoma. The prominence of these cells in cholesteatomatous squamous epithelium is, perhaps, more an indication of the marked exposure of the epithelium to foreign antigens than of its mode of origin.

b) Retraction pockets have been observed as a phase in the development of some cholesteatomas¹³. Sadè et al.¹⁴ in a prospective study of 201 retraction pockets found that only three developed into small attic cholesteatomas. Histological examination of 12 retraction pockets in *post-mortem* temporal bones¹⁵ showed no evidence of development of cholesteatoma. In two of them extensions of stratified squamous epithelium with keratin cysts have been traced from the tympanic membrane deep into the middle ear.

c) Sadè stated that he has frequently observed islands of squamous cell epithelium in the middle ear¹⁶. These were said to be in continuity with the middle ear columnar epithelium, indicating an origin by metaplasia. He has suggested that cholesteatoma develops by such metaplasia in the tympanic cavity and that when drainage of keratin is not possible externally, secondary infection develops in the middle ear.

Glandular transformation is often present in the attic and is frequently seen in associa-

tion with cholesteatoma. Sack has also suggested that the epithelium of submerged glands may become epidermoid by metaplasia and initiate miniature cholesteatomas¹⁷. It must be admitted that Sack's concept is appealing in its simplicity, but there has been little support published by other observers. Until that has been done the concept of metaplasia as a source of cholesteatoma must be considered unproved.

d) Cell rests of epidermoid tissue have been suggested from time to time as the origin of the primary form of cholesteatoma¹⁸. An absence of the connective tissue layer of the tympanic membrane allowing inward migration of the stratified squamous epithelium of the ear canal during development has recently been suggested as a mechanism of squamous epithelium entry into the middle ear to produce cell rests during development¹⁹. In a study of perinatal temporal bones it has been noticed²⁰ an epidermoid formation in the developing middle ear. This was seen between 10 and 33 weeks gestation in 37 out of 68 fetal ears in step section. The epidermoid cell collection is always in the same position in the epithelium of the middle ear adjacent to the anterior limb of the osseous tympanic ring. It is single or double, the latter separated by a short space of normal epithelium. The epidermoid formation may show extensive keratinization or vesicle formation²⁰. All the cases described by Levenson et al.³ of primary cholesteatoma arose in the upper anterior mesotympanum and so probably from the epidermoid formation. Secondary cholesteatoma is usually an attic lesion and thus seems unlikely to arise from the epidermoid formation.

Chemical factors in bone resorption

A number of chemical factors have been incriminated in the bone resorption of cholesteatoma. All of these are derived from the accompanying chronic otitis media or the infection associated with it. Specimens of cholesteatoma, which include the underlying matrix, have been found to show strong collagenase activity. This enzyme has been located by immunofluorescent methods in the connective tissue, particularly around blood vessels²¹. It is likely that this collagenase plays a part in resorption of bone. Endotoxins may also play a part and this is particularly likely

because they are derived from Gram-negative bacilli, which are prominent in infection associated with cholesteatoma²².

Conclusion

The primary cholesteatoma is a congenital disease, with no serious symptoms and consequences. In this case a "wait and see" policy is suggested.

On the other side the chronic cholesteatomatous otitis is a serious infection that can lead to severe complications: labyrinthitis, facial nerve palsy, meningitis, sinus thrombophlebitis, extradural abscess or brain abscess. In this case, the surgical treatment is mandatory. The aggressive behaviour of cholesteatomatous cells suggest to stage the operation²³⁻²⁵. This is indicated in chronic otitis media with a major mucous membrane problem and much more in cholesteatomatous chronic otitis media, were the operation can leave some cholesteatomatous cells, not visible even at the microscope, with consequent recurrent cholesteatoma²⁶⁻²⁷. To stage the operation permit a "second look" for removing the disease and for reconstructing the ossicular chain, which permits the recovery of the transmissive hearing loss.

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