Chapter 157: Chronic Otitis Media, Mastoiditis, and Petrositis

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Otitis media is the most common disease of childhood, with the exception of viral upper respiratory infections. The acute bacterial infection occurs in 80% of children between the ages of 1 and 6 years, and it is the most frequent disease treated with antibiotics in the USA. The infectious and noninfectious complications of otitis media result in significant morbidity. The infectious complications, including acute and chronic mastoiditis, petrositis, and intracranial infection, still occur despite the widespread use of antibiotics for this disease. The noninfectious sequelae, including chronic perforation of the tympanic membrane, ossicular erosion, labyrinthine erosion, and tympanosclerosis are significant causes of hearing loss throughout the world.

Further, some cases of acute otitis media (AOM) result in persistent otitis media with effusion (OME), which is now recognized as the leading cause of childhood hearing loss. The exact cause of OME is not clear; although eustachian tube dysfunction alone may lead to effusion of the middle ear, there is mounting evidence that the majority of cases of OME occurs as a sequela of acute otitis media, or at least share the same etiologic factors (see Chapter 156).

In most children AOM and OME subside spontaneously or after medical or surgical intervention. It is unknown how many children with OME eventually have complications. Sequele of otitis media may result in auditory deprivation during early childhood or direct effects of the localized process. Otitis media may be complicated by acute or chronic perforation of the tympanic membrane, acute mastoiditis, middle ear atelectasis, adhesive otitis media, tympanosclerosis, ossicular erosion or fixation, petrous apicitis, cholesteatoma, chronic otomastoiditis, labyrinthitis, facial paralysis, and intracranial infection. There is also evidence that sensorineural hearing los may result from chronic otitis media with or without cholesteatoma. Indirect sequelae include language delays and complications from septicemia.

Effects on Mastoid Pneumatization

It has been observed that children with chronic OME have more sclerotic mastoids with decreased pneumatization as compared to normal children. Two suggestions have been made to explain this observation: (1) the "hereditary theory", which states that children with hypoaeration of the mastoid are prone to OME (Diamant, 1940) and (2) the "environtmental theory", which states that chronic OME results in hypopneumatization of the mastoid (Wittmaak, 1918). Although a measurable correlation between mastoid hypocellularity and OME has been proven (Tos et al, 1985), a cause-and-effect relationship is not clear. Available evidence generally supports the concept that chronic inflammation may lead to new bone formation within the middle ear and mastoid and, subsequently, diminished size of mastoid air cells. However, Shatz and Sadé (1990) measured the distance from the lateral sinus to the external auditory canal and found it to be significantly smaller in individuals with sclerotic mastoids; they felt that this finding supported the hereditary theory in that it was unlikely that otitis would change the position of the lateral sinus.

Middle Ear Atelectasis and Adhesive Otitis Media

Middle ear atelectasis (Fig. 157-1) is thought to result from long-standing eustachian tube dysfunction. The tympanic membrane becomes retracted onto the promontory and the ossicles of the middle ear. In atelectatic ears the middle ear space is partially or completely obliterated but the tympanic membrane is not adherent to the medial wall of the middle ear and the mucosal lining of the middle ear is intact. In contrast, adhesive otitis media exists when the middle ear space is totally obliterated and the tympanic membrane is adherent to the ossicles and promontory; mucosal surfaces are not present. Retraction of the tympanic membrane may lead to erosion of the long process of the incus and the stapes suprastructure (Fig. 157-2). Not all individuals with chronic OME develop atelectasis; in most cases of OME, retraction of the tympanic membrane is limited. It may be that repeated bouts of AOM lead to weakening and thinning of the membrane, which allows atelectasis. Sadé and Bercoo (1976) demonstrated destruction of the collagen-containing fibrous layer of the tympanic membrane in some ears with recurrent infection. It is interesting to note that collagen destruction within the tympanic membrane may lead to another complication of OME, namely, tympanosclerosis.

Sadé and Berco (1976) described four states of tympanic membrane retraction: stage I: retracted tympanic membrane; stage II: retraction with contact onto the incus; stage III: middle ear atelectasis, and stage IV: adhesive otitis media (Fig. 157-3).

Middle ear atelectasis may be reversible with ventilating tubes. Sadé (1979) showed that ventilating tubes improved the state of atelectatis ears. Graham and Knight (1981) reported three cases in which atelectatic tympanic membranes were restored to their normal position by administration of nitrous oxide during anesthesia and insertion of a ventilating tube.

Atelectasis and adhesive otitis media usually coexist with OME. However, OME may resolve in these ears, allowing aeration of the attic and mastoid but leaving a collapsed middle ear. In extreme cases, when hearing loss or ossicular erosion occurs, a myringoplasty for the reinforcement of atelectatic tympanic membrane may be indicated (Donaldson, 1986; Paparella and Jung, 1981).

Cholesteatomas may arise from deep retraction pockets in which desquamated keratin debris does not migrate into the ear canal; these retraction pockets may occur in the pars tensa or pars flaccida of atelectatic ears and must be considered as precursors to cholesteatomas (see discussion of cholesteatoma).

Chronic Otitis Media with Cholesteatoma

Aural cholesteatomas are epidermal inclusion cysts of the middle ear or mastoid. (In the case of a retraction pocket cholesteatoma the "cyst" opens into the external auditory canal.) They contain the desquamated debris (principally keratin) from their keratinizing, squamous epithelial lining. Aural cholesteatoma was first described by Cruveilhier (1829) as a "pearly tumor" of the temporal bone. The term *cholesteatoma* is a misnomer since this entity does not contain cholesterol; the white-yellow keratin flakes found within cholesteatomas grossly resemble cholesterol crystals. Cholesteatomas of the temporal bone

may be congenital or acquired. Acquired cholesteatomas are the consequence of OME or AOM or both.

An understanding of the pathogenesis and pathophysiology of aural cholesteatoma is particularly important since it is the destructive nature of this entity that is responsible for much of the morbidity associated with chronic otitis media. The propensity of cholesteatomas to erode bone and the lack of effective, nonsurgical treatment add importance to the understanding of this disease.

Diagnosis

The diagnosis of aural cholesteatoma is made on otoscopic examination or surgical exploration. Special imaging procedures, such as high-resolution computed tomographic (CT) scanning and magnetic resonance imaging (MRI), may suggest the presence of cholesteatomas within the temporal bone and may be used to complement the clinical examination. High-resolution CT scanning is useful for operative planning and is recommended for all revision mastoid operations. The symptoms of cholesteatoma vary; some cholesteatomas are asymptomatic, whereas others become infected and rapidly cause bone destruction. Some patients will present to the physician with slowly progressive conductive hearing loss. However, most patients with cholesteatomas consult a physician because of chronic otitis with purulent otorrhea. The otorrhea from an infected cholesteatoma is often malodorous because of the frequent infection with anaerobic bacteria (Harker and Koontz, 1977). Patients with an infected cholesteatoma are occasionally misdiagnosed as having external otitis. Therefore careful follow-up and thorough canal debridement of a patient with otorrhea is mandatory, since the cholesteatoma may not be evident during an acute flare-up. Some patients will have signs and symptoms oof the sequelae of a cholesteatoma: vertigo and hearing loss caused by a labyrinthine fistula, facial nerve paralysis, or intracranial infection.

The otoscopic appearance of an aural cholesteatoma is also variable. A typical attic retraction cholesteatoma (Fig. 157-4) appears as a defect of variable size adjacent to the posterosuperior portion of the tympanic membrane; the center of the defect contains keratin debris: *primary acquired cholesteatoma.* In other cases, keratinizing epithelium has migrated through a perforation into the middle ear (Fig. 157-5): *secondary acquired cholesteatoma.* Cholesteatomas sometimes appear behind or within an intact tympanic membrane: so called *congenital cholesteatoma* (Fig. 157-6). These cholesteatomas have been considered to be congenital, but recent experimental evidence raises the possibility that they may arise during an inflammatory process. An infected cholesteatoma will sometimes present as an "aural polyp"; these "polyps" are actually granulation tissue at the junction between an eroding cholesteatoma and bone. The presence of an aural polyp in a chronically infected ear should be considered to be a cholesteatoma until proven otherwise. Occasionally, a cholesteatoma cannot be seen otoscopically but will be discovered during tympanomastoid surgery.

The prevalence of cholesteatoma is unknown. In 1978 there were 4.2 hospital discharges/100.000 population with cholesteatoma (Ruben, 1982). Additionally there were 13.8 hospital discharges/100.000 population with chronic otitis media without cholesteatoma.

Pathogenesis

It is generally accepted that cholesteatomas may be congenital or acquired. Congenital cholesteatomas, by definition, arise from areas of keratinizing epithelium wiithin the middle ear cleft. Michaels (1986) showed that a small area in the anterior tympanum in the developing fetus often contains a small area of keratinizing epithelium. He found epidermoid formation in 37 of 68 temporal bones of fetuses at 10 to 33 weeks of gestation. This region may give rise to congenital cholesteatomas.

The pathogenesis of acquired cholesteatoma has been debated for over a century. There four basic theories of the pathogenesis of acquired aural cholesteatoma: (1) invagination of the tympanic membrane, (2) basal cell hyperplasia, (3) epithelial ingrowth through a perforation, and (4) metaplasia of middle ear epithelium (Fig. 157-7).

Invagination theory

The invagination theory (Wittmaack, 1933) of the genesis of cholesteatoma is generally regarded as one of the primary mechanisms of the formation of attic cholesteatomas. Retraction pockets of the pars flaccida deepen because of negative middle ear pressure and possibly repeated inflammation (see Fig. 157-2); as the retraction pocket deepends, desquamated keratin cannot be cleared from the recess and a cholesteatoma results. The origin of such retraction pocket cholesteatomas is thought to be eustachian tube dysfunction (or OME) with resultant negatiive middle ear pressure ("ex vacuo" theory). The pars flaccida, being less fibrous and less resistant to displacement, is usually the source of the cholesteatoma. The result of this type of cholesteatoma (so-called primary acquired cholesteatoma) is an apparent defect in the posterosuperior quadrant of the tympanic membrane and erosion of the adjacent canal wall. Although these defects have the appearance of a marginal perforation, it is not a perforation but rather an invagination. Sadé (1979) showed that epithelial migration patterns within attic retraction pockets are altered. This failure of epithelial migration may allow the accumulation of keratin within a retraction pocket with subsequent enlargement merely from the accumulation of keratin within a relatively closed space. Recent laboratory data support this mechanism; it has been found that the gerbil spontaneously develops keratin accumulations on the tympanic membrane, which lead to invasive aural cholesteatomas (Chole et al, 1981).

Epithelial invasion theory

The epithelial invasion theory (Habermann, 1889) states that keratinizing squamous epithelium from the surface of the tympanic membrane invades or migrates into the middle ear from a perforation in the tympanic membrane. The theory is supported by clinical observation and experimental evidence. Weiss (1958) showed that epithelial cells will migrate along a surface by a process that he called *contact guidance* and that when they encounter another epithelial surface they will stop migrating, for which he used the term *contact inhibition.* Jackson and Lim (1978) give histologic and ultrastructural evidence that keratinizing epithelium can migrate into the cat bulla by contact guidance. It is likely that in some tympanic membrane perforations, inflammation damages the inner mucosal lining of the tympanic membrane, allowing the outer keratinizing epithelium to migrate inward and generate a cholesteatoma. Palva et al (1982) have shown histologic evidence for this theory

in human temporal bones. Cholesteatomas arising after temporal bone fractures may arise from this mechanism; fractures within the ear canal may allow ingrowth of keratinizing epithelium by contact guidance (McKennan and Chole, 1989).

Basal cell hyperplasia theory

Another possible mechanism for the histogenesis of cholesteatoma was suggested by Lange (19250. In this theory, he proposed that epithelial cells (prickle cells) of the pars flaccida could invade the subepithelial tissue by means of proliferating columns of epithelial cells. Ruedi (1959) supported this hypothesis with clinical and experimental evidence. In order for epithelium to invade into the lamina propria, the basal lamina (basement membrane) must be altered. Basal lamina disruptions have now been documented in human (Lim et al, 1977) and animal (Chole and Tinling, 1984) cholesteatomas. Huang et al (1988) and Masaki et al (1989) provided experimental support for this theory by demonstrating that epithelial ingrowth from the tympanic membrane can be induced by instillation of propylene glycol into the middle ear of chinchillas. These basal lamina breaks allow the invasion of epithelial cones into the subepithelial connective tissue and the formation of micro-cholesteatomas. This mechanism may explain some types of human cholesteatomas, even those occurring behind and intact tympanic membrane. According to this theory, microcholesteatomas may enlarge and then perforate secondarily through the tympanic membrane, leaving the typical appearance of an attic cholesteatoma; this sequence of events has not been documented.

Squamous metaplasia theory

Wendt (1873) theorized that the simple squamous or cuboidal epithelium of the middle ear cleft could undergoo a metaplastic transformation into keratinizing epithelium. Sadé (1971) supported that theory, pointing out that epithelial cells are pluripotent and can be stimulated by inflammation to becoming keratinizing. According to this theory, an area of keratinizing epithelium within the middle ear would enlarge because of accumulated debris and contact the tympanic membrane. With intercurrent infection and inflammation, the cholesteatoma would lead to lysis of the tympanic membrane and perforation resulting in the typical appearance of an attic cholesteatoma. Sadé (1979) supports this theory by demonstrating that biopsy specimens from the middle ear of children with OME sometimes contain islands of keratinizing epithelium. Some experimental evidence supports the contention that middle ear mucosa can become metaplastic and keratinize. Chole and Frush (1982) showed that severe vitamin A deficiency leads to the formation of keratinizing epithelium within the middle ear and eustachian tube of rats. Nevertheless, confirmation of the theory of vitamin A deficiency as a significant cause of human aural cholesteatoma is still lacking.

Clinically it appears that each of these pathogenic mechanisms accounts for a proportion of acquired cholesteatomas. Regardless of the pathogenesis of aural cholesteatomas, they all share certain properties in common. Cholesteatomas are prone to recurrent infection, and they characteristically erode the bone of the ossicles and the otic capsule.

Since cholesteatomas contain keratin debris enclosed in a tissue space, they are subject to recurrent infection. The bacteria found in infected cholesteatomas are different from those found in AOM or OME. Significant anaerobic bacteria are present. The most common aerobic bacteria is *Pseudomonas aeruginosa,* and the most common anaerobic bacteria is *Bacteroides sp.* (Table 157-1) (Harker and Koontz, 1977).

Aural cholesteatomas arising from the vicinity of the tympanic membrane exhibit typical growth patterns into the temporal bone. Since most acquired cholesteatomas ariise by invagination of the pars flaccida, their growth is limited by the mucosal folds and suspensory ligaments of the ossicles. The pars flaccida may invaginate into the lateralmost portion of the epitympanum (Prussak's space) and then into the recesses of the epitympanum posteriorly, lateral to the body of the incus, inferiorly into the middle ear via the pouch of VonTroeltsch (Fig. 157-8), or anteriorly into the protympanum (Fig. 157-90) (Jackler, 1989; Proctor, 1964).

Management

Cholesteatomas can only be eradicated from the temporal bone by surgicalresection (see Chapter 169). In some cases a cholesteatoma can be debrided of entrapped keratin by direct removal or by irrigation. In some cases, surgical intervention is not possible or advisable; the patient may not be medically able to withstand surgery, or the risks of surgery may not outweigh the benefits in some only-hearing ears. Irrigation with 1:1 distilled white vinegar and 70% isopropyl alcohol may keep some cholesteatomas stable if their opening into the ear canal is sufficiently large.

Chronic Otitis Media Without Cholesteatoma

Acute or recurrent infection of the middle ear may result in a permanent perforation of the tympanic membrane. Ears with chronic perforations without cholesteatomas may be chronically or intermittently infected. Three times as many operations were performed in the USA in 1978 for this disease as was performed for cholesteatoma (Ruben, 1982). Paparella and Kim (1977) reported that out of 375 primary tympanomastoid operations for chronic mastoiditis, two thirds were performed in ears with granulation tissue and without cholesteatoma.

Diagnosis

Tympanic membrane perforation (Fig. 157-10) may result from AOM, chronic otitis media, or trauma (injury or surgery). In some instances a dry, simple perforation will result from a single episode of AOM, that is, necrotizing otitis media. Perforation of the tympanic membrane, especially involving the tympanic annulus, may allow ingrowth of the keratinizing epithelium of the ear canal or tympanic membrane leading to cholesteatoma (see the section on cholesteatoma pathogenesis). An ear with a simple perforation may become infected because of contamination from the ear canal or because of a smoldering infection in the mastoid.

Pathogenesis

Chronic otomastoiditis without cholesteatoma is marked by the presence of irreversible inflammatory changes within the middle ear and mastoid. The factors that allow acute infections within the middle ear and mastoid to develop into chronic infections are not clear. The most common finding in temporal bones with chronic otomastoiditis was osteitis. In a review of 123 temporal bones with chronic otomastoiditis, Meyerhoff et al (1978) found osteitis in 90.2%, mucoperiosteal fibrosis in 76.4%, granulation tissue in 69.1%, tympanosclerosis in 27.6%, and cholesterol granuloma in 13%. Aeration of the middle ear, antrum, and mastoid depends on the free movement of air from the eustachian tube into the mastoid air cells. In the human temporal bone, air must travel around the ossicles in the epitympanic space to get into the antrum (Fig. 157-11). Proctor (1964)) demonstrated that the middle ear is separated from the antrum not only by the ossicles but also by mucosal folds. He found that there were only two constant openings: (1) between the tendon of the tensor tympani muscle and the stapes and (2) between the short process of the incus and the stapedial tendon. Hence edema and inflammation with granulation tissue may block these communicating openings, preventing drainage of the antrum and mastoid. Chronic obstruction of the attic and antrum with infection then leads to "irreversible" changes in the mucosa and bone of the antrum and mastoid. Granulation tissue within the temporal bone can lead to bone erosion: 4 of 123 temporal bones in this series had active bone erosion (see the discussion of bone erosion in cholesteatoma). Thomsen et al (1981) found that bone erosion in chronic otitis media was more prevalent when cholesteatoma was present, but it still occurred in the absence of cholesteatoma. Moriyama et al (1984b) found osteoclastic bone resorption in rats with chronic otitis media.

Chronic otitis media may occur in children who have indwelling tympanostomy tubes. Otorrhea is a common complication of tympanotomy tube insertion, occurring in 15% to 74% of children undergoing this procedure (Gates et al, 1988). Chronic otorrhea that is resistant to therapy has been reported to occur in 5.5% of children with tubes (McLelland, 1980). It is unclear whether such chronic infection is due to the indwelling tube or merely the drainage of an already smoldering infection. The bacteria that are found in such cases are those found in chronic otitis media generally: *Pseudomonas aeruginosa* and *Staphylococcus aureus.*

Management

Most infected perforations can be treated conservatively with topical antibiotics. Antibiotic otic suspensions with or without hydrocortisone are usually effective. The antibiotics should be chosen to eradicate the most common pathogens, *P. aeruginosa* and *S. aureus.* In recurrent or chronic infections, cultures should be used to adjust antibiotics. Irrigation of an infected ear with a perforation with a dilute acidic solution (for example, distilled vinegar and water, 1:1) is often effective in refractory cases. Many topical otic antibiotic preparations contain potentially ototoxic substances including aminoglycoside antibiotics and propylene glycol. Studies of these substances applied to the middle ear have shown ototoxicity in rodents (Wright and Meyerhoff, 1984) and primates (Wright et all, 1987). Although there are reports suggesting that sensorineural hearing loss may occur after topical use of these preparations (Dumas et al, 1980; Murphy, 1984)), thus far no conclusive evidence is available proving ototoxicity of commercially available otic preparations in the human middle ear. Potentially ototoxic topical preparations should be applied to the middle

ear only when potential benefits outweigh the potential risks. Topical antibiotics can also be applied in powder form by insufflation. Various agents are available individually or in combination including boric acid, sulfa, chloramphenicol, and hydrocortisone. This technique is particularly useful in the presence of epithelitis and in a moist mastoid cavity. Systemic antibiotics should be used in refractory cases when specific pathogens are found on culture. In ears that become repeatedly infected but clear between episodes, tympanoplasty should be considered. Ideally, an ear with a tympanic membrane perforation should be free from infection for a period of 3 months before tympanoplasty. In some instances, chronic infection with otorrhea, but without cholesteatoma, will persist in spite of aggressive medical therapy. In these cases two options should be considered: long-term intravenous antibiotics or tympanomastoid surgery. Antibiotic therapy can be administered at home or in the hospital. Aggressive local debridement is required. The goals of tympanomastoidectomy include aeration of the middle ear and mastoid, removal of irreversibly diseased tissue, closure of the middle ear, and reconstruction of the sound-conducting mechanism. These goals are not always achieved in a single stage.

Posttympanostomy tube otorrhea can usually be treated with topical and systemic antibiotics. If infection persists, intravenous antibiotic therapy directed at specifically identified organisms should be considered. Removal of the tympanostomy tube may be necessary in some refractory cases (Gates et al, 1988).

Bone Erosion in Cholesteatoma and Chronic Otitis Media

In Virchow's description of aural cholesteatoma in 1864 (VonTroltsch, 1864) he noted that the cholesteatoma "... extended through the bone to the external auditory canal, sometimes, also, in the cranial cavity ...". Since that time clinicians and investigators have studied the pathophysiology of bone resorption from this disease. Although much progress has been made in the understanding of the resorptive process, the actual sequence of events and their relative importance are unknown.

It was long held that the bone resorption seen adjacent to cholesteatomas was a result of pressure necrosis (Kirchner, 1891; Walsh et al, 1951). However, clinical observations led to the abandonment of the pressure necrosis theory since it was thought to be highly unlikely that cholesteatomas could exert pressure exceeding capillary perfusion pressure (approximately 25 mm Hg). Indeed, Orisek and Chole (1987) have measured pressure exerted by experimental cholesteatomas and found it to be 1.3 to 11.9 mm Hg. Lautenschlager (1927) first suggested that cholesteatomas may elaborate enzymes that erode bone, but direct evidence for the existence of such enzymes was lacking until Abramson (1969) showed that cultured human cholesteatoma could degrade guinea pig collagen. Several early human temporal bone studies revealed osteoclastic bone resorption adjacent to cholesteatoma matrix (Grippaudo, 1058; Pollack, 1959). Because of the relative paucity of osteoclasts seen in surgical specimens, Thomsen et al (1974) proposed the mononuclear histiocytes with notched nuclei were the predominant cell associated with erosive cholesteatomas; they later identified acid phosphatase activity in the vicinity of these cells and concluded that they might mediate bone resorption in cholesteatoma (Thomsen et al, 1975). Holtrop et al (1982) have shown that mononuclear cells in rat calvaria may be capable of bone resorption. Hence there was a discrepancy between these studies and earlier temporal bone studies; did mononuclear cells resorb bone in the vicinity of cholesteatomas or was resorption osteoclastic? Bernstein et al

(1977) pointed out that recent studies were based on biopsy material taken during tympanomastoid surgery; surgery is often preceded by attempts to control active inflammation; hence biopsy material may represent the reparative phase instead of the resorptive phase. Chole (1984) has shown ultrastructural evidence in human and experimental cholesteatomas that bone resorption is primarily due to the action of multinucleated osteoclasts on bone (Fig. 157-12). Although many mononuclear cells (histiocytes and fibroblasts) were present in the vicinity of active bone resorption, only multinuncleated osteoclasts were seen to disrupt the lamina limitans of bone and cause resorption lacunae. Therefore it is likely that multinucleated osteoclasts (Chole, 1984, 1988) cause bone resorption in cholesteatoma and chronic otitis media. In order for bone resorption to occur, enzymatic removal of the organic and inorganic components must occur. It is likely that these enzymes are elaborated or activated by the resorbing cells (osteoclasts) in their immediate microenvironment. These enzymes include acid phosphatase (Chole, 1984; Thomsen et al, 1975), collagenase (Abramson and Huang, 1977; Moriyama et al, 1987), and acid proteases (Blair et al, 1986). In studies by Blair and colleagues, a cathepsin-like proteolytic enzyme with maximal activity at pH 4.0 was shown to be active in the microenvironment of the osteoclast. In a recent study, Moriyama et al (1984a) localized collagenase in the vicinity of osteoclasts and mononuclear cells in regions of bone resorption in chronic otitis media. An elaboration of neutral collagenase by resident osteoclasts may trigger osteoclastic resorption (Kahn and Partridge, 1987).

A controversy still exists as to whether bone resorption exists only within the microenvironment of the ruffled border of the osteoclast (Chole, 1988) or by an elaboration of acids and enzymes into the subepithelial space (Ohsaki et al, 1988; Moriyama et al, 1989).

Yuasa et al (1978) demonstrated that the pH of keratin debris within cholesteatoma was acidic, which might lead to demineralization of the hydroxyapatite of bone. Moriyama et al (1984b) have shown that the keratin itself may induce an inflammatory reaction (foreign body granuloma), which leads to cellular bone resorption. Iino et al (1990) have presented experimental evidence to support this theory by demonstrating that cholesteatoma debris and alpha-keratin can stimulate the accumulation of mouse peritoneal macrophages. Additionally, Ohsaki et al (1988) found evidence that bone adjacent to cholesteatomas is demineralized; they suggest that demineralization by acidic cholesteatomas explains bony destruction. However, intimate contact of the cholesteatoma matrix with bone does not appear to be necessary for bone resorption to ensue. Thomsen et al (1981) showed that bone resorption can occur in chronic otitis media with or without cholesteatoma. Macri and Chole (1985) showed that an implanted silicone barrier between a cholesteatoma and underlying bone did not prevent osteoclastic bone resorption in experimental cholesteatoma. Therefore it is likely that indirect effects (for example, pressure) may activate the cellular events of bone resorption. recent studies have shown that pressure with (Huang et al, 1990; Moriyama et al, 1985) or without (Chole and McGinn, 1985; Wolfman and Chole, 1986) inflammation is sufficient to induce bone resorption in experimental animals and that the cellular pattern of pressure-induced bone resorption is similar to that seen in cholesteatoma: osteoclasts and granulation tissue (Chole, 1988). The physical effects (pressure) of cholesteatomas may lead to transient electrical potentials (Binderman et al, 1984) and the recruitment of monocytes into the subepithelial space. These monocytes may activate the cellular events of bone resorption. Activated monocytes can produce prostaglanding E2 (Moriyama et al, 1984a), which is a stimulator of bone remodelling. Other osteoclast-activating factors, such as interleukin-1alpha

and -1beta and tumor necrosis factor-alpha and beta, may be produced, which then lead to localized osteoclastic activity (Pfeilschifter et al, 1989). Interleukin-1 was found in cholesteatoma matrix (Ahn et al, 1990b) and was shown to stimulate fibroblasts and macrophages to produce PGE2 and collagenase (Ahn et al, 1990a). Neutral collagenase may stimulate osteoclastic resorption by degrading the osteoid surface of bone, thus allowing osteoclastic activity (Kahn and Partridge, 1987); neutral collagenase has not been found within osteoclasts (Sakamoto and Sakamoto, 1982) but has beenlocalized in the vicinity of resorbing bone (Fig. 157-13) (Moriyama et al, 1987).

The role of other cells in the pathophysiology of chronic otitis media is unclear. For example, Gantz (1984) suggested that Langerhans' cells within the matrix of cholesteatomas may initiate an immunologic response to the presence of antigens (keratin and bacterial debris); these cells in turn may induce the cellular events outlined above. However, Aberg et al (1988) found no increase in Langerhans' cells as compared to ear canal epitheliuim, suggesting that these cells may not have a primary role in the development of cholesteatoma. Mast cells are seen in cholesteatoma matrix but their role is unknown (Berger et al, 1985).

The destructive effects of an expanding cholesteatoma within the middle ear or mastoid and concomitant chronic infection are not limited to the bony structures of the temporal bone. Paparella et al (1969) observed sensorineural hearing loss in patients with chronic otitis media, and Chole and Chiu (1988) observed loss of cochlear hair cell stereocilia in animals with experimental cholesteatomas with or without infection. In a study of age-matched, staged cholesteatomas, McGinn and Chole (1991) showed loss of cochlear hair cells in areas subjacent to areas of bone erosion suggesting that ototoxic substances may traverse the bony wall of the cochlea directly.

Sensorineural Hearing Loss

Paparella et al (1969) showed that chronic otitis media may result in permanent sensorineural hearing loss from the passage of toxic substances through the round window membrane. Meyerhoff et al (1978) fround that 17.9% of temporal bones with chronic otitis media had histologic evidence of labyrinthitis. Vartianinen and Karjalainen (1987) compared 874 chronically infected ears with and without cholesteatoma to 609 controls and found significantly worse bone conduction in the infected group; ears with cholesteatomas were generally worse than those without cholesteatomas. However, after correcting for the artificial elevation of bone conduction thresholds from conductive hearing loss, the Carhart effect, Browning and Gatehouse (1989) found no difference in the bone conduction thresholds between 395 ears with chronic otitis media and 920 control ears.

Rahko et al (1989) studied bone conduction thresholds in 359 children with a history of recurrent acute otitis media and found no correlation between the number of bouts of infection and permanent sensorineural hearing loss. In contrast, Fria et al (1984) found that there was a tendency for bone conduction thresholds to be elevated at 2 kHz and 4 kHz in the ears with chronic OME compared bone conduction thresholds in children with or without OME. In animal experiments the inner ear is particularly sensitive to injury by middle ear infection. Morizono et al (1984) found that otitis media in chinchillas resulted in significant elevation in tone-burst-elicited compound action potentials after the otitis had cleared, indicating a sensory hearing loss.

Tympanosclerosis

Diagnosis

Tympanosclerosis is thought to be a complication of otitis media in which acellular hyalin and calcified deposits accumulate within the tympanic membrane and the submucosa middle ear. In most cases these plaques are clinically significant and cause little or no hearing impairment. Tympanosclerotic plaques within the tympanic membrane appear as a semicircular crescent or horsehoe-shaped white plaque within the tympanic membrane (Fig. 157-14).

Pathogenesis

Tympanosclerosis is a consequence of resolved otitis media or trauma. Hussl and Mueller (1980) found tympanosclerosis to be a frequent sequela of chronic OME, and they found it in 19.7% of drumheads 6 to 8 years after the insertion of ventilating tubes for OME. They also noted that middle ear tympanosclerosis was often seen after recurrent bouts of AOM. Tos and Stangerup (1989) found a significant increase in tympanosclerosis in ears in which grommets were placed (59%) compared to the contralateral ears in which only myringotomy was performed (13%). The incidence of tympanosclerosis in chronic otitis media has been reported from 9% to 38%. In patients undergoing surgery for chronic otitis media or its sequelae, Kinney (1978) found that 20% of 1495 cases had tympanosclerosis.

Tympanosclerosis appears histologically as a hyalinization of the subepithelial connective tissue of the tympanic membrane and middle ear; in most instances calcification is present. Osteogenesis can also occur within these lesions. The bone deposition and ossicular fixation occur most frequently in the attic associated with the heads of the malleus and incus. When plaques occur within the tympanic membrane, they are limited to the lamina propria. Hussl and Lim (1984) found these plaques to be a degenerative process resulting in calcification in connective tissue of the middle ear. They hypothesized that OME or AOM led to a destructive process within connective tissue. This led to degeneration of collagen and subsequently dystrophic calcification and tympanosclerosis. The degeneration of collagen may be a direct result of inflammation or infection within the middle ear (for example, by bacterial proteinases and collagenases). Wielinga et al (1988) showed that eustachian tube obstruction alone, without infection, caused tympanosclerosis in rats; they hypothesized that deformation alone was sufficient to cause the plaques to form. Another possible cause of tympanosclerosis in an autoimmune process occurring within the tympanic membrane. Schiff et al (1980) prepared antisera to guinea pig lamina propria and passively immunized guinea pigs. When the tympanic membranes of these animals were traumatized, tympanosclerotic plaques developed. Chole and Henry (1983) found the LP/J inbred mice spontaneously develop middle ear lesions that resemble tympanosclerosis and may be immunologically mediated (Brodie and Chole, 1987). Hussl and Lim (1984) proposed two possible mechanisms for the formation of tympanosclerotic plaques beginning with collagen degeneration (Fig. 157-15).

Management

Tympanosclerosis within the middle ear (Fig. 157-16) is histologically similar to that occurring within the tympanic membrane, but it often leads to conductive hearing loss caused by ossicular fixation. Although some authors have stated that tympanosclerosis tends to recur after surgical removal, others have reported stable hearing results in these patients. Smyth et al (1982) reported excellent hearing results in 79% of tympanosclerotic ears in which ossicular reconstruction (stapedectomy and total ossicular reconstruction) was performed in two stages. However, Gormley (1987) found that only 7% of his cases had an air-bone gap of less than 21 dB on long-term follow-up, questioning the advisability of stapedectomy in ears with tympanosclerosis. It should be noted that in the earlier series (Smyth, 1972) in which one-stage procedures were performed. 21% of 57 cases result in cochlear losses. Tympanoplasty and ossicular reconstruction can be performed in ears with tympanosclerosis, but the risks of cochlear damage appear to be greater than in other middle ear diseases because of the extensive dissection that is required in tympanosclerotic ears and the coexistence of labyrinthine erosion.

Petrositis

Infection of the mastoid and middle ear may be complicated by the spread of infection within the temporal bone into the petrous apex. Petrous apicits is an extension of infection from the mastoid air cell tract into a pneumatized anterior or posterior petrous apex.

In the preantibiotic ear, otitis media was often complicated by a sprad into the petrous apex and then further intracranial complications. The classic symptoms of petrous apicitis include deep facial pain, otitis media, and ipsilateral abducens nerve paralysis. This triad, called Gradenigo's syndrome (Gradenigo, 1907) is rare; however, suppurative processes in the petrous apex occur in patients with acute and chronic otitis media but most often manifest as chronic infection with otorrhea and sometimes deep pain after adequate surgery.

Historical note

The history of petrous apicitis and its treatment has been reviewed recently (Chole and Donald, 1983). A patient with petrous apicitis and Gradenigo's triad was first described by Goriis (1903). In Gradenigo's series of 57 patients, 24 actually had the pure triad; others had multiple complications. In the early part of this century, there was a controversy as to whether petrous apicitis can develop in diploic (marrow-filled) or pneumatic (air-filled) petrous apices. It is generally believed now that petrous apicitis occurs in patients who have pneumatized petrous apices. In the 1930s, Almour (1931) and Kopetsky and Almour (1931) described surgical approaches for petrous apicitis in which fistulous tracts were followed into the petrous apex. In 1933 Ramandier and later Lempert (1936 and 1937) described the now classic operation for exenteration of the anterior petrous apex. The histopathology of petrous apicitis was described by Lindsay (1938). An additional surgical approach for suppuration of the petrous apex was described in a case report by Hendershot and Wood (1973) in which they drained an osteomyelitis of the petrous apex through the middle cranial fossa.

Anatomy

The petrous apex is a truncated pyramid that is the portion of the temporal bone medial to the inner ear labyrinth (see Fig. 157-17). The petrous apex is the most surgically inaccessible portion of the temporal bone (Chole, 1985). The apex may be arbitrarily bisected by a coronal plate through the internal auditory canal (Fig. 157-17). This plane divides the apex into an anterior portion, the "peritubal" area, and a posterior portion, the "perilabyrinthine" area. The posterior petrous apex, which is pneumatized in 30% of individuals, is just medial to the semicircular canals. The anterior apex, which is pneumatized in 10% of individuals, is anterior and medial to the cochlear. The carotid artery traverses the anterior petrous apex.

The petrous apex may be pneumatic (air cell filled), diploic (marrow filled), or sclerotic (solid bone). Direct extension of infection from the mastoid and middle ear through pneumatized air cell tracts into the petrous apex is thought to be the etiology of petrous apicitis. It has been estimated that 30% of posterior petrous apices are pneumatized, and in a study of 84 normal human temporal bones, 9% of anterior petrous apices were found to be pneumatized (Fig. 157-18).

The anatomic relationships at the petrous tip may explain some of the symptoms of petrous apicitis. An undetected and poorly drained infected air cell of the petrous apex must trail through small air cell tracts into the middle ear and mastoid. These cell tracts consist of the infralabyrinthine air cell tract, the retrofacial tract, and the peritubal air cells superior to the eustachian tube. If the bony cortex of the anterior petrous apex is involved by the extension of infection, the infection may cause an epidural abscess in the region or damage nearby cranial nerves. On the superior aspect of the petrous tip lies the trigeminal or gasserian ganglion. Damage or irritation to the ganglion may explain the deep facial pain that some patients with apicitis experience. Extending from the tip of the petrous apex to the clinoid is the petroclinoid ligament. The abducens nerve travels below the petroclinoid ligament in a small canal called Dorello's canal (Dorello, 1906). Entrapment or inflammation in the ear of Dorello's canal is thought to account for the presence of abducens paralysis in some patients with petrous apicitis.

Diagnosis

Symptoms oof petrositis are usually subtle. Typically, a patient who has had prior mastoid surgery will complain of persistent infection and deep facial pain. In a series of eight patients, four patients had deep facial pain; only two had abducens paralysis, and two had meningitis (Table 157-2) (Chole and Donald, 1983).

Patients with suppuration may manifest a variety of symptoms, none of which are pathognomonic for the syndrome. In patients with long-standing chronic otomastoiditis, deep pain, and persistent infection, the diagnosis of petrositis should be considered. In a recent series of patients with petrous apicitis, the predominant organism was *Pseudomonas aeruginosa.*

The physical findings of petrositis usually include those of chronic otitis media with chronic otorrhea. In some case the infection can be limited to the anterior petrous apex, and

the middle ear is normal (Chole and Donald, 1983). Involvement of cranial nerves V, VI, and VII occurs in many cases.

Diagnostic tests

Once the diagnosis of petrouos apicitis is suspected on clinical grouns, the most appropriate diagnostic procedure is computerized axial tomography. High-resolution CT scanning usually shows details of the petrous apex. A pneumatized petrous apex on the uninvolved side can sometimes be contrasted with a fluid-filled or sclerotic petrous apex on the involved side; however, Roland et al (1990) have shown that asymmetry of the petrous apex is not necessarily diagnostic for apicitis since asymmetric pneumatization of the apex can occur in normal individuals. If the CT scan indicates a potential apicitis, magnetic resonance imaging (MRI) may add information about the nature of the fluid or tissue within the apex (Fig. 157-19). A gallium bone scan may provide additional information, showing increased uptake on the side of apicitis.

Management

The management of petrous apicitis is directed toward control of the infection. If topical and systemic antibiotic treatment is inadequate to control the suppuration, a variety of surgical approaches are available. The principal means of surgical drainage of the petrous apex approach long air cell tracts through the mastoid and middle ear into the petrous apex. These air cell tracts have been well defined anatomically (Chole, 1985)). They include the subarcuate and sinodural angle cells toward the posterior petrous apex; and the peritubal, retrofacial, and infralabyrinthine tracts toward the anterior petrous apex. The anterior apex may be widely exposed through the glenoid fossa using the approach of Ramandier (1933) and Lempert (1936, 1937). If adequate air cells cannot be identified through the middle ear and mastoid, the middle cranial fossa approach can be used to enter the roof of the anterior petrous apex (Hendershot and Wood, 1973).