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The Pathology of Silent Otitis Media: A Predecessor to Tympanogenic Meningitis in Infants

Muzeyyen Yildirim-Baylan, MD^{1,2}, Patricia Schachern, BS¹, Vladimir Tsuprun, PhD¹, Dai Shiabata, MD. PhD^{1,3}, Michael M Paparella, MD^{1,4}, and Sebahattin Cureoglu, MD¹

¹ Department of Otolaryngology, University of Minnesota, Minneapolis MN, USA

² Department of Otolaryngology, University of Dicle, Diyarbakir, Turkey

³ Department of Otolaryngology, Kawasaki University, Japan

⁴ Paparella Ear, Head and Neck Institute, Minneapolis MN, USA

Introduction

Otitis media (OM) is a common disease; accounting for more than 16 million doctor office visits in the US in a year [1]. In spite of the finest medical and/or surgical care, some patients with OM suffer from persistent and recurrent middle ear infections. In addition, intracranial complications of otitis media are not uncommon and can be potentially fatal [2]. Meningitis is the most common intracranial complication of otitis media and carries the risks of life-changing morbidity and death [2]. The mortality rate of tympanogenic meningitis has been reported between 10% - 41% [2-5]. Complications of tympanogenic meningitis are associated with the chronicity of middle ear infection, etiological agents of the infection, the patient's age, and comorbidities [6,7].

Bacteria within the fibrous matrices (BFM), which are adhered to the mucosal surface and embedded within a matrix of extracellular material, can be associated with the disease progression and persistence of inflammation in chronic otitis media. The fibrous matrix around the bacterial communities can act as a barrier by reducing the clearance of the bacteria by the host immune system. In this study, we investigate the occurrence, frequency, and location of BFM in the middle and inner ear in temporal bones from infants with tympanogenic meningitis. Because human temporal bone studies will allow us evaluate the entire middle and inner ear components, we can see clearly if there is an association between the presence of BFM in the middle and inner ear and tympanogenic meningitis.

Methods

Human temporal bones had been previously removed at autopsy. They were fixed in formalin solution, decalcified, embedded in celloidin, and serially sectioned in the horizontal

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Correspondence: Sebahattin Cureoglu MD, Department of Otolaryngology, University of Minnesota, 2001 6th Street S.E., Lions Research Building, Room 210, Minneapolis, MN 55455 cureo003@umn.edu Phone: 612-626-9883.

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plane from superior to inferior at a thickness of 20µm. Every 10th section was stained with hematoxylin and eosin and mounted on glass slides for light microscopic observation. Additional sections were stained with Weigert's Gram stain. Case histories were reviewed, and temporal bones from patients who had died of meningitis were selected. Thirty-one cases with meningitis from the human temporal bone collection at the University of Minnesota were screened to select those with tympanogenic meningitis. We excluded cases that had surgery of the temporal bone, leukemia, and other systemic diseases, which might infiltrate into the temporal bone. Of these, 17 temporal bones, from 9 cases that included 2 females and 7 males, ranging in age from 5 to 23 months, met our criteria of tympanogenic meningitis in infants. Meningitis was considered to be of tympanogenic origin if we found clinical and histological evidence of chronic otitis media, indicating that it existed prior to the acute meningitis, with no other source of infection. The presence of labyrinthitis and pathologic changes such as granulation tissue, fibrosis, cholesterol granuloma, cholesteatoma, tympanic membrane perforation, and tympanosclerosis were noted.

BFM composed bacterial aggregates, embedded in a network of fibrous material, were found adjacent to the mucosal surface in temporal bones with chronic silent otitis media. Many rounded bacterial particles were darkly stained with gram Weigert stain for gram-positive bacteria (Fig. 1a,b) and hematoxylin-eosin (H-E). Free-floating bacteria and scattered neutrophils, monocytes, and other inflammatory cells infiltrated in fibrous network were often seen throughout the entire structures. These structures frequently occupied the large areas of the middle or inner ear (Fig. 1a,b).

The following anatomical locations were examined for the presence of BFM: epitympanum, supratubal recess, Eustachian tube, facial recess, sinus tympani, the areas near the oval and round windows, mesotympanum, hypotympanum, aditus ad antrum, mastoid antrum, mastoid cells, inner ear, cochlear aqueduct, and internal auditory canal. Results of blood cultures were documented.

Results

Out of 62 temporal bones from 31 cases, 17 temporal bones, from 9 cases that included 2 females and 7 males, ranging in age from 5 to 23 months, met our criteria of tympanogenic meningitis in infants. Eighty-two percent (14/17) of the temporal bones with tympanogenic meningitis had BFM. Gram stains in those BFM cases showed gram-positive bacteria (Fig 1b; Fig 2a,b). Table 1 shows the findings of the temporal bones with tympanogenic meningitis. BFM were located in 1 anatomical region in 1 temporal bone and within multiple anatomic regions in 16 temporal bones. The most common locations were oval and round window areas, followed by the epitympanum, supratubal recess and facial recess. BFM within the inner ear were observed in the scala tympani and modiolus in the middle and basal turns of the cochleae of 9 temporal bones. In 1 of these temporal bones, BFM was seen in the internal auditory canal. Labyrinthitis was seen in all patients. The tympanic membrane was intact in all cases. BFM were not seen in 3 temporal bones from 2 patients. In one case, only 1 side was available for the study.

The blood culture results for cases with meningitis were as follows: *H. influenzae* was positive in 5 cases and *S. pneumoniae* was positive in 4 cases. During autopsy, none of the patients had any foci of different infection that was suggestive as a cause of meningitis.

Discussion

Meningitis is the most common intracranial complication of otitis media [2-5,8]. In our study we found BFM in 82% of the temporal bones from infants with tympanogenic

meningitis. The presence of BFM in a high percentage of the temporal bones of infants with tympanogenic meningitis suggests that bacteria embedded within a fibrous matrix may contribute to the pathogenesis of meningitis due to otitis media.

The concept of chronic silent otitis media depends on the basis of clinical and otopathologic evidence of chronic infection in the middle ear cleft in the absence of obvious pathologic findings in the tympanic membrane [9]. Because the tympanic membrane is intact, the chronic pathology in the middle ear cleft may not be detected, and due to a lack of clinical treatment, there is an increased risk of complications and sequelae [9]. The concept of silent otitis media may be especially significant in children under the age of 2 years because they often fail to communicate minor symptoms. Meningitis ran a very rapid course in all of the patients, with survival time up to a week after admission. Irreversible otopathologic changes in the middle ear indicated that the otitis media had been present for some time. These findings suggest a form of meningitis of tympanogenic origin.

Although it is often difficult to determine the route of bacterial infection from the middle ear to the meninges in the presence of middle ear infection, possible routes are: 1) hematogenous seeding; 2) direct spread or invasion a) through bony defect or connections [10]; b) through the round window membrane and into the inner ear and then through perivascular and perineural invasion or via the cochlear aqueduct. In animal models, *S. pneumoniae* have been shown to pass through an intact round window membrane into the inner ear and then into the modiolus through the small pores in the osseous spiral laminae [11]. Interestingly, in our cases with meningitis there was a high percentage of BFM located near the round and oval windows. All of our cases with tympanogenic meningitis had labyrinthitis. We also observed BFM within the basal turn, middle turn, and modiolus of the cochlea in some cases. Bacterial dissemination from the middle to inner ear may occur through the round and oval windows into the modiolus, finally ending up in the meninges. The fact of BFM's high percentage of presence in the epitympanum and supratubal recess suggests the possible route of crossing the tympanic tegmen to reach the dura. Neither route precludes the possibility of hematogenous spread. In fact, these findings may represent a cause-and-effect relationship between otitis media with BFM and meningitis. The clinician should, therefore, be aware that an intact tympanic membrane does not necessarily preclude the presence of pathologic changes including BFM in the middle ear cleft, and that the clinical definition of chronic otitis media may not encompass the majority of infants with this condition.

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Figure 1.

A) A lower magnification shows chronic purulent otitis media and bacteria within a fibrous matrix in round window area. Note the thickened sub-epithelial space in the middle ear mucosa. (TM: Tympanic Membrane; ME: Middle Ear; C: Cochlea; * shows location of bacteria within a fibrous matrix) (Hematoxylin eosin).

B) A higher magnification of the area shows bacterial aggregates and single bacteria (arrows) in bacteria within a fibrous matrix revealed with H-E (a) and gram Weigert (b) stains. Bars: 20 μ m (a, b).

Figure 2.

A) A low-power view of a human temporal bone section shows purulent effusion and a bacteria within a fibrous matrix in middle ear, facial recess, and sinus tympani (FN: Facial nerve, M: Malleus, I: Incus, C: Cochlea* shows location of the bacteria within a fibrous matrix in the scala tympani).

B) A higher magnification of the area shows bacteria (arrows), web like structures, and inflammatory cells including mononuclear cells and polymorphonuclear leukocytes in the cochlea.

Table 1

Findings in temporal bones (TBs) from patients with tympanogenic meningitis

		TBs with meningitis N=17 (%)
Labyrinthitis	(+)	17 (100)
	(-)	0 (0)
Location of BFM in Middle ear cleft	Oval window	12 (70.6)
	Epitympanum	9 (52.9)
	Round window	9 (52.9)
	Aditus ad Antrum	9 (52.9)
	Mesotympanum	8 (47.1)
	Facial recess	6 (35.3)
	Sinus tympani	6 (35.3)
	Supratubal recess	6 (35.3)
	Mastoid antrum	5 (29.4)
	Mastoid cells	3 (17.6)
	Eustachian tube	0 (0)
Location of BFM in Inner ear	Modiolus	6 (35.3)
	Scalas	4 (23.5)
	Internal auditory canal	1 (5.9)
Pathologic findings	Mucopurulent secretion	16 (94.1)
	Granulation tissue	8 (47.1)
	Thickened TM	8 (47.1)
	Fibrocystic tissue	4 (23.5)
	Ossicular changes	2 (11.8)
	Cholesterol Granuloma	1 (5.9)
	Sclerosis	1 (5.9)
	Retracted TM	1 (5.9)
	Perforated TM	0 (0)
	Cholesteatoma	0 (0)

BFM: Bacteria within the Fibrous Matrices

TM: Tympanic Membrane