

Chronic otitis media and immunoglobulin E-mediated hypersensitivity in adults: Is it a contributor of cholesteatoma?

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OBJECTIVES: The aim of this study was to determine the relationship between chronic otitis media (COM) and immunoglobulin E (IgE)-mediated hypersensitivity in adults.

STUDY DESIGN: A prospective comparative study.

SUBJECTS AND METHODS: One hundred seventeen patients with COM from July 2005 to April 2007 were enrolled. All subjects had a questionnaire on allergic rhinitis symptoms and performed allergy tests that included a total IgE and the multiple radioallergosorbent chemiluminescence assay to check the presence of IgE-mediated hypersensitivity.

RESULTS: The prevalence of IgE-mediated hypersensitivity and allergic rhinitis were 22.2% and 7.7% in patients with COM, respectively. The mean total IgE was 157.2 ranging from 3 to 1833. The prevalence of IgE-mediated hypersensitivity was similar with regard to the recurrence or bilaterality. However, patients with cholesteatoma had a higher prevalence of IgE-mediated hypersensitivity than patients without that condition.

CONCLUSION: The prevalence of IgE-mediated hypersensitivity and allergic rhinitis in adults with COM appeared to be higher than in the general population. Allergy might contribute to COM especially in cases with a cholesteatoma.

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Allergy is characterized by a state of hypersensitivity induced by exposure to a particular antigen (allergen) that results in harmful immunologic reactions on subsequent exposures; the term is usually used to refer to hypersensitivity to an environmental antigen. Atopy is a genetic predisposition to the development of immediate (type I) hypersensitivity reactions against common environmental antigens. The term “allergy” is usually used for patients with atopy that means immunoglobulin E (IgE)-mediated hypersensitivity.

Abnormal function of the Eustachian tube appears to be the most important factor in the pathogenesis of middle ear disease in all age groups.¹ The etiology of Eustachian tube dysfunction (ETD) includes causes such as infections, mechanical (obstructive), genetic, reflux, iatrogenic, and allergic factors. Although numerous reports have shown a relation-

ship between IgE-mediated hypersensitivity and ETD,^{2–7} this information is mostly based on the cases of otitis media with effusion (OME) in children. This appears to result from the higher incidence of ETD, OME, and allergy at a young age.

Reports in the English literature on the relationship between allergy and COM with or without cholesteatoma in adults are very limited. Based on the hypothesis that the Eustachian tube is an important factor in regulating the middle ear physiology and that allergy contributes to ETD, the role of allergy in the pathogenesis of COM needs to be determined in adults also.

The following specific questions were addressed in this article: (1) Is allergy more frequent in patients with COM than in the general population? (2) Is allergy more frequently diagnosed in recurrent COM? (3) Assuming that allergy is a systemic phenomenon and contributes to otitis media, is allergy more frequent in patients with bilateral COM? and (4) Is allergy more frequent in patients with cholesteatoma?

MATERIALS AND METHODS

Subjects

A prospective comparative study was conducted from July 2005 to April 2007. The Institutional Review Board of Samsung Medical Center granted approval for this study. One hundred seventeen patients, who were prearranged to undergo tympanomastoidectomy for COM including chronic suppurative otitis media (CSOM) or cholesteatoma with CSOM, were enrolled. Subjects enrolled included 49 men and 68 women, and their mean age was 47.6 years ranging from 18 to 72 years. The diagnosis of CSOM was made by a history of otorrhea, by otoscopic findings including chronic perforation (for three months or more) and inflammation in the middle ear cleft, and by soft-tissue density of mastoid and/or tympanum on high-resolution

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Table 1
Age and sex distribution of subjects grouped by three different characteristics

	Number	Age (Mean $\pm$ SD)	Sex (Male:Female)	P value	
				Age	Sex
Primary	70	48.9 $\pm$ 11.8	33:37	0.158	0.184
Recurrent	47	45.8 $\pm$ 10.8	16:31		
Cholesteatoma with CSOM	53	45.9 $\pm$ 11.3	26:27	0.129	0.189
CSOM	64	49.1 $\pm$ 11.5	23:41		
Unilateral	89	47.0 $\pm$ 11.0	35:54	0.382	0.251
Bilateral	28	49.8 $\pm$ 13.0	14:14		

No differences between subgroups were shown.

temporal bone computed tomography. Cholesteatoma with CSOM was diagnosed by otoscopic findings including deep retraction pockets whose extent was not visualized and not self-cleaned and by soft-tissue density of mastoid and/or tympanum on temporal bone computed tomography.⁸

Study Design

A questionnaire on the history and symptoms of COM and allergic rhinitis was obtained. A physical examination including otoscopy and nasopharyngoscopy was performed. Blood samples were analyzed for serum total IgE concentrations and the multiple radioallergosorbent chemiluminescence assays (MAST-CLA; Hitachi Chemical Diagnostics Inc, Mountain View, CA, USA). All patients underwent tympanomastoidectomy and tympanoplasty under general anesthesia. Tissue samples were sent to pathology to rule out and confirm the diagnosis of cholesteatoma.

The MAST-CLA was performed by using 36 common inhalant allergens in Korea including *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cockroach, *Aspergillus*, *Cladosporium*, *Alternaria*, dog fur, and cat fur. Values of MAST-CLA were assigned from 0 to 4 based on the amount of light emitted by the individual threads in the test chamber; this value is directly proportional to the amount of allergen-specific IgE in the patient's serum. The result of the MAST-CLA was considered positive when the value to one of the allergens was more than class 2, which represents a moderate or higher concentration.^{9,10}

Allergic rhinitis was diagnosed when the MAST-CLA was positive, and the subjects frequently complained of two or more symptoms including sneezing, runny nose, nasal obstruction, and itchy nose.

Nasopharyngoscopic examination was performed on all patients to observe the Eustachian tube orifice and determine the presence of a significant pathology or mechanical obstruction. No patient had abnormality of the nasopharynx.

Analysis

The data were analyzed by grouping the patients by the following characteristics: (1) recurrent or primary COM, (2) unilateral or bilateral disease, and (3) CSOM or cholesteatoma with CSOM.

Statistical analysis was performed by using SPSS 13.0 version (SPSS Inc, Chicago, IL). The chi-square test was used to compare the prevalence of IgE-mediated hypersensitivity in each of the groups. The independent *t* test was used to compare the serum total IgE concentration in each group. Statistical significance was defined as *P* values less than 0.05.

RESULTS

There were no significant differences in age and sex distribution among the patients in each of the subgroups (Table 1).

The average serum total IgE was 157.2 IU/mL with a range of 3 to 1838 IU/mL. There were no significant differences in serum total IgE among the subgroups for all three kinds of analysis (Table 2). The prevalence of allergic rhinitis in our series was 7.7% (9/117), which is almost 2-fold higher than the prevalence of 3.93% reported in a study of 71,120 patients in Korea.⁹

Among the 117 patients with COM, 26 (22.2%) had a positive MAST-CLA indicating IgE-mediated hypersensitivity to one or more inhalant allergens, which is higher than the national average of 17% in the United States.¹¹ The frequent allergens reported to be positive in the MAST-CLA were *Dermatophagoides farinae* (*n* = 18, 69.2%), *Dermatophagoides pteronyssinus* (*n* = 17, 65.4%), cockroach (*n* = 4, 15.4%), and cat fur (*n* = 3, 11.5%) in order of frequency. The comparative analyses of each subgroup showed that the cholesteatoma with the CSOM group had a higher prevalence of IgE-mediated hypersensitivity than CSOM group (*P* = 0.007, χ^2 test). There were no significant differences identified in the prevalence of IgE-mediated hypersensitivity with regard to the recurrence or bilaterality (Table 2).

DISCUSSION

The goal of this study was to investigate the relationship between IgE-mediated hypersensitivity (allergy) and the

Table 2
Serum total IgE concentration and prevalence of IgE-mediated hypersensitivity confirmed by MAST-CLA in subgroups grouped by three different characteristics

	N	Serum total IgE (mean $\pm$ SD)	<i>P</i> value	MAST-CLA (2+ or more)	<i>P</i> value
Primary	70	159.1 $\pm$ 265.0	0.922	15 (21.4%)	0.824
Recurrent	47	154.1 $\pm$ 264.4		11 (23.4%)	
Cholesteatoma with CSOM	53	199.3 $\pm$ 360.2	0.148	18 (34.0%)	0.007*
CSOM	64	125.7 $\pm$ 153.3		8 (12.5%)	
Unilateral	89	150.6 $\pm$ 245.0	0.648	21 (23.6%)	0.611
Bilateral	28	177.4 $\pm$ 318.4		5 (17.9%)	

occurrence, recurrence, bilaterality, and presence of cholesteatoma in patients with COM. The prevalence of IgE-mediated hypersensitivity was 22.2% in our series. Although we could not find data regarding the prevalence of IgE-mediated hypersensitivity in the Korean general population, the prevalence in our series appears to be higher than that quoted for the general population in the United States (17%).¹¹ Howard et al¹² reported the incidence of IgE-mediated hypersensitivity in patients with neuro-otologic symptoms (vertigo, tinnitus, hearing loss, aural fullness, Meniere's disease, and Eustachian tube dysfunction) as 38%, which was more than double the published national average data. However, in their study, radioallergosorbent test (RAST) was used for screening, and all RAST results of class I or greater were considered to be positive results. We set the criteria for a positive result as class 2 or more, which is generally used for MAST-CLA in other studies.^{9,10} If we considered the MAST-CLA results that were class I or more (mild or higher concentration) as positive, the prevalence of IgE-mediated hypersensitivity in our study would increase to 50.4% (59/117).

In addition, the prevalence of allergic rhinitis in patients with COM (7.7%) was higher than in the published data of 1.13%¹¹ to 3.93%,⁹ which are average prevalence rates in the United States and in Korea, respectively. This suggests a close relationship between allergy and the pathogenesis of COM in adults.

The role of IgE-mediated allergic reactions, in the pathogenesis of OME, is supported by a high prevalence of OME among patients with allergies.⁵ These observations may further explain the high prevalence of IgE-mediated hypersensitivity and allergic rhinitis in adults with COM considering the close relationship between OME and COM. The role of allergy in OME may involve one or more of the following mechanisms: (1) middle ear mucosa as a target organ; (2) inflammatory swelling of the Eustachian tube with resultant obstruction; (3) inflammatory obstruction of the nose and nasopharynx; or (4) reflux, insufflation, or aspiration of bacteria-laden allergic nasopharyngeal secretions into the middle ear cavity.⁵ However, there is little evidence to support that the middle ear mucosa functions as an allergic shock organ, making the first suggested mecha-

nism least likely.^{13,14} The latter three mechanisms are associated with abnormal Eustachian tube function, and retraction pockets are well known to result from ETD.¹⁵ We found a high prevalence of IgE-mediated hypersensitivity in 34.0% of the cholesteatoma with CSOM group, which was about 3-fold higher than the CSOM group (12.5%, *P* = 0.007). Although the criteria used for a positive result are different, this positive rate is about two times the published prevalence in the general population of the United States (17%).¹¹ These results suggest that allergy may be a contributing factor to the pathogenesis of cholesteatoma.

In our study, the higher prevalence of IgE-mediated hypersensitivity in the cholesteatoma with CSOM group can be explained by ETD caused by IgE-mediated hypersensitivity. Bluestone² suggested a sequence of pathogenesis in cholesteatoma formation, involving functional failure of the Eustachian tube, leading to increased negative middle ear pressure, atelectasis of the tympanic membrane (TM), and formation of a retraction pocket in the attic or posterior-superior quadrant.

Allergic inflammation is reported to occur on both sides of the nasopharynx, the Eustachian tube, and the middle ear in atopic patients with OME.¹⁶ In addition, the contralateral ear in patients with unilateral cholesteatoma showed signs of retraction pockets in 72% of cases.¹⁷ Although a higher prevalence of atopy could be expected in patients with bilateral COM, no difference in the prevalence of atopy was observed between bilateral and unilateral COM. A possible explanation is that atopy is just one of the many contributing factors for the development of COM.

Although our observation has a prospective design and a relatively large number of patient samples, we could not show a local allergic inflammation of the middle ear or the Eustachian tube. A histologic confirmation of allergic inflammation from those regions or accurate evaluation of E-tube function may enhance our hypothesis. However, because most cases of COM result from E-tube dysfunction, allergy likely affects a continuum of these pathologic conditions. More research on the specific immunologic mechanisms underlying the pathogenesis of COM in adults is required to explain our observations.

CONCLUSION

The prevalence of IgE-mediated hypersensitivity and allergic rhinitis appears to be higher in patients with COM than in the general population. Allergy may contribute to the development of cholesteatoma with CSOM.

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AUTHOR CONTRIBUTIONS

Sang Duk Hong, data collection, writer; **Yang-Sun Cho**, study design; **Sung Hwa Hong**, study design, writer; **Won-Ho Chung**, study design, data collection; **Kyu-Wan Chung**, chart and data review for revision.

FINANCIAL DISCLOSURE

None.

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