

ORIGINAL ARTICLE

The Role of Allergy in the Pathogenesis of Chronic Suppurative Otitis Media

Orhan Gorgulu, Mediha Ozelci, Suleyman Ozdemir, Mehmet Yasar, Mustafa Kemal Olgun, Osman Kursat Arikian

Adana Numune Education and Research Hospital, Department of Otorhinolaryngology, Adana, Turkey (OG, MO, MY, MKO, OKA)
Cukurova University School of Medicine, Department of Otorhinolaryngology, Adana, Turkey (BO)

Objective: The etiological role of allergy in the pathogenesis of chronic suppurative otitis media (CSOM) has not been clearly shown. The aim of this study was to assess the role of allergy in the etiology of CSOM.

Materials and Methods: In this study, total and allergen specific IgE levels, as well as blood eosinophil counts of 61 consecutive patients with CSOM and 31 healthy controls were measured. Endoscopic evaluations of the rhinopharynx were done in both groups.

Results: The difference in mean total serum IgE levels and blood eosinophil counts between patients with CSOM and healthy controls were statistically insignificant ($p=0,611$, $p=0,804$ consecutively). More patients with CSOM had serum total IgE levels greater than 300 IU/ml compared to healthy controls, and this difference was statistically significant ($p=0,031$). Positivity rates against any of the allergens were higher in the CSOM patient group compared to healthy control. The difference between two groups was statistically significant ($p=0,042$). Evaluation of allergen-specific IgE levels found in the Turkish Mixed 20 respiratory allergy panel only revealed a significant difference between patients with CSOM and healthy controls with regards to allergy against house dust mites (pteron and farinae) ($p=0,037$ for two values).

Conclusion: The present study shows that some of our results support a role of allergy in the etiology of CSOM. Thus, the possibility of allergy should be considered in CSOM patients preoperatively, the drug treatment of allergy might be helpful in addition to the operational treatment of CSOM patients in case of allergy.

Submitted : 11 October 2011

Accepted : 13 May 2012

Introduction

Chronic suppurative otitis media (CSOM) is characterized by the presence of eardrum perforation, purulent discharge in the external ear canal and hearing loss, mainly of the conductive type [1]. Although several factors play a role in the etiology of the disorder, it is most commonly associated with recurrent attacks of otitis media during childhood. Such attacks result in impaired mucociliary activity and the development of mucosal metaplasia, eventually leading to irreversible mucosal changes [2,3]. Conditions which decrease the body's resistance such as diabetes mellitus and immune system disorders, nutritional disorders, allergy, craniofacial

malformations, adenoid hypertrophy, inappropriate or incomplete treatment of acute and recurrent otitis media are all independent factors which contribute to the development of CSOM [4]. Eustachian tube disorders and poor mastoid aeration are additional local factors that have also been implicated [5, 6]. Abnormal Eustachian tube function is an important factor in the pathogenesis of middle ear disorders in all age groups [7]. Common etiologies of Eustachian dysfunction include infections, obstructive causes, genetics, reflux disease, allergy and iatrogenic causes [6, 8]. Several studies have reported on a link between Eustachian tube dysfunction and IgE-mediated hypersensitivity [5,9,10]. The likelihood of having IgE-mediated hypersensitivity and allergic rhinitis is

Corresponding address:

Orhan Gorgulu
Department of Otorhinolaryngology, Adana Numune Education and Research Hospital Adana, Turkey.
Hacı Ömer Sabancı Caddesi No: 2
Seyhan Adana, 01500, Turkey
Phone: + 90-505-2730548 , Fax: +90-322-2252986
E-mail: drorhan76@yahoo.com

Copyright 2005 © The Mediterranean Society of Otolaryngology and Audiology

higher in patients with CSOM than in the general population [11].

Despite many studies, there is no established cause-effect relationship of allergy with CSOM. Few studies have focused on the association of allergic rhinitis and CSOM, and this motivated us to investigate to further clarify the subject. In this study, blood eosinophil counts, serum total IgE levels and allergen-specific IgE levels along with reactions to allergens found in the Turkish mixed 20 respiratory allergy panel were evaluated in adults with CSOM and healthy controls, to determine the role of allergy in the etiopathogenesis of CSOM. The aim of this study was to investigate the role of allergens in the development of CSOM and their potential as targets for the prevention of this disorder.

Materials and Methods

Our study population consisted of 61 consecutive patients who were diagnosed with CSOM in the Otorhinolaryngology Department at Adana Numune Teaching and Research Hospital, and 31 healthy controls. This study was undertaken with the approval of the local ethics committee, and written informed consent was obtained for each patient prior to enrollment. Patients were questioned regarding smoking status before undergoing rhinopharyngeal endoscopic examination for any signs of conchal hypertrophy or pallor, investigation of Eustachian tube dysfunction and the presence of a serous discharge was noted. Blood samples were collected for the determination of eosinophil count, and after centrifugation, the resultant sera were tested for total IgE levels and for levels of allergen-specific IgE for 19 allergens contained in the Turkish mixed 20 respiratory protocol.

As for inclusion criterion we considered chronic unilateral or bilateral otorrhea in patients with less than 60 years of age. Patients with the following conditions were excluded from the study: presence of cholesteatoma, previous ear surgery, history of nasal polyposis, presence of severely deviated septum, adenoid vegetation. All control subjects had no history of upper respiratory infection in the last 3 months.

Total and allergen specific IgE serum levels were measured by electrochemiluminescence immunoassay (ECLIA) using the Elecsys 2010 system (Roche, Hitachi High Technologies Corporation, Tokyo, Japan). This method utilizes monoclonal antibodies targeted against human IgE to provide a quantitative measure.

Positive responses against any of the allergens were accepted as positivity in the evaluation of allergen specific Ig E levels. The normal range for blood eosinophil count was considered as 0.04-0.36 (cells x 10⁻³ µl) for females and 0.04-0.54 (cells x 10⁻³ µl) for males. The normal range for serum total IgE levels was accepted as 0.01-300 IU/ml.

Allergy was defined as a presence of history of persistent sneezing on exposure to irritants, a positive physical examination such as pale or watery nasal mucosa in the absence of common cold in the past 12 months; in addition, a positive reaction to at least one of the 20 regional aeroallergens in allergen specific IgE tests or total IgE level more than 300 IU/ml or positive rate of blood eosinophil count.

Statistical analysis

Analysis of the data was performed using the Statistical Package for the Social Sciences for Windows (SPSS 15.0) program (SPSS, Inc, Chicago, IL, USA). Comparison between groups for categorical variables was performed using the Pearson's Chi-square, Fisher's exact and Monte Carlo's tests. In the presence of abnormal distribution, comparison of numerical variables between independent groups was done using the Mann-Whitney U test. Statistical significance was defined as a pvalue of less than 0.05.

Results

A total of 61 patients with CSOM were enrolled in the study. Thirty-five were female, and 26 were male, with a mean age of 36.7 ± 13.8. The control group consisted of 31 patients, 12 male and 19 female, with a mean age of 41.1 ± 13.0. There was no statistically significant difference between the groups in terms of age and gender distribution.

Otosopic examination revealed left-sided CSOM in 34.4%, right-sided CSOM in 34.4% and bilateral

CSOM in 31.2% of patients. Mean duration of the ear disease was of 11.6 (SD=10.3), varying from 1 to 43 years. Findings encountered on nasal endoscopic evaluation included conchal hypertrophy in 19.7%, pale conchae in 44.3% and the presence of serous discharge in 41.5% of patients. Endoscopic evaluation of the control group was normal. There was no mechanical obstruction of the nasopharyngeal orifice of the Eustachian tubes of the patients. The rate of smokers among the patients with CSOM was 39.3%. Control subjects had the smoking rate at 33.4%. There was no significance between the two groups with regards to smoking status (p= 0.83). Radiographic evaluation was done with the axial section of computed tomography of temporal bone in all patients with CSOM. Mastoid bone pneumatization types were aerated (n= 18, 29.5%), sclerotic (n= 26, 42.6%), and diploic (n= 17, 27.9%).

All subjects enrolled into the study were tested for 19 allergens found in the Turkish Mixed 20 respiratory

allergy panel as shown in Table 1. The most frequently encountered allergic reaction in the CSOM patient group was against house dust mites. Healthy controls manifested a reaction more commonly to house dust mites followed by oak tree pollen. There was only statistically significant difference between the patients with CSOM and control subjects with regards to house dust mites (*D.pterony* and *D.farinaea*) allergy (p= 0.037 for two values). No statistically significant difference was observed with any of the remaining allergens on the Turkish Mixed 20 respiratory allergy panel. Positivity rates against any of the allergens were 29.5% in the CSOM patient group compared to 22.3% in healthy control. The difference between two groups was statistically significant (p= 0.042). (Table 2)

Patients with CSOM had a mean total serum IgE level of 248.7 ± 372.6 IU/ml compared to 224.2 ± 437.9 IU/ml in healthy controls, a statistically insignificant difference was found between groups (p= 0.611). But more patients with CSOM had serum total IgE levels

Table 1. Turkish Mixed 20 respiratory allergy panel results in the study and control groups.

	Patients (n=61)	Controls (n=31)	P
	n (%)	n (%)	
Penicillium	1 (1.6)	0 (0.0)	1.000
Milk	3 (4.9)	0 (0.0)	0.548
Egg white	0 (0.0)	0 (0.0)	0.000
Barley pollen	2 (3.3)	1 (3.2)	1.000
Ribwort plantain pollen	2 (3.3)	1 (3.2)	0.716
Wheat pollen	3 (4.9)	1 (3.2)	1.000
Rye pollen	3 (4.9)	1 (3.2)	1.000
Oat pollen	2 (3.3)	1 (3.2)	1.000
Grass pollen	3 (4.9)	1 (3.2)	1.000
Willow tree pollen	3 (4.9)	2 (6.5)	1.000
Pine tree pollen	5 (8.2)	2 (6.5)	0.339
Oak tree pollen	4 (6.6)	5 (16.1)	0.397
Poplar tree pollen	2 (3.3)	3 (9.7)	0.592
Cockroach	1 (1.6)	2 (6.7)	0.258
Bird feather	1 (1.6)	2 (6.5)	0.402
Dog hair	5 (8.2)	2 (6.5)	1.000
Cat hair	6 (9.8)	2 (6.5)	0.887
House dust mites-pterony	11 (18.0)	5 (16.1)	0.037
House dust mites-farinaea	11 (18.0)	5 (16.1)	0.037

greater than 300 IU/ml compared to healthy controls, and this difference was statistically significant (26.2% vs. 16.1%; $p= 0.031$). The mean eosinophil count in the CSOM patient group was 0.8 ± 0.11 (cells $\times 10^{-3} \mu\text{l}$) in comparison to a count of 0.20 ± 0.15 (cells $\times 10^{-3} \mu\text{l}$) in healthy controls. This difference was deemed statistically insignificant ($p= 0.804$). Blood eosinophilia was observed in 1.6% of patients with CSOM compared to 9.7% in the control group. The difference between the groups with regards to eosinophil count was statistically insignificant ($p=0.109$). These results have been summarized in Table 2.

If the allergy was defined as a presence of history of persistent sneezing on exposure to irritants, any positivity of a positive physical examination findings (pale-hypertrophic concha, watery nasal mucosa, serous discharge) or positive responses against any of the allergens in the evaluation of allergen specific Ig E levels or high level of serum total IgE levels (≥ 300 IU/ml) or higher level of blood eosinophil count than values mentioned above, the difference between two groups were found statistically significant ($p=0.019$).

Discussion

The high prevalence of chronic otitis media with effusion (COME) in patients with allergies suggests a possible role for IgE-mediated hypersensitivity in the

pathogenesis of COME [8, 12]. In the light of these observations, it may be easier to explain the high prevalence of IgE-mediated hypersensitivity and allergic rhinitis in adults with CSOM [13]. Allergy contributes to the development of COME by promoting Eustachian tube dysfunction, and retraction pockets are known to occur as a result [5-14]. Although the effect of allergic inflammation on the Eustachian tube dysfunction is well established, there is still a lack of evidence on the effect of the allergy in development of the CSOM.

Some studies have identified allergy a risk factor for COME and CSOM. In a study by Khalil et al., it was demonstrated that allergic inflammation occurs on both sides of the nasopharynx, in the Eustachian tube and in the middle ear of atopic patients with COME [15]. In another study on patients with CSOM, the prevalence of allergic rhinitis was reported at 7.7%, which is higher than previously reported rates in studies from the USA and Korea (1.13% and 3.93%, respectively) [8, 12]. The findings of these studies are suggestive of a close link between allergy and the pathogenesis of CSOM in adults. Yet another study demonstrated a higher prevalence of IgE-mediated hypersensitivity and allergic rhinitis in patients with CSOM, compared to the general population [11, 16].

The prevalence of IgE-mediated hypersensitivity was reported at 34% in study on a group of patients with

Table 2. Serum total IgE levels, Blood eosinophil count (mean \pm standard deviation), Allergen-specific IgE (+) persons (%) in blood samples taken from patients with and without chronic otitis media

Average values	Patients (n=61)	Controls (n=31)	p-value
Total IgE levels (IU/ml)	248.7 \pm 372.6	224.2 \pm 437.9	0.611*
Total Ig E \geq 300 IU/ml (%)	16(26.2%)	5(16.1%)	0.031**
Blood eosinophil count (cells $\times 10^{-3} \mu\text{l}$)	0.18 \pm 0.11	0.20 \pm 0.15	0.804*
Allergen-specific IgE (+) persons (%)	18 (29.5%)	7 (22.3%)	0.042**
Positivity of Allergy***	36 (59.0%)	7 (22.3%)	0.019**

*Mann-Whitney U test,

**Chi-square test

***presence of history of persistent sneezing on exposure to irritants, positive physical examination such as pale or watery nasal mucosa; in addition, a positive laboratory tests

CSOM and cholesteatoma^[17]. This rate is nearly three times higher than that observed in a group with COME (12.5%). It is also twice as high as the prevalence in the general population, reported from the USA (17%)^[12]. Bernstein et al, on the other hand, observed elevations in serum IgE levels in 22.8% of patients with COME^[17]. All of the above studies suggest a possible role for allergy in the pathogenesis of CSOM. The prevalence of allergy in our study, as determined by the criteria mentioned above was 59.0% in patients with CSOM, significantly higher than in our control group (22.3%). According to our clinical and laboratory findings, we found a positive significant correlation between allergy and CSOM.

Becker et al. reported on elevated eosinophil counts in 83% of children with COME who had positive skin prick tests^[18]. In our study on CSOM patients, however, the difference between groups with regards to blood eosinophilia was statistically insignificant. These findings are consistent with those of other studies where an increase in eosinophil count was not established in blood or in middle ear effusion samples.

In a study on patients with COME, an allergic reaction to at least one inhaled allergen was detected in 46.6% of patients^[19]. Hurst reported on the presence of house dust allergy in most cases of COME, also associated with positive skin prick test reactions to dust, grass, mold and trees^[20]. Among the allergen specific Ig E test parameters investigated in our study, the only statistically significant difference observed between patient and control groups was in the frequency of allergic reactions to house dust mites (*D. pterony* and *D. farinea*) ($p= 0.037$).

The present study shows that some of our results support a role of allergy in the etiology of CSOM. Thus, some positive findings in our study encourage us to propose that preoperative endoscopic evaluation of nasal passage is useful to detect allergic situation. If the allergic signs are found in patients, allergy treatment may be helpful to the surgical success rate. Prospective, double blinded randomized trials are required to fully establish the role of allergy in the etiopathogenesis of CSOM.

References

1. Proctor B. Chronic otitis media and mastoiditis. In: Paperella MM, Schumrick DA, eds. Otolaryngology, 3rd ed. Philadelphia: W.B. Saunders Co. 1991: 1349-76.
2. Tanaka A, Ohashi Y, Kakinoki Y, et al. Influence of the allergic response on the mucociliary system in the eustachian tube. *Acta Otolaryngol Suppl.* 1998; 538: 98–101.
3. Meyerdohoff WL, Kim CS, Paperella MM. Pathology of chronic otitis media. *Ann Otol Rhinol Laryngol.* 1978; 87: 749-60
4. Fliss DM, Shoham I, Leiberman A, Dagan R. Chronic suppurative otitis media without cholesteatoma in children in southern Israel: incidence and risk factors. *Pediatr Infect Dis J.* 1991; 10: 895-899.
5. Bluestone CD. Eustachian tube function and allergy in otitis media. *Pediatrics* 1978; 61: 753– 60.
6. Seibert JW, Danner CJ. Eustachian tube function and the middle ear. *Otolaryngol Clin North Am.* 2006; 39: 1221–35.
7. Bluestone CD. Pathogenesis of otitis media: role of eustachian tube. *Pediatr Infect Dis J.* 1996; 15: 281–91.
8. Fireman P. Otitis media and eustachian tube dysfunction: connection to allergic rhinitis. *J Allergy Clin Immunol.* 1997; 99: S787–97.
9. Corey JP, Adham RE, Abbass AH, et al. The role of IgE-mediated hypersensitivity in otitis media with effusion. *Am J Otolaryngol* 1994; 15: 138-144.
10. Lazo-Saenz JG, Galvan-Aguilera AA, Martinez-Ordaz VA, et al. Eustachian tube dysfunction in allergic rhinitis. *Otolaryngol Head Neck Surg.* 2005; 132: 626–9.
11. Hong SD, Cho YS, Hong SH, Chung WH. Chronic otitis media and immunoglobulin E-mediated hypersensitivity in adults: is it a contributor of cholesteatoma? *Otolaryngol Head Neck Surg.* 2008 ; 138: 637-640.
12. Min YG, Choi BY, Kwon SK, et al. Multicenter study on the prevalence of perennial allergic rhinitis and allergy-associated disorders. *J Korean Med Sci.* 2001; 16:697–701.

13. Bluestone CD. Eustachian tube function: Physiology, pathophysiology and role of allergy in pathogenesis of otitis media. *J Allergy Clin Immunol.* 1983; 72: 242-51.
14. Knight LC, Eccles R, Morris S. Seasonal allergic rhinitis and its effects on eustachian tube function and middle ear pressure. *Clin Otolaryngol Allied Sci.* 1992; 17: 308 –12.
15. Khalil HM, Saleh MA, Sakr AA. A clinico-radiological study of the contralateral ear in acquired unilateral cholesteatoma. *Rev Laryngol Otol Rhinol (Bord).* 2004; 125: 17–22.
16. El-Kabarity RH, El-Kabarity RH. Diagnostic Value of Serum Anti-Heat Shock Protein 70 (Anti-HSP70) in Cases of Autoimmune Inner Ear Disease (AIED). *Int. Adv. Otol.* 2011; 7:55-61.
17. Bernstein JM. The role of IgE-mediated hypersensitivity in the development of otitis media with effusion. *Otolaryngol Clin North Am.* 1992; 25:197-211.
18. Becker S, Koch T, Philipp A. Allergic origin of recurrent middle ear effusion and adenoids in young children. *HNO.* 1991; 39: 182-4.
19. Nguyen LH, Manoukian JJ, Sobol SE, et al. Similar allergic inflammation in the middle ear and the upper airway: evidence linking otitis media with effusion to the united airways concept. *J Allergy Clin Immunol.* 2004; 114:1110 –5.
20. Hurst DS. Allergy management of refractory serous otitis media. *Otolaryngol Head Neck Surg.* 1990; 102:664-8.