

Atopy in children with otitis media with effusion

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Summary

Background Contrasting data have been found on the prevalence of atopy in children with otitis media with effusion (OME). A major issue would be to determine whether screening for atopy should be recommended.

Setting Centre for Study of Otitis Media with Effusion, Tabiano Terme, Parma, Italy.

Objective The purpose of this study was to investigate the relation of OME to atopy.

Methods The subjects were 172 children with OME and a control group of 200 children. The protocol included a questionnaire survey of diseases associated with atopy, a skin-prick test and a clinical evaluation of allergic symptoms and hypersensitivity to aeroallergens.

Results No significant difference between patients and control group was observed for family history of atopy or positive skin-prick test reactions. Symptoms associated with atopy occurred significantly more frequently in the group with OME ($P < 0.001$), though only the presence of rhinitis or atopic eczema was significantly associated with OME.

Conclusions Prevalence of positive skin-prick tests results is not enhanced in children with OME. Nevertheless, the association of OME with symptoms associated with atopy suggests that such concomitant diseases may play a part in the pathogenesis of the disorder. Children with allergic rhinitis or atopic eczema should be investigated by tympanometry for OME.

Keywords: atopic disease, otitis media with effusion, skin-prick test

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Introduction

Otitis media with effusion (OME) is a common disease in childhood with a prevalence ranging from 15 to 20% [1] and it is the most frequent reason for surgery [2] and hearing loss in children [3]. Heterogenous factors are involved in the origin of serous otitis media. It has been shown that cultures of middle ear secretion demonstrate bacterial growth in 28–43% of instances [4,5] and viral isolates were obtained in 16–19% of cases [4,6]. The role of an IgE-mediated hypersensitivity in the development of serous otitis media has been discussed for years. A number of clinical studies showed that incidence of allergy in otitis media with effusion patients varied from almost zero to more than 80% [7–13]. High levels of total and specific IgE have been found [12–14]. However, the connection between

allergy and otitis media with effusion (OME) has been criticized by other investigators who found different results in terms of IgE levels [15,16]. Limitations of these studies concern lack of controls or inadequate criteria for diagnosis of allergy and OME. In the present study, to test the hypothesis that OME is associated with atopy, we compared atopic family history, atopic diseases and skin-prick tests of children with OME and control subjects.

Materials and methods

Study population

One hundred and seventy-two children (93 females, 79 males) attending at the Centre for the Study of Otitis Media with Effusion, Tabiano Terme (Parma, Italy) were consecutively enrolled in the patient group between May and November 1993. Ages ranged from 4 to 14 years (mean age 6.3 years). All children had a history of OME and hearing

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loss of more than 5 months duration. They had an otoscopy examination to establish existence or absence of glue ear.

In addition, 200 healthy children (114 females, 86 males; age range 6–11 years, mean 7.8 years) were recruited at an annual school health examination as controls between January 1994 and April 1994. Children were examined by an ENT specialist. None of these children had either active OME on examination or a history of previous otitis media with effusion. These examinations were always conducted in the presence of a parent, whose permission to take part in the study was requested.

Tympanometry was performed on all children. Children included in the study group had a type B or C tympanograms; in the control group, type A tympanograms.

Diagnostic criteria

A questionnaire was handed out to parents of all children. All parents completed their questionnaire. Simple questions covered family history of atopy. Presence of symptoms often associated with atopy were sought with 'yes/no' questions. Allergic rhinitis was established through the question: 'Does your child have any "allergy-like" symptoms affecting the nose? Tick 'yes', if your child has a itchy and/or runny and/or blocked nose, not associated with a cold'. Asthma was identified by the question 'Does your child have asthma? Tick 'yes', if your child has wheezing (noisy breathing with a whistling sound coming from the chest) and/or a recurrent cough at night and/or is coughing or breathless during exercise'. A history of allergic conjunctivitis was established by asking whether the child had any 'allergy-like' symptoms affecting the eyes (e. g. itching, redness, watery). Eczema was defined as itching, chronic or chronically relapsing red patches with flaking and scaling of the skin. Urticaria was established by asking whether their child had a itching rash, consisting of weals surrounded by variable red circles. For every symptom information was obtained regarding the age of onset, number of episodes, seasonality, whether symptoms occurred after contact with animals. Before the study, the questionnaire had been completed by the parents of 60 children with suspected allergy. Answers agreed with medical findings.

Children underwent skin-prick tests for the common aero-allergens relevant in the area of northern Italy.

A single paediatric allergy specialist examined all children for allergic disorders on the basis of the history, clinical examination and skin-prick tests results. Parents were interviewed to check the trustworthiness of the answers to the questionnaire. The physical examination included inspection of skin and conjunctivae, anterior rhinoscopy and auscultation of the lungs.

Asthma, rhinitis, conjunctivitis, atopic eczema and urticaria were defined as allergic if they appeared after exposure

to a particular allergen, in combination with positive skin-test reactions to such allergen.

Asthma was defined as two or more of the following symptoms paroxysmal cough, wheezing, shortness of breath, breathless or wheezing or cough induced by exercise. Auscultatory, prevalently expiratory wheezes and diminished breath sounds could confirm the diagnosis. Eczema was diagnosed according to the criteria of Hanifin and Rajka [17]. Urticaria consisted of hives and irregular weal-like lesions. Allergic rhinitis consisted of nasal obstruction or congestion, rhinorrhoea, pruritus and sneezing not due to infections [18]. Swelling and pallor of mucosae and turbinates could confirm the diagnosis. The possibility of a non-allergic rhinitis eosinophilic syndrome (NARES) was excluded [19]. Allergic conjunctivitis consisted of excessive lacrimation, conjunctival redness, pruritus, swelling of the eyelids not due to infections [18].

Skin-prick test

All children were skin-prick tested using commercial extracts (1:10 w:v; Bayropharm Italiana, Milano, Italy) for the following allergens: grasses, plantain, *alternaria*, *parietaria*, birch, hazelnut, *artemisia*, *cladosporium*, *aspergillus*, *Dermatophagoides pteronyssinus* and *farinae*, cat and dog epithelium. The positive control was histamine 1 mg/mL. The negative control was diluent.

The results were evaluated after 15 min. Weals at least 3 mm greater in diameter than weals at the site of the negative control were considered positive [20].

Skin-prick tests were performed if patients were free from medication with antihistamines for 7 days.

Statistics

The χ^2 test, with or without Yates' correction was used to test the significance of the differences between the two groups. The Fischer exact test was used when expected number of individuals in all the cell was less than 5. Odds ratio and 95% confidence intervals were also calculated. Ages were compared by analysis of variance. Values of *P* less than 0.05 were considered significant.

Results

The otitis media with effusion and the control groups were comparable concerning both sex and age.

No significant difference between the patient and the control group was observed for family history of atopy (95 [55.2%] vs 95 [47.5%]). No difference at all was found between the groups regarding atopic history in father, mother, grandfather, grandmother, father + mother or father + mother + grandparents.

Table 1. Number of children with a positive skin-prick test to aeroallergens

Positive skin-prick test reaction	Otitis media with effusion group (n = 172)	Control group (n = 200)	Odds ratio	95% confidence interval	P value
Grasses	24 (13.95%)	31 (15.5%)	0.884	0.497–1.574	NS
<i>Alternaria</i>	8 (4.65%)	11 (5.5%)	0.838	0.329–2.134	NS
House dust mites	21 (12.21%)	35 (17.5%)	0.656	0.366–1.176	NS
Patients positive	46 (26.74%)	61 (30.5%)	0.833	0.529–1.308	NS

NS, not significant.

Forty-six (26.74%) of the children with serous otitis media had at least one positive skin-prick test to any antigen. No association was found between the occurrence of OME and positive skin-prick test reactions to grasses, house dust mites or *alternaria* (Table 1). Since positive skin-prick test reactions to plantain, *parietaria*, birch, hazelnut, *artemisia*, *cladosporium*, *aspergillus*, cat and dog epithelium were observed only occasionally, data were not shown.

The symptoms often associated with atopy reported by parents of children with glue ear and controls are shown in Table 2. Overall, these symptoms occurred significantly more frequently in the group with OME. However, only the presence of rhinitis and atopic eczema was significantly associated with OME.

The medical examination and skin-prick test results confirmed the presence of allergic rhinitis in 28 of 30 positive questionnaires in the OME group and in 11 of 15 in the control group. Allergic conjunctivitis was diagnosed

in 18 of 20 positive questionnaires in the OME group and 12 of 21 in the control group. The presence of asthma, atopic eczema and urticaria was confirmed in all cases.

The proportion of children with allergic rhinitis (28 of 172) in the patient group was significantly higher ($P < 0.001$) than that in the control children (11 of 200). The odds ratio was 3.341 and the 95% confidence limit was 1.609–6.935. The number of children with non-allergic rhinitis, allergic or non-allergic conjunctivitis or asthma did not differ significantly in two groups.

Children with rhinitis in the patient group were more likely to have allergic rhinitis than in the control group (Table 3). In the otitis media with effusion group, allergic rhinitis was provoked by house dust mites in 18 (10.46%) children and by grasses in 18 (10.46%); in the control group, by house dust mites in four (2%) children and by grasses in 10 (5%).

Sex or age (<6 years vs >6 years) grouping did not show

Table 2. Prevalence of manifestations associated with atopy in 172 children with Otitis Media with Effusion (O) and in 200 Control Children (C)

	Groups	Odds ratio	95% confidence interval	P value
Rhinitis	O: 30 (17.44%) C: 15 (7.5%)	2.605	1.350–5.025	<0.01
Asthma	O: 13 (7.55%) C: 11 (5.5%)	1.404	0.612–3.221	NS
Conjunctivitis	O: 20 (11.62%) C: 21 (10.50%)	1.121	0.586–2.146	NS
Atopic eczema	O: 19 (11.04%) C: 9 (4.50%)	2.635	1.159–5.990	<0.05
Urticaria	O: 20 (11.63%) C: 14 (7%)	1.748	0.854–3.576	NS
Any symptom	O: 64 (37.21%) C: 42 (21%)	2.229	1.408–3.530	<0.001

NS, not significant.

Table 3. Comparison of children with allergic and non-allergic respiratory symptoms

		OME group	Control group	Odds ratio	95% confidence interval	P value
Rhinitis	Allergic	28 (93.3%)	11 (73.3%)	3.72	0.975–38.12	<0.001
	Non-allergic	2 (6.7%)	4 (26.7%)			
	Total	30	15			
Asthma	Allergic	8 (61.5%)	8 (72.7%)	0.6	0.382–12.28	NS
	Non-allergic	5 (38.5%)	3 (27.3%)			
	Total	13	11			

NS, not significant.

an association with the presence of atopic family history, positive SPT or atopic diseases.

Discussion

The results of the present study provide evidence that allergic rhinitis and atopic eczema are more common in children with OME compared with normal control subjects. Our findings are consistent with many, but by no means all, previous reports [7–10,12,13]. However, these reports did not take into account the risk of bias due to lack of healthy control subjects or of well-defined diagnostic criteria for allergic disease and OME. To avoid this bias, we included a random control group and observed rigid diagnostic criteria. Among children in the general community, the diagnosis of asthma has an incidence varying from 0.7% to 9.5% [21–25]. The prevalence of asthma in our OME group (7.55%) and in the control group (5.50%) is consistent with these figures. Epidemiological surveys reported that 5% to 10% of children have allergic rhinitis [26–28]. In our control group this prevalence was lower (4%). A possible explanation is that these differences may be related to genetic and environmental factors. Another possibility is that a questionnaire survey may have limitations such as universally accepted question items and lack of objectivity. Therefore, to validate the questionnaire, in the second part of the study we matched the questionnaire with a medical examination. On the other hand, there are many problems even comparing internationally objective tests such as skin-prick test results. The prevalence of positive skin-prick test reactions in different studies widely varied, ranging from 9% to 49% [25,29,30], because of differences in study populations, kinds of allergens tested and technique of skin-prick testing. However, in the present study we analysed factual data obtained by the same procedures in children with and without OME, so we believe that other factors did not introduce any bias.

There has been much debate about the role of allergy in the aetiology of OME. Our findings of no relationship between OME and positive skin-prick tests to aeroallergens or atopic family history, may indicate that there is no a direct connection between OME and allergy. At present, there is no convincing data that an IgE-mediated reaction induces middle ear inflammation. IgE antibodies were rarely detected in the ear effusion. No histopathological alteration was elicited by challenge with relevant allergen at the site of the middle ear mucosa in sensitized primates [14]. Therefore, an elevated concentration of histamine [31] or eosinophil cationic protein [32] in the ear effusion has an uncertain value. On the other hand, OME was associated with elevated serum IgE antibodies, suggesting a systemic reaction [12].

There is some support for the view that an abnormal eustachian tube function may alter gas exchange in the middle ear with resultant underpressure and, if prolonged, otitis media with effusion [33]. A tubular obstruction occurs in children with allergic rhinitis, as demonstrated after challenge with intranasal allergens [34] or during natural seasonal exposure to ragweed in allergic patients [35]. It has been suggested that eustachian tube blockage may be the result of mediators of inflammation released by inflammatory cells in the nasal mucosa. These molecules may reach the eustachian tube via the nasal mucociliary system or nasal microcirculation causing mucosal inflammation [33]. In accordance with these studies, our findings suggest that a nasal inflammation due to aeroallergens may cause a long-standing eustachian tube obstruction which is required to induce otitis media with effusion [34,35].

However, OME developed only in a subset of children with allergic rhinitis. It is possible that anatomic factors may predispose the onset of the disease [36]. This factor would tend to confound the relation between allergic rhinitis and serous otitis media.

As it has been cautiously suggested that food allergy may

play a role in the pathogenesis of a few cases of OME only in the first two years of age [10], we did not test this hypothesis in our older group of patients. However, we found an association between glue ear and atopic eczema in which adverse reaction to foods are frequent.

Whatever the outcome of our further investigations, we believe that two important considerations may be drawn from this study. First, that children with allergic rhinitis or atopic eczema should be screened by tympanometry for otitis media with effusion. Secondly, since our results show that about one-third of children with glue ear have allergic rhinitis, we think that further studies on the treatment of OME should be based on the separate identification of such patients. Several studies have reported that OME with positive skin-prick test or specific IgE antibodies to aero-allergens, responded to an antiallergic treatment [13,37]. In our view, it is likely that the disorder in children with allergic rhinitis could benefit from antihistamines, steroids and immunotherapy.

Conclusions

We failed to find any association between OME and skin-prick test results. Nevertheless, symptoms often associated with atopy are more common in OME children. This higher rate may reflect a pathogenetic role of these concomitant diseases in OME. Children with allergic rhinitis or atopic eczema should be investigated by tympanometry for OME.

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