

.....
Serous Otitis media and Food Allergy

J.A. Bellanti, S.M. Nsouli, T.M. Nsouli

Departments of Pediatrics and Microbiology-Immunology and
The International Center for Interdisciplinary Studies of Immunology,
Georgetown University School of Medicine, Washington, D.C., USA

Introduction

Serous otitis media (SOM) is a chronic inflammatory disease of the muco-periosteal lining of the eustachian tube, middle ear, and mastoid air cells [1] and is today one of the most leading causes of acquired hearing loss in children, including acquired irreversible hearing loss [1-3]. Although the precise pathogenesis of SOM is unknown, the condition has provoked considerable controversy. One school of thought suggests that the serous accumulation of fluid is the result of an unresolved or an inadequately treated acute otitis media [4]. A second possible etiology for the condition has been linked to an allergic predisposition [5]. Neither of these mechanisms, however, is mutually exclusive of the other and both could contribute to or be caused by viral or bacterial infections in which allergy may be the underlying basis.

Viral or bacterial infections can be secondary to poor drainage of the middle ear secretions, with stasis and bacterial proliferations resulting in acute otitis media. The age distribution of SOM has two peaks: the first peak occurring between 6 and 24 months of age and the second between 5 and 6 years of age. SOM is more frequent in boys than in girls and occurs more frequently in Eskimos, American Indians, and Whites than in Blacks [6]. These findings support the role of genetic factors contributing to the pathogenesis of SOM.

The role of food allergy in SOM has been less well studied. The purpose of this presentation is to provide evidence in favor of the proposition that there is a causal relationship of food allergy in the pathogenesis of recurrent SOM [1].

Materials and Methods

Patients

A total of 104 unselected patients with recurrent SOM ranging in age from 1.5 to 9 years (mean 4.6) were evaluated for the presence of food allergy by means of skin testing and/or specific IgE and open food challenge.

Entry Criteria

The patients included in this study were those who presented with a history of chronic middle ear effusion of greater than 3 months in duration and/or recurrent or repeated acute otitis media greater than one episode per month for more than 5 months. All patients were unselected for food hypersensitivity. In order to obviate possible bias of the study which could result from known seasonal variations in disease expression of SOM, patients were entered into the study throughout the year but were challenged primarily during the summer season (i.e. May to July) avoiding the winter and spring periods of time when SOM is known to more likely occur [7].

Exclusion Criteria

Patients with the following conditions were excluded from the study: (1) history of anaphylaxis to foods; (2) generalized severe urticaria/angioedema; (3) Down's syndrome; (4) cleft palate; (5) bifid uvula; (6) smoker parents; (7) severe deviated nasal septum; (8) cystic fibrosis; (9) nasal polypsis; (10) hypertrophic adenoids, and (11) IgG, IgA, IgM and/or IgG2, IgG2, IgG3, IgG4 subclass deficiency.

Criteria Used for Diagnosis of SOM/Secretory Otitis media/Otitis media with Effusion

Tympanometry: Tympanometric abnormalities were required for the diagnosis of middle ear effusion and testing was performed using a Welch-Allyn tympanometer using a sound transmission of 226 Hz [1].

Audiometry: Audiometry was also used for the evaluation of middle ear effusion by testing the hearing at four different frequencies: 500, 1,000, 2,000 and 4,000 Hz at the sound intensity of 20 dB [1].

Otologic Parameters Monitored during the Study

Tympanometry and audiometry were monitored once monthly during elimination and challenge diet phases. The otologic parameters that were monitored during the study included the following: tympanometry as a major criterion, audiometry, color and position of the tympanic membrane, and air fluid/air bubbles as minor criteria.

Criteria for Diagnosis of Food Allergy

The criteria used for the diagnosis of food allergy in this study included historical, clinical and laboratory findings[8]. Laboratory criteria included positive RAST ($\geq$ class 2+ reactions to IgE to specific food allergens) and positive ($\geq$ 5 mm) epicutaneous testing (prick testing) as major criteria; history of urticaria and/or pruritus and history of nausea, diarrhea, abdominal pain (after ingestion of specific foods), one to two episodes (following natural food challenges) as minor criteria. One major criterion and two minor criteria were required for the diagnosis.

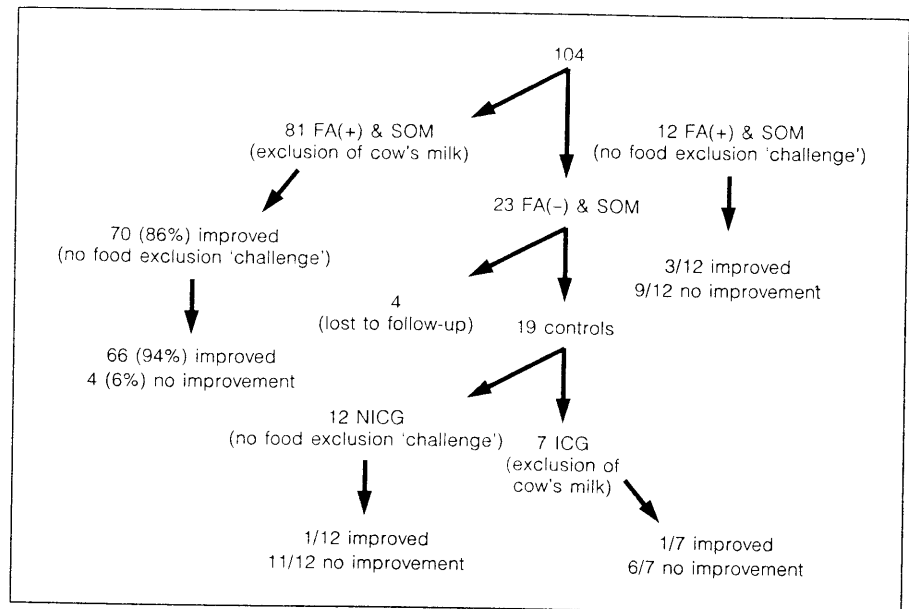


Fig. 1. Schematic representation of experimental design and various study groups.

Study Design

Of the total of 220 patients initially screened, 104 were found to meet criteria for SOM. These 104 unselected patients with SOM were screened for food allergy by means of allergy skin prick testing to cow's milk, wheat, egg white, peanut, soy, corn, orange, tomato, chicken, apple, specific serum IgE antibodies (RAST), and open food challenge.

Two groups of methodologic controls were included in this study. The first included 23 food allergy-negative subjects with SOM (FA(-) & SOM) (fig. 1). Of these, 4 were lost to follow-up and 19 were assigned to two groups: (1) a non-interventive control group (NICG) consisting of 12 patients in whom no dietary manipulation was performed, and (2) an inter-ventive control group (ICG) consisting of 7 patients in whom cow's milk was eliminated. A second type of methodologic control was included consisting of 12 food allergy-positive (FA(+)) & SOM patients who were not subjected to dietary restriction (fig. 1).

Food Allergen Elimination/Challenge

The foods that were selected for elimination were those that were demonstrated to be most positive either by skin prick testing or by in vitro specific IgE testing. For challenge studies, those foods (up to two) showing the highest degree of reactivity either by skin prick testing or RAST were employed.

Table 1. Role of food allergy in SOM: frequency distribution of allergies to individual foods in 81 subjects with food allergy

Food	Patients, n	%
Cow's milk	31	38
Wheat	27	33
Egg white	20	25
Peanut	16	20
Soy	14	17
Corn	12	15
Orange	8	10
Tomato	4	5
Chicken	4	5
Apple	3	4

Table 2. Frequency distribution of positive reactions to foods in study population according to number of food allergens

Positive food allergens, n	Allergic patients/total	
	n	%
1	11/81	13.6
2-4	66/81	81.5
5-7	3/81	3.7
8-10	1/81	1.3

Results

Prevalence of Food Allergy in Study Population

Of the 104 unselected patients with SOM originally screened, 81 (78%) were found to meet entry criteria of food allergy. The frequency distribution (percentage) of allergy to a variety of common food antigens in the 81 subjects with food allergy is shown in table 1. It can be seen that the highest frequencies (> 10%) were seen with milk, wheat, egg, peanut, soy and corn, and < 10% were seen with orange, tomato and chicken. Shown in table 2 is the distribution in the study population of food antigen reactivity grouped according to the number of foods encountered. It can be seen from table 2 that the vast majority of patients were allergic to from two to four foods.

Clinical Responses to Food Allergen Elimination/Challenge

An exclusion diet of the offending foods for a period of 16 weeks led to a significant amelioration of their middle ear disease (effusion) in 70 of the 81 patients (86%) as assessed by tympanometric testing, audiometric testing, clinical evaluation of position/mobility, color of the tympanic membrane, and monitoring of air fluid bubbles and/or air bubbles in the middle ear; a total of 11/81 (14%) did not improve. Seven of the 81 patients discontinued the diet; 4 did not improve. Only 17% of the patients with middle ear effusion diagnosed by tympanometry presented with an air fluid level or bubbles of air, but almost always mobility was affected as assessed by pneumatic otoscopy.

Following a non-double-blinded open food challenge with the suspected potential offending food allergens in 70 of patients who initially showed improvement, a recurrence of SOM was seen in 66 (94%) over a 16-week period. Of the 4 patients showing no recurrence of SOM, 2 did not have activation of their SOM and 2 discontinued the food challenge.

Effect of Dietary Elimination or Maintenance in Food Nonallergic (FA(-)) and Food-Allergic (FA(+)) Patients with SOM

The data were studied utilizing two lines of analysis assessing: (1) the effects of the exclusion diet and (2) the effects of the challenge diet in food allergy-positive subjects (FA(+)) & SOM) compared to that observed in food allergy-negative subjects with SOM (FA(-)) & SOM).

The effect of an exclusion diet was evaluated by comparing the nature of change of objective parameters between the 81 (FA(+)) & SOM) exclusion diet participants in comparison to that seen among the 7 food nonallergic (FA(-)) & SOM) patients in the ICG in whom cow's milk was eliminated. Of the 7 patients in the ICG group, 1 showed improvement and 6 showed no improvement. A highly significant χ^2 was obtained ($\chi^2 = 21.51$; d.f. = 1; $p < 0.001$) indicating a statistically strong linkage between the presence or absence of the food allergy and SOM symptom improvement during the exclusion diet (fig. 1).

The effect of the challenge diet was determined by comparing the nature of symptom change between the 70 (FA(+)) & SOM) challenge diet participants to that found among the 12 NICG food nonallergic (FA(-)) & SOM) subjects in the NICG (fig. 1). Of the 12 NICG patients, 1 showed improvement and 11 showed no improvement in SOM. This analysis also yielded a highly significant χ^2 ($\chi^2 = 73.00$; d.f. = 2; $p < 0.001$), suggesting an association between the nature of symptom change and participation in the challenge diet. A separate group of 12 food-allergic patients with SOM (FA(+)) & SOM) was studied to evaluate the effect of lack of elimination of specific foods. In this group, improvement of SOM was observed in 3 and a persistence of SOM was seen in 9 subjects ($p < 0.01$).

Although the role of food allergy in SOM has been suggested by Bernstein [6], particularly in otitis-prone children under the age of 2, its precise incidence is unknown. The results of the present study suggest that in a cohort of unselected patients with recurrent SOM, a sharply high prevalence of food hypersensitivity was detected in 81/104 (78%) of patients. The spectrum of reactivity to specific foods (table 1) is consistent with that reported by other authors [8–12] with the most prevalent foods including milk, wheat, egg, peanut, soy and corn. Over 95% of the patients in the present study demonstrated a pattern to multiple food reactions, i.e. 54. The unusually high incidence of food allergy in SOM patients in the present study may be explained on the selected nature of the study population which was drawn from a group of patients highly refractory to conventional forms of medical and surgical therapy referred to an allergy clinic. In a similar study of patients with refractory recurrent SOM, Hurst [10] detected an allergic basis in all 20 patients studied on the basis of RAST testing and skin testing. In this study, 65% had normal hearing and normalization of tympanometry following immunotherapy to inhalants, and SOM resolved in the remaining 35% of subjects. In the present study, 70/81 patients (86%) improved following food elimination and of 70 rechallenged with the offending food(s), 66 (70%) had recurrence of SOM following provocation.

Otitis media, in conclusion, may be secondary to a variety of factors that cause eustachian tube obstruction. Allergic inflammation, because of its obstructive effects particularly at the orifice and within the eustachian tube, probably is the most common cause of eustachian tube obstruction. Although such inflammation often is associated with recurrent upper respiratory infection, the present study indicates that food allergy may contribute significantly to a proportion of cases. Thus, the possibility of a food allergy should be considered in all patients with recurrent SOM and a diligent search for the putative food allergen made for the proper diagnostic and therapeutic management of these patients.

References

- 1 Nsouli TM, Nsouli SM, Linde RE, O'Mara F, Scanlon RT, Bellanti JA: Role of food allergy in serous otitis media. *Ann Allergy* 1994;73:215–219.
- 2 Donaldson J, Bierman CW: Diseases of the ear; in Bierman CW, Pearlman DS (eds): *Allergic Diseases from Infancy to Adulthood*. Philadelphia, Saunders, 1988, pp 483–497.
- 3 Gates G, Wachtendorf C, Holt GR, et al: Medical treatment of chronic otitis media with effusion. *Otolaryngol Head Neck Surg* 1986;94:350–354.
- 4 Bernstein JM: Immunologic reactivity in otitis media with effusion. *Clin Rev Allergy* 1984;2: 303–318.
- 5 Bluestone CB: Microbiology in Otitis media in Infants and Children. Philadelphia, Saunders, 1988, pp 45–58.

- 6 Bernstein JM: Recent advances in immunologic reactivity in otitis media with effusion. *J Allergy Clin Immunol* 1988;81:1004-1009.
- 7 Teele DW, Marshall R: Epidemiology of otitis media in children. *Ann Otol Rhino Laryngol* 1980; 89:5-6.
- 8 Bluestone CD, Fireman P: Otitis media; in Middleton EM, Reed CE, Ellis ET, Adkinson NF, Yunginger JW (eds): *Allergy Principles and Practice*. St Louis, Mosby, 1988, pp 1305-1325.
- 9 Sampson H: Adverse reactions to foods; in Middleton E, Reed CE, Ellis EF, Adkinson NF, Yunginger JW, Busse WW (eds): *Allergy Principles and Practice*. St. Louis, Mosby, 1993, pp 1675-1678.
- 10 Hurst DS: Allergy management of refractory serous otitis media. *Otolaryngol Head Neck Surg* 1990;102:664-669.
- 11 Bock SA, May CD: Adverse reactions to food caused by sensitivity; in Middleton EM, Reed CE, Ellis EF (eds): *Allergy Principles and Practice*. St Louis, Mosby, 1988, pp 1415-1427.
- 12 Fireman P: Update on middle ear disease. *Allergy Proc* 1991;12:159-161.

Dr. Joseph A. Bellanti, Georgetown University Medical Center,
3800 Reservoir Road, NW Washington, DC 20007 (USA)