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ORIGINAL RESEARCH

Nasal polyposis: Prevalence of positive food and inhalant skin tests

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OBJECTIVES: To investigate the etiology of nasal polyps and its relationship to allergy. The prevalence of positive food and inhalant skin tests in patients with nasal polyps and nonatopic controls was compared.

STUDY DESIGN AND SETTING: Prospective controlled study in tertiary referral rhinology clinic.

RESULTS: Seventy percent (70%) of the patients with nasal polyps had positive skin tests to an average of four foodstuffs, compared to 34 percent of controls ($P = 0.006$). Only 35 percent of the nasal polyp patients also had positive inhalant skin tests. Overall, the prevalence of positive inhalant skin tests was similar in the nasal polyp patients and controls.

CONCLUSIONS: These findings suggest that the positive skin tests to foods are not merely a reflection of the general atopic status of patients with nasal polyps. It may be that non–IgE-mediated hypersensitivities, such as to ingested foods, play a role on the basis of a significant number of patients with positive intradermal skin tests to foods.

SIGNIFICANCE: Evaluation of the allergic status of patients with polyposis is important. Dietary manipulation may be indicated, though its role needs further investigation.

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The etiology of nasal polyposis (NP) remains obscure, but NP can be considered as the end result of a chronic inflammatory process in the sinonasal mucosa, seen in a variety of disease states such as infection, allergy, asthma, aspirin hypersensitivity, and cystic fibrosis.[1]

In 90 percent of NPs eosinophils comprise the most prevalent inflammatory cell type. These cells have a demonstrable ability to synthesize and release mediators and powerful regulatory molecules. This marked self-perpetuating eosinophilia and the noted association with atopic states has led to allergy being implicated in the pathogenesis of NP. This role is debated, however, as positive skin prick test (SPT) and raised IgE and RAST (radioallergosorbent tests) levels are not found in the majority of patients with nasal polyps.[2] In fact, asthmatic patients with negative SPTs to inhalant allergens have significantly more NP than asthmatic patients with positive SPTs.[3] Some authors have in fact suggested that there is a more frequent association between NP and food allergies than the typical IgE-mediated inhalant allergies,[4] and that treatment leads to decreased symptoms and slower progression of the polyps.[5]

A previous study of patients with nasal polyps in our center found that 80 percent had positive intradermal food tests (IDFT) to a range of foods, mostly wheat, potato, and tomato, compared to 11 percent of control volunteers.[4] It may be that this finding merely reflects the general atopic diathesis of this group of patients. However, the status of these patients with respect to inhalant SPTs or IgE-mediated atopy was not examined. We would expect to see a difference in the prevalence of positivity to IDFTs and SPTs in patients with nasal polyps and controls, as it is suggested that food hypersensitivities are mediated mainly by non–IgE-mediated mechanisms. Since it is suggested that they have different immunological bases, it may be the case that a genuine difference in prevalence exists.

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The aims of our study were to prospectively compare patients with nasal polyps and controls for the prevalence of 1) positive reactions to food allergens by intradermal food tests and 2) positive reactions to inhalant allergens by skin prick tests.

MATERIALS AND METHODS

Subjects and Controls

Forty patients were recruited to the study from the outpatient rhinology clinic at a tertiary referral center. All the patients were about to undergo endoscopic sinus surgery for nasal polyposis refractory to medical treatment and had inflammatory nasal polyps confirmed by endoscopic examination, CT scanning, and histology. Patients with other sinonasal pathologies or with chronic rhinosinusitis without polyposis were excluded. The patients were selected consecutively from the waiting list and not according to atopic/allergic status as the intention was to compare the patients for objective reactions to food and inhalant allergens.

The controls were recruited from members of the otolaryngology staff and students attached to the department. The controls had no nasal symptoms and were defined as nonatopic from the absence of a history of hayfever, asthma, or eczema. They had not had their atopic status defined by prior SPTs or RAST.

Food Allergy

Forty patients with confirmed nasal polyposis, 21 male and 19 female (mean age 51 years), and 21 sex-matched nonatopic volunteer controls (mean age 39 years) underwent intradermal food allergy tests to a panel of 16 food allergens. Each subject completed a 14-day food diary. All foods eaten were documented and subjects were asked not to change their eating habits. The diaries were analyzed and grouped into constituent foodstuffs (eg, wheat, egg). Foods that were not usually eaten at least twice a week were excluded from the allergen panel. Any food known to give an anaphylactic reaction was also excluded and subjects were required not to use any antihistamine during the preceding week. Biodiagnostics (Bio-diagnostics Ltd, Worcester, UK) manufacture a range of commercially prepared test allergens and those foodstuffs identified by the diaries were selected from that range. Some foodstuffs, such as additives and preservatives, are not available as a test allergen for intradermal testing.

The test allergens (Biodiagnostics) are supplied in 1:10 w/u strength with 50 percent glycerine as a solvent. The test allergen is diluted five times with saline. The negative control used was 50 percent glycerine in the same strength as the solvent in the test reagents. A 0.05-mL quantity of each test allergen is injected intradermally on the flexor surface of the forearm to produce a wheal size of 7 mm diameter, measured and documented. The size of the wheal is read at 20 minutes. A growth of two mm in diameter in excess of the negative control is considered a positive test.[4]

Inhalant Allergy

The same 40 patients with nasal polyps and 21 controls underwent skin prick tests to a panel of 12 inhalant allergens. A drop of solution of test allergen (Biodiagnostics) was placed on the flexor surface of the forearm, and a Medipoint used to prick the skin. Histamine was used as a positive control and saline as a negative control. Skin prick tests were read at 20 minutes. A wheal of more than three mm in diameter is considered a positive test. SPTs are the most widely used technique for inhalant allergy testing in the outpatient setting in the UK.

The subjects were unaware of the nature of each test allergen at each test site. Adrenaline 1:1000 was available and a member of the medical team was present to deal with any problems.

The study had the approval of the local ethical committee and informed consent was obtained from each patient.

Two-by-two tables were constructed and χ^2 tests performed to look for statistical significance.

RESULTS

Twenty-eight (70%) of the patients with nasal polyps had positive intradermal food tests vs seven (34%) of the controls ($\chi^2 = 7.57$, $P = 0.006$); see Table 1.

Significantly more of those patients with nasal polyps with positive IDFT reactions had negative SPT, compared with the controls (35% vs 19%, Table 1). Whether or not the patients with nasal polyposis had positive or negative SPTs, they still had the same likelihood of having positive IDFTs.

Table 1
Comparison of numbers of subjects with positive intradermal food tests and skin prick tests

	Nasal polyps N = 40	Controls N = 21
+ve IDFTs	28 (70%)*	7 (34%)
−ve IDFTs	12 (30%)	14 (66%)
+ve SPTs	17 (43%)	10 (48%)
−ve SPTs	23 (57%)	11 (52%)
+ve SPTs		
& +ve IDFTs	14 (35%)*	3 (14%)
& −ve IDFTs	3 (7.5%)	7 (33%)*
−ve SPTs		
& +ve IDFTs	14 (35%)*	4 (19%)
& −ve IDFTs	9 (22%)	7 (33%)

IDFT, intradermal food test; *SPT,* skin prick test.
χ^2 tests on 2 × 2 tables: *statistically significant difference (if any of the expected values is less than 5, Fisher's exact test was performed).

Table 2
Pattern of positive responses to food intradermal tests and inhalant skin prick tests

Nasal polyp patients (n = 40)				Controls (n = 21)			
Food	No +ve	Inhalant	No +ve	Food	No +ve	Inhalant	No +ve
Wheat	15	Grass	9	Wheat	7	Mite 1	8
Tomato	12	Weeds	9	Potato	4	Mite 2	7
Potato	11	Mite 1	9	Banana	3	Grass	7
Milk	9	Mite 2	7	Egg	2	Dog	6
Chicken	8	House dust	5	Chicken	2	Cereal	6
Pea	8	Molds	4	Orange	1	Weeds	5
Banana	8	Tree	3	Peanut	1	House dust	4
Oats	7	Dog	3	Tomato	1	Cat	4
Egg	6	Cat	2	Apple	1	Feathers	4
Orange	6	Feathers	2	Beef	1	Flowers	1
Pork	4	Flowers	1				
Beef	3	Aspergillus	1				
Peanut	3						
Corn	3						
Apple	2						

There was no significant difference in the prevalence of positive SPT overall: 17 (43%) nasal polyp patients and 10 (48%) of the controls. Positive SPTs in isolation occurred in only 3 (7.5%) of the nasal polyp patients compared to 7 (33%) of the controls ($\chi^2 = 6.71$, $P < 0.01$).

The average number of food substances tested was 12 in the nasal polyp group and 13 in the controls. Both patients with nasal polyps and controls were tested with 12 inhaled allergens. Subjects reacted to an average of four foodstuffs and to an average of four inhaled allergens (see Table 2).

DISCUSSION

This prospective, controlled study provides further objective evidence to support the opinion of other authors that nasal polyps may have a more common relationship with food allergies than typical IgE-mediated inhalant allergies.[4,5] Our patients with nasal polyps were no more likely to react to skin prick tests for inhalant allergens (ie, be atopic) than controls (43% vs 48%), but were twice more likely to have positive IDFTs (70% vs 34%). Furthermore, only half the patients with nasal polyps and controls with positive IDFTs also had positive SPTs. This suggests that IDFT positivity is more than a simple marker of atopic status, and does reflect a specific response to foodstuffs. Whether or not the patients with nasal polyposis had positive or negative SPTs, they still had the same likelihood of having positive IDFTs.

Three-quarters of control subjects with positive SPTs were positive to inhaled allergens alone, compared to one-sixth of patients with nasal polyps, again implying that IgE-mediated atopy is not more prevalent in the nasal polyp group. Although other evidence also suggests nasal polyps are not caused by the allergic IgE or non-IgE antibody response,[2,6] when nasal polyps and atopy occur together, allergies appear to aggravate the nasal polyposis and increase the chance of recurrence.[6-9] The evaluation of both inhaled and ingested allergen response is therefore appropriate in patients with nasal polyps.

Since there was a slight male predominance in our patients with nasal polyposis, our controls were sex matched. Although the mean age of our control group (39 years) was younger than the patient group (51 years), we did not control for this as we felt it would not influence the results. A number of publications document the fact that the incidence of nasal polyps and allergy is comparable in patients in their 30s, 40s, and 50s.[3,7]

The diagnosis of atopy in clinical practice is based on a number of in vivo and in vitro tests, namely skin prick tests, RAST (radioallergosorbent test) for specific IgE, and oral challenge food tests. In response to SPTs, a skin wheal response is conveniently regarded as an IgE-mediated response. For inhaled allergens, the SPT correlates well with the clinical history and RAST.[10]

In the case of skin tests for food allergy, debate has existed over whether provocation of the skin wheal response is an appropriate test outcome. Though oral challenge tests are seen as the gold standard, they are expensive and time-consuming, avoidance is difficult with certain foods, and compliance with exclusion diets is hard to ensure.[11,12] In 1988, the American Academy of Otolaryngologic Allergy reported that the skin response was the more dependable method of test interpretation than symptom provocation, providing a validity coefficient of 0.78 and a reliability coefficient of 0.68.[5,13] There is evidence to suggest that intradermal testing rather than skin prick testing is the more sensitive testing method in food tests, as the latter technique does not deliver a big enough dose to register a response.[5] For these reasons SPTs were used for the inhaled allergens and IDFTs used for the food tests in our study.

It has been shown that food allergen intradermal tests match the results of oral challenges more closely than those of RAST tests for specific IgE.[11] Most reliable and validated tests are those demonstrating IgE antibodies,[11,14] but in food allergies the pathophysiology of these reactions is unclear—Type II, III, and IV delayed hypersensitivity have all been proposed and 95 percent of food reactions are thought to be mediated by these other immunological mechanisms.[5,11,15]

It seems, therefore, that IDFTs are not solely dependent on IgE but other immunological mechanisms are involved that justify their use in the detection of food allergies and delayed food hypersensitivities.[12] Sampson concluded that skin tests and immunoassays have an excellent negative predictive value, though less good positive predictive value, and can be regarded as a good guide to identifying food allergies.[15] Many of these patients and controls do not volunteer a history of hypersensitivity on direct questioning. If delayed mechanisms are involved a clear time relationship between ingestion of the food and symptoms may not be apparent. Ultimately there remains no ideal method for food allergy testing.

CONCLUSIONS

The data from this prospective controlled study indicate that IgE- and non–IgE-mediated immunological mechanisms such as food allergy and delayed food hypersensitivity may play a part in the etiology of nasal polyps, as patients with nasal polyps were significantly more likely to have positive intradermal food tests than controls. However, patients with nasal polyps were no more likely to be atopic than controls, as gauged by skin prick test positive response, and therefore the non–IgE-mediated delayed food hypersensitivity may be the more important. A trial of food exclusions based on the results of the intradermal testing would be warranted, especially in the patient with more severe disease. The ultimate relevance can only be determined by the symptom benefit of manipulation of the patient's diet.

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