

Hypersensitivity to molds in patients with nasal polyposis: A clinical study

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Nasal polyposis is a rather frequent disorder. Although it is generally believed that allergy plays a pathogenetic role in nasal polyps, allergic reactions seem to occur infrequently in affected subjects.¹ Previous studies found that only a small proportion of atopic patients have nasal polyps² and that patients with polyposis do not show an increased incidence of allergic disorders.³

More than 200,000 mold species have been identified so far. The allergenic significance of most airborne fungi is still uncertain and difficult to ascertain because of the lack of good-quality extracts for in vivo or in vitro allergologic testing. Thus, although there is a feeling that many molds might be allergenically relevant, skin tests with extracts of fungi other than *Alternaria*, *Cladosporium*, or *Aspergillus* are frequently not carried out during routine assessment of possible allergic patients. The current study aimed to investigate the immediate skin reactivity to a series of 15 fungi in a group of patients with nasal polyposis.

PATIENTS AND METHODS

Patients and skin tests

Twenty consecutive patients (male/female ratio 12:8; age 28-77 years, mean 50.5 years) with severe nasal polyposis seen at the ENT outpatient department from October 1, 1998, to June 30, 1999, were studied. None of them had undergone allergologic investigations before, but a woman with a history of birch pollen allergy had been treated with injection immunotherapy up to February 1997. Patients underwent a thorough interview to detect aspirin intolerance (asthma, rhinitis, or urticaria/angioedema) or possible respiratory allergies (seasonal or perennial rhinoconjunctivitis or asthma). Skin prick tests (SPT) with commercial extracts of the main airborne allergens present in this geographic area, including pollens (grass, pellitory, mugwort, ragweed, cypress, birch, hazel, plantain, and olive tree), house dust mites, and cat and dog dander (Allergopharma, Reinbeck, Germany, 50,000 biological units [BU]/mL in all cases but dog dander, 10,000 BU/mL) were performed. Moreover, SPT with a series of 15 commercial mold extracts (Table I, all by Allergopharma 10,000 BU/mL, except *Mycogone* and *Pae-*

Abbreviations used

BU: Biological units
SPT: Skin prick tests

TABLE I. Mold extracts tested in patients with nasal polyps

<i>Alternaria tenuis</i>
<i>Aspergillus fumigatus</i>
<i>Botrytis cinerea</i>
<i>Candida albicans</i>
<i>Cladosporium herbarum</i>
<i>Curvularia lunata</i>
<i>Fusarium moniliforme</i>
<i>Helminthosporium halodes</i>
<i>Mycogone</i>
<i>Mucor mucedo</i>
<i>Paecilomyces varioti</i>
<i>Penicillium notatum</i>
<i>Pullularia pullulans</i>
<i>Rhizopus nigricans</i>
<i>Tricophyton mantagrophytes</i>

cilomyces, which were manufactured by Dome/Hollister-Stier, 10,000 protein nitrogen units/mL) were carried out as well. All SPTs were performed with 1-mm tip disposable prick lancets (Bayer). Readings were taken at 15 minutes, and wheals >+ by comparison with histamine 10 mg/mL were considered positive.⁴

Controls

A total of 409 consecutive patients (male/female ratio 198:211; age 6-70 years, mean age 32.2 years) with respiratory allergy seen at the allergy department from January 1, 1996, to June 30, 1999, were used as control subjects. All of them underwent SPT with a standard series of airborne allergens (see before), including 5 mold extracts (*Alternaria*, *Aspergillus*, *Cladosporium*, *Candida*, *Penicillium*). All SPTs were carried out with the same extracts used in patients (Allergopharma, Reinbeck, Germany).

Statistical methods

Proportions were compared by the 2-tailed chi-square test with Yates' correction. *P* values <.05 were considered significant.

RESULTS

Clinical features and SPT results are shown in Table II. No patient had a history of aspirin intolerance (whether asthma, rhinitis, or skin disorders). One patient (5%) had recurrent perennial asthma. Three of 20 (15%) patients had a typical clinical history of seasonal rhinoconjunctivitis and asthma; in these patients respiratory allergy was confirmed by positive SPTs (Table II). Altogether, 55% (11/20) of patients demonstrated skin reactivity to at

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TABLE II. Clinical features and skin reactivity in 20 patients with nasal polyps

Patient	Sex/age (y)	Aspirin intolerance	Asthma	SPT	
				Molds	Other allergens
B. V.	M/61	No	No	Negative	Negative
C. D.	M/66	No	No	Negative	Negative
C. T.	F/36	No	No	Negative	Negative
F. M.	M/42	No	No	Negative	Negative
G. A.	F/56	No	No	Can++	Negative
G. P.	M/28	No	No	Negative	Negative
G. E.	F/52	No	No	Negative	Negative
M. R.	M/51	No	No	Negative	Negative
M. F.	F/52	No	Seasonal (B)	Can++	BGRP++++
M. G.	M/41	No	Seasonal (G)	Can+++	BGMR+++
P. G.	M/59	No	No	Can++++	Mite+++
P. L.	F/54	No	Perennial	Can++	Mite++
P.R.	M/61	No	No	Asp++	Negative
R. F.	M/41	No	No	Negative	M+++
R. P.	M/30	No	No	Negative	Negative
S. C.	F/72	No	No	Can++	Negative
S. G.	M/77	No	No	Can+++	Negative
S. L.	F/32	No	No	Negative	Negative
S. M.	F/39	No	Seasonal (B + R)	Alt++++/Can++	BGR+++
T. M.	M/60	No	No	Negative	Negative

M, Male; F, female; Can, *Candida*; B, birch; G, grass; R, ragweed; P, plantain; M, mugwort; Asp, *Aspergillus*; Alt, *Alternaria*.

least one airborne allergen; 9 (45%) of them were positive on SPT with mold extracts (8 *Candida* [40%], 1 *Aspergillus* [5%], and 1 *Alternaria* [5%]). No skin reactivity to the remaining 12 molds was observed among patients with nasal polyps. Reactivity to house dust mite and mugwort pollen was observed in 2 and 1 cases, respectively.

Forty-three of 409 (11%) control subjects were positive on SPT with mold extracts: *Alternaria* in 36 (9%) cases, *Aspergillus* in 6 (1%), *Candida* in 4 (1%), *Cladosporium* in 3 (1%), and *Penicillium* in 2 cases. A significantly higher proportion of patients than control subjects demonstrated mold sensitivity on SPT (45% vs 11%, respectively; $P < .001$; Table III); this striking difference could be totally ascribed to *C albicans* sensitivity (40% vs 1%, $P < .001$), whereas no difference in the prevalence of skin reactivity against other fungi was observed.

Patients were significantly older than control subjects (mean age 50.5 vs 32.2 years, respectively). To exclude a possible influence of age on *C albicans* sensitivity, controls aged >35 years were analyzed separately; only 2 of 169 (1%) were positive for *Candida* on SPT.

Sixty-six of 409 (16%) control subjects were seen for obstructive rhinitis. Small monolateral polyps and a severe bilateral obstructing polyposis were found in 4 and 1 subjects, respectively; interestingly, the patient with severe polyposis was 1 of the 4 control subjects positive on SPT with *C albicans* extract.

DISCUSSION

In this study a surprisingly high proportion (40%) of patients with severe nasal polyposis showed immediate

TABLE III. Comparison between mold sensitivity in patients and control subjects

Positive SPT	Patients (n = 20)	Controls (n = 409)	Statistical significance
<i>Alternaria</i>	1 (5%)	36 (9%)	NS
<i>Aspergillus</i>	1 (5%)	4 (1%)	NS
<i>Cladosporium</i>	0 (0%)	3 (1%)	NS
<i>Candida</i>	8 (40%)	4 (1%)	$P < .001$
<i>Penicillium</i>	0 (0%)	2 (1%)	NS
Any mold	9 (45%)	43 (11%)	$P < .001$

NS, Not significant.

skin reactivity against a commercial extract of the yeast *C albicans*. Such reactivity was rare in a large group of control subjects with respiratory allergy, and severe nasal polyposis was found in 1 of 4 positive controls. *Candida* sensitivity was not associated with an increased frequency of skin reactivity to different common mold genera such as *Alternaria*, *Aspergillus*, *Cladosporium*, or *Penicillium*. Moreover, patients with nasal polyps did not show any skin reactivity to 10 further mold genera. The incidence of asthma among patients with nasal polyposis (20%) was identical to that found in other studies.¹

Although reaginic responses to *C albicans* are well documented, the role of this yeast as an airborne allergen remains controversial.⁵ Most patients with nasal polyps demonstrating a positive SPT with *Candida* extract did not report typical symptoms of acute allergic rhinitis, such as sneezing and itching, but rather chronic rhinorrhea and a progressively worsening obstructive rhinitis, often associated with hyposmia. *C albicans* is a common saprophytic inhabitant of the human upper respiratory tract.⁵ The continuous contact between small amounts of

this (maybe weak) allergen and a weakly or moderately allergic nasal mucosa might have induced chronic inflammation in the absence of episodes of acute rhinitis in these patients. Moreover, *C albicans* is scarcely present in the environmental air,⁵ a fact that might explain the total absence of perennial conjunctivitis or perennial asthma in most *Candida*-sensitive subjects.

Only a few fungi were tested in this study, but the series used here included most of commercial mold extracts available on the market. Our findings suggest that other molds, possibly normal inhabitants of the upper respiratory tract as well, might also play a role in patients with nasal polyposis. Studies that use much larger series of mold extracts will be needed to test this hypothesis. Finally, this study supports an allergic patho-

genetic mechanism in several patients with nasal polyposis.

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