

TISSUE-SPECIFIC IMMUNOGLOBULIN E IN HUMAN NASAL POLYPS

CHIH-YEN WEI, MD

SHEEN-YIE FANG, MD

TAINAN, TAIWAN (ROC)

Allergy is generally believed to be an underlying cause of nasal polyps. The objective of this study was to define allergic nasal polyps. We investigated specific immunoglobulin E (sIgE) in polyp tissue. Thirty pieces of polyp tissue were taken from patients with positive allergic symptoms, and 30 from patients without allergic symptoms. Nasal polyp tissue homogenate and serum from these patients were prepared for detecting sIgE by a CAP method. For patients with allergic symptoms and/or positive serum CAP test results, the rates of positive tissue CAP tests were low: 36.7% and 35.7%, respectively. However, nearly all of the tissue CAP-positive subjects had allergic symptoms and positive serum CAP tests. We conclude that the local tissue sIgE profile reflects more specifically the allergic status of patients with nasal polyps than does the systemic serum test or the presentation of allergic symptoms. Thus, polyp tissue CAP tests might be performed in patients with positive allergic symptoms and positive serum CAP tests to define an allergy-induced polyp precisely. Then, specific antiallergic treatment could be administered to prevent polyp recurrence.

KEY WORDS — allergy, CAP, immunoglobulin E, nasal polyp.

INTRODUCTION

Nasal polyposis is a common disorder that occurs in association with many diseases of the upper respiratory tract. Its cause, however, remains largely unknown, perhaps because the specific cause is not the same for all patients.^{1,2} Allergy is generally believed to be an underlying cause of nasal polyps, but the connection between allergy and nasal polyps is still speculative. Previous studies have found that only a small proportion of atopic patients have nasal polyps and that patients with polyposis do not typically show an increased incidence of allergic disorders.^{3,4} In 1982, Lee and Pitcher-Wilmott⁵ found no evidence of an increased incidence of allergic disorders among 200 consecutive patients admitted for polypectomy. However, some investigators have confirmed local production of allergen specific immunoglobulin E (sIgE) in the nasal secretions and the polyp fluid of polyp sufferers; they have suggested that allergy might play an important role in producing nasal polyps.⁶⁻¹¹

Since the precise relationship between allergy and nasal polyps is still debatable, multiple investigations have been performed to study the occurrence of positive allergy tests among patients with polyps. Such investigations typically used a radioallergosorbent test (RAST) in order to detect sIgE in nasal secretions and in the patients' serum.⁶⁻⁹ Moreover, positive serum test results have frequently been used to define an allergic nasal polyp in clinical practice. In 1988, the CAP system (Pharmacia Diagnostics, Uppsala, Sweden) was developed for the measurement of sIgE and is characterized by a new solid phase (consist-

ing of a hydrophilic polymer encased in a capsule). Since its development, it has been used more and more frequently in clinical practice for the identification of the presence of sIgE. Consequently, the CAP system was compared with the RAST system for the detection of serum sIgE. The former revealed itself to be more sensitive and either equally as specific as or more specific than the RAST system.^{12,13}

The appropriate treatments for nasal polyps with different causes are diverse, and thus it is critical to attempt to identify the cause clinically. It is not always appropriate to determine nasal polyps as being allergic or nonallergic by clinical symptoms or serum allergic test results alone. In order to obtain a better profile of allergic nasal polyps, we measured sIgE in nasal polyp tissue using the CAP system and compared the results to the patients' serum sIgE levels and the patients' clinical manifestations.

MATERIALS AND METHODS

Sixty patients with nasal polyps — 30 with allergic symptoms (including frequent sneezing, itchy nose, and watery rhinorrhea for a period of at least 1 year) and 30 without allergic symptoms — were selected for this study. The mean ($\pm$ SD) age of the patient group with allergic symptoms was 29.5 ± 4.2 years; 18 of 30 patients were male. The mean age of the patient group without allergic symptoms was 31.6 ± 5.7 years; 17 of 30 patients were male. All participating patients underwent endoscopic sinus surgery to remove the nasal polyps. Serum and nasal polyp tissue sIgE levels specific to five common aeroaller-

From the Department of Otolaryngology, National Cheng Kung University Hospital, Tainan, Taiwan (ROC). This study received a grant from the National Science Council, Taiwan (NSC92-2314-B006-049).

CORRESPONDENCE — Sheen-Yie Fang, MD, Dept of Otolaryngology, National Cheng Kung University Hospital, No. 138, Sheng-Li Road, Tainan 70428, Taiwan (ROC).

TISSUE AND SERUM CAP TEST RESULTS IN 60 PATIENTS WITH NASAL POLYPS

Patient Status	No. of Patients	Tissue CAP—Positive		Allergic Symptom—Positive		Serum CAP—Positive	
		No.	%	No.	%	No.	%
Serum CAP—positive	28	10/28	35.7	28/28	100		
Serum CAP—negative	32	1/32*	3.1	2/32	6.3		
Allergic symptom—positive	30	11/30	36.7			28/30	93.3
Allergic symptom—negative	30	0/30	0			0/30	0
Tissue CAP—positive	11			11/11	100	10/11	91
Tissue CAP—negative	49			19/49	38.8	18/49	36.7

*This patient did reveal allergic symptoms.

gens in Taiwan — *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Candida*, *Aspergillus*, and *Penicillium* — were investigated with the CAP system.

The nasal polyp tissue was frozen at -70°C immediately after removal. When selected for experimentation, the samples were thawed, ground, and homogenized with lysis buffer (120 mmol/L sodium chloride, 10 mmol/L Tris–hydrochloric acid, Nonidet P40, 1% deoxycholate, 0.1% sodium dodecyl sulfate [pH 6.8]) and were stored at 4°C for about 30 minutes. Then these samples were centrifuged at 14,000 rpm for a period of 20 minutes. The upper liquid layer was removed and used to run the CAP system (Pharmacia Diagnostics). Serum and polyp tissue sIgE levels corresponding to the five kinds of allergens were determined. A positive result was defined as an sIgE level of 0.35 kU/L or greater.

RESULTS

The correlation of clinical symptoms, serum CAP test results, and tissue CAP test results is shown in the Table. Virtually all of the sIgEs that were detected in polyp tissue from individual patients were also found in the serum of the same patients.

Of the 30 patients with allergic symptoms, 36.7% (11/30) had positive tissue CAP test results for sIgE and 93.3% (28/30) had positive serum CAP test results. The prevalence of allergic symptoms among patients correlated well with a positive serum CAP test, but poorly with a positive tissue CAP test.

Of the 60 patients who participated in the study, 28 exhibited positive serum CAP test results, and 10 of these (10/28; 35.7%) demonstrated a positive tis-

sue CAP test. Thus, we determined that positive serum CAP test results correlated poorly with positive tissue CAP test results. Of patients with negative serum CAP test results, only 1 patient demonstrated a positive tissue CAP test result. However, this patient also exhibited allergic symptoms.

There were 11 patients who had positive tissue CAP test results. Ten of the 11 patients demonstrated positive serum CAP test results. All 11 patients revealed allergic symptoms. A high incidence of allergic symptoms and positive serum CAP test results was noted for the tissue CAP–positive patient group.

The 30 patients with no allergic symptoms had negative serum and tissue CAP test results.

DISCUSSION

A nasal polyp is the ultimate form of inflammation of the upper airway. It arises for unknown reasons, although multiple possible etiologic factors have been suggested.⁷ Although allergy is one of the factors most frequently suggested as an underlying cause, the connection between allergy and nasal polyps would still appear to be somewhat ambiguous at this time.

The diagnosis of allergy in clinical practice is usually based on a skin test and the determination of serum sIgE antibody presence. The RAST was first developed by Wide et al¹⁴ in 1967. Multiple subsequent studies have shown a high concordance between results of skin testing and the serum RAST for a host of allergens. Serum RAST results have been widely used in clinical practice for allergy investigation in Taiwan. Another method, the Pharmacia CAP technique, is an in vitro sIgE test that was introduced in 1988.^{15,16} This technique uses a 3-dimensional cellulose solid allergen phase and has revealed a greater level of sensitivity than the RAST and at least as high a level of specificity as the RAST in regard to the detection of sIgE in serum. The superiority of CAP has been demonstrated in a number of different investigations.^{12,13} Furthermore, the Pharmacia CAP technique system allows for the rather quick provision of test results (ie, within 6 hours) as compared to the modified RAST (around 3 days). Hence, the CAP technique represents a test procedure that is both expeditious and convenient to operate in clinical practice.

Since CAP has been successfully used to detect sIgE in serum in a number of previous studies^{12,13} and also in clinical practice, it appears sensible to attempt to use the CAP test for the measurement of sIgE in nasal polyp tissue. The CAP technique is more sensitive than the RAST alternative without losing

any degree of specificity when 0.35 kU/L is used as the cutoff value for the detection of serum sIgE.¹⁷ We used the CAP technique to detect sIgE in serum and nasal polyp tissue with the selected cutoff value set at 0.35 kU/L in this study. However, we do suggest that further quantitative studies be performed to confirm the relative sensitivity and specificity of the CAP test for polyp tissue.

Allergy has consistently been proposed as a cause of polyps since Younge's original article on the cause of nasal polyps, published in 1907.¹⁸ Several previous studies also demonstrated that polyps are characterized by mast cell degranulation and high local levels of IgE, histamine, and eosinophilic inflammation.⁷⁻¹⁰ However, there are strong counterarguments against this idea. Nasal polyps do not occur with an increased frequency in allergic patients, and a positive allergic skin test is not more frequent in nasal polyp patients than in control subjects.^{19,20} Although allergy as a cause of nasal polyposis has yet to be confirmed, physicians often presume that the demonstration of allergic symptoms and/or a positive serum test in a patient with nasal polyps demonstrates that the polyp is allergy-induced. Our study has demonstrated that the rates of positive tissue CAP test results are typically low in the patient groups with allergic symptoms and positive serum CAP test results: 36.7% and 35.7%, respectively. Furthermore, of the 60 polyp patients, only 18.3% (11) demonstrated positive tissue CAP test results. This finding suggests that a cause-and-effect relationship between nasal polyposis and the presence of allergy may not necessarily exist. It is likely that there may be several possible underlying explanations. First, nasal polyposis is a disease that is not necessarily associated with a specific allergy, but may arise as a consequence of the influence of certain other, nonallergic, factors. Second, nasal polyposis, either among patients with positive serum CAP test results or patients with allergic symptoms, may not necessarily be induced by an allergy. The positive tissue CAP results for nasal polyp patients revealed in this study may be merely coincidental. Third, only five kinds of sIgE were detected in our study, and it may be possible that other kinds of sIgE among these study participants were omitted.

In contrast, of those patients who demonstrated positive tissue CAP test results, all had allergic symptoms and 91% had positive serum CAP test results. It is feasible that the tissue CAP test may actually have represented the presence of an allergic reaction not only in the nasal polyp tissue, but also, systemically, for the study subjects. In 2001, by using a CAP technique, Bachert et al¹⁰ evaluated nasal tissue from 20 patients with nasal polyps and also from 20 pa-

tients who revealed no evidence of nasal polyps. They found an association between an increased level of sIgE and eosinophilic inflammation within nasal polyp tissue and suggested that if increased levels of sIgE were noted in nasal tissue, immunologic inflammation would likely occur and may have some connection with the production of nasal polyps. For the same reason, if nasal polyp tissue reveals positive CAP test results, it would mean that there is an elevation of sIgE levels and an immunologic inflammation within this polyp tissue. Thus, it would appear reasonable to assume that this nasal polyp was allergy-induced.

Since tissue CAP-positive nasal polyps are more likely to be allergy-induced nasal polyps than are polyps from patients with positive clinical symptoms and/or positive serum CAP test results, and the treatment regimens for allergic and nonallergic nasal polyps are diverse, the validity of a polyp tissue CAP test as a routine clinical practice is inevitably questioned. Our study demonstrated that among patients who did not show any allergic symptoms, none had a positive tissue CAP test result. For patients with negative serum CAP test results, only 1 patient had a positive tissue CAP test result, and this patient exhibited allergic symptoms. However, among patients with allergic symptoms and patients with positive serum test results, 36.7% (11/30) and 35.7% (10/28) revealed positive tissue CAP test results, respectively. On the other hand, Shatkin et al²¹ performed a meta-analysis of nine studies that investigated mucosal allergy with the RAST, and they found strictly mucosal allergy in about 19% of the total allergic (systemic and mucosal) patients; however, up to 55% to 60% of patients in the studies had a positive polyp fluid RAST. They suggested that tests of local allergy have more significance in patients who have histories consistent with allergy but do not demonstrate positive results on systemic tests. According to our findings and the previous study, we recommend that tissue CAP tests be reserved specifically for those patients with a clinical history consistent with allergic disease, because we believe that this is more cost-effective and is more practicable clinically than such testing for all presumed polyp cases. Once the tissue CAP test yields a positive result, allergy control is critical for the patient. Allergen avoidance and antiallergic treatments such as antihistamines, decongestants, anti-inflammatory drugs, and immunotherapy are especially important for the patient in order to prevent the recurrence of nasal polyps. A follow-up study that examines the results of aggressive allergy management, recurrence rates, and other clinical parameters is necessary to substantiate the usefulness of such a treatment regimen.

CONCLUSIONS

Positive polyp tissue CAP test results are highly associated with nasal polyp sufferers with allergic symptoms and positive serum CAP test results. In addition, the local tissue sIgE profile reflects more precisely the allergic reaction within the nasal polyp tissue than does the systemic serum test or the presentation of clinical symptoms. Thus, the adminis-

tration of a nasal polyp tissue CAP test is suggested as routine practice for patients who exhibit positive allergic symptoms and a positive serum CAP test result. This will allow clinicians to define an allergic nasal polyp precisely. Afterward, a specific antiallergic treatment constituting an integral part of the post-operative course may be administered in order to prevent the recurrence of nasal polyps.

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