

The role of allergy in the severity of nasal polyposis

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ABSTRACT

Background: Although patients with nasal polyposis frequently exhibit concomitant allergy, there is limited information about the impact of allergy on the severity of nasal polyposis. The goal of this study was to evaluate the role of allergy in the severity of nasal polyposis.

Methods: Polyp sizes, computed tomography (CT) scores, skin-prick test results, blood total eosinophil count, serum levels of total immunoglobulin E, symptom scores, and recurrences were analyzed in 83 patients with nasal polyposis. The results were compared between allergic and nonallergic patients with nasal polyposis.

Results: No association was found between the presence of allergy per skin-prick testing and polyp size, CT opacification, symptom scores, or recurrences ($p > 0.05$). In allergic patients, only the serum total eosinophil count correlated strongly with the results of CT ($p = 0.005$) but not with other parameters ($p > 0.05$).

Conclusions: The results of this study show that, although patients with nasal polyposis frequently have allergies, the presence of allergy does not correlate with polyp size, symptom scores or rate of recurrence.

(Am J Rhinol 21, 686–690, 2007; doi: 10.2500/ajr.2007.21.3062)

Key words: Allergic rhinitis, allergy, nasal polyposis, pathogenesis, quality of life, rate of recurrence, skin-prick test, symptom scores

Nasal polyposis (NP), a chronic inflammation of the nasal and paranasal sinus mucosa, is characterized by edematous masses in the nasal cavities.¹ NP occurs clinically in 2–4% of the population.^{2,3} NP affects all races, and its prevalence increases with age. The pathogenesis of NP is multifactorial, and the condition itself is frequently seen with asthma, aspirin intolerance, and cystic fibrosis.⁴ Genetic factors, allergy, environmental factors, and viral, bacterial, or fungal antigens may contribute to the development of nasal polyps.⁵

Allergy plays a role in the development of respiratory diseases and is frequently a predisposing factor in rhinosinusitis.⁶ The prevalence of allergy in individuals with chronic rhinosinusitis (CRS) is high, and allergy is exacerbated by CRS.⁷ The prevalence of allergy in patients with NP varies from 10% to 64%.⁵

Nasal endoscopy and computed tomography (CT) are used in the diagnosis of sinonasal diseases. However, those objective tools of assessment are not always adequate to determine the severity of disease or predict the outcome of treatment.⁸ Therefore, both symptom scores and quality of life (QOL) scales have been suggested in the evaluation of the severity of sinonasal diseases. QOL measurements are used in either general health evaluations or disease-specific health evaluations. Disease-specific health evaluations are used to assess the patient's symptoms and the effects of those symptoms on the patient's general health. NP impairs the QOL in patients through symptoms such as nasal obstruction or congestion, hyposmia, and headache.⁹ Because there is limited knowledge regarding the role of allergy on the clinical course of NP, we

aimed to compare the severity between allergic and nonallergic patients with NP.

MATERIALS AND METHODS

Participants

At the Baskent University Konya Teaching and Research Center otolaryngology outpatient clinic, 4210 new patients 18 years and over were examined between November 2004 and January 2006. NP was diagnosed in 116 of those patients (2.7%). Eighty-three patients who completed diagnostic work-up and a questionnaire including sinonasal symptoms were enrolled in the study. Individuals with an antrochoanal polyp, mental retardation, cystic fibrosis, or an inverted papilloma were excluded from the study. Patients who had undergone sinus surgery within the previous 12 months were also excluded. Patients who underwent sinus surgery before, used topical steroid treatment for at least 6 months postoperatively, and had polyps in the nasal cavities were considered to have recurrent disease. None of the patients was using medical treatment at least during the last 1 month. All participants provided written informed consent.

Allergy Testing

We used skin-prick test to determine the presence of allergy in patients with nasal polyposis. Skin-prick tests were performed using the Quintest multiple skin-prick test device (Hollister-Stier Laboratories LLC, Spokane, United Kingdom) in all patients diagnosed as having NP. Each patient was evaluated for sensitivity to 18 allergens (ALK Abello, Madrid, Spain) that were based on our geographic area. Allergenic extracts were stored at 4°C. The panel used for skin-prick test included house dust mites, animal epithelia, mold, and pollen, as well as positive (histamine) and negative (glycerin/saline) controls. Results were read after 20 minutes. Test results were considered positive when at least one of the induration diameters was 3 mm higher than that in the negative control. Serum total eosinophil counts and serum total

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This study was presented at the 5th Balkan Congress of Otorhinolaryngology Head and Neck Surgery on September 7–10, 2006, Edirne, Turkey

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immunoglobulin E (IgE) values using the chemiluminescent immunoassay were also obtained.

Objective Evaluation of NP

In this study, the definition of NP was applied to bilateral polyps that were endoscopically identified as originating from the middle meatus. Polyp size was classified as follows: zero, no polyps; 1, polyps only in the middle meatus; 2, polyps that reached to the upper surface of the inferior turbinate; or 3, polyps that completely obstructed the nasal cavity.¹⁰

The results of paranasal sinus CT scans were staged according to the Lund-Mackay system.¹¹ That system scores the opacification of each paranasal sinus as follows: zero, no abnormalities; 1, partial opacification; or 2, total opacification. The ostiomeatal complex was scored as zero (no occlusion) or 2 (occlusion). The highest total score with this system is 24. NP was considered extensive when the CT score was higher than 16.¹²

Subjective Evaluation of NP

Nasal obstruction, nasal congestion, hyposmia, rhinorrhea, postnasal drip, facial fullness or pain, and headache symptoms were scored. Responses were scored from zero to 4 (zero, no symptoms; 1, mild symptoms; 2, moderate symptoms; 3, severe symptoms; or 4, intolerable symptoms), and the highest possible total score was 28.

Statistical Evaluation

All analyses were performed with SPSS software (Statistical Package for the Social Sciences, version 11.0, SSPS Inc, Chicago, IL). The impact of allergy on serum total eosinophil counts, serum total IgE, polyp size, CT score, and symptom scores was evaluated with the Student *t* test. The Fisher exact test was used to assess the association of allergy with gender, extensive NP, presence of asthma, aspirin intolerance, and recurrences. Pearson analysis was used to assess the correlation of serum total eosinophil counts and serum total IgE with polyp size, CT score, and symptom scores. One-way ANOVA and Kruskal-Wallis test were used for comparisons of symptom scores in allergic and nonallergic patients with matched subgroups of polyp size. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Thirty patients (36.1%) were women and 53 were men (63.9%). The mean patient age was 43.8 ± 11.6 years (range, 19–78 years). The mean age at symptom onset was 36.7 ± 12.5 years (range, 14–68 years), and the duration of disease was 7.1 ± 5.7 years (range, 1–25 years). The clinical characteristics of patients with NP are provided in Table 1.

The results of the skin-prick test were positive in 55 patients (66.3%). Thirty-seven male patients (69.8%) and 18 female patients (60%) were allergic, and there was no statistical difference with regard to gender ($p = 0.469$, Fisher exact test). The serum total eosinophil count was $365.07 \pm 245.73/\mu\text{L}$, and the serum total IgE level was 162.95 ± 200.58 IU/mL. The values of the serum total eosinophil count and the serum total IgE level were higher in allergic patients than in nonallergic patients ($p < 0.05$, Student *t* test) (Table 2).

Table 1 Clinical characteristics of patients with nasal polyposis

Mean age (y)	43.8
Sex (M/F)	53/30
Polyp stage	
Stage 1 (%)	28 (33.7)
Stage 2 (%)	35 (42.2)
Stage 3 (%)	20 (24.1)
Computed tomographic score	17.51
Prevalence of allergy (%)	55 (66.3)
Asthma (%)	30 (36.1)
Aspirin intolerant	12
Aspirin tolerant	18

Nineteen allergic patients (35.8%) and 11 nonallergic patients (39.3%) had asthma, and there was no statistical difference between the 2 groups ($p = 0.810$, Fisher exact test). The prevalence of allergy in aspirin-intolerant and aspirin-tolerant patients was 58.3% (7 of 12 patients) and 67.6% (48 of 71 patients), respectively. Difference in prevalence of allergy was not statistically significant with regard to presence of aspirin intolerance ($p = 0.528$, Fisher exact test).

Twenty-two (26.5%) of the patients with NP had undergone repeated surgery (range, 1–5) to treat recurrences of that disorder. Patients with recurrent disease had undergone repeated nasal examinations after sinus surgery for a period changing from 6 months to 9 years. Recurrences of NP were noted in 5 (17.8%) of the nonallergic patients and in 17 (30.9%) of the allergic patients, however difference was not significant ($p = 0.294$, Fisher exact test).

Objective Evaluation of NP

There was no association between allergy and larger polyp size or higher Lund-Mackay CT score (Table 2) ($p > 0.05$, Student *t* test). There was a strong correlation between the blood total eosinophil count and the CT score in allergic patients with NP ($p = 0.005$, Pearson correlation analysis), but there was no correlation between the serum total eosinophil count and other parameters of severity (Table 3) ($p > 0.05$, Pearson correlation analysis). Serum total IgE values had no impact on the severity of NP in allergic patients with NP ($p > 0.05$, Pearson correlation analysis). In nonallergic patients, the serum total IgE level and the serum total eosinophil count did not correlate with polyp size or CT score (Table 3) ($p > 0.05$, Pearson correlation analysis). NP was considered extensive in 53 patients (63.8%), of whom 35 were allergic and 18 were nonallergic. There was no correlation between allergy and extensive NP ($p = 1.0$, Fisher exact test).

Subjective Evaluation of NP

The primary complaints of the patients studied were nasal congestion and hyposmia in both allergic and nonallergic subjects (Table 2). Symptom scores were compared between each polyp stage in overall patients with NP. All symptom scores increased in patients with larger polyp size. However, significant differences were found only in nasal congestion and hyposmia ($p < 0.05$, Kruskal-Wallis test). There was no

Table 2 Correlation of allergy with severity of nasal polyposis

	Allergic Patients*	Nonallergic Patients*	P Value
Total IgE (IU/mL)	200.99 ± 231.78	89.58 ± 82.21	0.02 (<i>t</i> = 3168)
Serum total eosinophil count (/μL)	402.87 ± 276.28	293.54 ± 154.28	0.025 (<i>t</i> = 2285)
NP recurrence	1.65 ± 1.05	1.20 ± 0.44	0.187 (<i>t</i> = 1375)
Polyp stage	1.84 ± 0.78	2.04 ± 0.693	0.242 (<i>t</i> = 1182)
Computed tomographic score	17.31 ± 5.02	17.89 ± 5.72	0.649 (<i>t</i> = 458)
Nasal obstruction	2.69 ± 1.2	2.71 ± 1.08	0.929 (<i>t</i> = 90)
Nasal congestion	2.76 ± 1.08	2.96 ± 0.96	0.394 (<i>t</i> = 859)
Facial pain or fullness	1.55 ± 1.23	1.75 ± 1.48	0.533 (<i>t</i> = 629)
Headache	1.38 ± 1.11	1.68 ± 1.41	0.339 (<i>t</i> = 967)
Postnasal drip	2.00 ± 1.23	1.89 ± 1.42	0.736 (<i>t</i> = 339)
Rhinorrhea	2.11 ± 1.41	2.07 ± 1.38	0.908 (<i>t</i> = 116)
Hyposmia	2.80 ± 1.40	2.96 ± 1.29	0.597 (<i>t</i> = 532)
Total symptom score	15.29 ± 6.02	16.04 ± 6.17	0.603 (<i>t</i> = 524)

*Values are given as the mean ± SD. *t* = *t* statistical odds value for the hypothesis

Table 3 Correlation coefficients of total IgE level, serum total eosinophil count, and severity of disease in patients with nasal polyposis

	Allergic Patients		Nonallergic Patients	
	Total IgE	Eosinophilia	Total IgE	Eosinophilia
Polyp stage	0.102	0.242	0.290	0.088
Computed tomographic score	0.178	0.379*	0.005	0.026
Nasal obstruction	0.102	0.123	0.190	0.185
Nasal congestion	0.018	0.099	0.170	0.013
Facial pain or fullness	0.034	0.110	0.030	0.144
Headache	0.078	0.002	0.078	0.049
Postnasal drip	0.130	0.175	0.221	0.145
Rhinorrhea	0.069	0.182	0.132	0.206
Hyposmia	0.045	0.109	0.327	0.429*
Total symptom score	0.009	0.167	0.059	0.089

**p* < 0.05

association of allergy with symptom scores (Table 2) (*p* > 0.05, Student *t* test). There was no significant difference when symptom scores were compared between allergic and nonallergic patients with matched polyp stage (*p* > 0.05, one-way ANOVA test). The serum total IgE level and the serum total eosinophil count also did not correlate with symptom scores (Table 3) (*p* > 0.05, Pearson correlation analysis). However, there was a correlation of the serum total eosinophil count with hyposmia in nonallergic patients with NP (*p* = 0.023, Pearson correlation analysis).

DISCUSSION

The role of allergy in CRS has been a focus of research for some time. Ramadan and colleagues⁷ have suggested that discounting the role of allergy in patients with CRS might result in insufficient treatment and a lack of symptom resolution. According to Newman and colleagues,¹³ allergy is associated with CRS but that association is limited only to

extensive CRS. NP, which is sometimes considered to be a subgroup of CRS, is associated with varying rates of concomitant allergy. However, the pathogenesis of NP is multifactorial, and allergy is only one of the possible causes of that disorder.

In study findings reported in 2003, Krause⁶ stated that 55% of the subjects with polyps had allergies, and that patients with an allergy should receive medical treatment before they undergo extensive surgery. We agree that testing for allergies should be a part of the diagnostic algorithm in patients with NP. The rate of allergy in patients with NP was high (66.3%) in our series. In the present study, skin-prick testing was used to determine the presence of allergic reaction to antigens present in our geographic area. The other skin testing techniques include scratch testing, single intradermal testing, single intradermal testing after skin-prick test, and intradermal dilutional testing. Skin-prick testing is safe and easy, and allows the evaluation of many antigens quickly.¹⁴ However, it

may miss low-level allergies leading to false-negative results. Various rates of allergy in NP reported previously may be due to this weakness of skin-prick testing.

In our study, we found that the serum total IgE level and the serum total eosinophil count were higher in allergic patients than in nonallergic patients. This finding is similar to that of a study by Voegels and colleagues.¹⁵ However, in Voegels' research, the impact of allergy tests on the severity of NP was not evaluated. In our series, there was a high correlation of the serum total eosinophil count with the CT score in allergic patients with NP ($p = 0.005$). This correlation is similar to that in studies showing a correlation of allergy with the CT score in patients with CRS.^{7,13} The total IgE level was not correlated with polyp size or CT score in either allergic or nonallergic patients. Thus, the serum total IgE level can be an indicator of allergy in patients with NP, but it cannot be said that the serum total IgE level has an impact on the severity of NP.

Bernstein and colleagues¹⁶ found that the difference of lymphocyte subpopulations in polyp tissue was not statistically significant in allergic versus nonallergic patients with NP. Those authors also found that the percentage of lymphocytes producing TH1 and TH2 cytokines were higher in nasal polyp tissue than in peripheral blood. In light of those data, they suggested that a local mucosal immune system may be present in polyps. The lack of correlation of systemic allergy with polyp size or CT score could be due to the effect of that local immune system. In a recent study, Wei and Fang¹⁷ concluded that the local tissue-specific IgE profile more specifically reflects the allergic status of patients with NP than does systemic examination, and that specific antiallergic treatment could be given with polyp tissue-specific IgEs.

Radenne and colleagues¹⁸ showed that NP impairs QOL to a greater degree than does perennial allergic rhinitis. However, those authors did not investigate allergy in patients with NP. In fact, studies assessing the impact of allergy on the severity of NP are limited in number. In a recent study, Alobid and colleagues¹⁹ reported that allergy increases the negative impact of NP on QOL but noted no correlation of allergy with polyp size or CT score. In the present study, nasal congestion and hyposmia scores were significantly associated with polyp size in overall study subjects. However, we failed to find a correlation of allergy with symptom scores. Instead, we found a correlation of the serum total eosinophil count with hyposmia in nonallergic patients, although we could not explain the reason for that finding. Symptom scores may be less valuable than validated disease-specific QOL scales to evaluate the impact of co-morbidities on severity of NP, and comparative research is needed.

Duration of follow-up and use of appropriate medical treatment after sinus surgery are important factors to evaluate recurrences in NP. Duration of follow-up after sinus surgery was different for each patient with recurrent disease in this study. Although patients had undergone nasal examinations on a regular basis postoperatively, these data were based on history obtained from the patients. To reduce weakness of the present study, patients who had undergone sinus surgery within the previous 12 months and did not use medical treatment for at least 6 months postoperatively were not included. After all, we could not show the impact of allergy on recurrences. This finding was contrary to previous data^{20,21} indi-

cating poor outcomes of endoscopic sinus surgery in allergic patients with CRS. Further studies need to compare the effect of allergy on recurrences in CRS without polyps and nasal polyposis.

CONCLUSIONS

NP is a multifactorial disease that frequently exhibits concomitant allergy. However, presence of allergy was not associated with objective or subjective severity of NP in the present study. We concluded that, although the prevalence of allergy is high in NP, the presence of allergy is not associated with larger nasal polyp size, recurrences, or symptom scores.

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