

Allergic vs nonallergic rhinitis: which is more predisposing to chronic rhinosinusitis?

Asli Gelincik, MD*; Suna Büyüköztürk, MD*; İsmet Aslan, MD†; Salih Aydın, MD†; Ferhan Özşeker, MD*; Bahattin Çolakoğlu, MD*; and Murat Dal, MD*

Background: The impact of allergy on chronic rhinosinusitis (CRS) is controversial.

Objective: To evaluate whether a history of CRS is more prevalent in patients with allergic rhinitis than in those with nonallergic persistent rhinitis.

Methods: A total of 115 patients (78 females; mean age, 31.9 years; age range, 14–64 years) with persistent rhinitis were included in the study. A 7-point analog scale was used to report the severity of individual and global CRS symptoms and to determine the impact of rhinosinusitis symptoms on quality of life. The allergic status of the patients was evaluated using skin prick tests for common inhalant allergens, and asthma was evaluated by means of history, physical examination, and respiratory function tests. Rhinoscopy and paranasal sinus computed tomography were used to determine CRS.

Results: Asthma and CRS were not significantly different in allergic and nonallergic patients. Nasal polyps were found equally in both groups (8 patients). However, mean Lund-Mackay staging scores, postnasal drainage, dental pain, and global CRS scores were significantly higher in patients with nonallergic rhinitis ($P = .045$, $P = .001$, $P = .02$, and $P = .01$, respectively). No significant correlations, except for dental pain (correlation coefficient, 0.250; $P = .008$), were found between Lund-Mackay scores and CRS symptoms. In rhinoscopy, the only conspicuous difference was nasal purulence in allergic patients ($P = .002$).

Conclusion: Allergic and nonallergic rhinitis may contribute similarly to the development of CRS.

Ann Allergy Asthma Immunol. 2008;101:18–22.

INTRODUCTION

Rhinosinusitis is characterized by inflammation of the nasal mucosa and paranasal sinuses. If symptoms last 12 weeks or longer, the disease is defined as chronic rhinosinusitis (CRS),^{1,2} a prevalent disease that is associated with major physical, emotional, and economic morbidity.³ The disease reflects a spectrum of inflammatory and infectious disturbances of the nose and paranasal sinuses. Consequently, the pathogenesis of CRS is not fully understood.⁴

The contribution of allergy to the pathogenesis and symptom expression of CRS has long been controversial.^{1,3} A variety of studies^{5–7} report that markers of atopy are more prevalent in populations with CRS. In an early study,⁸ it was shown that acute rhinosinusitis is more common in allergic than in nonallergic individuals. Ten years later, Suzuki and colleagues⁹ noted an increased prevalence of allergy (39%) in patients with CRS. These findings were confirmed in several other studies.^{7,10–13} However, the pathogenetic mechanism of the causative role of allergy was not explained in these studies. On the other hand, other studies^{14–16} showed no increase in the incidence of CRS in allergen-sensitized patients. In addition, eosinophilic infiltration into nasal mucosa,

which is the major characteristic of CRS, occurs with or without nasal polyposis and independent of atopy.¹

Because of these controversial data on the relationship between allergy and CRS, we aimed to evaluate whether a history of CRS is more prevalent in patients with allergic rhinitis than in those with nonallergic persistent rhinitis. For this purpose, we compared patients with persistent nonallergic rhinitis and those with allergic rhinitis in terms of CRS existence. The diagnosis of CRS depends on typical nasal symptoms and either endoscopic findings or computed tomographic (CT) changes.¹⁷ Because not all sinus areas can be evaluated properly, endoscopy alone cannot be used as the sole dependable diagnostic tool. Similarly, CT changes determined in CRS can be present without any associated symptoms.¹ To prevent contradiction, both diagnostic tools were used together to determine the presence or absence of current CRS in this detailed prospective study.

METHODS

Patient Recruitment

Consecutive patients initially referred to the Allergy Division, Department of Internal Medicine, Faculty of Medicine, Istanbul University, for persistent rhinitis symptoms between November 1, 2006, and March 31, 2007, were enrolled in the study according to the following inclusion criteria: (1) has not received any medications for the rhinitis symptoms, (2) has not undergone surgery for CRS or any nasal anatomical abnormalities, (3) has not fulfilled the diagnostic criteria for acute rhinosinusitis, and (4) has not had serious underlying medical conditions, such as malignancy and severe renal/

Affiliations: * Allergy Division, Department of Internal Medicine, Faculty of Medicine, Istanbul University, Istanbul, Turkey; † Department of Otolaryngology, Faculty of Medicine, Istanbul University, Istanbul, Turkey.

Disclosures: Authors have nothing to disclose.

Received for publication June 22, 2007; Received in revised form December 28, 2007; Accepted for publication January 10, 2008.

hepatic disorders. This investigation was approved by the ethical committee of Istanbul University. Written informed consent was obtained from the study participants.

Symptoms and Quality-of-Life Assessments

A detailed history concerning CRS, allergic rhinitis, and asthma symptoms was taken from the patients. A 7-point analog scale, which was endorsed by the Joint Task Force on Practice Parameters, was used to report the severity of individual CRS symptoms, including nasal obstruction/blockage/congestion, anterior or posterior nasal mucoid/purulent drainage, facial pain/pressure/fullness, headache, fatigue, decreased sense of smell, ear pain/pressure/fullness, cough, halitosis, dental pain, and fever.¹ On this scale, 1 indicates no symptoms (an occasional limited episode); 3, mild symptoms (steady symptoms but easily tolerable); 5, moderately bothersome symptoms (symptoms hard to tolerate, may interfere with activities of daily living or sleeping); and 7, very severe symptoms (symptoms are so bad that the person cannot function most of the time). A global severity score was also used to obtain additional information on CRS symptoms.¹ The severity of allergic rhinitis symptoms, such as sneezing, nasal itching, nasal drainage, and obstruction, was also evaluated using a 7-point scale. Finally, the same scale was used to determine the impact of rhinosinusitis symptoms on quality of life.¹ This simple visual analog scale was used to evaluate quality of life in terms of sleep disturbance at night, impairment of work or school performance, and impairment of social and recreational activities.

Evaluations

The allergic status of the patients was evaluated using skin prick tests for common grass, tree, weed, cereal pollens, mites, mold, cockroach allergens, and, when necessary, animal dander. Prick test results were regarded as positive when the wheal diameter was at least 3 mm and equal to 60% of that induced by histamine without reaction of the negative control. Patients with compatible positive skin prick test results and clinical symptoms were considered to have allergic rhinitis.¹⁸

The lower airways were examined by means of a thorough physical examination, and respiratory function tests were applied to all patients. Asthma diagnosis was made according to the recent Global Initiative for Asthma reports.¹⁹ Forced expiratory volume in 1 second, forced vital capacity, and the ratio of forced expiratory volume in 1 second to forced vital capacity were measured, and, when necessary, reversibility was evaluated according to the rapid improvements in forced expiratory volume in 1 second measured 15 minutes after inhalation of 200 µg of salbutamol.

All the patients were examined using nasal endoscopy by a single ear, nose, and throat specialist (S.A.) who was unaware of their allergic status. Nasal erythema, edema, polyps or polypoid swelling, crusting, mucopus or pus deep in the nasal cavity (nasal purulence), and all anatomical

variations were evaluated. All the patients also underwent paranasal CT. The CT scans were scored using the Lund-Mackay staging system by a single radiologist who was unaware of their clinical and rhinoscopic findings.¹ The radiologic scoring of the patients ranged from 0 to 24 according to the Lund-Mackay staging system (Table 1).¹ The diagnosis of CRS was based mainly on clinical symptoms, CT changes, and endoscopic findings.

Statistical Analyses

Statistical analysis was performed using a software program (SPSS 11.0; SPSS Inc, Chicago, Illinois). The statistical significance of differences between the types of rhinitis regarding history of CRS prevalence and other categorical outcomes was evaluated using either the Fisher exact test or the χ^2 test. Differences in means for Lund-Mackay staging scores and other continuous outcome variables were evaluated using 2-sample *t* tests.

RESULTS

A total of 120 patients were enrolled during the study period. Data concerning 115 patients (78 females; mean age, 31.9 years; age range, 14–64 years) who fulfilled the inclusion criteria and completed the whole study procedure were evaluated. Seventy-nine patients (68.7%) were diagnosed as having allergic rhinitis, 26 (22.6%) as having asthma, and 52 (45.2%) as having CRS. No patients were diagnosed as having allergic fungal rhinosinusitis. According to the 7-point analog scale, the most severe symptom was nasal congestion (mean [SD] score, 4.34 [1.73]), and the least severe was dental pain (mean [SD] score, 1.38 [1.05]).

Patients with allergic rhinitis were found to be mostly sensitized to mites (*n* = 58), followed by grass (*n* = 31), cereal (*n* = 31), tree (*n* = 27), weed pollens (*n* = 27), mold (*n* = 18), and cockroach allergens (*n* = 8). Among these patients, 13 (11.3%) were sensitized to only pollens, 31 (27.0%) to only perennial allergens, and 35 (30.4%) to both.

Table 1. Lund-Mackay Staging System¹

Lund-Mackay Staging System	Right	Left
Sinus systems (0–2)		
Maxillary		
Anterior ethmoids		
Posterior ethmoids		
Sphenoid		
Frontal		
Ostiomeatal complex		
Total		
Anatomical variations (0–1)		
Absent frontal sinus		
Concha bullosa		
Paradoxical middle turbinate		
Everted uncinate process		
Haller cells		
Agger nasi cells		

There was no correlation between CRS and the type of allergen sensitivity.

Asthma and CRS were not significantly different between allergic and nonallergic patients. However, of the CRS symptoms, postnasal drainage, dental pain, and the global CRS score were significantly higher in patients with nonallergic rhinitis than in allergic patients ($P = .001$, $P = .02$, and $P = .01$, respectively) (Table 2). The other CRS symptoms, and the patients' quality-of-life scores, did not significantly differ between the 2 groups. The mean (SD) duration of rhinitis symptoms reported by the patients was 7.02 (6.07) years (range, 1–30 years). No correlation between symptom duration and CRS and asthma was found.

CT Staging Results

Lund-Mackay staging scores were higher in nonallergic patients than in allergic patients ($P = .045$) (Table 2). No significant correlation, except for dental pain (Spearman correlation coefficient, 0.250; $P = .008$), was found between Lund-Mackay scores and CRS symptoms. Tomographic abnormalities, including absent frontal sinuses, concha bullosa deformity, Agger nasi cells, and Haller cells, were not different in allergic and nonallergic patients. In addition, the allergen sensitivities and IgE levels in patients with allergic rhinitis did not display any correlation with either CRS symptoms or CT findings.

Rhinoscopic Findings

Nasal polyps, hypertrophic concha, mucosal congestion, and anatomical variations, such as septal deviation, paradoxical middle turbinate, and ostiomeatal complex obliteration, were found in similar frequency between the allergic and nonallergic patients and in patients with and without CRS. In rhinoscopy, the only conspicuous difference was nasal purulence in allergic patients ($P = .002$) (Table 2).

DISCUSSION

This study indicates that for the development of CRS, allergic rhinitis does not seem to be a more predisposing type of nasal

inflammation than does nonallergic rhinitis. We believe that the comprehensive diagnostic evaluation of the patients in this study confirms the scientific reliability of the results. These results are also compatible with the clinical observations.

The role of allergy in the pathogenesis and symptom expression of CRS has been discussed for many years.³ Some studies reported higher positive allergy skin test reactions in patients with rhinosinusitis, and others examined the incidence of sinusitis in allergic patients and concluded that chronic sinusitis could represent a complication of perennial allergic rhinitis.⁸ Comparing 40 perennial allergic patients with 30 nonallergic nonrhinitis controls, Berrettini and colleagues¹⁰ demonstrated that allergic rhinitis is often associated with sinusitis. In another study,⁷ a retrospective review was performed on 200 consecutive patients with CRS refractory to medical therapy who subsequently underwent functional endoscopic sinus surgery. The authors concluded that perennial allergy contributes to the development of CRS.⁷ More recently, Gutman et al²⁰ concluded that perennial allergy has a statistically significant association with chronic and acute rhinosinusitis. In this study, perennial and seasonal allergen sensitivities did not differ regarding the existence of CRS. However, the finding that all the patients with nasal purulence in endoscopy were allergic, mostly to mites, was highly conspicuous.

Allergic rhinitis is common, affecting 50% of patients with persistent rhinitis and 10% to 40% of the general population.²¹ This condition is an IgE-mediated inflammatory disease and is diagnosed by the determination of allergic sensitivity to aeroallergens in patients with nasal symptoms. Nonallergic rhinitis or idiopathic rhinitis, another form of persistent rhinitis, is characterized by the absence of specific IgE to aeroallergens. The pathogenesis of this disease has been ascribed as unknown. Histopathologic studies have revealed some dissimilarity between allergic and nonallergic rhinitis. The principal differences involve a greater degree of

Table 2. Comparison of Clinical, Radiologic, and Rhinoscopic Findings in Patients With Allergic and Nonallergic Rhinitis

	Allergic rhinitis patients (n = 79)	Nonallergic rhinitis patients (n = 36)	P value
Clinical diagnosis, No. (%)			
CRS	34 (43)	18 (50)	>.99
Asthma	19 (24)	7 (19)	>.99
Radiologic evaluation			
Lund-Mackay staging score, mean (SD)	2.0 (3.3)	4.5 (6.9)	.045
Obliteration of ostiomeatal complex, No. (%)	11 (14)	5 (14)	.64
Rhinoscopic findings			
Purulence in rhinoscopy, No. (%)	9 (11)	0	.002
Symptom severity scores, mean (SD)			
Postnasal drainage	3.5 (1.9)	4.9 (2.0)	.001
Dental pain	1.1 (0.6)	1.8 (1.5)	.02
Global assessment of rhinosinusitis	4.1 (1.3)	4.8 (1.4)	.01
Quality of life	4.9 (1.3)	5.3 (1.3)	.18

Abbreviation: CRS, chronic rhinosinusitis.

neutrophilic inflammation and a lesser degree of eosinophilic inflammation in nonallergic patients.¹ Similarly, T-cell cytokine profiles also differ in the 2 types of rhinitis: a predominance of T_H2 cytokines is found in allergic individuals and a mixed T_H1/T_H2 profile exists in nonallergic individuals. However, some researchers have shown that a subpopulation with idiopathic rhinitis has a nasal mucosal inflammatory infiltrate similar to that found in allergic rhinitis,²² with a prevalence of IgE-positive cells, mast cells, and eosinophils. They proposed the term *entopy* to define the concept of localized nasal allergy in nonatopic rhinitis. Recently, Rondon et al²¹ presented data supporting the same hypothesis. Meanwhile, no consensus exists for the concept of local IgE-mediated allergic disease present in some individuals with nonatopic rhinitis.²³ In the present study, we were unable to know whether some nonallergic patients have local allergy without systemic atopy. Thus, we can propose that persistent rhinitis is a risk factor for CRS on its own regardless of whether atopy exists. However, the high total CRS symptom and radiologic scores in nonallergic patients suggested that the degree of sinonasal inflammation may be higher in nonallergic rhinitis. This raises the question again of whether a local ongoing nasal allergy plays a role in those patients. However, we could not determine whether nonatopic patients have localized nasal allergy.

In CRS without nasal polyps, a range of mediators and cytokines, including interleukin 1 (IL-1), IL-6, IL-8, tumor necrosis factor α , IL-3, granulocyte-macrophage colony-stimulating factor, intercellular adhesion molecule 1, myeloperoxidase, and eosinophil cationic protein have been shown to be increased in nasal mucosa.¹ These findings have been announced to suggest that the underlying pathologic process might involve unresolved inflammation after infection or a response to chronic infection. The inflammation in nasal polyposis is different, with the presence of abundant eosinophils and local production of IgE. Analysis of specific IgE revealed a multiclonal IgE response in nasal polyp tissue and IgE antibodies to *Staphylococcus aureus* enterotoxins in approximately 60% of the patients and in approximately 80% of those with nasal polyps with asthma. We think that these results cannot reflect the relation of the nasal polyps with CRS because of the low number of patients with nasal polyps.

In the present study, a correlation between chronic sinusitis and asthma diagnosis was not seen. This might be attributed to the low severity of asthma in these patients. Bresciani et al²⁴ demonstrated that sinonasal involvement was significantly greater in patients with serious corticosteroid-dependent asthma than in those with mild-to-moderate asthma. Similarly, Dixon et al²⁵ concluded that allergic rhinitis and sinusitis are associated with more severe asthmatic symptoms and with poorly controlled asthma. The fact that nasal polyposis was very low in the present patients also might play a role in the absence of a correlation between chronic sinusitis and asthma.

In conclusion, the results of this study suggest that allergic and nonallergic rhinitis may not differ significantly in their predisposing effects on the propensity for developing CRS. Therefore, the role of atopy does not seem to predominate in the pathogenesis of CRS, and allergy-specific treatments may not be effective in most patients with CRS.

REFERENCES

1. Meltzer EO, Hamilos DL, Hadley JA, et al. Rhinosinusitis: establishing definitions for clinical research and patient care. *J Allergy Clin Immunol*. 2004;114:S155–S212.
2. Meltzer EO, Hamilos DL, Hadley JA, et al. Rhinosinusitis: developing guidance for clinical trials. *J Allergy Clin Immunol*. 2006;118: S17–S61.
3. Krouse JH. Computed tomography stage, allergy testing, and quality of life in patients with sinusitis. *Otolaryngol Head Neck Surg*. 2000;123: 389–392.
4. Krouse JH. Allergy and chronic rhinosinusitis. *Otolaryngol Clin North Am*. 2005;38:1257–1266.
5. Beninger M. Rhinitis, sinusitis and their relationship to allergies. *Am J Rhinol*. 1992;6:37–43.
6. Grove R, Farrior J. Chronic hyperplastic sinusitis in allergic patients: a bacteriologic study of 200 operative cases. *J Allergy Clin Immunol*. 1990;11:271–276.
7. Emanuel IA, Shah SB. Chronic rhinosinusitis: allergy and sinus computed tomography relationships. *Otolaryngol Head Neck Surg*. 2000; 123:687–691.
8. Savolainen S. Allergy in patients with acute maxillary sinusitis. *Allergy*. 1989;44:116–122.
9. Suzuki M, Watanabe T, Suko T, et al. A clinical and pathologic study of chronic sinusitis: the role of the eosinophil. *Am J Otolaryngol*. 1999;20: 112–115.
10. Berrettini S, Carabelli A, Sellari-Franceschini S, et al. Perennial allergic rhinitis and chronic sinusitis: correlation with rhinologic risk factors. *Allergy*. 1999;54:242–248.
11. Ramadan HH, Fornelli R, Ortiz AO, et al. Correlation of allergy and severity of sinus disease. *Am J Rhinol*. 1999;13:345–347.
12. Lane AP, Pine HS, Pillsbury HC. Allergy testing and immunotherapy in an academic otolaryngology practice. *Otolaryngol Head Neck Surg*. 2001;124:9–15.
13. Zacharek MA, Krouse JH. The role of allergy in chronic rhinosinusitis. *Curr Opin Otolaryngol Head Neck Surg*. 2003;11:196–200.
14. Karlsson G, Holmberg K. Does allergic rhinitis predispose to sinusitis? *Acta Otolaryngol Suppl*. 1994;515:26–28.
15. Hinriksdottir I, Melen I. Allergic rhinitis and upper respiratory tract infections. *Acta Otolaryngol Suppl*. 1994;515:30–32.
16. Robinson S, Douglas R, Wormald P-J. The relationship between atopy and chronic rhinosinusitis. *Am J Rhinol*. 2006;20:625–628.
17. Fokkens W, Lund V, Bachert C, et al. EAACI position paper on rhinosinusitis and nasal polyps executive summary. *Allergy*. 2005;60: 583–601.
18. Pratter MR. Chronic upper airway cough syndrome secondary to rhinosinus diseases (previously referred to as postnasal drip syndrome): ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129: 63S–71S.
19. Global Initiative for Asthma (GINA), National Heart, Lung, and Blood Institute (NHLBI). Diagnosis and classification. In: *Global Strategy for Asthma Management and Prevention*. Bethesda, MD: Global Initiative for Asthma, National Heart, Lung, and Blood Institute; 2006:15–26.
20. Gutman M, Torres A, Keen K, Houser SM. Prevalence of allergy in patients with chronic rhinosinusitis. *Otolaryngol Head Neck Surg*. 2004; 130:542–552.
21. Rondon C, Romero JJ, Lopez S, et al. Local IgE production and positive

-
- nasal provocation test in patients with persistent nonallergic rhinitis. *J Allergy Clin Immunol.* 2007;119:899–905.
22. Powe DG, Jagger C, Kleinjan A, et al. “Entropy”: localized mucosal allergic disease in the absence of systemic responses for atopy. *Clin Exp Allergy.* 2003;33:1374–1379.
23. Powe DG, Jones NS. Local mucosal immunoglobulin E production: does allergy exist in non-allergic rhinitis [review]? *Clin Exp Allergy.* 2006; 36:1367–1372.
24. Bresciani M, Paradis L, Des Roches A, et al. Rhinosinusitis in severe asthma. *J Allergy Clin Immunol.* 2001;107:73–80.
25. Dixon AE, Kaminsky DA, Holbrook JT, Wise RA, Shook DM, Irvin

CG. Allergic rhinitis and sinusitis in asthma: differential effects on symptoms and pulmonary functions. *Chest.* 2006;130:429–435.

Requests for reprints should be addressed to:

Asli Gelincik, MD

Eytam Street

No. 31/5

Macka, Istanbul, Turkey 80200

E-mail: gelincik@istanbul.edu.tr
