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Atopic profile of patients failing medical therapy for chronic rhinosinusitis

Bruce K. Tan, MD^{1,*}, Whitney Zirkle, BS², Rakesh K. Chandra, MD¹, David Lin, BS², David B. Conley, MD¹, Anju T. Peters, MD³, Leslie C. Grammer, MD³, Robert P. Schleimer, PhD³, and Robert C. Kern, MD¹

¹Department of Otolaryngology, Head and Neck Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL

²Northwestern University-Feinberg School of Medicine, Chicago, IL

³Division of Allergy-Immunology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL

Abstract

Background—Chronic rhinosinusitis (CRS) is an inflammatory condition of the nasal airway and paranasal sinuses that can broadly be classified into Chronic rhinosinusitis with Nasal Polyps (CRSwNP) and Chronic rhinosinusitis without Nasal Polyps (CRSsNP). The relationship between CRS and atopy to inhalant allergens remains unclear. We sought to examine the presence of atopy in patients failing medical therapy for both types of CRS.

Objective—To analyze the frequency and distribution of allergen sensitivity in patients failing medical therapy for CRSwNP and CRSsNP in comparison to rhinitis patients without CRS and the general population.

Methods—A prospectively collected database of 334 consecutive CRS patients who had surgery after failing maximal medical therapy was queried to identify those who met inclusion criteria: a Sinus Computed Tomography(CT), an endoscopy consistent with CRS and skin-prick testing with 24 common inhalant allergens in 8 classes at our institution (n=125). Additionally, data from these CRS patients were compared to a group of 50 patients diagnosed with rhinitis who had similar symptoms but radiologically normal CT scans, as well as published normative population skin prick testing data obtained from the National Health and Nutrition Examination Study III (NHANES III). The relationship between atopy, as assessed by the frequency of skin test positivity, and radiological disease severity was assessed for several allergen classes in CRSwNP, CRSsNP and rhinitis patients.

Results—One or more positive skin results were observed in 103/125 (82.4%) CRS patients who underwent surgery- a prevalence significantly higher than that found in the NHANES III study ($p<0.05$) but not different from the rhinitis control group (36/50 -72.0 %). The most prevalent positive skin test results were to dust mites and ragweed in CRSwNP, CRSsNP and rhinitis patients. Comparing these three patient groups, there were no significant differences in the rates of positive skin test results to any single allergen. However, the median number of skin test positive results was higher in CRSwNP patients compared to CRSsNP and rhinitis patients. Consistent

Corresponding author for proofs and reprints: Bruce K. Tan M.D., Instructor, Department of Otolaryngology –Head and Neck Surgery, Northwestern University- Feinberg School of Medicine, 676 N. St. Clair, Suite 1325, Chicago, IL 60611. btan76@gmail.com.

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with other studies, we found that CRSwNP patients were more likely to be male and have concurrent asthma.

Conclusions—In our series of patients failing medical therapy for CRS, we found higher rates of atopy compared with the general population but not compared with rhinitis patients. CRSwNP patients with medically refractory sinusitis were more likely to have multiple positive skin tests and asthma as compared to the general population or patients with either CRSsNP or rhinitis. Host barrier dysfunction may play a role in enabling multisensitization.

Keywords

Endoscopic Sinus Surgery; Atopy; Asthma; Upper Airway; Chronic Rhinosinusitis; Nasal Polypsis

Introduction

Chronic rhinosinusitis (CRS) is a clinical syndrome associated with persistent inflammation of the mucosa of the nose and paranasal sinuses. This definition of CRS encompasses both polypoid (CRSwNP) and non-polypoid (CRSsNP) forms of the disease, which may represent distinct diseases with separate pathophysiological mechanisms. The role of atopy in CRS is controversial, with some studies suggesting that atopic CRS patients have more inflammatory changes on CT, have worse prognosis following surgery and decreased quality of life¹⁻⁸. Other studies however, show that disease severity correlates weakly with CT scan findings, and do not demonstrate increased atopy in CRS patients^{9,10}. Studies into this association are complicated by lack of uniform definitions for both CRS and atopy, variability in allergy testing methodologies and potential referral bias in patients receiving allergy testing.

CRS is a disease that until recently was defined primarily by symptoms lasting >12 weeks, but this definition was recently revised to require inflammatory changes of the paranasal sinuses on computed tomography (CT) and/or endoscopy, since up to 50% of patients with symptoms compatible with CRS do not have discoverable sinus inflammation¹¹⁻¹⁴.

Although a concise definition of atopy is not uniformly accepted- for this study we adopted the definition that atopy is the genetically mediated predisposition to produce specific IgE that is clinically defined as having evidence of allergic sensitization to at least one allergen. While atopy is fundamental to the pathogenesis of allergic disorders, clinical presentations of allergies can occur its absence¹⁵. Regardless of its definition, the prevalence of atopy is rising in the US population- the most recent National Health and Nutrition Examination Study III (NHANES III), demonstrated that 54.3% of 10,508 test subjects undergoing skin-prick allergy testing were sensitive to one or more allergens compared with 20.2% of patients in the NHANES II study performed a decade earlier¹⁶.

Unlike CRS, atopy is clearly implicated in the pathophysiology of other inflammatory diseases of the upper airway diseases such as allergic rhinitis and asthma¹⁷⁻¹⁹. Interestingly, patients who have CRS have a 20% prevalence of concurrent asthma- a rate approximately three to four times greater than the general population. Conversely, up to 90% of asthmatics have abnormal findings on CT scans of the sinuses²⁰. Our group is interested in the complex interplay between CRS and atopy and has previously published studies comparing atopy patterns in allergic rhinitis with those of patients with CRSwNP; as well as on the influence of atopy on the radiologic severity of CRS^{21,22}. In this study, we sought to query an expanded database of 334 well-characterized patients (about three times the size of our previously published study) and included a control group of rhinitis patients without radiographic or endoscopic evidence of CRS to account for the inherent referral patterns

intrinsic to our previous study. Additionally, we compared our data to the NHANES III dataset, the latest iteration of a large population-based study of the US population, for perspective on our findings¹⁶.

Methods

All protocols and studies discussed in this paper were reviewed and approved by the Northwestern University IRB. Patients included in this database gave informed consent for enrollment at the time of inclusion.

CRS Patients

A retrospective review was performed on 334 consecutive patients enrolled prospectively into a tertiary allergy and sinus center database at the time of nasal surgery. The CRS patients enrolled in this database received endoscopic sinus surgery for idiopathic CRS that was not attributable to a discrete cause, e.g.: antrochoanal polyps, complications of a dental procedure, cystic fibrosis, or sinonasal neoplasm. All patients failed maximal medical therapy that in general, consisted of a three week-course of antibiotics and oral corticosteroids followed by nasal corticosteroids. Some patients with CRSwNP without signs of infection had been treated primarily with oral corticosteroids. The enrollment period for this study was between January 2007 and August 2009.

The patients in the database were then screened for those carrying a diagnosis of CRS with or without nasal polyps and possessed a complete sinus and allergic workup at our institution consisting of nasal endoscopy to classify patient's polyp status, a CT-scan to evaluate the full extent of sinus inflammation and a documented allergy test to determine atopy.

Rhinitis control group

To provide a non-CRS control group that adequately reflected the patients in our practice who were getting comprehensive evaluation of their sino-nasal complaints and allergy, we reviewed the medical records of 227 consecutive patients who were referred to our joint Otolaryngology and Allergy clinic for sino-nasal complaints between January 2009 and March of 2010. Fifty consecutive patients with a final diagnosis of rhinitis (allergic and non-allergic) were identified who met symptomatic criteria for evaluation with both allergy testing and a CT-scan to evaluate the presence of sinus disease. All patients in this rhinitis control group had CT scans that *did not* show any evidence of CRS.

Evaluation of patients

All patients included in this study had a history suggestive of allergic rhinitis and were evaluated at our institution using a standard skin prick panel of 24 commonly inhaled aeroallergens in 8 major classes (dog, cat, dust mite, grass, tree, ragweed, mold and cockroach), a positive histamine and a negative saline control. A positive test was considered to be a wheal diameter of 5 mm with flare at 20 minutes. If skin prick testing was negative and the history implicated the presence of atopy to a specific allergen, further evaluation was carried out using intradermal testing using 0.02 mL of extract. The same criteria outlined previously were used to define a positive intradermal skin reaction. Demographic data, CRS subtype, skin test results, asthma status and CT radiologic disease score using the scoring criteria proposed by Lund and Mackay were recorded and tabulated²³.

NHANES III

NHANES III is the latest iteration of a population-based survey conducted by the National Center for Health Statistics for which normative skin testing data from a sample of the US population has been published. This survey used a complex design to sample the civilian, non-institutionalized population. In NHANES III, a total of 31,311 individuals aged 2 months to 90 years were interviewed and examined; prick-puncture allergy skin tests for 10 allergens and 2 controls (positive and negative) were administered to all subjects aged 6 to 19 years and a random half-sample of subjects aged 20 to 59 years for a total of 10,508 valid skin test panels¹⁶.

Statistical analysis

In the present analysis, patients were separated into three groups based on the presence of nasal polyposis- CRS with nasal polyposis (CRSwNP) and CRS without nasal polyposis (CRSsNP), and on the presence of rhinitis. Within each group, demographic data, and the Lund-Mackay scores (excluding the rhinitis patients) were compared between skin test positive patients and skin test negative patients using the student's t-test. The frequencies of asthma, atopy and skin test reactivity to each allergen were compared using multiple contingency tables using the Fisher's exact test in binary comparisons or the Chi-squared test for non-binary comparisons. Additional analysis was then performed to evaluate the distribution of multi-allergen sensitivity using a Kruskal-Wallis test, and a post-hoc Mann-Whitney U test was then performed to determine the binary comparisons driving the positive Kruskal-Wallis test. All analysis was performed using software provided by GraphPad Prism (La Jolla, CA) and publically available online statistical tools (StatTools <http://obg.cuhk.edu.hk>). A p-value of less than 0.05 was considered statistically significant. P-values were 2-tailed and corrected, where appropriate, for multiple comparisons.

Results

Patient characteristics

A total of 125 CRS patients who failed medical therapy were identified as having completed a sinus and allergic workup at Northwestern. Of these, 62 patients had CRSwNP and 63 had CRSsNP based on endoscopic and CT findings. Compared with the rhinitis control group (n=50), CRSwNP patients were more likely to be male (Odds Ratio of 3.074; 95% CI 1.413-6.685). Comparisons of patients with CRSsNP with the rhinitis control group showed no statistically significant differences in gender distribution. CRSwNP patients in this study were slightly older than the CRSsNP patients (44.1 years vs 38.2 years, p<0.001). As expected, patients with CRSwNP had a higher presenting Lund-Mackay score than patients with CRSsNP (14.9 and 9.2 respectively p<0.001). Table 1 summarizes these findings.

Prevalence of atopy and individual allergen sensitivity across subgroups of patients

The relationship of sensitivity to each aeroallergen class on Lund-Mackay score within CRSwNP, CRSsNP was analyzed. There were no differences in Lund-Mackay scores among patients who tested positive for any of the allergen classes examined when compared to those who tested negative for the allergen. Chi-squared analysis of the rate of reactivity to each specific allergen was analyzed across CRS subtypes using 3×2 contingency tables showing no association between CRS subtype and skin test positivity. Post-hoc testing comparing patients with CRSwNP to rhinitis subjects did reveal higher rates of tree, grass, ragweed, mold and dog sensitization but after correcting for multiple testing, these relationships were not statistically significant. The distribution of skin test results is summarized in figure 1.

Prevalence of allergen class sensitivity

The overall rate of skin test reactivity to one or more allergens was 82.4% among all CRS patients (85.5% in CRSwNP, 79.4% in CRSsNP) and 72.0% in rhinitis patients ($p=0.21$). Reactivity to one or more perennial allergens was seen in 80.6%, 68.3% and 68.0% of CRSwNP, CRSsNP and rhinitis patients respectively ($p=0.21$). Reactivity to perennial allergens only was seen in 14.5%, 15.9% and 24.0% of these patients respectively ($p=0.38$). Reactivity to one or more seasonal allergens was seen in 71.0%, 63.5% and 48.0% of CRSwNP, CRSsNP and rhinitis patients respectively ($p<0.05$). However, when examined for the prevalence of sensitivity to seasonal allergens only, there was no statistically significant difference seen between the three groups ($p=0.44$). We defined atopy to perennial allergens as those patients who exhibited positive skin test reactions to dust mites, cockroach, dog and cat allergens. Atopy to seasonal allergens were defined as reactivity to trees, grass, ragweed and mold since most mold in Chicago is seasonal in nature. These results are summarized in Table 1 and represented in figure 2.

Number of positive skin test results across patient groups

Across all disease groups, the most common positive skin test results were to dust mites and ragweed, demonstrating that the overall allergic profile of our rhinitis control population was similar to that of our CRS patients. The median number of positive skin test results was 3, 2 and 2 (mean: 3.7, 2.9 and 2.4) for CRSwNP patients, CRSsNP patients and rhinitis patients respectively ($H=6.50$, $p=0.038$). Post-hoc testing revealed that this difference was driven by the binary comparisons of CRSwNP and CRSsNP ($U=1.84$, $p=0.033$) and of CRSwNP and rhinitis ($U=2.81$, $p<0.01$). In figure 3, a graphical representation of these results is provided.

Influence of asthma

Asthma was seen in 62.9%, 30.2% and 14% of CRSwNP, CRSsNP and rhinitis patients respectively ($p<0.001$). The overall rate of asthma was significantly higher in patients with CRSwNP compared with rhinitis and CRSsNP patients (Odds Ratio 10.42; 95% CI 4.025-26.96, and 3.927; 95% CI 1.864–8.273 respectively) even though only 5 of the 62 CRSwNP patients were known to have Samter's triad. Compared with rhinitis patients, CRSsNP patients did have a slightly higher overall incidence of asthma (Odds Ratio 2.653; 95% CI 1.012-6.951).

Comparison with NHANES III dataset

The NHANES III dataset utilized a skin prick panel of 9 aeroallergens that corresponded to 7 of the 8 major allergen categories we utilized in this study. Although the exact skin prick mixtures used in our study and those used for the NHANES III dataset are nonidentical, comparisons of our dataset with the NHANES III dataset enables us to understand our dataset in the context of normative population data. Comparing skin prick testing data from our patients with the NHANES III dataset revealed higher rates of sensitivity to all aeroallergens tested (Relative Risk between 2.0 and 4.3) with the exception of cockroach for which patients in our dataset had a lower rate of sensitization (Relative Risk = 0.6; 95% CI 0.44-0.87). The prevalence of sensitivity to perennial or seasonal allergens only was similar between the NHANES III study population and our study populations. The prevalence of skin test positive reactions to both seasonal and perennial allergens was elevated in CRSwNP and CRSsNP relative to the findings of the NHANES III dataset ($p<0.001$). Additionally, the median number of skin test positive results was higher in all three patient groups compared to the NHANES data ($p<0.001$)-there was a trend toward increased rates of multi-sensitization progressing from rhinitis, to CRSsNP to CRSwNP.

Discussion

Historically, CRSsNP was considered to result from an incompletely treated case of acute infectious rhinosinusitis resulting in chronic infection while CRSwNP was considered a non-infectious disorder of unclear etiology, perhaps related to atopy. In a minority of CRS cases, distinct host genetic or systemic disorders are identified as the cause of sinonasal inflammation but the overwhelming majority of CRS cases are idiopathic. Specific proposed mechanisms for persistent inflammation include obstruction of the osteomeatal complex, impaired mucociliary clearance, microbial resistance, biofilm formation, *Staphylococcus aureus* superantigens, fungal hypersensitivity and epithelial barrier dysfunction²⁴.

This study sought to further investigate the association between CRS and atopy using the updated Rhinosinusitis Task Force criteria for the diagnosis and classification of CRS and a standard skin test panel for the diagnosis of atopy in all of our patients. In light of growing evidence for patho-physiologically distinct mechanisms underlying CRSsNP and CRSwNP, we analyzed the skin-test sensitivity profiles of these subgroups separately. Additionally, we also compared our findings to both a rhinitis control group that controls for the inherent referral bias in patients receiving skin testing in our practice, as well as normative population data obtained from the NHANES III study. Analysis of the demographics of our patients continues to suggest that CRSwNP is more common in men and presents in older individuals than CRSsNP— an observation that is consistent with the findings of several other studies^{25,26}. We want to stress that our population of patients with CRS does not represent the typical CRS population as they had disease of sufficient severity *after* medical therapy to justify surgical intervention.

The relationship between CRS and atopy is controversial but previously published retrospective studies consider atopy a potential risk factor or negative prognostic factor in patients with CRS. No prospectively enrolled study has been performed to date examining atopy and CRS. Kennedy reported that inhalant allergy testing was positive in 57% of 120 patients undergoing functional endoscopic sinus surgery (FESS) for CRS without differentiating between subtypes⁶. Berrettini *et al.* compared CT sinus scans from 40 adult patients with perennial allergic rhinitis with scans from 30 controls and found evidence of CRS in 67.5% of the allergic patients versus 33.4% of the control group ($p = 0.017$)²⁷. Gutman *et al.* found that on review of 48 voluntary study participants with chronic or recurrent acute rhinosinusitis, 57.4% of participants had positive allergy testing either by RAST or intradermal endpoint titration⁵. An additional uncontrolled case series by Emmanuel and Shah, reported on a series of 200 CRS patients requiring FESS for CRS refractory to medical therapy who were evaluated by CT and allergy testing³. They found that 84% of patients undergoing FESS had positive allergy tests using a combination of skin testing and RAST testing with 58% of patients having multiple allergen sensitivities.

Our study demonstrated an overall skin-prick positivity rate of 82% among our CRS patients, which was significantly higher compared to the NHANES III population (54.3 %) but comparable to other studies of similar design¹⁶. However, when compared to our rhinitis control group, the CRS patients had similar overall rates of atopy, suggesting that referral patterns may account for the higher rates of atopy observed in our study and the other published studies of similar design. While there was a trend toward increasing atopy rates going from rhinitis to CRSsNP to CRSwNP, the overall atopy rates were similar across groups suggesting that higher atopic rates are not confined to CRSwNP. Furthermore, the skin test positivity rate to each allergen was similar across the three diagnostic groups studied. This finding supports some of our earlier studies and does not suggest that atopy, or sensitivity to any specific allergen, predisposes patients toward CRS or a specific subtype of CRS²¹.

Upon classifying allergens into perennial and seasonal allergens, we did find differences in the prevalence of seasonal allergen sensitivity driven by a higher incidence of seasonal allergen sensitivity in the CRSwNP group relative to rhinitis patients. However, when the prevalence of isolated sensitivity to seasonal allergens was examined, we found that most patients with seasonal allergen sensitivity had concurrent perennial allergen sensitivity and that seasonal allergen sensitivity in isolation was relatively uncommon. Given these findings, we conclude that the development of multiple allergen sensitivity was more relevant to the disease process than the seasonal nature of the allergen.

Several studies support a positive correlation between atopy and disease severity. One such study by Ramadan *et al.* revealed that of 25 atopic and 17 non-atopic rhinosinusitis patients analyzed by CT scanning and modified RAST, the atopic patients were found to have a higher mean Lund-Mackay score than non-atopic patients ($p = 0.03$)⁷. A study by Krouse *et al.* involving 48 CRS patients who underwent SET and CT scanning also showed a significant correlation between CT score and SET mean end point ($r = 0.42, p < 0.01$)²⁸. There was also a positive association between SET mean end point and the Rhinosinusitis Disability Index physical scale score ($r = 0.32, p < 0.05$), a measure of sinus-related disability. This suggests that atopic patients not only exhibit more severe disease on CT scanning but have a greater extent of symptoms as well. Contrary to these findings, Robinson *et al.* showed a very modest difference in CT score and no difference in quality of life between atopic and non-atopic rhinosinusitis patients¹⁰. Our study also fails to demonstrate a relationship between atopy or sensitivity to any specific positive allergen and Lund-Mackay score severity within each CRS subtype. Interestingly, some studies suggest that more extensive sinus disease is found (including nasal polyps) in nonallergic CRS patients and asthmatics as opposed to allergic CRS patients^{4,29}. In the Emanuel and Shah study there was a trend toward a relatively lower rate of positive allergy testing among patients with the most severe sinus disease (based on the Glicklich CT grading system) in comparison to less severe disease. Our study does show a similar trend with our non-atopic patients having slightly higher Lund-Mackay scores than their atopic counterparts, although these observations did not reach statistical significance³.

While some studies suggest a greater role for certain allergens, specifically perennial allergens and mold, in the pathogenesis of CRS, the data reported here showed no significant differences in the frequency of skin test positivity to any individual allergen between the CRSsNP, CRSwNP and rhinitis groups. Our data also suggest that the rates of perennial allergen sensitivity was grossly similar across groups and contrary to these studies the rate of seasonal allergens sensitivity was actually higher in the CRS populations although most of these patients had concurrent perennial allergen sensitivities. Compared to the NHANES normal controls, the frequency of skin test positivity was higher in all aeroallergen classes except cockroach. In all three groups, the most common reactivity among our patients was to dust mites and ragweed and overall profiles suggest that perennial allergen sensitivity is slightly higher than seasonal allergen sensitivity. In the NHANES III dataset, the most common positive skin tests were to dust mites (27.5%) followed by perennial rye (26.2%) and ragweed (26.1%). In Gutman *et al.*'s study, 92% of the study participants with CRS and positive allergy testing were sensitized to one or more perennial aeroallergens, particularly molds and dust mites⁵. Several studies support higher rates of sensitization to dust mites among patients with CRS compared to asymptomatic normal individuals, but as demonstrated in our study, a referral bias cannot be completely excluded^{1,3,30}. Asero and Bottazzi showed a higher prevalence of perennial aeroallergen sensitivity among 43 patients with nasal polyps in comparison to 1128 controls (70% versus 19%, respectively; $p < 0.001$), while seasonal allergen sensitivity was higher in the control group (84% versus 60%, $p < 0.005$)². While our study does recapitulate similar findings of elevated rates of sensitivity to dust mite and other allergens when compared to normal

controls, the significance of these findings is less striking when compared to our rhinitis patients who are clinically more similar to our CRS patients being tested for atopy. Similarly, in one of our previous studies, while seasonal allergen reactivity was similar between participants with nasal polyps versus allergic rhinitis (AR), perennial allergen reactivity was actually more prevalent in the AR group²².

Munoz del Castillo *et al.* studied the characteristics of a group of patients with nasal polyposis and found a higher incidence of asthma in comparison to the healthy control group (48.9% versus 2.3%, $p < 0.001$) along with a higher prevalence of males than females among their nasal polyp patients (63.7% versus 36.3%)²⁶. We have recapitulated these findings but also demonstrate that the rate of asthma is significantly higher in CRSwNP even when compared to patients with CRSsNP and rhinitis patients. There is a well-known correlation between asthma and both rhinitis and rhinosinusitis^{18,20,31-37}. There are also several studies supporting an association between asthma and atopy^{17,18,35}. These observed relationships have led to the development of the concept of the “unified airway,” in which inflammatory processes of the upper airway such as allergic rhinitis and rhinosinusitis are found to commonly co-exist with inflammatory processes of the lower airway such as asthma and COPD.³⁸ This relationship encourages physicians to seek out the presence of lower respiratory processes in patients presenting with upper respiratory symptoms and vice versa in order to provide comprehensive treatment to improve quality of life.

Most strikingly, our data demonstrate an increased median number of skin test positive results among CRSwNP patients compared to CRSsNP and the rhinitis control group. Evidence for the multi-sensitization of the CRS population is further reflected in the elevated rates of concurrent seasonal and perennial allergen sensitivity relative to the rhinitis group. For example, 38.7% of CRSwNP patients demonstrated skin test positive reactions to more than half the panel tested compared with 16% in the rhinitis group and 18% in the NHANES III study. Similarly, while the rates of sensitization to seasonal or perennial allergens only were similar across our patient populations and the NHANES III data, our data demonstrate that 62.9% of CRSwNP patients demonstrated concurrent seasonal and perennial allergen sensitivity compared with 30.1% in the NHANES III study of the normal population. One possible explanation for these findings is the growing body of evidence for the role of mucosal epithelial barrier dysfunction in the pathogenesis of CRS, particularly in the CRSwNP subtype^{24,39,40}. A dysfunctional epithelial barrier may be more permissive to environmental allergens allowing sensitization of the host immune system to multiple allergens. Whether the environmental allergens are responsible for the breakdown of the host epithelial barrier through intrinsic proteases or whether intrinsic host deficits in protease inhibitors, such as SPINK5/LEKT1, are responsible for enabling allergen penetration in CRS is still unclear; both effects may occur to differing degrees in different patients. Furthermore, the temporal relationship between multi-sensitization and the onset of CRS is unclear – one possibility is that the inflammatory response secondary to multi-sensitization leads to CRS but it is also plausible that epithelial barrier dysfunction secondary to CRS allows multi-sensitization to aeroallergens. Since CRSwNP occurs frequently in the absence of atopy (14.5% in our series), the latter scenario appears to be more likely.

Conclusion

These data highlight the higher prevalence of atopy among our CRS patients failing maximal medical therapy when compared to the general population. However, unique to this study, we used a control population that accounts for potential referral bias and found no significant differences in atopic rates or rates of sensitization to individual classes of allergens. We also found no significant correlation between atopy and Lund-MacKay scores or the influence of sensitivity to any single allergen on CRS disease severity. In this study,

higher rates multiple allergen sensitivity are seen in CRSwNP patients and suggests that the previously reported mucosal barrier dysfunction may play a role in allowing multiple allergens to sensitize the host immune system. While this study delves further into the complex interactions between CRS and atopy, additional research must still be done to elicit an understanding of the causal relationship between the two.

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Figure 1.
Rates of skin test positivity by stratified by allergen and disease group

Figure 2. Comparison of the frequency distribution of perennial and seasonal allergen sensitivity by disease group. The NHANES III data is provided for comparison with normative population data.

Figure 3.

Comparison of the frequency distribution of multiallergen sensitivity by disease group. For clarity, the patient populations were divided into three groups: the non-atopic group, the oligo-sensitive group who were sensitized to between one and four aero-allergen classes, and the multi-sensitive group who were sensitized to five or more (more than half our tested panel) aeroallergens. The NHANES III data is provided for comparison with normative population data.

Table 1

Patient demographics and clinical information

Patient Characteristics	CRSwNP	CRSsNP	Rhinitis
n	62	63	50
Average age	44.1	38.2 *	42.9
Gender			
Male	38 (61.3%)	29 (48.0%)	17 (34.0%)
Female	24 (38.7%)	34 (54.0%)	33 (68.0%)
Average Lund-MacKay Score	14.9	9.2 *	N/A
Asthma	39 (62.9%)	19 * (30.2%)	7 * (14.0%)
Samter's Triad	5 (8.1%)	0	0
Skin testing results			
Skin test positivity	53 (85.5%)	50 (79.4%)	36 (72.0%)
Perennial allergen positivity	48 (77.4%)	42 (66.7%)	33 (66.0%)
Seasonal allergen positivity	44 (71.0%)	40 (63.5%)	24 (48%) *
Both Seasonal and Perennial	39 (62.9%)	32 (50.8%)	21 (42.0%)
Perennial allergens only	9 (14.5)	10 (15.9%)	12 (24.0%)
Seasonal allergens only	5 (9.1%)	8 (12.7%)	3 (6.0%)

*
p<0.05 in binary comparison with CRSwNP