

# Chronic rhinosinusitis with nasal polyps: elevated serum immunoglobulin E is associated with *Staphylococcus aureus* on culture

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**Background:** Recent data has implicated *Staphylococcus aureus* (SA) superantigen as a potential disease modifier in patients with chronic rhinosinusitis (CRS) with nasal polyps (CRSwNP). The objective of this work was to compare total serum immunoglobulin E (IgE) and serum eosinophils in patients with CRSwNP and CRS without nasal polyps (CRSsNP) based on culture results of the 3 most commonly isolated bacteria.

**Methods:** Retrospective review at a tertiary rhinology referral center of patients with CRS over a 4-year period.

**Results:** Bacterial cultures and immunologic data were obtained from 62 patients with CRSwNP and 34 patients with CRSsNP. SA was the most prevalent bacteria in the CRSwNP group, isolated in 19 patients (31%). Patients with elevated total serum IgE ( $>114$  IU/mL) were more likely to have SA on culture ( $p = 0.04$ ) in this population. The percent serum eosinophil levels in the SA + group compared with the SA – group was not significant (6.0 vs 5.1,  $p = 0.17$ ). Lund-Mackay computed tomography (CT) scores, but not Sino-Nasal Outcome Test 20 (SNOT-20) scores were sig-

nificantly higher in the SA + vs SA – group ( $p = 0.03$ ) in patients with CRSwNP. The CRSsNP group demonstrated no difference in IgE or serum eosinophils between different bacterial groups.

**Conclusion:** Our findings suggest that there is an association between SA sinonasal presence and elevated total serum IgE in patients with CRSwNP. In addition, SA + patients had higher Lund-Mackay CT scores, indicating a higher objective burden of disease in this group of patients.

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## Key Words:

superantigen; staphylococcus aureus; chronic rhinosinusitis; nasal polyps; immunoglobulin E; eosinophil; T-helper-2; sinus bacteria

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Chronic rhinosinusitis (CRS) contains numerous subsets and overlapping etiologies that remain poorly understood. CRS with nasal polyposis (CRSwNP) represents one of these subsets.<sup>1</sup> The common denominator in most patients with CRSwNP is the presence of eosinophilic inflammation associated with a predominant T-helper-2 (Th2)

inflammatory response.<sup>2</sup> *Staphylococcus aureus* (SA) is one of the most common organisms recovered from sinus cultures of patients with CRS.<sup>1,3</sup> In one study, the rate of SA colonization was shown to be over 60% in patients with CRSwNP, although it was unclear in that report whether the middle meatal swabs were obtained with endoscopic guidance using strict aseptic methodology.<sup>4</sup> The role of SA in sinonasal inflammation, as well as bronchial asthma and atopic dermatitis has been shown to go beyond the traditional model of pathogenic induction of infectious neutrophilic inflammation.<sup>5–7</sup> There is increasing evidence that SA enterotoxins, known as superantigens (SAG) amplify eosinophilic inflammation in patients with CRSwNP.<sup>8,9</sup> The identification of SA enterotoxin-specific immunoglobulin E (IgE) within the sinonasal mucosa supported the presence of the enterotoxins, with known SAG activity, within the local tissue.<sup>8</sup> Also, SA enterotoxins were shown to induce local polyclonal IgE production and further shift the local cytokine profile in nasal polyps toward a Th2 milieu.<sup>10</sup> Interestingly, when combined with deficient innate immune

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barriers, presence of a Th2 adaptive response correlated with SA colonization in atopic dermatitis (AD).<sup>11,12</sup> This relationship, however, has never been studied in inflammatory chronic rhinosinusitis although recent data implicate defects in innate immune barriers in the pathogenesis of CRS.<sup>13,14</sup>

This study investigates potential association between positive SA sinonasal cultures and peripheral markers of Th2 polarity (namely total serum IgE and peripheral eosinophilia) in patients with CRSwNP as compared to patients with chronic rhinosinusitis without nasal polyps (CRSsNP). In addition, this study assesses the relationship between disease severity and the presence of SA on sinonasal cultures in patients with CRSwNP.

## Patients and methods

A 4-year retrospective review of patients diagnosed with CRSwNP in whom bacterial cultures were obtained was performed at a tertiary rhinology referral center. Patients were included in the review if they met the diagnostic criteria of CRSwNP according to established guidelines.<sup>1</sup> Bacterial isolates from middle meatal cultures were then used to divide the study population into 3 groups: (1) cultures yielding SA; (2) cultures yielding *Pseudomonas aeruginosa* (PA); and (3) cultures yielding coagulase-negative *Staphylococcus* (CNS). Each of these bacteria represents 1 of the 3 most commonly obtained isolates. Similar culture data was obtained from a sample of patients with CRSsNP for comparative purposes. The following Th2 polarity data parameters were compared between the groups: (1) total serum IgE and (2) percent serum eosinophils. The following were considered to be threshold levels indicative of significant Th2 polarity: total serum IgE >114 IU/mL and percent serum eosinophils >4. These threshold numbers are above the normal range for the laboratory that performed the test. One laboratory was used for all the immunologic testing of our patients.

Additional data parameters analyzed and compared in the CRSwNP group included: (1) demographic data including age, sex, and ethnicity; (2) medical history including asthma, aspirin sensitivity, as well as previous treatment (surgical as well as medical); (3) symptom scores and computed tomography (CT) findings evaluated via Sino-Nasal Outcome Test 20 (SNOT-20) and Lund-Mackay scores,<sup>15</sup> respectively.

Subjective data was obtained from patient charts via a standardized institutional sinonasal questionnaire, which collects demographic and medical information as part of a routine clinic intake protocol. This instrument also includes a validated assessment of symptom and disease impact via the validated SNOT-20.<sup>16</sup>

All patients underwent rigid nasal endoscopy with a 3-mm or 4-mm 30-degree rigid telescope, after topical application of 0.05% oxymetazoline and 4% lidocaine solution using an atomizer. Cultures were obtained aseptically

using either a Tami Sinus Secretion Collector (Medtronic ENT, Jacksonville, FL) or a standard 40-cc Kendall-Argyle suction trap (Tyco Healthcare Group LP, Mansfield, MA). In our clinical practice, cultures are obtained routinely on patients with CRSwNP as these patients often have mucus, mucin, and/or purulence associated with nasal polyps. In patients with CRSsNP, cultures are obtained if there is evidence of infection on nasal endoscopy, specifically purulent drainage visualized within the middle meatus or open sinus cavities. Secretions were collected from any of the following areas: middle meatus, sphenoethmoidal recess, ethmoid, frontal, maxillary, or sphenoid sinuses. Laboratory analysis of specimens included: Gram stain, fungal cultures, as well as bacterial culture and sensitivity. The first recorded culture prior to antibiotic therapy, including intraoperative cultures, was used for data analysis. The use of systemic steroids was not considered grounds for exclusion. Serum IgE and eosinophil levels were obtained prior to systemic steroid initiation. All patients underwent preoperative prednisone dosing the week prior to surgery.

Exclusion parameters included patients with reported history of immunodeficiency, cystic fibrosis, ciliary dysmotility syndromes, or autoimmune inflammatory disease, such as Wegener's granulomatosis, sarcoidosis, or systemic lupus erythematosus. Finally, patients who received antibiotics in the 2 weeks prior to the date of culture were excluded to limit the possible alteration of intranasal flora, as well as the possible selection of resistant bacteria.

Statistical analysis was performed using SPSS software (Version 13, SPSS, Inc., Chicago, IL). Correlations were assessed utilizing the Spearman's rank correlation coefficient to measure the correlation between serum IgE and percent serum eosinophils. The resulting correlation coefficient is 0.17 ( $p = 0.19$ ), indicating these 2 variables are independent. The Shapiro-Wilk normality test and Bartlett's test for equal variance were used to verify continuous variables. Age was the only variable with normal distribution. A 1-way analysis of variance was performed for patient demographic variables to compare SA+ patients vs SA- patients in the CRSwNP group. The SA- group included patients whose cultures grew: PA, CNS, "other" bacteria, and "no growth." For other comparisons in the manuscript, Wilcoxon rank-sum test was used to compare means between groups with continuous variables. The Fisher's exact test was employed for the categorical variables. Odds ratios were performed, analyzing association between presence of SA and Th2 biomarkers (IgE and eosinophilia) in the entire study population as well as in the CRSwNP and CRSsNP groups. Similar analysis was performed in each of the groups to evaluate the association between asthma and Th2 biomarkers. This study was conducted with Institutional Review Board (IRB) approval from the Committee for the Protection of Human Subjects Office of Research Support Committees at the University of Texas Health Science Center at Houston.

TABLE 1. Characteristics of Patient Population of CRSwNP

|                            |      |        | SA—       |         |      |         |      |         |       |         |                   |
|----------------------------|------|--------|-----------|---------|------|---------|------|---------|-------|---------|-------------------|
| Variable                   | SA + |        | No Growth |         | PA   |         | CNS  |         | Other |         |                   |
| N                          | 19   |        | 11        |         | 11   |         | 8    |         | 13    |         | p-value           |
| Age                        |      |        |           |         |      |         |      |         |       |         |                   |
| Mean (SD)                  | 45.9 | (16.4) | 49.2      | (17.7)  | 52.6 | (13.1)  | 35.5 | (13.4)  | 47.8  | (11.6)  | 0.17 <sup>a</sup> |
| Sex                        |      |        |           |         |      |         |      |         |       |         |                   |
| Male (%)                   | 10   | (52.6) | 5         | (45.5)  | 7    | (63.6)  | 4    | (50.0)  | 6     | (46.2)  | 0.93 <sup>b</sup> |
| Female (%)                 | 9    | (47.4) | 6         | (54.5)  | 4    | (36.4)  | 4    | (50.0)  | 7     | (53.8)  |                   |
| Race                       |      |        |           |         |      |         |      |         |       |         |                   |
| African American (%)       | 7    | (41.2) | 0         | (0.0)   | 4    | (40.0)  | 2    | (28.6)  | 3     | (23.1)  | 0.11 <sup>b</sup> |
| Caucasian (%)              | 10   | (58.8) | 10        | (100.0) | 5    | (100.0) | 4    | (57.1)  | 8     | (61.5)  |                   |
| Other (%)                  | 0    | (0.0)  | 0         | (0.0)   | 1    | (10.0)  | 1    | (14.3)  | 2     | (15.4)  |                   |
| Asthma                     |      |        |           |         |      |         |      |         |       |         |                   |
| No (%)                     | 9    | (47.4) | 7         | (63.6)  | 5    | (45.5)  | 4    | (57.1)  | 9     | (75.0)  | 0.56 <sup>b</sup> |
| Yes (%)                    | 10   | (52.6) | 4         | (36.4)  | 6    | (54.5)  | 3    | (42.9)  | 3     | (25.0)  |                   |
| Aspirin sensitivity        |      |        |           |         |      |         |      |         |       |         |                   |
| No (%)                     | 17   | (89.5) | 9         | (81.8)  | 8    | (72.7)  | 8    | (100.0) | 13    | (100.0) | 0.21 <sup>b</sup> |
| Yes (%)                    | 2    | (10.5) | 2         | (18.2)  | 3    | (27.3)  | 0    | (0.0)   | 0     | (0.0)   |                   |
| Previous Surgery           |      |        |           |         |      |         |      |         |       |         |                   |
| No (%)                     | 4    | (22.2) | 2         | (18.2)  | 2    | (18.2)  | 3    | (37.5)  | 3     | (23.1)  | 0.89 <sup>b</sup> |
| Yes (%)                    | 14   | (77.8) | 9         | (81.8)  | 9    | (81.8)  | 5    | (62.5)  | 10    | (76.9)  |                   |
| Previous Medical Therapy** |      |        |           |         |      |         |      |         |       |         |                   |
| No (%)                     | 1    | (5.3)  | 0         | (0.0)   | 0    | (0.0)   | 0    | (0.0)   | 1     | (7.7)   | 0.99 <sup>b</sup> |
| Yes (%)                    | 18   | (94.7) | 11        | (100.0) | 11   | (100.0) | 8    | (100.0) | 12    | (92.3)  |                   |

\*Designation of Other included Asian, Indian and Middle Eastern descents.

\*\*Previous Medical therapy includes antibiotics or oral steroids within one year of presentation.

<sup>a</sup>One-way ANOVA.

<sup>b</sup>Fisher's exact test.

SA + = Growth of *Staphylococcus aureus* on culture; SA– = No growth of *Staphylococcus aureus* on culture; PA = *Pseudomonas aeruginosa*; CNS = coagulase-negative *Staphylococcus*.

## Results

### CRSwNP patient population

#### Demographics

During the study time period, 79 patients met the inclusion criteria for the CRSwNP group, having documented evidence of endoscopic culture sampling. Of these, 17 we excluded based on absence of immunologic data in the chart; therefore, 62 patients were analyzed for the study. There was no statistical difference in the prevalence of asthma and aspirin sensitivity between the SA + and SA– group (asthma,  $p = 0.56$ ; aspirin sensitivity,  $p = 0.21$ ). There was no statistical difference between the SA + and SA– groups in any of the demographic parameters, including age, sex, race, or prior medical or surgical therapy (Table 1). Similarly, there was no statistical difference in the rate of prior surgery between PA + and PA– patients, nor between CNS + and CNS– patients.

### Microbiology

Of the 62 intranasal cultures obtained, 11 had no growth on final report. The total number of individual bacterial species obtained from the 51 samples yielding growth resulted in 67 distinct isolates. *Staphylococcus aureus* grew on 19 (31%) out of the 62 total cultures and was found to be the most commonly obtained bacterial isolate. *Pseudomonas aeruginosa* was the second most recovered bacteria growing in 11 (18%) cultures, followed by coagulase-negative *Staphylococcus* species, accounting for 8 (13%) of 62 samples. Table 2 summarizes the bacterial data.

#### Th2 biomarkers: serum IgE and percent serum eosinophils

Total serum IgE level was available on 62 patients, 19 from the SA + and 43 from the SA– group. Of the 19

**TABLE 2.** Comparison of prevalence of SA, PA, and CNS in patients with CRSwNP vs CRSsNP

|                        | CRSwNP(%) | CRSsNP(%) | <i>p</i> <sup>a</sup> |
|------------------------|-----------|-----------|-----------------------|
| SA                     |           |           |                       |
| Present on culture     | 19 (31)   | 8 (24)    | 0.49                  |
| Not present on culture | 43 (69)   | 26 (76)   |                       |
| PA                     |           |           |                       |
| Present on culture     | 11 (18)   | 5 (15)    | 0.78                  |
| Not present on culture | 51 (82)   | 29 (85)   |                       |
| CNS                    |           |           |                       |
| Present on culture     | 8 (13)    | 11 (32)   | 0.03                  |
| Not present on culture | 54 (87)   | 23 (68)   |                       |

<sup>a</sup>Fisher's exact test.CNS = coagulase-negative *Staphylococcus*; CRSsNP = chronic rhinosinusitis without nasal polyps; CRSwNP = chronic rhinosinusitis with nasal polyps; PA = *Pseudomonas aeruginosa*; SA = *Staphylococcus aureus*.

patients in the SA + group, 17 (89.5%) were noted to have elevated total serum IgE (>114 IU/mL) compared to 27 of the 43 patients (62.8%) from the SA− group (*p* = 0.04). The mean total serum IgE was higher in the SA + (1048 IU/mL) compared to the SA− group (574 IU/mL), but the difference did not reach statistical significance (*p* = 0.054). The percent serum eosinophil levels in the SA + and SA− groups were not statistically different (Table 3). In addition, there was no difference in total serum IgE, elevated serum IgE, or percent serum eosinophils when

the following groups were compared: PA + vs PA− patients; CNS + vs CNS− patients; and PA vs CNS patients. Finally, allergy status based on ImmunoCap-specific IgE blood testing did not show a difference between any of the following groups: SA + vs SA−, PA + vs PA−, or CNS + vs CNS−.

### Disease severity

Lund-Mackay CT scores were statistically higher in the SA + group, in comparison to SA− group, (12.3 vs 9.7, *p* = 0.03). There was no difference in Lund-Mackay scores between PA + and PA− patients, CNS + and CNS− patients, or CNS and PA patients (*p* = 0.84 and *p* = 0.49, respectively). SNOT-20 scores were statistically higher in the PA + group, in comparison to PA− (2.8 vs 1.8, *p* = 0.01). There was no statistical difference between the SA + and SA− groups or CNS + and CNS− groups in the respective SNOT-20 scores (2.1 vs 2.0, *p* = 0.45; 1.4 vs 2.1, *p* = 0.12).

### CRSsNP patient population

#### Microbiology

Chart analysis identified 34 patients meeting the criteria for inclusion into the CRSsNP group. Cultures yielded 8(24%) patients with SA, 5(15%) with PA, and 11(32%) with CNS. The remaining 10 patients grew other species of bacteria (*n* = 9, 26%) or had no growth (*n* = 1, 3%). The prevalence of SA, PA, and CNS in this group was then compared to the prevalence of SA, PA, and CNS in the CRSwNP group.

**TABLE 3.** Immunology results for CRSwNP and CRSsNP patients

|                           | CRSwNP    |           |                                |                       | CRSsNP    |          |                                |                       |
|---------------------------|-----------|-----------|--------------------------------|-----------------------|-----------|----------|--------------------------------|-----------------------|
|                           | Total     | SA        | No growth, PA, CNS, and others | <i>p</i> <sup>a</sup> | Total     | SA       | No growth, PA, CNS, and others | <i>p</i> <sup>a</sup> |
| Total serum IgE (IU/mL)   |           |           |                                |                       |           |          |                                |                       |
| n                         | 62        | 19        | 43                             | 0.054                 | 34        | 8        | 26                             | 0.78                  |
| Mean                      | 719.3     | 1048.2    | 574.0                          |                       | 262.2     | 188.9    | 284.8                          |                       |
| Percent serum eosinophils |           |           |                                |                       |           |          |                                |                       |
| n                         | 62        | 19        | 43                             | 0.17                  | 28        | 8        | 20                             | 0.26                  |
| Mean                      | 5.3       | 6.0       | 5.1                            |                       | 4.2       | 4.2      | 4.2                            |                       |
|                           | n (%)     | n (%)     | n (%)                          | <i>p</i> <sup>b</sup> | n (%)     | n (%)    | n (%)                          | <i>p</i> <sup>b</sup> |
| Serum IgE                 |           |           |                                |                       |           |          |                                |                       |
| Not elevated (≤114)       | 18 (29.0) | 2 (10.5)  | 16 (37.2)                      | 0.04                  | 20 (58.8) | 4 (50.0) | 16 (61.5)                      | 0.69                  |
| Elevated (>114)           | 44 (71.0) | 17 (89.5) | 27 (62.8)                      |                       | 14 (41.2) | 4 (50.0) | 10 (38.5)                      |                       |
| Serum eosinophils         |           |           |                                |                       |           |          |                                |                       |
| Not elevated (≤4%)        | 24 (38.7) | 6 (31.6)  | 18 (41.9)                      | 0.57                  | 20 (71.4) | 6 (75.0) | 14 (70.0)                      | 0.99                  |
| Elevated (>4%)            | 38 (61.3) | 13 (68.4) | 25 (58.1)                      |                       | 8 (28.6)  | 2 (25.0) | 6 (30.0)                       |                       |

<sup>a</sup>One-way ANOVA.<sup>b</sup>Fisher's exact test.ANOVA = analysis of variance; CNS = coagulase-negative *Staphylococcus*; CRSsNP = chronic rhinosinusitis without nasal polyps; CRSwNP = chronic rhinosinusitis with nasal polyps; IgE = immunoglobulin E; PA = *Pseudomonas aeruginosa*; SA = *Staphylococcus aureus*.

Though the prevalence of SA was higher in CRSwNP vs CRSsNP (31% vs 24%), this was not statistically significant ( $p = 0.49$ ). However, there was a statistically higher number of CNS in the CRSsNP group (32% vs 13%,  $p = 0.03$ ). The prevalence of PA was not significantly different between the groups ( $p = 0.78$ ). This data is presented in Table 2.

### *Th2 biomarkers: serum IgE and percent serum eosinophils*

There was no difference in total serum IgE, elevated serum IgE, or percent serum eosinophils when the following groups were compared: SA + vs SA–, PA + vs PA–, and CNS + vs CNS–. Additionally, asthma was evaluated in this population as a possible Th2 inflammatory driver. Thirteen patients out of 34 patients (38%) with CRSsNP also had asthma, of these 4 were SA positive. Of these 4 patients, 3 had total IgE greater than the laboratory limit for normal ( $>114$  IU/mL), and of the remaining 9 SA negative patients, 4 had elevated IgE. However given the limited number of cases, stratified analysis could not be performed. The SA + vs SA– immunologic data for CRSsNP are presented in Table 3.

### *Correlation of elevated IgE and/or eosinophilia with SA vs asthma*

Odds ratio were calculated for the presence of SA and elevated IgE or eosinophilia in the entire study population, the CRSwNP group and the CRSsNP group. Similar calculation was performed for the presence of asthma and elevated IgE or eosinophilia across the same patient groups. Odds ratio (with confidence interval) for presence of SA and elevated IgE or eosinophilia were as follows: total study population 1.55 (0.5–6.0), CRSwNP 4.1 (0.5–192.5), and CRSsNP 0.6 (0.9–4.2). For asthma, the odds ratios were: total study population 1.45 (0.5–4.5), CRSwNP 0.6 (0.1–3.0), and CRSsNP 3.67 (0.7–25.8). To summarize these results, there was no statistical association with SA or asthma with Th2 markers of inflammation.

## **Discussion**

This retrospective study lends support to several important observations. The findings suggest that there is an association between SA sinonasal presence and elevated serum IgE ( $>114$  IU/mL) in patients with CRSwNP. The relationship between SA superantigens and both the local nasal polyp Th2 tissue milieu and the serum SA enterotoxin-specific IgE is well-documented in the literature.<sup>8–10,17,18</sup> The correlation, however, between SA colonization and nonspecific systemic Th2 biomarkers has never been reported in the upper airway. Interestingly, one study recently confirmed a similar relationship between SA colonization and systemic Th2 biomarkers in atopic dermatitis (AD).<sup>11</sup> Numerous published reports confirm the role of SA enterotox-

ins in modulating the Th2 immune responses in CRSwNP, bronchial asthma, and AD.<sup>5–9</sup> The exact mechanisms, however, remain to be elucidated. It has been suggested that the Th-2 inflammatory profile in CRSwNP contributes to the likelihood of SA colonizing the sinonasal mucosa.<sup>2</sup> In fact, there is evidence that Th2 cytokines suppress innate immune and host barriers, therefore increasing the risk of colonization with SA and other microbes.<sup>19–21</sup> Our results may be interpreted in this context, whereby a Th2 systemic profile facilitated SA colonization. It is also feasible that the relationship between SA and a Th2 phenotype is bidirectional and the presence of SA, through superantigenic mechanisms, accentuates the local and systemic Th2 polarity, further suppressing innate immune mechanisms. In this context, it is interesting to consider the capacity of SA to reside intraepithelially and potentially evade immune surveillance.<sup>18</sup> As such, SA can be a possible source of sustained immune response to superantigens in the tissue leading to persistent eosinophilic inflammation.<sup>22,23</sup> It is interesting that our data did not show an association between PA or CNS colonization and Th2 immunologic markers in patients with CRSwNP. Also, such an association was not found for any of the bacterial isolates (including SA) in the CRSsNP group. It is intriguing to note that the prevalence of SA was similar in the CRSwNP and CRSsNP groups despite their presumably different phenotypic profiles. It is possible that SA superantigenic effect leading to amplification of the Th2 response is selective to patients with Th2 skewing, such as CRSwNP, asthma, and allergic rhinitis. We may also speculate that SA may be inducing infectious neutrophilic inflammation in patients with CRSsNP who are experiencing an acute clinical exacerbation. However, the role of SA in eliciting differing immunogenic responses is beyond the scope of this retrospective review. It should also be cautioned that the apparent association of SA colonization within the sinuses of CRSwNP patients and elevated total serum IgE described in this review does not warrant any firm conclusions about the role of SA in CRSwNP.

The recognized association between asthma and elevated IgE as well as allergic rhinitis and IgE deserve consideration as potential confounding variables in this study. However, odds ratio analysis did not show that the presence of asthma had a higher correlation with serum IgE or eosinophils than the presence of SA in any of the patient groups. A separate analysis looking at the association between elevated IgE in CRSsNP patients with asthma that were SA positive vs those without SA could not be performed due to a limited number of patients meeting this criteria, but could have been helpful in further delineating the association of IgE and SA. For this analysis, as well as the odds ratio, it is possible that a larger patient population may have achieved statistical significance.

Allergic rhinitis, though not specifically evaluated, could have contributed to the Th2 inflammatory response seen in this study. However, aside from physical findings of nasal polyps, it is difficult to weigh the differential contribution of

allergic rhinitis and CRSwNP to the resultant Th2 inflammation considering the highly similar molecular substrate of these 2 conditions.<sup>1</sup>

Our results also indicate that the presence of SA on sinonasal cultures of CRSwNP patients were associated with higher Lund-Mackay scores suggesting a higher objective disease burden in this group of patients. Subjective assessment of disease burden through SNOT-20 was similar in the SA+ and SA− groups but statistically higher in PA+ compared to PA− patients. There is paucity of data in the literature about the specific relationship between CRS severity and presence of SA on sinonasal cultures. Recent data has found a higher prevalence of SA in nasal tissue of CRSwNP patients with aspirin sensitivity, a condition known to carry a higher burden of eosinophilic inflammation and a poorer prognosis.<sup>18</sup> This was not observed in our CRSwNP population, as there was no difference in prevalence of aspirin sensitivity or asthma in the SA+ compared to the SA− group. This study suffers from all the limitations inherent to a retrospective review. Also, in light of recent reports demonstrating local inflammatory responses in nasal polyps to SA superantigen in tissue, it is possible that sys-

temic markers of Th2 polarity may not correlate with local markers. In addition our results reveal lack of association between SA and elevated serum eosinophil levels, an important marker of Th2 inflammation. Unfortunately, tissue eosinophil counts were not systemically obtained and as such were not available for inclusion in this study. Finally, this study focuses on the presence of SA, but superantigens have been described for other bacteria including common isolates obtained from nasal culture such as *Streptococcus pyogenes* (Group A strep).<sup>24</sup> It is conceivable that other bacteria may have contributed to the results described in this review.

## Conclusion

Many factors including SA superantigen likely play a role in the development of inflammatory chronic rhinosinusitis. The reported findings suggest that there is an association between SA sinonasal presence and elevated total serum IgE in patients with CRSwNP. In addition, presence of SA correlates with higher burden of objective disease based on Lund-Mackay CT scores. ③

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