

Radiographic Nuances in Allergic Fungal Rhinosinusitis

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Abstract

Background: Allergic fungal rhinosinusitis (AFRS) is characterized by higher revision endoscopic sinus surgery (ESS) rates and unique radiographic features when compared to chronic rhinosinusitis with nasal polypsis (CRSwNP) or chronic rhinosinusitis without nasal polypsis (CRSsNP).

Objective: We hypothesized that an increased frequency of concha bullosa in AFRS or other radiographic nuances might allow for accumulation of allergic mucin and contribute to increased ESS revision rates.

Methods: A retrospective cohort study was performed. Patient diagnosis (AFRS, CRSwNP, and CRSsNP), basic demographics, and prior ESS rates were collected.

Results: A total of 210 consecutive patients were included (AFRS = 70, CRSwNP = 70, and CRSsNP = 70). Pediatric AFRS patients had more unilateral disease (38.1% vs 4.4%; $P = .007$) and anterior ethmoid skull base erosion (23.8% vs 6.7%; $P = .047$) than adult AFRS patients. AFRS patients were more likely to be younger (24.9 ± 10.1 years vs 45.6 ± 14.4 years vs 48.7 ± 18.2 years; $P < .001$), African American (70% vs 14.3% vs 11.4%; $P < .001$), and have undergone prior ESS (54.3% vs 45.7% vs 31.4%; $P = .02$) than CRSwNP or CRSsNP patients. Concha bullosa were more prevalent in AFRS patients than CRSwNP or CRSsNP patients across the population (42.9%, 18.6%, and 14.3%; $P < .001$) and in the setting of no previous surgery (53.1%, 31.6%, and 16.7%; $P < .001$).

Conclusion: In this cohort, pediatric AFRS patients had more unilateral disease and anterior ethmoid skull base erosion. Concha bullosa prevalence was significantly higher in AFRS as compared to those with CRSwNP or CRSsNP, despite prior ESS. Surgeons should consider concha bullosa as a potential anatomical subsite to harbor recurrent or residual disease.

Keywords

allergic fungal rhinosinusitis, allergic fungal sinusitis, chronic rhinosinusitis, chronic sinusitis, nasal polypsis, nasal polyps, endoscopic sinus surgery, concha bullosa

Introduction

Allergic fungal rhinosinusitis (AFRS) is a distinct clinical entity with a unique presentation and management strategy that distinguishes it from other forms of chronic rhinosinusitis (CRS).¹ Patients with AFRS are typically immunocompetent, younger adults who present with nasal polypsis and thick, eosinophilic mucin in the setting of environmental allergies. Patients may also present with disfiguring facial features such as orbital proptosis or telecanthus secondary to extreme polyp burden in severe cases.²

The radiographic features of AFRS have been well studied. Computed tomography (CT) images of the sinuses demonstrate dense heterogeneous opacifications

with areas of hyperattenuation as well as characteristic metallic-type densities on soft tissue windowing. Not uncommonly, patients present with dramatic local

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bony erosion and expansion into critical nearby structures such as the orbit and skull base. These characteristics served as the basis for a dedicated AFRS radiographic staging system.³

Beyond clinical presentation, AFRS is further distinguished from other forms of CRS by increased surgical revision rates.⁴ With revision rates cited as high 100% in older studies,⁵ more contemporary studies suggest that current revision rates range from 20% to 50%.^{4,6} The etiology of these high recurrence rates has yet to be fully elucidated; however, we hypothesize that advanced disease at the time of presentation and anatomic variability may play a contributory role. In our practice, we began to notice that many patients undergoing revision surgery for AFRS had a concha bullosa filled with allergic mucin, contributing to middle meatal inflammation. These concha bullosa were present despite extensive prior procedures. This led to speculation that patients with AFRS may have concha bullosa at greater rates than other CRS patients, which could fill with allergic mucin and contribute to ongoing disease at various points in time. We further speculated that these concha bullosa may be overlooked surgically given the burden of disease typical on CT scan which can often obscure subtle nasal anatomy.

In this study, we sought to identify radiographic nuances and anatomical correlates unique to the AFRS population. Our objectives were to compare (1) the prevalence of both concha bullosa and radiographic features of disease between AFRS and other forms of CRS and (2) patient clinical presentation, demographics, and diagnosis with rates of previous sinus surgery.

Methods

Study Design

This retrospective case-control study was performed at the Medical University of South Carolina (MUSC). Adult and pediatric patients with CRS were included in this study and designated as CRS with nasal polypsis (CRSwNP), CRS without nasal polypsis (CRSsNP), or AFRS. All patients with CRS met diagnostic criteria for CRS according to the Clinical Practice Guideline of the American Academy of Otolaryngology – Head and Neck Surgery.⁷ Meanwhile, patients with AFRS met diagnostic criteria as defined by the International Consensus Statement on Allergy and Rhinology: Rhinosinusitis, with type I hypersensitivity determined by formal testing or a reported history of environmental allergies.⁸ All patients had been treated at MUSC between January 1, 2009, and May 1, 2018, and were identified prior to undergoing endoscopic sinus surgery (ESS). The most recent 70 patients undergoing ESS for

each diagnosis, with complete records, were included in this study. All patients had preoperative fine cut CT images available. In general, these images were acquired as 0.625 to 1.25 mm slice thickness. Patients without complete records or radiographic images for review were excluded.

Outcome Measures

The primary outcome measure was the presence of a concha bullosa. Patient demographics including age, sex, race, and insurance status were extracted from the medical record. Disease characteristics including the need for revision surgery, radiographic laterality of disease, and the extent of skull base erosion in AFRS patients were documented.

Radiographic images were evaluated and viewed in axial, coronal, and sagittal planes by a single reviewer and confirmed by a second, blinded, otolaryngologist to establish interobserver reliability. Mucosal disease and laterality were determined as present or absent. The presence of a concha bullosa was characterized as present, absent, or cannot be determined (representative images, Figure 1(a) to (d)). A concha bullosa was considered present if greater than 50% of the height of the middle turbinate, measured in a coronal plane, was pneumatized (Figure 1(b) and (c)). A distinction of cannot be determined was recorded when definitive boundaries of the middle turbinate could not be determined by both reviewers (Figure 1(d)). Skull base erosion was identified similar to prior study and characterized as either present or absent.³ Skull base erosion was defined as present when there was clear loss of bony integrity with obvious replacement with radiographic soft tissue density in the expected location of bone, when CT images were viewed in bone window algorithm.

Statistical Analysis

All data analyses were performed with SPSS 24.0 (IBM Corporation, Armonk, NY). The age at diagnosis variable was tested for normal distribution as determined by the Kolmogorov–Smirnov test. Descriptive statistics of patient demographics were performed, and χ^2 test was used to compare categorical variables. An analysis of variance test was used to compare the age at diagnosis variable between cohorts in this study. Multivariate regression was used to determine the relationship between concha bullosa and disease type while adjusting for relevant covariates. A *P* value of <.05 was considered to indicate a statistically significant difference for all statistical tests.

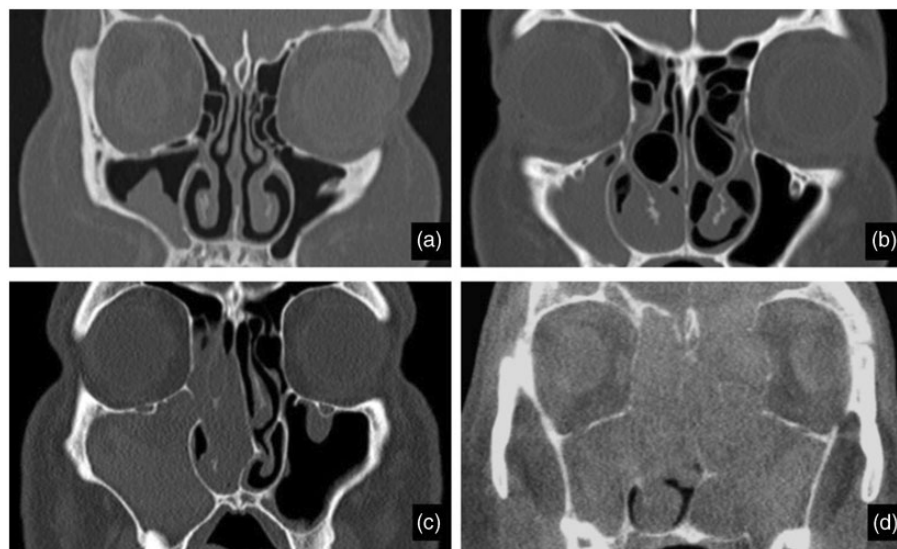


Figure 1. Pneumatization patterns of middle turbinate. (a) Normal middle turbinate. (b) Bilateral concha bullosa. (c) Right opacified concha bullosa. (d) Cannot determine pneumatization pattern secondary to the extent of disease.

Table 1. Patient Demographics Stratified by Disease Type.

	Total	CRSwNP	CRSSNP	AFRS	P
Cases, n	210	70	70	70	
Mean age (SD)	39.7 (18.0)	45.6 (14.4)	48.7 (18.2)	24.9 (10.1)	<.001 ^a
Sex, n (%)					.17
Female	95 (45.2)	26 (37.1)	37 (52.9)	32 (45.7)	
Race, n (%)					<.001 ^a
White	139 (66.2)	59 (84.3)	61 (87.1)	19 (27.1)	
Black	67 (31.9)	10 (14.3)	8 (11.4)	49 (70.0)	
Other	3 (1.4)	1 (1.4)	0 (0.0)	2 (2.9)	
Unknown	1 (0.5)	0 (0.0)	1 (1.4)	0 (0.0)	
Insurance, n (%)					<.001 ^a
Private	150 (71.4)	61 (87.1)	48 (68.6)	41 (58.6)	
Medicare	26 (12.4)	7 (10.0)	17 (24.3)	2 (2.9)	
Medicaid	25 (11.9)	1 (1.4)	4 (5.7)	20 (28.6)	
Uninsured	6 (2.9)	0 (0.0)	0 (0.0)	6 (8.9)	
Other	3 (1.4)	1 (1.4)	1 (1.4)	1 (1.4)	
Prior surgery, n (%)					.02 ^a
Yes	92 (43.8)	32 (45.7)	22 (31.4)	38 (54.3)	

Abbreviations: AFRS: allergic fungal rhinosinusitis; CRSsNP: chronic rhinosinusitis without nasal polyposis; CRSwNP: chronic rhinosinusitis with nasal polyposis; SD: standard deviation.

^aStatistical significance.

Results

Patient Demographics

In total, 210 patients were included, with 70 patients in each diagnosis category: CRSwNP, CRSsNP, and AFRS. The mean age of the total cohort was 39.7 years (standard deviation: 18.0, range: 5.8–75.1; Table 1). There were no differences in distribution of sex with 26 (37.1%) females in the CRSwNP cohort, 37 (52.9%) in

the CRSsNP cohort, and 32 (45.7%) in the AFRS cohort ($P = .17$). As compared to CRSwNP and CRSsNP, AFRS patients were more likely to be younger (45.6 ± 14.4 years vs 48.7 ± 18.2 years vs 24.9 ± 10.1 years; $P < .001$), African American (14.3% vs 11.4% vs 70%; $P < .001$), and have Medicaid or be uninsured (1.4% vs 5.7% vs 37.5%; $P < .001$). The prevalence of previous sinus surgery was highest in the AFRS cohort (54.3%) when compared to the CRSwNP cohort (45.7%) and CRSsNP cohort (31.4%) ($P = .02$; Table 1).

Prevalence of Concha Bullosa

Concha bullosa were detected in all subgroups of CRS. The complete description of concha bullosa presence, absence, or inability to determine stratified by disease type is listed in Table 2. Concha bullosa were more prevalent in patients with AFRS as compared to patients with CRSwNP or CRSsNP across the study population (42.9%, 18.6%, and 14.3%; $P < .001$). Meanwhile, the inability to determine the presence of concha bullosa was also the most common in patients with AFRS (45.6%).

When stratifying the study population by both disease type and on the basis of prior sinus surgery, patients with AFRS and no previous sinus surgery were more likely to have the presence of a concha bullosa (53.1%) as compared to patients with CRSwNP (31.6%) or CRSsNP (16.7%; $P < .0001$). Similarly, when examining patients who had previously undergone sinus surgery, concha bullosa were more prevalent in AFRS patients (42.9%) as compared to patients with CRSwNP (18.6%) or CRSsNP (14.3%; $P < .0001$; Table 3). After controlling for relevant covariates and assessing the importance of disease type, the odds of the presence of at least one concha increased by 35.1 times in the setting of a diagnosis of AFRS (odds ratio [OR] = 35.1; 95% confidence interval [CI]: 6.48–190.58). Meanwhile, patients with prior surgery had 5 times lower odds of having the presence of a concha bullosa (OR = 0.2; 95% CI: 0.07–0.57; Table 4).

Radiographic Characteristics of AFRS

In the total study population, bilateral disease was more common than unilateral disease and found in 89% of the population. When comparing laterality across the

3 disease types, bilateral disease was the most common in the CRSwNP cohort (95.7%) compared to the CRSsNP (87.1%) and AFRS (84.3%) cohorts ($P = .01$; Table 2). When examining AFRS patient cohort alone, pediatric patients were more likely to have unilateral disease (38.1% vs 4.4%; $P = .01$) and anterior ethmoid skull base erosion (23.8%) as compared to adult patients with a diagnosis of AFRS (6.7%; $P = .047$). A complete comparison of the presence of concha bullosa, skull base, and anatomical subsite involvement is listed in Table 5 and without other statistically significant differences between pediatric and adult patients with AFRS.

Discussion

AFRS is a distinct clinical entity with unique patient demographics and radiographic nuances that distinguish it from other forms of CRS. This study further

Table 3. Prevalence of Concha Bullosa Stratified by Disease and Previous Surgery.

	CRSwNP	CRSsNP	AFRS	P
Previous surgery				
No (n)	38	48	32	<.0001 ^a
No concha	22 (57.9)	39 (81.3)	2 (6.3)	
Concha present	12 (31.6)	8 (16.7)	17 (53.1)	
Cannot determine	4 (10.5)	1 (2.1)	13 (40.6)	
Yes (n)	32	22	38	<.0001 ^a
No concha	49 (70.0)	58 (82.9)	8 (11.4)	
Concha present	13 (18.6)	10 (14.3)	30 (42.9)	
Cannot determine	8 (11.4)	2 (2.9)	32 (45.7)	

Abbreviations: AFRS: allergic fungal rhinosinusitis; CRSsNP: chronic rhinosinusitis without nasal polyps; CRSwNP: chronic rhinosinusitis with nasal polyps.

^aStatistical significance.

Table 2. Radiographic Characteristics Stratified by Disease Type.

	Total	CRSwNP	CRSsNP	AFRS	P
Cases, n	210	70	70	70	
Disease laterality, n (%)					.01 ^a
Unilateral right	8 (3.8)	1 (1.4)	6 (8.6)	1 (1.4)	
Unilateral left	15 (7.1)	2 (2.9)	3 (4.3)	10 (14.3)	
Bilateral	187 (89.0)	67 (95.7)	61 (87.1)	59 (84.3)	
Presence of any concha bullosa, n (%)					<.001 ^a
None	115 (54.8)	49 (70.0)	58 (82.9)	8 (11.4)	
Concha present	53 (25.2)	13 (18.6)	10 (14.3)	30 (42.9)	
Cannot determine	42 (20)	8 (11.5)	2 (2.8)	32 (45.7)	
Concha bullosa description, n (%)					<.001 ^a
None	115 (54.8)	49 (70.0)	58 (82.9)	8 (11.4)	
Right concha bullosa	11 (5.2)	6 (8.6)	1 (1.4)	4 (5.7)	
Left concha bullosa	26 (12.4)	5 (7.1)	5 (7.1)	16 (22.9)	
Bilateral concha bullosa	16 (7.6)	2 (2.9)	4 (5.7)	10 (14.3)	
Cannot determine	42 (20)	8 (11.5)	2 (2.8)	32 (45.6)	

Abbreviations: AFRS: allergic fungal rhinosinusitis; CRSwNP: chronic rhinosinusitis with nasal polyps; CRSsNP: chronic rhinosinusitis without nasal polyps.

^aStatistical significance.

characterizes the demographic subtleties of the AFRS patient population as well as differences in disease presentation between adult and pediatric AFRS patients. The most notable finding of this study, however, is the increased prevalence of a pneumatized middle turbinate, or concha bullosa, in patients with AFRS. This latter finding may provide some insight into the characteristically high revision surgery rates in AFRS and increase

surgeon awareness of potential anatomical subsites that may harbor residual disease.

Concha bullosa is a well-recognized anatomical variant with reported rates of prevalence ranging from roughly 20% to 50%.^{9–12} Despite its commonality, the clinical significance of this structure is unknown. Traditionally, it was suggested that given the relatively larger size of a concha bullosa, as compared to a non-aerated middle turbinate, this may lead to ostiomeatal complex narrowing and subsequently CRS of the obstructed sinus.^{9,13–15} Although there is evidence of a correlation between a deviated nasal septum and concha bullosa,^{12,16} there are a relatively large number of studies which demonstrate a lack of correlation between the presence of concha bullosa and CRS.^{12,14,16–20} Other authors have attempted to demonstrate an adaptive and protective effect of a concha bullosa to environmental allergies; however, these studies have also failed to demonstrate a correlation.^{19,21}

Although existing evidence suggests lack of correlation between CRS and concha bullosa in general, the data presented here are compelling with regard to AFRS specifically. This study demonstrates an association between concha bullosa and patients with AFRS as compared to other forms of CRS, even in the presence of prior surgery. The latter is especially surprising, as it might be assumed that the prevalence of concha bullosa

Table 4. Odds Ratio Estimates for Clinical Characteristics Associations With Concha Bullosa.

	Odds Ratio	95% CI	P
Type of disease			
CRS _{swNP}	1.65	0.62–4.36	.32
AFRS	35.14	6.48–190.58	<.001 ^a
Age at presentation	0.97	0.95–1.002	.07
Sex, n (%)			.19
Female	0.55	0.23–1.35	
Race, n (%)			.37
Black	0.52	0.13–2.13	
Other	0.88	0.05–14.8	.93
Previous sinus surgery			.003 ^a
Yes	0.20	0.07–0.57	

Abbreviations: AFRS: allergic fungal rhinosinusitis; CI: confidence interval; CRS_{swNP}: chronic rhinosinusitis without nasal polyps; CRS_{NP}: chronic rhinosinusitis with nasal polyps.

^aStatistical significance.

Table 5. Radiographic Characteristics in AFRS Patients.

	Total	Pediatric AFRS	Adult AFRS	P
Sex, n (%)				.07
Female	29 (43.9)	7 (29.2)	22 (52.4)	
Race, n (%)				.07
White	17 (25.8)	10 (41.7)	7 (16.7)	
Black	47 (71.2)	13 (54.2)	34 (81.0)	
Other	2 (3.0)	1 (4.2)	1 (2.4)	
Laterality, n (%)				.007 ^a
Unilateral	10 (15.2)	8 (33.3)	2 (4.8)	
Bilateral	56 (84.8)	16 (66.7)	40 (95.2)	
Presence of any concha bullosa, n (%)				.11
None	8 (12.1)	1 (4.2)	7 (16.6)	
Concha present	26 (39.4)	13 (54.2)	13 (31.0)	
Cannot determine	32 (48.5)	10 (41.7)	22 (54.4)	
Frontal sinus skull base erosion, n (%)				.38
Yes	10 (15.2)	2 (9.5)	8 (17.8)	
Anterior ethmoid skull base erosion, n (%)				.047 ^a
Yes	8 (12.1)	5 (23.8)	3 (6.7)	
Posterior ethmoid skull base erosion, n (%)				.34
Yes	17 (25.8)	7 (33.3)	10 (22.2)	
Orbital erosion, n (%)				.31
Yes	38 (57.6)	14 (66.7)	24 (53.3)	
Sphenoid erosion, n (%)				.71
Yes	20 (30.3)	7 (33.3)	13 (28.9)	

Abbreviation: AFRS: allergic fungal rhinosinusitis.

^aStatistical significance.

would be similar in all postoperative patients given the generalized need for reduction of the concha bullosa for surgical access.

Although this cross-sectional study is not designed to determine the mechanism by which concha bullosa form within patients with AFRS, we suspect that the presence of this anatomical variation in patients with AFRS may contribute to disease phenotype differently than other types of CRS and potentially even play a role in the pathogenesis of recurrent disease. For instance, if the typically air-filled space of the concha bullosa was filled with fungal particles or allergic mucin, as is typically seen at the time of presentation, one might assume that this site of disease would be relatively sheltered from typical route of delivery of topical therapies, from anterior to posterior. In turn, if this site is not recognized during a sinus surgery, this untreated site of local disease could lead to propagation of disease by local tissue inflammation, causing narrowing of the middle meatus and thereby blocking access to the majority of the sinuses for topical therapies, thus allowing for unregulated progression of disease.

Beyond the association between concha bullosa and the diagnosis of AFRS alone, concha bullosa prevalence was increased in postoperative patients with AFRS as compared to CRSwNP and CRSsNP. One potential explanation for this is relatively increased technical complexity of sinus surgery in patients with AFRS. Characterized by thick, tenacious mucin, often described akin to "peanut butter," this eosinophilic mucin may inhibit the surgeon's ability to fully appreciate a patient's anatomy both radiographically and intraoperatively. It is notable that in this study, the presence of a concha bullosa could not radiographically be determined in 45.6% of patients with AFRS. This was significantly increased as compared to patients with CRSwNP and CRSsNP in whom the presence of a concha bullosa could not be determined in 11.5% and 2.8%, respectively. This is not unexpected given the typical appearance of AFRS radiographs and the potential difficulty in identifying any landmarks; however, this may represent a potential source of bias and either over- or underestimation of the true incidence of concha bullosa in the AFRS population. Nonetheless, failure to recognize these structures radiographically in patients with AFRS may lead to incomplete intraoperative reduction of these potential spaces that could potentially harbor mucosal inflammation and tenacious eosinophilic mucin, in turn serving as a nidus for recurrent disease.

The cause of recurrent disease and increased revision rates in AFRS has yet to be fully elucidated, but it has several potential causes beyond our hypothesis regarding the role of concha bullosa detailed above. First, this may be secondary to a fundamentally more aggressive and recalcitrant disease process than other forms of CRS.

Another consideration is lack of patient compliance with topical therapies, especially considering that the AFRS is typically younger, and may represent a less compliant patient population. Adding to this, AFRS patients both in this study and in the reported literature come from a lower socioeconomic status,² which may present barriers to access to the care and therapies needed to prevent disease recurrence. Finally, though there is no evidence that rates of intraoperative cerebrospinal fluid leaks are higher among patients with AFRS, the oftentimes impressive skull base erosion on preoperative scans can be daunting. This finding may make sinus surgeons more cautious and thereby more likely to leave residual disease at the skull base and contribute to the higher rates of revision surgery.

The radiographic staging system for patients with AFRS described by Wise et al. delineated many of the radiographic nuances found in AFRS.³ This current report highlights several other notable distinctions. First, in this review, similar to prior reports, pediatric patients were more likely to demonstrate unilateral disease as compared to their adult counterparts.²² More common unilateral disease in pediatric patients suggests that the disease process may represent a continuum and begin as a unilateral process, ultimately transitioning to become bilateral disease. Furthermore, this review demonstrated increased prevalence of anterior ethmoid skull base erosion in pediatric patients. Although this cross-sectional study cannot determine the etiology of this finding, we suspect that this finding may be a reflection of the development pattern of pediatric sinuses, in that the sphenoid and frontal sinuses may yet to be fully developed thereby leading to a relatively higher epicenter of disease in the ethmoid sinuses. Furthermore, the relatively small sample size of pediatric patients should be acknowledged and can potentially limit this study and its statistical robustness. A more reliable but substantially more intensive study would prospectively characterize the radiographic features of AFRS disease in a large group of patients as they transition from pediatric to adult patients.

Certainly, as a retrospective review, there are inherent limitations to this type of study. Also, the tertiary care nature of this patient population may limit the generalizability of these findings. A prospective anatomic study of intraoperative findings could help support the conclusions of this investigation. Nonetheless, this study provides insight into the subtleties of the clinical findings in the AFRS population that may help guide surgeons as they consider their operative plan.

Conclusions

Sinus surgeons should be aware of the radiographic and anatomical nuances of the AFRS population. In this

study, concha bullosa was more prevalent in patients with AFRS, both pre- and postoperatively as compared to other forms of CRS. Furthermore, surgeons should be aware that it may be more difficult to determine the presence of a concha bullosa in patients with AFRS compared to other forms of CRS. We suspect that this anatomical subsite may harbor untreated disease that could potentially contribute to the high rates of revision sinus surgery common in this population. Even in the setting of prior sinus surgery, surgeons should be aware that an unresected concha bullosa may be present and serve as a reservoir for additional disease. As such, careful preoperative radiographic assessment is imperative, and residual concha bullosa should be appropriately addressed during revision surgery.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: ZMS is a consultant for Olympus and 480 Biomedical as well as on the advisory board for Regeneron. RJS is consultant for Olympus and Arrinex and has received grant support from Entellus and Intersect.

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