

The Role of Allergic Rhinitis in Chronic Rhinosinusitis



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KEYWORDS

- Allergy • Atopy • Allergic rhinitis • Chronic rhinosinusitis • Nasal polyposis
- Sinusitis

KEY POINTS

- There is limited evidence linking allergic rhinitis (AR) and chronic rhinosinusitis in general; however, certain endotypes of chronic rhinosinusitis with nasal polyps (CRSwNP) may be better linked.
- The hypersensitivity reactions of AR and the cytokine pathways of some CRSwNP subtypes are both subserved by a type 2 inflammatory response involving eosinophils and interleukins 4, 5, and 13, among others.
- Intranasal allergens may not penetrate the paranasal sinuses, but instead exert their effects indirectly by means of downstream, systemic factors that then feedback to the sinuses.
- Allergic fungal rhinosinusitis and the newly characterized central compartment atopic disease have immunologic differences from other types of CRS, and may be most related to AR.

INTRODUCTION

Allergic rhinitis (AR) is an inflammatory condition mediated by IgE pathways. It is a disease characterized by nasal obstruction, nasal itching, nasal discharge, and sneezing. Although AR may exist in isolation, rhinitis theoretically may worsen chronic rhinosinusitis (CRS) by adding more fuel to the inflammatory milieu. CRS has been defined as lasting 12 weeks or more and is characterized by nasal discharge, nasal obstruction, hyposmia, or anosmia, and facial pressure. CRS is diagnosed with the support of computed tomography (CT) or endoscopic findings of inflammation, polyps, or active infection.^{1,2}

CRS, such as AR, is an inflammatory process with an indolent course. Chronic rhinosinusitis is frequently parsed into 2 phenotypic groups, namely CRS with nasal polyps

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Immunol Allergy Clin N Am 40 (2020) 201–214

<https://doi.org/10.1016/j.iac.2019.12.010>

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(CRSwNP) and CRS without nasal polyps (CRSsNP). The mechanism behind CRS is multifactorial, and increasing evidence has mounted to suggest inflammation as a common manifestation of this disease process. Generally speaking, local tissue aberrations, such as epithelial tissue hypersensitivity, disruptions of innate immunity, the presence of bacterial colonization and biofilm, and genetic and environmental factors may all play a role in disease pathogenesis. CRSwNP and CRSsNP paint the disease process in broad strokes, however, and recent data suggest that there are discrete endotypes within these categories that better refine treatment and management strategies.³ Nonetheless, inflammation serves as a common denominator for these seemingly disparate causes of sinusitis. Therefore, it is reasonable that allergy may produce or exacerbate CRS. However, data are conflicting when analyzing this relationship, particularly when patients are placed into broad phenotypic categories, such as CRSsNP and CWRwNP.⁴

Better evidence exists when looking at the relationship between AR and specific CRS subtypes, such as allergic fungal rhinosinusitis (AFRS) and the newly characterized central compartment atopic disease (CCAD). This article focuses on the confluence of these entities, with attention to the symptoms that characterize this phenomenon, the mechanism by which they synergize, and suggestions for the management of these patients. Special attention will be placed on CCAD, which lends itself well to characterize the synergistic relationship of allergy and CRS.

EPIDEMIOLOGY AND RISK FACTORS

Epidemiology

Allergic rhinitis is a common pathologic condition, with an estimated prevalence of 10% to 40% of adults worldwide, and 5% to 22% in the United States.^{5,6} The prevalence of AR peaks in childhood and adolescence, and troughs in the elderly. Allergic rhinitis is most frequently triggered by trees, grasses, or weeds for seasonal AR and by dust mites or mold for perennial AR.⁶ CRS is a common and costly disease process, affecting 5% of the United States populace, or approximately 31 million patients, and costs an estimated \$8.6 billion per annum.^{7,8} Allergic rhinitis is also costly, with estimates of \$5.9 to \$7.9 billion for direct patient care and upward of \$3.4 billion in indirect costs (work/school absenteeism) in the treatment of this disease.^{6,9}

PATHOPHYSIOLOGY

Allergy is a hypersensitivity to an antigen that yields reproducible symptoms at a dose that is otherwise tolerated by nonallergic individuals. In the case of AR, nasal allergy is the result of an allergen-specific IgE. Chronic rhinosinusitis *without* nasal polyposis and CRSwNP can be broadly differentiated based on the different cytokine pathways involved in inflammation. CRS *without* nasal polyposis is generally characterized by type 1 inflammation, with neutrophils serving as the common cell type and releasing cytokines, such as interferon-gamma. CRS *with* nasal polyposis is most often mediated by a type 2 inflammatory response involving eosinophils and cytokines, such as interleukin (IL-4), IL-5, and IL-13. Atopic and allergic responses, such as AR, also involve type 2 inflammation. In the AR patient, inhaled allergen activates nasal dendritic cells or other antigen presenting cells. Eosinophils, macrophages, B lymphocytes, and mast cells involved in this process activate downstream T-helper lymphocytes.¹⁰⁻¹²

Putative Mechanism Supporting a Relationship Between Allergic Rhinitis and Chronic Rhinosinusitis

Several studies have implicated allergens and cytokine mediators of allergy in CRS. A putative mechanism is that inhaled allergens are processed by nasal immune cells,

which in turn activate T-helper lymphocytes that then migrate to the bone marrow, leading to the release of type 2 inflammatory mediators, such as IL-4, IL-5, and IL-13. This in turn yields the production of eosinophils, mast cells, and basophils, which precipitates nasal eosinophilia. Moreover, nasal and paranasal mucosal cells express cell surface molecules that attract inflammatory mediators and also release inflammatory cytokines leading to a feedback loop.^{12,13} In patients with CRS, these cell surface adhesion molecules (such as vascular cell adhesion molecule-1 or VCAM-1) and chemotactic molecules are expressed in abundance and have been postulated to underlie the mechanism by which AR mediates CRS.^{10–12} Changes in cellular transcription may serve to further link AR and CRS. As an example, eotaxin, an eosinophil-specific chemokine that directly recruits eosinophils to target tissues, is upregulated in both allergic and nonallergic sinusitis, and is correlated to eosinophil cell infiltration commonly observed in CRS. Eotaxin mRNA is also upregulated following aeroallergen exposure in patients with AR.¹³

The above mechanism is supported in part by several animal models and human studies. Klemens and colleagues¹⁴ demonstrated a hyper-responsiveness to histamine in a murine model of acute bacterial sinusitis, and Blair and colleagues¹⁵ described an enhanced sinusitis disease state in mice exposed to aeroallergens. Several studies have demonstrated an increased rate (60%–63.2%) of positive skin prick testing in patients with CRSwNP when compared with a control cohort.^{16–18} However, systemic allergy symptoms or testing is neither necessary nor solely sufficient for detecting intranasal IgE. Indeed, there are instances in which patients test negative for systemic allergy, but nonetheless demonstrate local sinonasal IgE. In this scenario, called local AR or “entopy,” there is a confined IgE-mediated nasal inflammatory response.^{19,20} This phenomenon could also explain why some patients who test negative for systemic allergen could still have a local inflammatory response that could worsen CRS.

Kennedy and Borish¹² suggest that aeroallergens may have limited access to the sinuses as a result of physical barriers, inability for allergen particles to diffuse adequately into adjacent sinus cavities, and mucociliary flow. The authors suggest that a systemic inflammatory process is more likely the cause of sinusitis. In their estimation, a nasally triggered allergen response leads to nasal eosinophilia by several downstream effector mechanisms. Newly created eosinophils are also nonspecifically recruited by tissues displaying addressins and chemotactic factors, as can occur in patients with sinusitis. The authors also posit that *Staphylococcus* species residing in the nose and paranasal sinuses can create a biofilm and serve as a source of superantigen, suggesting an active inflammatory role for these bacteria and their enterotoxins, despite being in an indolent, biofilm-associated state. The superantigens trigger IL-4, IL-13, and T_H2 cytokines further leading to IgE in the sinus tissues and further promoting the inflammatory response.^{12,21}

Conflicting Data Regarding the Relationship Between Allergic Rhinitis and Chronic Rhinosinusitis

Although the pathways described above seem convincing, this relationship is controversial as several studies do not correlate allergy and atopy with CRS, and indeed only 0.5% of patients with atopy develop nasal polyposis.²² Adkins and colleagues²³ used radiolabeled allergen to demonstrate that inhaled allergen is unable to permeate the adjoining sinuses and remained sequestered in the nasal cavity and oropharynx, suggesting that there is a natural physical limitation to allergy exacerbating disease of the sinuses. There is additional evidence that demonstrates no relationship between allergies and CRSwNP, including the extent of nasal polyposis, sinonasal symptom

severity, or CRS disease recurrence.^{24,25} Li and colleagues,²⁶ characterized the relationship of atopy, or the state of being sensitized to an allergen but not being symptomatic, to clinical severity and disease recurrence in CRSwNP patients. Their data showed no correlation between atopy test results (total IgE, eosinophil cationic protein levels, or Phadiatop testing) and disease severity score as measured by visual analog scoring, Lund-Kennedy endoscopy, or Lund-Mackay CT scoring. In a recent systematic review of CRSwNP, 7 of 18 studies showed no relationship between allergy and CRSwNP, 10 studies demonstrated a relationship between allergy and CRSwNP, and 1 study was equivocal.⁴

Less intuitive is the relationship between allergy and CRS without nasal polyposis. Indeed there is a dearth of literature addressing this question. Some studies suggest that inflammation on imaging seems worse in CRSsNP patients with allergy.^{27,28} However, of 9 reviewed studies, only 4 demonstrated a relationship between CRSsNP and allergy.⁴ Gelincik and colleagues²⁹ demonstrated no difference in the rates of CRS in allergic and nonallergic rhinitis patients. In a recent consensus statement, the evidence linking allergy to CRSsNP is quite low (level D).¹ What is more likely is the association between allergy and CRSwNP, or to be more specific, with select subtypes of CRSwNP, such as AFRS and CCAD.³⁰

The missing link: AR is better associated with discrete endotypes of CRSwNP—Allergic Fungal Rhinosinusitis and Central Compartment Atopic Disease.

AFRS and CCAD are subtypes of CRSwNP that seem to be linked to allergen-mediated inflammation. AFRS is a known CRSwNP entity with strong geographic associations. Bent and Kuhn established 5 criteria for AFRS, among which is a type 1 hypersensitivity reaction to aeroallergens as confirmed by history, serologic testing, or skin prick testing.³¹ Hutcheson and colleagues³² demonstrated a heightened fungal responsiveness (including increased total serum IgE and IgG anti-*alternaria* antibodies) in AFRS compared with CRS, thus distinguishing AFRS as having a clear immunologic difference from other forms of CRS and tying the disease process closely with allergy.

In 2014, White and colleagues³³ demonstrated a correlation between isolated middle turbinate polypoid edema and polyps and positive skin or in-vitro testing to inhalant allergy. Hamizan and colleagues,³⁴ in a large retrospective study, showed that increasing degrees of middle turbinate polypoid edema on nasal endoscopy were associated with significant likelihood of AR. Brunner and colleagues³⁵ compared groups of patients with isolated middle turbinate polyps or with diffuse sinonasal polyposis, and found that these were 2 distinct entities, with the isolated middle turbinate polyp group having a significantly higher incidence of allergy (83% versus 34%), significantly lower incidence of sinusitis (10% versus 100%), and significantly lower Lund McKay scores (2.8 versus 14.9).

DelGaudio and colleagues³⁶ in 2017 first coined the term “central compartment atopic disease” in patients demonstrating polyps or polypoid changes of the superior nasal septum, along with the middle and superior turbinates, with a strong association to inhalant allergy. In the original paper on CCAD, 15 of 15 patients in the series suffered from AR symptoms and had positive allergy testing.

The central compartment structures include the superior nasal septum, the middle turbinate, and superior turbinate. These structures are involved because they are in the path of normal nasal airflow. Nasal airflow arcs over the head of the inferior turbinate to enter the area between the nasal septum and middle and superior turbinates, then descends over the posterior tail of the inferior turbinate to enter the nasopharynx. In a more recent publication, DelGaudio and colleagues³⁷ reported that 80.6% of patients with aspirin-exacerbated respiratory disease (AERD) have endoscopic evidence

of central compartment disease, and over 80% have clinical AR. Among patients with AERD with central compartment involvement and with available allergy data, 100% had clinical AR and 93.8% had positive allergy testing.

CLINICAL FEATURES

CRS *without* nasal polyposis is defined as at least 12 consecutive weeks of 2 or more symptoms of nasal drainage, congestion, attenuated smell or loss of smell, sinus pressure, and evidence of inflammation on CT scan or on nasal endoscopy. Chronic rhinosinusitis *with* nasal polyposis mirrors that of CRSsNP, except with the presence of sinonasal polyposis.² Diagnosis of AR hinges of the presence of atopy, or the characteristic of becoming triggered to an allergen and mounting an IgE response.⁴ The presence of atopy can be supported by skin prick or serum testing. To further complicate the diagnosis, there may be discord between the systemic response to an allergen and the intranasal release of IgE in response to an allergen, a response termed local AR. This discordance has been well characterized, and indeed in 1 study, using a nasal allergen provocation test, 26.5% of previously determined nonatopic individuals had an intranasal IgE response to an allergen.^{34,38} Diagnosing AR concomitant with CRS is, therefore, complex, and requires thoughtful evaluation.

History and Physical Examination

A thorough history and physical examination can identify features of both CRS and AR occurring in unison. From the patient's history, the presence of seasonal or perennial allergy symptoms, rhinitis associated with specific triggers, itchy eyes and nose, responsiveness to anti-allergy medications, and comorbid asthma can help tease out atopic individuals.

Determining the time course and type of allergen exposure is also helpful. Indeed, CRS seems to be more associated with perennial rather than seasonal allergies.³⁹ It follows that chronic exposure to perennial allergens, such as cockroaches, dust mites, pets, and house mold, can yield a chronic inflammatory environment that reinforces CRS. In patients undergoing functional endoscopic sinus surgery for medically refractory CRSwNP, 56.4% of patients had a perennial allergy, a value that exceeds that of the general population, which is estimated between 5% and 22%.⁴⁰ In 1 study, among 225 patients undergoing surgery for CRS, 59.6% demonstrated sensitivity to 1 or more antigens, and among these patients 61.2% had perennial and seasonal allergies, 33.6% had perennial allergies only, and 5.2% had seasonal allergies only.⁴⁰

AFRS can present with varying clinical severity ranging from nasal obstruction, taste and smell disturbance, to facial deformity, proptosis, and vision changes.² Questioning should ascertain a history of airway reactivity. In conjunction with the aforementioned history, the physical examination finding of nasal polyposis or polypoid edema is important for a diagnosis of AFRS or CCAD. Patients with endoscopic findings of central compartment polyposis, with involvement of structures, such as the superior nasal septum, and the middle and/or superior turbinate, in conjunction with allergic symptoms speaks to the disease entity of CCAD.^{33,36,41} This finding in conjunction with positive allergy testing should lead the clinician to suspect CCAD (Figs. 1 and 2).

Allergy Testing

Allergy testing is the initial step in determining allergen sensitivity to correlate with clinical symptoms. There are several mechanisms to test for inhalant allergen sensitivity, including skin prick testing, intradermal testing, and serum allergen-specific IgE

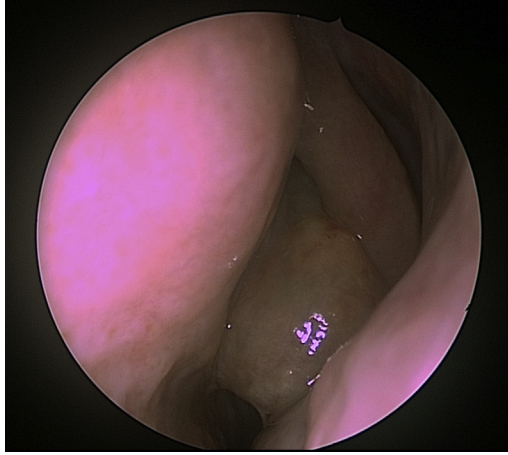


Fig. 1. Left-sided endoscopy image of central compartment atopic disease.

testing (described below). Testing for local AR involves nasal provocation, quantification of allergen-specific IgE in nasal secretions/tissues, and/or basophil activation testing. These methods to detect local AR are most commonly used in research protocols at the present time.

Systemic allergy testing

A combination of serum and skin prick testing is considered most accurate to correctly identify offending allergens. Some allergic sensitivities may be missed if only 1 type of testing modality is performed.⁴² Although clinically this may not always be practical, there is potential variance between the 2 techniques; with controversy regarding which technique is superior.^{16,18} A thorough discussion of the benefits, downsides, and specific techniques for skin and in-vitro allergy testing is beyond the scope of this article.

DeGaudio and colleagues demonstrated that, in patients with CCAD, 100% of this cohort had a clinical history of AR and had positive allergy testing. Conversely, there

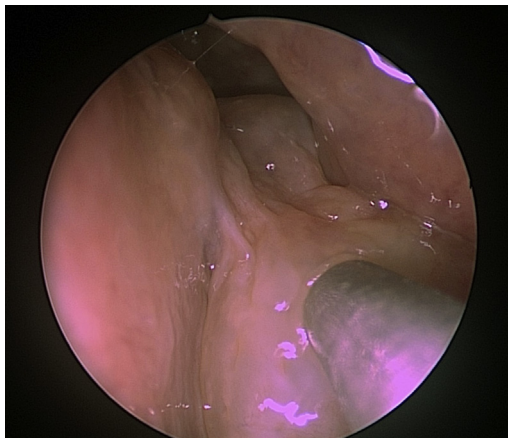


Fig. 2. Left-sided CCAD; suction demonstrates polyp attachment to septum.

are data to suggest a lack of association between allergy and CRSwNP as a broad phenotype, with no association between positive skin prick testing and polyposis, sinus imaging opacification, sinusitis symptoms, or likelihood for recurrent disease.^{24,25,43} Although these 2 statements may seem to be contradictory at first, we now understand that CRSwNP describes a general phenotype of CRS that should be further broken down into subtypes (ie, AFRS, CCAD, AERD, nonatopic CRSwNP). Association of allergy with specific CRSwNP subtypes (namely CCAD, AFRS, and AERD with CCAD features) has been demonstrated. Attempting to associate AR and CRSwNP broadly is problematic because of the various disease processes and causes contributing to CRSwNP as a whole. Future studies and approaches may reduce the issues that have been present in the past.

Intranasal provocation with allergens and its relationship to sinonasal inflammation

Although geographic and regional differences exist, up to 85% of nasal polyps have a high concentration of IL-5.^{26,44} Interestingly, nasal polyps can also express Th17- and Th1-associated cytokines, such as IL-17 and interferon-gamma, and in CRSsNP, tissues can express profiles associated with Th1, Th2, and Th17 signatures, suggesting a veritable cross-pollination of cytokine profiles.⁴⁴ Nonetheless, in CRSwNP, in response to a unilateral intranasal allergen challenge, there is a robust eosinophilic response that occurs in bilateral sinonasal cavities and renders a high tissue concentration of eosinophil cationic protein, IL-5, and tissue IgE.^{45–47} Baroody and colleagues⁴⁵ observed an increased eosinophil count after cannulating the maxillary sinuses of seasonal allergy patients treated with an allergen challenge. The authors postulate that increased albumin, eosinophil cationic protein, histamine, and eosinophilia are not directly from allergen entering the sinus cleft but rather the result of a downstream reaction to a localized allergen challenge. Although these methodologies of intranasal testing provide excellent pathophysiologic information, commercial testing for intranasal cytokines and inflammatory cell types is not currently used in everyday clinical practice.

Imaging Studies

Kirtsreesakul and Ruttanaphol²⁷ and Berrettini and colleagues²⁸ demonstrated the presence of increased sinonasal inflammation in allergic patients on plain film radiographs and CT, respectively, when compared with nonallergic patients (67.5% compared with 33.4% in the CT cohort). Patients sensitized to cypress pollens undergoing a nasal provocation test have demonstrable radiologic changes in their osteomeatal complexes and ethmoid sinuses.⁴⁸ CT studies are used to identify paranasal sinus disease and can serve as an adjunct in diagnosing different disease subtypes. For example, in the presence of endoscopic findings of polyposis and allergic mucin, CT of the paranasal sinuses can identify heterogeneous intrasinus densities with possible bone thinning and expansion of the sinuses that is characteristic of AFRS (Figs. 3 and 4). On MRI, a signal void may be present in regions of fungal involvement with allergic mucin on T2-rendered images.⁴⁹ CCAD has characteristic endoscopic and imaging correlates. On endoscopy and CT imaging these patients demonstrate central compartment soft tissue thickening and/or frank polyposis. Patients with the radiologic finding of central opacification with peripheral clearing have a high association with allergy, and predicts atopy with a 90.82% specificity, and a 73.53% positive predictive value.⁵⁰ In isolated CCAD, as this is primarily a nasal inflammatory process, the sinuses are only affected late in the disease process, when the central compartment polyps obstruct the sinuses by lateralization and/or extensive polypoid changes of the middle turbinates, and cause a secondary obstructive sinusitis (Figs. 5 and 6).³⁶

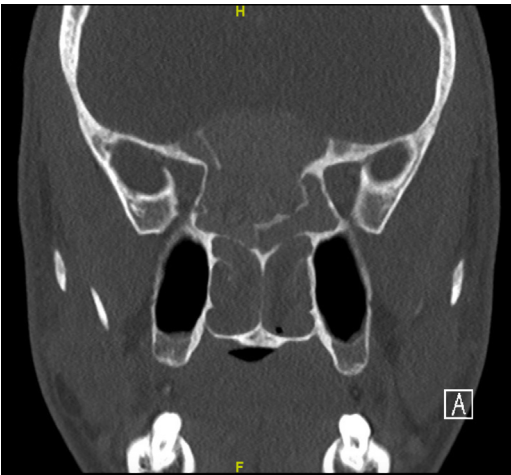


Fig. 3. Coronal computed tomography image of allergic fungal sinusitis with marked thinning of the skull base from local expansion of fungal mucin.

DIFFERENTIAL DIAGNOSIS

A patient with allergies and nasal polyposis may have various causes for their sino-nasal disease that should be elucidated. As stated above, AFRS and CCAD should be strongly considered if the characteristics of history, nasal endoscopy, and imaging fit these entities. Other CRSwNP entities should be taken into account—AERD, cystic



Fig. 4. Sagittal computed tomography image of allergic fungal sinusitis demonstrating expansion of allergic mucin above the sella.



Fig. 5. Coronal computed tomography image demonstrating mild central compartment atopic disease with sparing of lateral sinuses.

fibrosis, or CRSwNP not otherwise specified, depending on the individual patient evaluation. Inverted papilloma should be considered for unilateral polyposis or bilateral polyposis in the setting of a communicating nasal septal perforation. Respiratory epithelial adenomatoid hamartoma is a rare process that is, frequently identified in the upper nasal septum as a primary process or concomitant with mucosal inflammatory disease, such as CRSwNP. It can be unilateral or bilateral.^{51,52} It is further important to establish allergy as the underlying cause of rhinitis, since rhinitis may have nonallergic or mixed causes as well. Indeed, a careful history, physical examination, and allergy testing can be used to differentiate between infectious rhinitis, rhinitis medicamentosa, nonallergic vasomotor rhinitis, nonallergic inflammatory rhinitis with



Fig. 6. Coronal computed tomography image demonstrating severe central compartment atopic disease with postobstructive involvement of lateral sinuses.

eosinophilia, hormonal rhinitis associated with pregnancy or a hypothyroid state, and finally reactive rhinitis from structural considerations or neoplasm.^{1,6}

TREATMENT AND MANAGEMENT

The management for AR is multifactorial, and treatment is particularly nuanced as it relates to AR compounding CRS. Chronic aerosolized allergen exposure may lead to chronic inflammation, and indeed in patients with CRSwNP, 56.4% have a sensitivity to a perennial allergen compared with 5% of the general populace.⁴⁰ Therefore, reducing hypersensitivity to exacerbating allergens is an option, and the role of allergen immunotherapy has been well characterized in patients with AR.¹ Although immunotherapy is effective in AR, it is difficult to fully extrapolate this success to CRS. Nonetheless, immunotherapy may serve as an adjunct, particularly in the post-operative setting.

In the case of CCAD, allergen exposures and their sequelae are best addressed following surgical intervention. DelGaudio and colleagues³⁶ describes a cohort of patients with CCAD pretreated with intranasal corticosteroids, antihistamines, oral corticosteroids, antibiotics, and/or immunotherapy. Antibiotics were given for indication of endoscopic or CT imaging findings demonstrating purulence or air-fluid levels. Despite this pretreatment, medical management did not yield complete resolution of symptoms, and CT images obtained after treatment showed persisting thickening of the central nasal cavity and pathologic involvement of adjacent sinuses or sinuses whose outflow tracks were disturbed by middle turbinate lateralization by central compartment polyps. Therefore, surgical therapy was undertaken to remove obstructive sinonasal pathologic material with the goal of sculpting the polypoid central compartment. In some instances, and particularly in revision CCAD surgical cases, performing a Draf 2b or Draf 3 procedure is a helpful adjunct to clear frontal sinus disease, central compartment polyp and scar, and to resect the polyp-bearing upper nasal septum to provide better access for topical therapy to this portion of the central compartment. Postoperatively, these patients are treated with topical steroids and allergen immunotherapy. Maintenance of topical therapies and immunotherapy is essential, as opening the affected sinuses could in theory expose previously allergen-naïve mucosa to a greater burden of environmental allergens and lead to new or recurrent disease.^{23,36}

Surgery also has an essential role in the management of AFRS. Surgical relief of entrapped allergic mucin serves to halt progressive sinonasal symptoms as well as local tissue response to inflammatory mucin. Creating capacious and evacuated sinus cavities allows for irrigations to continuously remove debris and allergen and distributes topical anti-inflammatory medications to the mucosa. Just as in CCAD, patients with AFRS should undergo a regimen of preoperative systemic steroids and topical nasal steroid (preferably in rinse form), with allergen immunotherapy as an option postoperatively. Despite an underlying type I hypersensitivity reaction to fungal elements, allergen-specific immunotherapy has not undergone rigorous clinical trials in AFRS and currently carries a relatively low level of evidence in the treatment of this disease.^{2,53}

The role of targeted anti-IgE and anti-cytokine therapy deserves mention. In particular, the Food and Drug Administration approval of omalizumab in the treatment of refractory allergen-exacerbated asthma and chronic urticaria has led to the study of this agent in CRSwNP.⁵⁴ Bachert and colleagues⁴⁶ demonstrated a reduction in total nasal endoscopic polyp scores in the omalizumab cohort, suggesting the role of IgE levels in the pathophysiology of CRSwNP. In a subgroup analysis, allergic patients had

Table 1 Comparisons between allergic fungal rhinosinusitis and central compartment atopic disease		
	Allergic Fungal Rhinosinusitis	Central Compartment Atopic Disease
Presentation	Nasal obstruction, hyposmia/anosmia, Thick rhinorrhea, proptosis or telecanthus (in later stages)	facial pain/pressure Clear rhinorrhea, itchy nose, sneezing
Endoscopy	Large, diffuse nasal polyps with thick, yellow/brown, "allergic" or "eosinophilic" mucin	Mucosal edema or polypoid change of the middle turbinate, posterior-superior nasal septum, and/or superior turbinate
Imaging	Unilateral or asymmetric disease, bony remodeling, heterogenous signal in sinuses	Central nasal opacification with peripheral clearing of the sinuses, lateralization of the middle turbinates
Treatment	• Endoscopic sinus surgery to remove polyps and allergic mucin and widely open sinuses for postoperative irrigation • Topical corticosteroid irrigations • Allergen immunotherapy may be used but it is not well supported	• Endoscopic sinus surgery to sculpt the polypoid areas of the central sinonasal compartment and relieve obstructive sinusitis • Topical corticosteroid irrigations • Allergen immunotherapy is suggested but the role is currently unstudied

significant improvements in Lund-Mackay score compared with nonallergic patients (Table 1).

SUMMARY

This article highlights the pathophysiology, diagnosis, and management for AR associated with CRS. There are several putative links between AR and CRS. Although there are no definitive studies that prove this association, there are key features of the 2 disease processes that share common ground. Chronic inflammation may be a mechanism by which AR triggers or exacerbates CRS. Examples of this are the recently identified phenomenon of CCAD, as well as AFRS. Additional study of the relationship between AR and specific CRS subtypes will further our understanding of the interplay between these 2 entities in the future.

FINANCIAL DISCLOSURES AND POTENTIAL CONFLICTS OF INTEREST

None (S.N. Helman, E. Barrow, and T. Edwards). Medtronic (consultant); IntersectENT (stockholder) (J.M. DelGaudio). Research support by the Triological Society and National Center for Advancing Translational Sciences of the National Institutes of Health under award numbers UL1TR002378 and KL2TR002381. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH (J.M. Levy). OptiNose (scientific advisory board); SinopSys Surgical (scientific advisory board); ALK-Abello (scientific advisory board; Stryker (consultant); NeurENT (consultant) (S.K. Wise).

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