Central compartment atopic disease

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ABSTRACT

Background: *Isolated polypoid changes of the middle turbinate were recently reported as having a high association with inhalant allergy. A more advanced manifestation of this association may present as polypoid changes of the entire central sinonasal compartment (i.e., the middle and superior turbinates, and the posterosuperior nasal septum), while the lateral sinus mucosa remains relatively normal.*

Objective: *To introduce and describe this newly recognized variant of chronic rhinosinusitis (CRS), termed central compartment atopic disease (CCAD).*

Methods: *A case series of 15 patients from two institutions who presented with sinonasal symptoms and demonstrated central compartment polypoid mucosal changes on computed tomography (CT). The endoscopic appearance of central compartment edema was assessed. Allergy status was determined by skin or serum in vitro* testing.

Results: *The mean ± standard deviation patient age was 42.4 ± 14.8 years, and 47% of the patients were women. All 15 patients had a diagnosis of allergic rhinitis symptomatically, and those who underwent allergy assessment (14/15) tested positive. All the patients had central compartment polypoid edema on endoscopy and central nasal soft-tissue thickening with peripheral clearing on CT. Even with more severe sinus disease, a central focus of inflammatory change existed.*

Conclusion: *CCAD may represent a local inhalant allergy process that affects the central nasal structures of ethmoid origin. Although inhalant allergy changes mainly appear within the nasal cavity, medial-to-lateral progression to involve the sinuses can occur as a simple obstructive phenomenon. This is a pattern of CRS distinct from the more diffuse sinonasal inflammatory disease and likely requires allergy management as a core component.*

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Allergic rhinitis (AR) is the most prevalent of the atopic disorders and presents with symptoms such as nasal congestion, clear rhinorrhea, itchy nose, and/or sneezing.[1] AR is an immunoglobulin E (IgE) mediated process induced by environmental allergens, and treatment is aimed at allergen avoidance and management of allergic symptoms *via* pharmacotherapy or disease-modifying immunotherapy (IT).[2] The association between chronic rhinosinusitis (CRS) and allergy has been extensively studied, but is still ill-defined as there is a poor level of evidence that supports a link between the two.[3] For example, some studies found evidence of an association between allergy and CRS with nasal polyposis (CRSwNP)[4,5] as well as allergy and CRS without nasal polyposis (CRSsNP),[6–8] whereas others have not.[9–12]

In 2014, White *et al.*[13] described an association between isolated middle turbinate (MT) polypoid changes and atopic disease. More recently, Hamizan *et al.*[14] corroborated these findings in a larger series of patients that identified a greater association of positive allergy testing results with an increasing degree of isolated MT polypoid edema. A potential explanation for the etiology of MT edema in patients with AR is that the MT, especially its anterior surface, is exposed to inhalant allergens *via* routine nasal airflow. The MT represents ethmoid mucosa without the vascular sinusoidal spaces and fibrotic stroma of the inferior turbinate, and undergoes edematous changes that can be grossly polypoid in some patients (Fig. 1). The studies by White *et al.*[13] and Hamizan *et al.*[14] highlight the association between inhalant allergy and isolated MT polypoid changes. However, we more recently observed an advanced manifestation of this atopic process that also involves other structures of the central compartment of the nasal cavity - the superior turbinates (ST), and the posterosuperior nasal septum (PSNS). These central compartment polypoid changes are evident on both nasal endoscopy and radiographic imaging. We termed this process "central compartment atopic disease" (CCAD).

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METHODS

This study was conducted as a multi-institutional case series from tertiary care rhinology clinics in Atlanta, Georgia, and Sydney, Australia. Institutional review board approval was obtained at both sites. The patients in this series initially presented between January 2010 and June 2016.

Patient Screening and Recruitment

Patients were included if they had nasal endoscopic findings of polypoid edema or frank polyps that involved the MT, ST, and PSNS. The senior investigators [J.D., S.W., R.H.] at each institution assessed the sinonasal endoscopic findings in the office and surgical settings. Patient demographics (age, gender), available pre- and postoperative 22-item Sino-Nasal Outcome Test (SNOT-22) scores, medical history (presence of absence of asthma and/or AR), smoking history, presenting symptoms, results of allergy testing, and any previous allergy treatment were collected. Asthma status was determined by either a positive spirometry result with challenge testing or β-agonist use, or if the patient was currently using regular inhaled bronchodilator or corticosteroid therapy. Smokers were defined as any patient currently smoking or any patient who had ceased smoking within the past 12 months.

Qualitative Analysis of Computed Tomography

All patients underwent computed tomography (CT) scanning, and the images were evaluated for soft-tissue thickening of the central compartment of the nasal cavity (MT, ST, and PSNS) and the presence and pattern of sinus involvement. The assessors were asked to de-

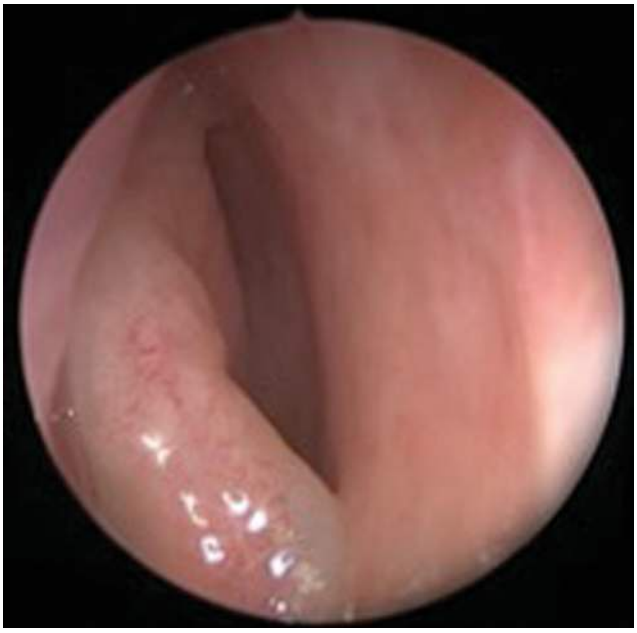

Figure 1. Polypoid changes of the middle turbinate.

scribe the pattern of mucosal involvement, including the central compartment, osteomeatal complex, medial sinus walls, sinus roof, and lateral sinus walls, to describe a pattern that might be associated with CCAD.

Allergy Status

Aeroallergen sensitization was defined by either serologic assessment or skin testing. Many patients were tested before presenting to our institutions, and confirmation of positive allergy testing was obtained. For those who were tested at our institutions, the following methods were used. For serologic assessment, serum IgE (>0.35 kU/L) for any mixed airborne antigen was considered a positive result. Skin allergy assessment was performed by using a skin-prick test, followed by selected intradermal testing in certain cases. Allergens in a 50% glycerin solution were applied to the volar forearm with a Multi-test II device (Lincoln Diagnostics, Inc. Decatur, Illinois). Appropriate positive and negative controls were used. The patients refrained from antihistamine use for at least 7 days before testing. The patients were grouped as allergic if either the serology or the skin test result was positive, and nonallergic if the allergy testing result was negative. The serologic profiles used at each institution are outlined in Table 1.

Management

Patient treatment after the diagnosis of CCAD was recorded. Preoperative medical management included intranasal corticosteroids, antihistamines, oral corticosteroids, antibiotics, and/or IT. Many patients had been medically treated before arriving at our institutions. If indicated, additional medical treatment was initiated after the patient's initial office visit at our institutions, and their symptoms were reevaluated ~4 weeks later. Surgical intervention on average took place ~1–2 months after the patient's initial office visit because it was recommended only after the patient had an extended course of medical therapy that failed. Surgical intervention aimed to reverse the sinonasal obstructive changes and included sculpting the polypoid central compartment disease and opening the affected sinuses. Post-

Table 1 **Allergy testing profiles**

	Emory University	Sydney, Australia
Skin-prick test profiles		
House-dust mite	*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*	*D. pteronyssinus* and *D. farinae*
Mold	*Alternaria, Aspergillus, Cladosporium, Curvularia, Penicillium, Dreschlera, Epicoccum*	*Alternaria, Aspergillus, Cladosporium, Penicillium*
Pet	Cat, dog	Cat, dog
Tree	White oak, pecan, red cedar, birch, white ash, Eastern cottonwood, American elm, red maple	Plane, olive, pine, birch
Grass	Timothy, Bermuda, Bahia	7-Grass mix (Kentucky blue/June, meadow, rye, sweet vernal, cocksfoot, timothy), Bermuda, Bahia, rye
Weed	Short ragweed, Lamb's Quarters, rough pigweed, English plantain	Plantain (*Plantago*), wall pellitory (*Parietaria judaica*)
Other	Mixed feather, cockroach	Mixed feather, cockroach
In vitro blood panels		
House-dust mite	*D. pteronyssinus* and *D. farinae*	*D. pteronyssinus* and *D. farinae*, cockroach (HX2 mix)
Mold	*Alternaria, Aspergillus, Helminthosporium, Penicillium*	*Alternaria, Aspergillus, Candida, Cladosporium, Helminthosporium, Penicillium, Setomelanomma,* Mold Mix 2 (MX2)
Pet	Cat, dog	Cat, dog, horse, cow
Tree	White hickory, oak, silver birch, white ash, cottonwood, elm, maple/box elder, willow	Not performed
Grass	Timothy, Bermuda, Bahia, Johnson, meadow fescue	Timothy, Bermuda, Bahia, Johnson, meadow fescue, rye
Weed	Short ragweed, giant ragweed, Lamb's Quarters, rough pigweed, English plantain	Not done
Other	Cockroach	Included in dust mix–HX2

operative treatment included the off-label use of high-volume topical steroid sinonasal rinses (budesonide 0.5–1.0 mg per 2 mL twice daily) to treat the inflammatory mucosa, and a recommendation for allergy IT.

Statistical Analysis

Statistical analyses were performed by using SPSS version 20.0 (SPSS, Inc., Chicago, IL). Age was represented as parametric and as mean ± standard deviation. All other statistics were nominal and expressed as percentages and/or proportions. No comparative analysis was performed.

RESULTS

Patients

Fifteen patients were identified (mean ± standard deviation, age 42.4 ± 14.8 years; range, 23–71 years; 47% women). All patients presented with the chief concern of nasal obstruction or congestion, and six patients endorsed allergic symptoms, such as itchy or watery eyes, sneezing, and itchy nose. All patients reported that their nasal symptoms had been present for many years. Seven patients (46.7%) had a diagnosis of asthma, of which all were controlled with simple inhaled therapy, and 15 of 15 (100%) had a diagnosis of AR. None had aspirin-exacerbated respiratory disease (AERD).

In terms of smoking status, 3 patients were smokers (1 former smoker and 2 current smokers) and the remaining 12 patients were nonsmokers. Fourteen patients underwent allergy testing either before presentation at our institutions or during further workup, and all had positive allergy testing results. One patient was lost to follow up before undergoing allergy testing. Thirteen patients had been treated for allergy symptoms with 1 or more allergy medication before presentation in the rhinology clinic: 11 with nasal sprays, 6 with oral allergy medication, and 2 with IT. None of these treatment modalities relieved the patients' symptoms of nasal obstruction and/or congestion. Patient demographics and allergy history are listed in Table 2. On nasal endoscopy, all patients had edematous or polypoid changes of the MT (Fig. 2, *A* and *B*), PSNS (Fig. 2, *A* and *C*, and Fig. 3 *A*), and ST (Fig. 3 *A*), and more advanced cases demonstrated frank polyposis. Due to the purely descriptive nature of this report, no control group was included.

Management

All the patients underwent medical therapy with a combination of topical and/or oral steroids before or after initial evaluation in our clinics. Antibiotics were given if indicated based on endoscopic and/or imaging findings of purulence or fluid. At the completion of medical management, no patients had complete resolution of their symptoms. Preoperative SNOT-22 scores were available for six patients (Table 2) and demonstrated a range of 4 to 79, with a mean of 40.2 and a median of 33. Sinus CTs were obtained for all patients and demonstrated a consistent pattern of soft-tissue thickening of the central nasal cavity bilaterally, although the degree of thickening was not always equal on both sides. If sinus involvement was present, then the distribution was more centrally located in the paranasal sinuses with a peripheral lucency in the lateral ethmoids, consistent with postobstructive medial-to-lateral progression (Fig. 3 *B*) This pattern was likely related to either lateralization of the MT from central polypoid changes or from direct extension of the polypoid changes into the sinus outflow tracts. In longer-standing disease, there was more extensive polypoid change to the point of frank

Table 2 **Patient demographics and allergy history**

Patient No.	Age, y	Gender	Presenting Symptoms	SNOT-22 Score	Asthma	Allergic Rhinitis	Smoker	Previous Allergy Testing	Previous Allergy Therapy
1	27	F	NO, PND	Preop, 74; postop, 46	Yes	Yes	Never	+	INS
2	37	F	NO, hyposmia, NC, SP	Preop, 18; postop, 13	No	Yes	Never	+	INS
3	33	M	NO	Preop, 79; postop, 25	No	Yes	Never	+	None
4	26	F	NO, ND, SP	Preop, 39; postop, 0	Yes	Yes	Never	+	None
5	31	M	NO, ocular symptoms	NP	No	Yes	Current	+	IT
6	41	F	NO, ND, nasal itchiness, ocular symptoms	NP	No	Yes	Never	+	INS
7	47	M	NO, NC, ND, nasal itchiness	NP	Yes	Yes	Never	+	INS
8	30	M	NO, PND, ND, sneezing, ocular symptoms	NP	Yes	Yes	Current	+	INS
9	44	M	NO, NC, ND, sneezing, ear itchiness	NP	Yes	Yes	Never	+	INS, oral, IT
10	50	F	NO, NC, ND	NP	Yes	Yes	Former	Lost to follow up	INS, oral
11	63	M	NO, NC	Preop, 4; postop, 11	No	Yes	Never	+	INS
12	71	M	NO, NC, PND	Preop, 27; postop, 3	No	Yes	Never	+	Oral
13	51	M	NC, ND, sneezing, ocular symptoms	NP	No	Yes	Never	+	INS, oral
14	62	F	NO	NP	Yes	Yes	Never	+	INS, oral
15	23	F	NO	NP	No	Yes	Never	+	INS, oral

SNOT-22 = 22-Item Sino-Nasal Outcomes Test; NO = nasal obstruction; PND = postnasal drainage; preop = preoperative; postoperative; + = positive; INS = intranasal steroid; NC = nasal congestion; SP = sinus pressure; ND = nasal drainage (clear); IT = immunotherapy; NP = not performed.

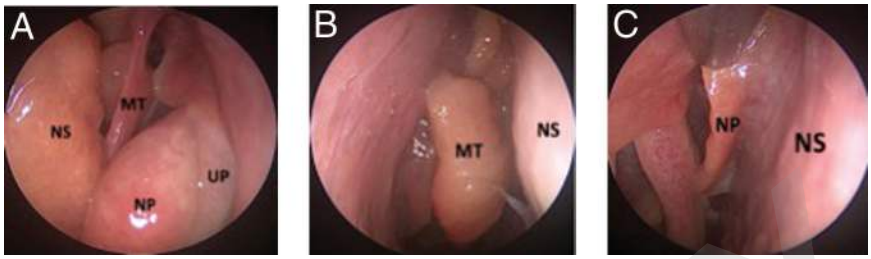

Figure 2. Endoscopic images of central compartment atopic disease. (A) Left nasal cavity, demonstrating nasal septum (NS), middle turbinate (MT), and uncinate process (UP) nasal polyps (NP). Of note, because the MT is narrow, this allows airflow into the middle meatus, which results in UP polyps. (B) Right nasal cavity, demonstrating MT polyps. (C) Right nasal cavity, demonstrating NS polyps.

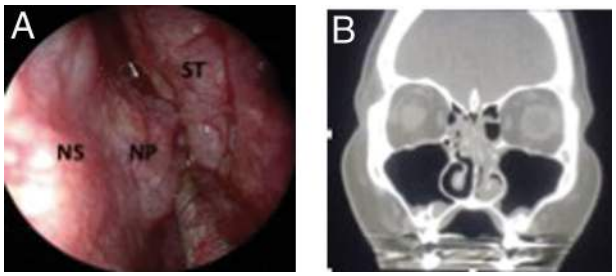

Figure 3. Endoscopic and radiographic images of early central compartment atopic disease (CCAD). (A) Left nasal cavity, demonstrating polypoid nasal septum (NS) and superior turbinate (ST). (B) Computed tomography (CT), showing localized central ethmoid disease; this would represent a relatively early stage of CCAD, with early progression to the ethmoid cavity and maxillary sinus outflow tract obstruction.

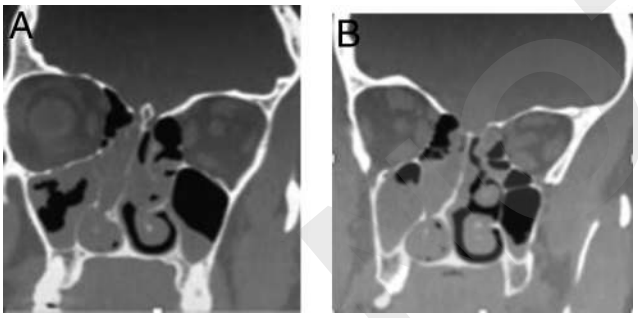

Figure 4. Radiographic images of medial-to-lateral sinus progression of central compartment atopic disease. (A and B) Bilateral nasal septal soft-tissue thickening due to polypoid edema, which is more distinct on the left due to severe right nasal septal deviation; the right maxillary sinus is obstructed due to central compartment polypoid changes and the deviated septum, causing osteomeatal complex obstruction; the ethmoid sinuses demonstrate medial involvement, with lateral aeration at the lamina and superior aeration at the ethmoid roof.

polyposis and more extensive involvement of the sinuses (Fig. 4, *A* and *B*) to the point of near-complete sinus opacification.

Most patients underwent surgical treatment to address the obstructive components related to this process, which included sculpting of the polypoid central compartment disease and opening of the affected sinuses. On follow-up, all of these patients reported improvement in their symptoms. Postoperative SNOT-22 scores for the six patients mentioned decreased in comparison with the preoperative SNOT-22 scores (Table 2): range, 0–46; and mean, 16.3 (compared with a preoperative score of 40.2) and a median of 12 (compared with a preoperative score of 33). At least one patient was noted to develop new polypoid changes in the ethmoid sinuses after surgery, which were well controlled with topical steroid rinses. This was potentially related to new exposure of the now open ethmoid sinuses to the inhalant allergens. All the patients were started on or were recommended to undergo allergy IT.

DISCUSSION

We defined CCAD as a variant of CRS strongly associated with allergy. On endoscopic and radiologic examination, CCAD demonstrates inflammation and edema of the central sinonasal compartment. The previously reported MT polypoid edema is likely a precursor or early stage of CCAD. Inclusion of ST and PSNS edema and/or inflammation is the next stage. Typically, in early CCAD, only edema and/or polypoid change is encountered, with discreet polyps occurring as the disease progresses.

Further progression of CCAD polypoid changes may lead to involvement of the central sinus cavities, such as the medial ethmoid region and the maxillary sinus ostium. At this stage, a rim of peripheral clearing along the orbit and skull base is usually maintained. This sinus involvement occurs when the central compartment polypoid changes encroach on the sinus outflow tracts, either by MT lateralization from central compartment polypoid disease or by direct extension of polyps from the lateral surface of the MT. With more-severe CCAD, near-complete sinus opacification can be found, with a progression of sinus involvement in a medial-to-lateral direction. The lateral sinus disease is postobstructive in nature rather than secondary to polypoid changes, which is demonstrated by the normal sinus mucosa found within these sinuses once they were surgically opened (Fig. 5, *A–D*).

A review of the current literature demonstrated an inconclusive association among allergy, CRSsNP, and CRSwNP. An evidence-based review by Wilson *et al.*[3] in 2014 evaluated the role of allergy in both CRSwNP and CRSsNP, and found that the literature was divided, with the recommendation of allergy testing and allergy treatment in CRSwNP and CRSsNP groups as an option only. Rosati and Peters[15] established that the literature supports a relationship between AR and CRS but found no direct evidence of causality between the two. Sedaghat *et al.*[16] followed up 59 patients with AR and found that 24 of these subjects eventually went on to develop CRS. Their findings demonstrated that CRS develops faster in patients with AR who have comorbid asthma and recommended that these patients be counseled to medically manage their AR to possibly prolong or stop the future development of CRS.[16] It is postulated that those patients with both sinus disease and inhalant allergy may have a greater symptom burden, but causality is still debated.

With regard to CRSwNP, a prospective study from 1978 did not find an association between atopy and nasal polyposis,[17] whereas more recent literature has focused on the strong evidence for the local expression of total and allergen-specific IgE in polypoid tissue.[18] Pumhirun *et al.*[5] performed skin-prick testing on 40 patients with nasal polyps and 30 control subjects, and found that 60% of patients with nasal polyps had positive skin-prick testing results compared with only 20% in the control group ($p = 0.0019$). However, Gorgulu *et al.*[9] found no difference in mean IgE levels ($p = 0.591$), serum total IgE positivity ($p = 0.680$), and allergy prevalence (present in 25% of the nasal polyp group and in 28% of the control group; $p = 0.722$) between 60 patients with nasal polyps who had undergone endoscopic sinus surgery and 50 control patients (25 smokers and 25 nonsmokers). They determined that smoking was a significant risk factor for the development of nasal polyps but that allergy was not.[9] Overall, no direct correlation between allergy and CRSwNP was established.

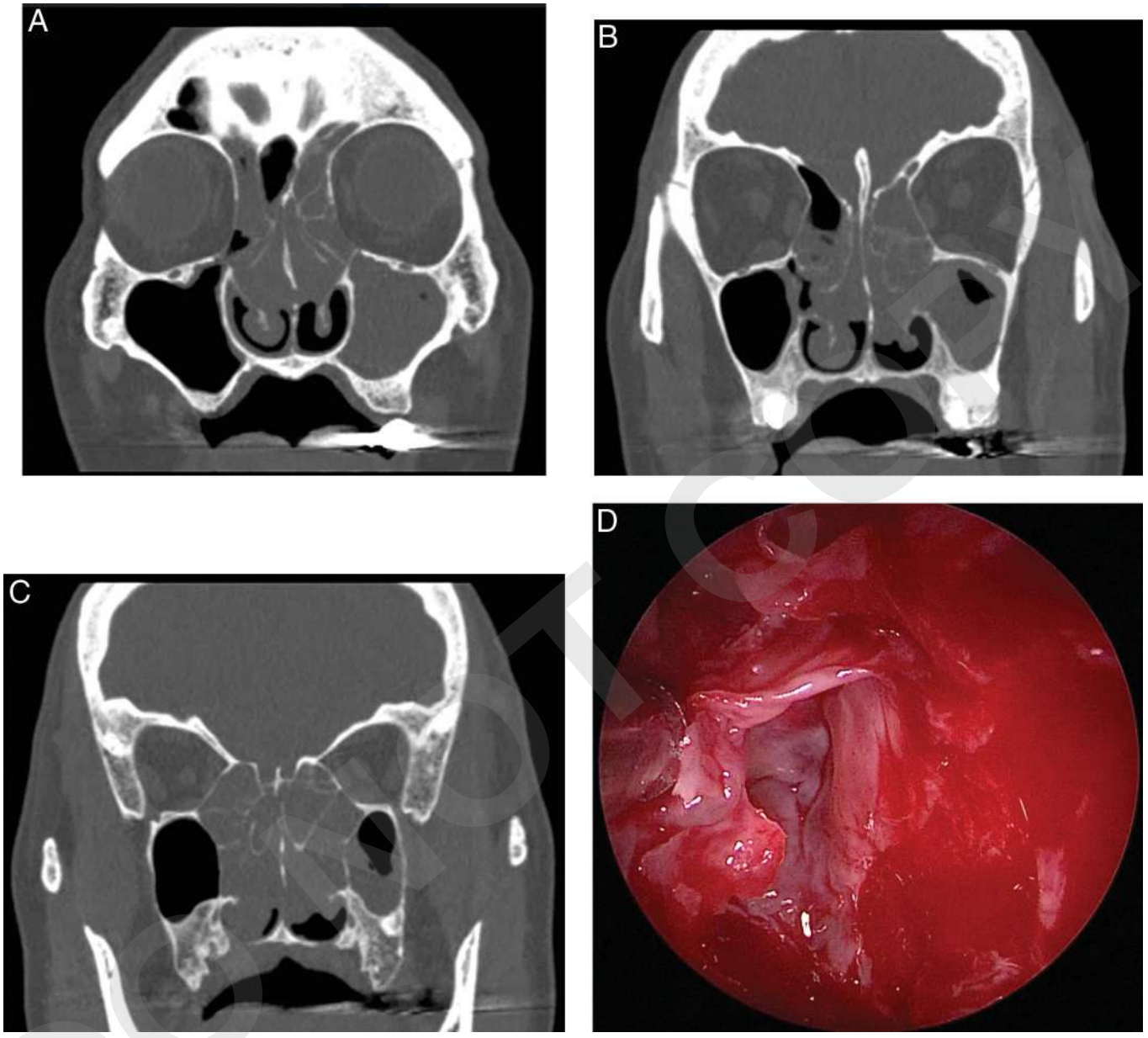

Figure 5. *Radiographic and endoscopic images of advanced central compartment disease. (A–C) Preoperative computed tomography (CT), showing progressively posterior cuts, demonstrating severe central compartment soft-tissue thickening, with lateral sinus clearing on the right side and postobstructive secretions in the left maxillary and ethmoid sinuses. Note the laterally displaced middle turbinates, especially anteriorly, with scalloping of the inferior turbinate bone due to the severe, chronic central polypoid disease. (D) The same patient during surgery, demonstrating fairly normal mucosa in the left ethmoid cavity; the opacification on CT was secondary to obstructed secretions, not polypoid disease.*

Regarding CRSsNP, Berrettini *et al.*[6] evaluated 40 patients with AR and 30 control patients by using CTs of the sinuses and found a statistically significant difference between the groups ($p = 0.017$), with 67.5% of the allergic group demonstrating findings of sinusitis on the CT compared with only 33.4% of the control subjects.[6] However, Gelincik *et al.*[12] compared a cohort of patients with AR with a cohort of patients with nonallergic rhinitis and found that CRS was equally prevalent in the patients with allergic (43%) as well as patients with nonallergic (50%) rhinitis. Similar to CRSwNP, no direct correlation between allergy and CRSsNP was established.

In the previously mentioned study by White *et al.*,[13] 16 patients with isolated MT polypoid edema on nasal endoscopy (68.8% bilateral and 31.2% right side only) all tested positive for both seasonal and perennial allergens on *in vitro* or skin allergy testing. In the study by Hamizan *et al.*,[14] 304 nasal cavities were assessed and the MTs were graded as having normal, focal, multifocal, diffuse, or polypoid edema by a blind assessor. The investigators found that the more severe findings of diffuse and polypoid edema demonstrated the strongest association with inhalant allergy and that MT edema on nasal endoscopy had an excellent positive predictive value for the presence of inhalant allergy.[14]

It seems that CCAD may represent a more advanced stage of the previously described isolated MT atopic polypoid changes, with additional involvement of the ST and PSNS. This may represent a local immune response related to antigen contact in these areas most exposed to inhaled air. We previously attributed the isolated MT

Table 3 **Comparison of CCAD with other sinonasal diagnoses**

	Endoscopic Findings	Radiographic Findings	Presence of Asthma	Aspirin Sensitivity	Allergy Status
CRSwNP	Diffuse watery polyps, middle and superior turbinates and posterior nasal septum likely spared	Diffuse pansinus disease, central compartment spared	±	−	±
CRSsNP	No polyposis	Diffuse pansinus disease, central compartment spared	±	−	±
AFRS	Diffuse watery polyps, middle turbinate may have polypoid changes but septum spared	Unilateral or asymmetric disease, bony remodeling, heterogenous signal in sinuses	±	−	+
AERD	Diffuse fibrous polyps, middle and superior turbinates, and posterior nasal septum frequently involved	Diffuse pansinus disease, including lateral sinuses and central compartment thickening	+	+	±
AR	No polyposis	Clear sinuses	±	−	+
CCAD	Watery polypoid changes of the middle and superior turbinates and posterior nasal septum	Central sinus dominance with peripheral clearing	±	−	+

CCAD = Central compartment atopic disease; CRSwNP = chronic rhinosinusitis with nasal polyposis; ± = may or may not be present; − = not present; CRSsNP = chronic rhinosinusitis without nasal polyposis; AFS = allergic fungal rhinosinusitis; + = present; AERD = aspirin exacerbated respiratory disease; AR = allergic rhinitis.

polypoid edema to the likely role of the MT as a protective structure that prevents inhaled particles from entering the middle and superior meatus, and possibly a role in antigen presentation.[13] As the MT edema increases, this may negatively impact normal function of the mucosa, which allows particles to find their way to surrounding structures, such as the ST, PSNS, and middle meatus (MM). The uncinate process can also be affected but less so than the more central structures, likely due to the shielding effect of the MT on the MM. However, if the MM is not shielded by the MT, then airflow can result in uncinate process polypoid changes, as seen in Fig. 2 *A*. It is interesting that these changes are localized to mucosa derived from the ethmoid complex: the MT, ST, and the PSNS (*i.e.*, the perpendicular plate of the ethmoid bone). The inferior turbinates are spared, potentially due to their nonethmoid origin, as was also shown in the study by Hamizan *et al.*[14] In more severe cases of CCAD, polypoid changes can manifest as frank polyposis in the central compartment structures.

When the sinuses become affected in CCAD, this seems to be due to lateral progression of the polypoid change, with secondary obstruction of the sinus outflow tracts and postobstructive secretions in the sinuses rather than from atopic and/or polypoid changes in the sinuses themselves (Fig. 5, *A–D*). This is reflected in the pattern of sinus involvement on the CT in patients with CCAD, especially in earlier stages of the disease. The soft-tissue thickening begins in the medial aspect of the ethmoid sinuses, likely related to polypoid changes of the lateral surface of the MT, with the lateral portion of the ethmoids being clear, and a halo of aeration along the orbits and skull base (Fig. 4, *A* and *B*). As stated, this is likely due to the lateralization of the MT from central compartment polypoid changes and/or from the direct extension of polypoid changes of the lateral MT into the sinus outflow tracts and causes obstruction.

This pattern of sinonasal soft-tissue involvement in CCAD is distinct from the nonatopic inflammatory sinus disease found in CRSwNP and CRSsNP, which more commonly diffusely affects the sinus cavities without significant involvement of the MTs and STs and nasal septum. However, the distinction between these disease processes can be difficult to determine when CCAD has advanced to the point that there is extension of the sinus disease laterally with complete opacification of the ethmoid sinuses. In these cases, the key to differentiating the entities is the presence of the central compartment polypoid edema, which is not commonly found in nonatopic inflammatory sinus disease. Typical CRSwNP presents with diffuse sinonasal polyposis within the sinus outflow tracts and sinuses, but the MTs and STs and the posterior nasal septum are usually spared or minimally affected by these polypoid changes. CCAD may represent a variant of CRSwNP (in advanced cases) in which the polypoid tissue does not primarily involve the sinus mucosa but rather involves the central compartment mucosa. Because no one has reported this differentiation previously, it is possible that this could represent one explanation for the failure to identify a consistent relationship between CRSwNP and allergy.

The involvement of the central compartment structures in CCAD also needs to be differentiated from AERD. Kountakis *et al.* presented a poster at the Triologic Society in 2014 which demonstrated that AERD recurrence frequently occur in the central compartment of the nose and olfactory region. Nonetheless, CCAD and AERD are easily distinguishable based on other factors. Polyps in CCAD (if present) are watery compared with the more fibrous polyps in recurrent AERD. In addition, AERD primarily affects the sinuses in a diffuse pattern similar to other forms of nonatopic inflammatory sinonasal disease. Also, none of our subjects with CCAD had been diagnosed as aspirin sensitive, and only 7 of 15 (46.7%) had a diagnosis of asthma, whereas 100% of the patients with AERD were originally described as being aspirin sensitive and with asthma in an early description by Samter and Beers.[19] A comparison between CCAD and other common sinonasal disease processes can be found in Table 3.

In our patient series, removing the polypoid tissue and/or frank polyps and opening the secondarily obstructed sinuses, followed by the use of topical steroid rinses and treatment of allergies, resulted in dramatic improvement in patient symptoms. Surgery was recommended in all the patients in this series because all had persistent nasal obstruction after medical therapy. Furthermore, we believe that opening the sinuses allows for better delivery of postoperative topical steroids for long-term maintenance of this disease process. However, it should be noted that, because allergen exposure is the likely cause of CCAD, further exposing the sinonasal mucosa to environmental allergens could, in theory, worsen the disease burden. If this were the case, then systemic therapy and maintenance of anatomic barriers would be a reasonable treatment option in these patients.

However, because the patients in our cohort did not demonstrate improvement in their subjective symptoms and continued to demonstrate objective findings of central compartment polypoid disease

after medical management, we believed that surgery was indicated in these patients when nasal obstruction or medically refractory CRS was present. Furthermore, in the six patients for whom both pre- and postoperative SNOT-22 scores were available, the mean score decreased from 40.2 before surgery to 16.3 after surgery. Although our patient cohort had significant symptomatic improvement in our short-term follow-up, long-term follow-up data on this patient cohort are not yet available. The major limitation of our study was the lack of a comparison group because this was a descriptive study with the main objective of introducing and describing this new subset of patients with CRS. Another limitation was the lack of complete patient-reported outcome measures for all 15 patients in this series. These data are currently being monitored for future evaluation and reporting.

CONCLUSION

CCAD is a distinct variant of inflammatory sinonasal disease. The findings include edematous and polypoid changes in the central sinonasal cavity associated with inhalant allergy. This disease process affects ethmoid derivatives, including the MTs and STs and the PSNS. The endoscopic and CT findings consist of central nasal cavity edema and/or polypoid changes. If left untreated, the central compartment polypoid disease can secondarily obstruct the sinuses by MT displacement or by extension of polyps from the lateral MT surface to the sinus outflow tracts. If the sinuses are involved, then there is a medial-to-lateral progression, with lateral sinus clearing until there is advanced sinus disease. The identification of CCAD as a variant of CRS may provide a step to help clarify the relationship of allergy to CRSwNP in some patients, and may also define a variant of CRS that requires allergy management as a core component. Further studies are underway to better define the association between aeroallergen sensitization and central compartment disease features.

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