

Chronic Rhinosinusitis

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Overall Purpose/Goal: To provide excellent reviews on key aspects of allergic disease to those who research, treat, or manage allergic disease.

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List of Design Committee Members: Christopher J. Ocampo, MD, PhD, and Leslie C. Grammer, MD.

Activity Objectives

1. Appreciate the multiple causes and differential diagnosis in patients presenting with nasal obstruction.
2. Recognize the presentation of the various subtypes of chronic rhinosinusitis.
3. Initiate appropriate treatment options for aspirin-exacerbated respiratory disease.

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A 50-year-old woman with nonallergic rhinitis, asthma, and aspirin intolerance presented with worsening symptoms of nasal congestion, purulent drainage, and anosmia. Nasal polyps were

visualized on anterior rhinoscopy, and there was evidence of chronic rhinosinusitis (CRS) on imaging studies during work-up for another medical condition. Over a 2-year period she had numerous bouts of acute exacerbations of CRS which required multiple courses of antibiotics; however, she was unwilling to undergo surgery to reduce polyp burden. She successfully underwent aspirin desensitization and experienced partial relief of symptoms with daily aspirin ingestion.

Nasal obstruction is a common symptom that can result from multiple causes, including mucosal disorders (eg, allergic and nonallergic rhinitis, rhinosinusitis, sarcoid) and structural disorders (eg, nasal septal deviation, tumors, mucocoeles). The various causes and work-up for nasal obstruction are discussed with emphasis placed on CRS, which is a prevalent disease characterized by inflammation of the nose and paranasal sinuses for a duration of >12 weeks. The different subtypes of CRS, including CRS with and without nasal polyps, allergic fungal rhinosinusitis, and aspirin-exacerbated respiratory disease, are discussed along with pathogenesis, diagnosis, and treatment options. © 2013 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol: In Practice 2013;1:205-11)

Key words: Aspirin-exacerbated respiratory disease; Aspirin intolerance; Asthma; Chronic rhinosinusitis; Nasal obstruction; Nasal polyps; Nonallergic rhinitis

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Abbreviations used

5-LO- 5-Lipoxygenase
ABRS- Acute bacterial rhinosinusitis
AERD- Aspirin-exacerbated respiratory disease
AFRS- Allergic fungal rhinosinusitis
AR- Allergic rhinitis
ARS- Acute rhinosinusitis
COX-1- Cyclo-oxygenase-1
CRS- Chronic rhinosinusitis
CRSwNP- Chronic rhinosinusitis with nasal polyps
CRSsNP- Chronic rhinosinusitis without nasal polyps
CT- Computerized tomography
FESS- Functional endoscopic sinus surgery
INCS- Intranasal corticosteroids
LTRA- Leukotriene receptor antagonist
MRI- Magnetic resonance imaging
NP- Nasal polyp
NSAID- Nonsteroidal anti-inflammatory drug

CASE

A 50-year-old white female minister presented to the Allergy-Immunology outpatient clinic for worsening symptoms of nasal congestion. She had been followed for 6 years; the initial diagnoses were nonallergic rhinitis and persistent asthma. She also described severe nasal congestion and profuse rhinorrhea after aspirin or ibuprofen ingestion. For the first 4 years, she had done relatively well in managing her rhinitis symptoms with intranasal steroids.

At that point, she had an urgent visit after a month of increasing nasal congestion, purulent discharge, and anosmia. She denied fever, facial pain, or sinus pressure. Nasal polyps (NPs) and pus were first visualized. She was treated with azithromycin (Z-Pak $\times$ 2) and prednisone (30 mg daily for 5 days) with improvement, but not complete resolution, of symptoms.

At follow-up 5 months later, she reported recurrence of uncontrolled sinusitis symptoms, with enlarged polyps visualized on examination. She was placed on a 3-week course of amoxicillin-clavulanate, and further evaluation with computerized tomography (CT) of the sinuses was recommended on at least 2 occasions, but the patient did not comply. She did not have exacerbations of asthma and was maintained on low-dose fluticasone-salmeterol; spirometry was normal.

Two months later she presented for increasing right eye swelling over a 3-week period and was noted to have proptosis of the right orbit. Magnetic resonance imaging (MRI) showed a soft tissue abnormality in the medial aspect of the right orbit (Fig 1, A). A biopsy of the right orbital mass obtained through a superior nasal-anterior orbitotomy showed noncaseating granulomatous changes, consistent with a diagnosis of ocular sarcoidosis.

The CT imaging studies showed near complete opacification of the right ethmoid sinuses and moderate mucosal thickening of the bilateral maxillary sinuses (Fig 1, B and C). In addition, multiple polypoid lesions were noted in the nasal cavity (Fig 1, C). Humoral immune function was evaluated. Total quantitative immunoglobulins were normal, and specific antibody titers to *Streptococcus pneumoniae* were adequate. Additional laboratory studies (comprehensive metabolic panel, complete blood cell count with differential, angiotensin-converting enzyme level, and anti-neutrophil cytoplasmic antibody) were within normal limits. She was treated for several months with a tapering schedule

of prednisone, which resolved the orbital sarcoid (as evidenced by resolution of abnormalities on repeat MRI studies and complete resolution of proptosis) and controlled her symptoms of chronic rhinosinusitis (CRS). However, after discontinuation of prednisone, the patient resumed having acute exacerbations of CRS which required antibiotics. She refused further prednisone and functional endoscopic sinus surgery (FESS).

Her nasal congestion showed some improvement with montelukast; however, she could not continue the medication because she believed it caused mood changes. Zafirlukast did not help; because of the need for liver function tests, she did not want zileuton. While she was taking montelukast, aspirin desensitization was performed. During the first attempt she ingested a total of 325 mg of aspirin but experienced significant rhinorrhea and sneezing; her spirometry did not change and she had no lower respiratory symptoms. She was maintained on 81 mg of aspirin twice daily, and 2 weeks later she tolerated progressively higher doses with minimal reaction. She took 650 mg of aspirin twice daily with improvement but experienced another exacerbation that required antibiotics. The plan was that she will agree to FESS to reduce her polyp burden; intensive medical therapy will continue.

DIFFERENTIAL DIAGNOSIS FOR NASAL OBSTRUCTION

The differential diagnosis for nasal obstruction is broad (Table 1). Causes for nasal obstruction can be divided into mucosal disorders: rhinitis (allergic and nonallergic), rhinosinusitis (acute and chronic, with multiple subtypes), and structural disorders such as nasal septal deviation or mucocele. Nasal congestion can also be due to the effects of medications (Table 1).

Mucosal disorders

Allergic and nonallergic rhinitis. Initially, the patient had symptoms of persistent rhinitis, which is characterized by at least one of the following: nasal congestion, rhinorrhea, sneezing, and pruritus.¹ An essential component of the history is identifying symptom triggers, because rhinitis can be caused by both allergic and nonallergic stimuli. It is important to work up allergic rhinitis (AR) in a person with CRS, because the prevalence of AR is estimated to be 60% in CRS.² However, it is important to note that the association of CRS with AR does not imply causation, because studies have failed to show causality.³⁻⁵ Evaluation for a possible allergic trigger for rhinitis symptoms includes a thorough history and physical examination, with confirmatory diagnostic skin prick testing for specific IgE to a panel of relevant environmental allergens.¹ The patient had negative skin prick testing to environmental allergens and thus her condition was initially diagnosed as nonallergic rhinitis, which can mimic AR, because symptoms can be similar and perennial or periodic.¹

Acute rhinosinusitis. Acute rhinosinusitis (ARS) is defined as the sudden onset of symptoms of nasal congestion/obstruction/congestion or nasal discharge, along with facial pain/pressure or hyposmia/anosmia for a duration of <12 weeks.⁵ Children may present with associated fever and cough. A diagnosis of ARS is made clinically on the basis of history and physical examination. In most cases, ARS is viral in origin, with only approximately 0.5% to 2% developing a secondary bacterial infection; acute bacterial rhinosinusitis (ABRS) is suspected when

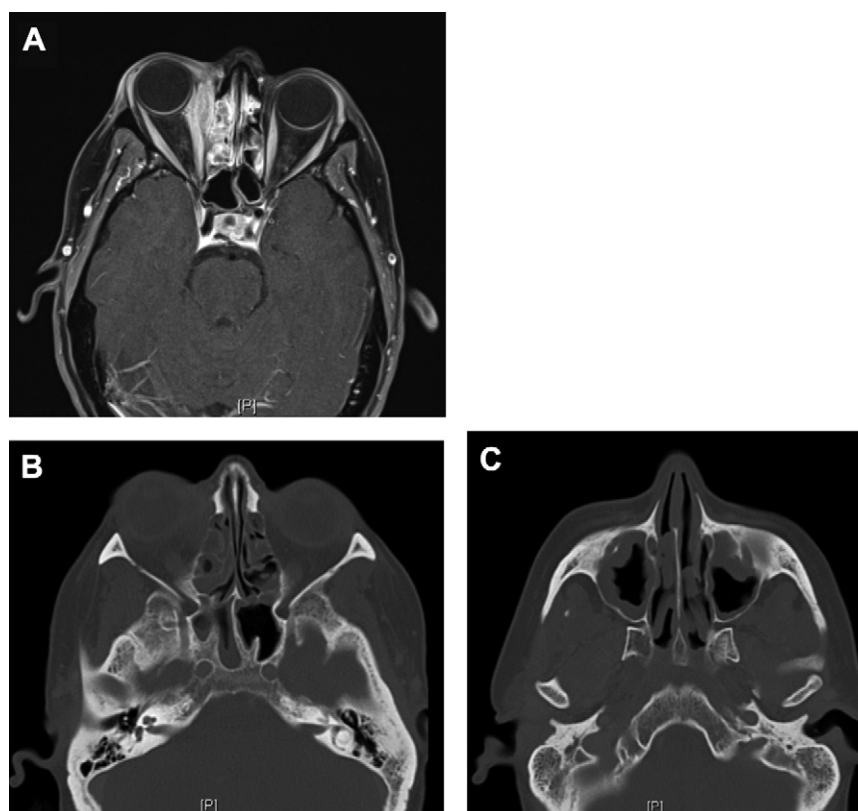


FIGURE 1. T1-weighted MRI shows infiltrative lesion in superior and medial aspects of the right orbit (A). CT evidence of extensive mucosal thickening of the ethmoid sinuses (B). CT evidence of moderate mucosal thickening of the maxillary sinuses with numerous polypoid lesions in the nasal cavity (C).

TABLE I. Differential diagnosis of nasal obstruction

Mucosal disorders
Rhinitis
Allergic: perennial; seasonal
Nonallergic: infectious; vasomotor; eosinophilic; hormonal
Rhinosinusitis
Acute: viral; bacterial
Chronic: without nasal polyps; with nasal polyps; allergic fungal rhinosinusitis; aspirin-exacerbated respiratory disease
Other: Wegener granulomatosis; sarcoid; Churg-Strauss syndrome
Structural disorders
Nasal septal deviation
Mucocoele
Other: concha bullosa, foreign body, adenoid hypertrophy, tumor
Medications
Aspirin, NSAIDs
Oral contraceptives
Vasodilators
Erectile dysfunction medications
Ocular topical beta blockers
Nasal decongestants (rhinitis medicamentosa)

the upper respiratory infection has persisted beyond 10 to 14 days (Table II).⁵

Because the patient's symptoms were >12 weeks in duration, the diagnosis is not ARS. However, she had frequent

exacerbations of sinusitis with worsening of symptoms that mimicked ABRS.

Chronic rhinosinusitis. CRS is defined as inflammation of the nose and paranasal sinuses lasting 12 weeks or longer. The prevalence estimates of CRS range from 5% to 15% of the adult population in the United States and Europe.⁵ The prevalence of physician-diagnosed disease with the use of objective criteria is estimated to be only 2%.⁵ The 4 characteristic signs and symptoms of CRS are nasal congestion, facial pain/pressure, anterior or posterior nasal drainage, and hyposmia or anosmia.^{2,5} At least 2 of these symptoms should be present for 12 weeks or longer, when considering the diagnosis of CRS. Objective measures, such as direct endoscopic examination or dedicated sinus CT imaging studies, can be used to confirm the diagnosis of CRS.^{6,7} However, dedicated imaging and rhinoscopy should be used only after initial treatment fails or with recurrence of symptoms.

CRS can be associated with a number of complications. Physical examination findings that suggest a possible complication include severe headache, facial swelling, significant peri-orbital edema, visual changes, proptosis, abnormal extraocular movements, ophthalmoplegia, and meningeal signs.⁸ In these cases emergent evaluation is indicated to prevent permanent visual impairment or infectious progression to meningitis, cavernous sinus thrombosis, or brain abscess. Our patient presented with CRS and an orbital mass, which has an extensive

TABLE II. Rhinosinusitis types and key features

Acute rhinosinusitis (<12 weeks' duration)
Viral origin in vast majority of cases
Symptomatic treatment, typically resolves without antibiotics
Consider antibiotics with symptoms lasting longer than 10-14 days
Chronic rhinosinusitis subtypes (>12 weeks' duration)
Chronic rhinosinusitis without nasal polyps
Predominantly T _H 1 inflammation
Prominent symptoms of facial pain and purulent drainage
Chronic rhinosinusitis with nasal polyps
Presence of nasal polyps
Predominantly T _H 2 inflammation
Prominent symptoms of nasal obstruction, hyposmia/anosmia
Allergic fungal rhinosinusitis
Fungal hyphae isolated from allergic mucin
Fungal-specific IgE present in the serum
Typically unilateral disease
Hyperdensities within opacified sinuses (allergic mucin)
Exclusion of other fungal diseases
Aspirin-exacerbated respiratory disease
Presence of nasal polyps
Idiosyncratic reaction to aspirin or other NSAIDs
Difficult to control asthma
Difficult to control sinus disease

TABLE III. Differential diagnosis of chronic rhinosinusitis with orbital mass

Orbital sarcoidosis
Orbital cellulitis
Wegener granulomatosis
Churg-Strauss syndrome
Graves disease
Lymphoma
Orbital apex syndrome (because of chronic invasive fungal rhinosinusitis)
Periocular xanthogranuloma associated with adult-onset asthma
IgG ₄ -related orbital inflammatory pseudotumor

differential diagnosis (Table III), but was found to have orbital sarcoidosis from which she recovered completely.

CRS remains a challenge to diagnose because its symptoms mimic many other conditions, its onset is often insidious in nature, physicians do not inquire about disease-specific symptoms such as anosmia, and/or clinicians lack the training to perform nasal endoscopy.⁵ Adding to the challenge, it is a disease composed of multiple phenotypes, each with unique characteristics that are lumped into the broad term chronic rhinosinusitis.⁹ These various subtypes of CRS have unique presentations and management options (Table II), although the exact division of subtypes remains controversial.

Chronic rhinosinusitis without nasal polyps. Chronic rhinosinusitis without nasal polyps (CRSsNP) is the most prevalent subtype, accounting for approximately 60% to 65% of cases of CRS. In general, persons with CRSsNP have more prominent symptoms of facial pain and purulent discharge.⁷

Histologically, the mucosal lining shows basement membrane thickening, goblet cell hyperplasia, limited subepithelial edema,

and prominent fibrosis and mononuclear cell infiltrate.⁷ Immunologically, more skewing occurs toward a T_H1 phenotype.^{7,10} Although both eosinophils and neutrophils are part of the inflammatory milieu, eosinophils are less prominent in the mucosa of patients with CRSsNP, suggesting this subtype can be characterized as having more of a neutrophilic process.^{5,7}

CRSsNP in the pediatric population has similar signs and symptoms as adult CRS, with chronic cough slightly more prominent than in adults.⁵ Diagnosis of CRS in children is more challenging, given the large overlap of symptoms with common childhood nasal diseases and difficulties with the physical examination.⁵ Another important distinction in pediatric CRS is the prominent role of the adenoids, because it is hypothesized they harbor biofilms that act as a bacterial reservoir.¹¹ In addition, biofilms may also contribute to chronic inflammation and increased resistance by protecting bacteria from host defense mechanisms and antibiotics.⁵

Chronic rhinosinusitis with nasal polyps. Chronic rhinosinusitis with nasal polyps (CRSwNP) occurs in approximately 20% of persons with CRS. In general, persons with CRSwNP present with symptoms of prominent nasal obstruction and hyposmia/anosmia and complain less of facial pain.⁷ This subtype tends to be more refractory to conventional medical treatment, requires more surgical intervention, and has greater morbidity.⁷ On physical examination large polyps can sometimes be visualized with anterior rhinoscopy alone. They appear translucent, have a yellow gray color, lack sensitivity, and typically arise around the ostiomeatal complex at the middle meatus.¹² Some polyps may only be detected with CT imaging studies.

In approximately 80% to 90% of white patients with CRSwNP there is a prominent tissue eosinophilia.¹³ In whites, CRSwNP occurs almost exclusively in adults; in children, cystic fibrosis should be considered. Histologically there is epithelial damage, a thickened basement membrane, edematous and fibrotic stromal tissue, and reduced numbers of vessels and glands.⁷ Immunologically, there is more of a T_H2 skewing; however, this likely is an oversimplification of a complex process.^{7,10} Markers of allergic inflammation, such as eosinophil cationic protein, IL-4, and IL-5, do not differ locally in the sinonasal mucosa between atopic and nonatopic persons with nasal polyposis.⁷

Allergic fungal rhinosinusitis. The histopathologic criteria required for the diagnosis of allergic fungal rhinosinusitis (AFRS) are (1) allergic mucin present on gross and/or histopathologic examination; (2) either (a) methenamine silver stain of allergic mucin positive for fungal hyphae but no fungal hyphae are seen in the mucosa (with or without positive fungal culture) or (b) silver stain negative and positive fungal culture; (3) sinus mucosal H&E stain characteristic for AFRS; and (4) exclusion of other histopathologic fungal diseases.¹⁴ An important acute process that should be excluded is acute invasive fungal rhinosinusitis in an immunocompromised host.¹⁵ It occurs over a time course of <4 weeks and is considered an emergency because predominant fungal vascular invasion occurs.¹⁵

AFRS is CRS accompanied by opacification of at least one sinus with allergic mucin. What distinguishes this condition from other CRS subtypes is that viable fungal hyphae can be isolated from the mucin and fungal-specific IgE is often present in the serum.¹⁶ In addition, CT imaging often shows

hyperdensities within opacified sinuses, suggestive of accumulations of allergic mucin; on MRI, T2-weighted images show marked low signal or even signal void.¹⁷ The pathogenesis of AFRS is thought to involve sensitization to fungal allergens, eliciting an IgE-mediated inflammatory response in the sinonasal cavity. On re-exposure to an environment with high fungal content hyperresponsiveness is increased in the upper and lower airways in sensitized persons.¹⁵ The patient in this case study did not meet criteria for AFRS because fungal stains and cultures were negative. In addition, acid-fast bacilli stain and culture were negative.

Aspirin-exacerbated respiratory disease. Aspirin-exacerbated respiratory disease (AERD) refers to the triad of asthma, CRSwNP, and aspirin sensitivity. The prevalence of AERD is unknown, with some estimates suggesting that 15% to 20% of patients with asthma and CRSwNP have AERD.^{18,19} Symptoms after aspirin ingestion vary, ranging from upper respiratory complaints of nasal congestion, rhinorrhea, and sneezing to more severe lower respiratory symptoms of bronchospasm. Aspirin-induced bronchospasm is generally more severe than bronchospasm induced by histamine inhalation, lasts longer, and responds poorly to bronchodilators.²⁰

The mechanisms that result in the development of respiratory symptoms with aspirin exposure are not completely understood. It is theorized that patients with AERD have a baseline increased level of circulating leukotrienes, which are synthesized from arachidonic acid via 5-lipoxygenase (5-LO). 5-LO is normally regulated by the inhibitory protein prostaglandin E₂, which is synthesized by the enzyme cyclo-oxygenase-1 (COX-1). Aspirin inhibits COX-1 activity, and in persons with AERD, this inhibition of COX-1 activity leads to profound inhibition of prostaglandin E₂ synthesis, unregulated activity of 5-LO, and continued production of leukotrienes, with resulting inflammation.²⁰ However, this mechanism does not explain why only a select group of persons with CRS have idiosyncratic reactions after ingesting aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs).

In terms of disease severity, persons with AERD have worse sinus disease than persons who tolerate NSAIDs. They have significantly worse outcomes, including preoperative CT scores (Lund-Mackay scoring) and nasal endoscopy scores (Lund-Kennedy scoring) compared with persons with CRSwNP tolerant to NSAIDs.^{21,22}

Sarcoidosis and CRS

Our patient met the international criteria for definite ocular sarcoid, which is defined as a biopsy-supported diagnosis with a compatible uveitis.²³ Ocular symptoms of sarcoidosis are relatively common with 25% to 50% of patients with sarcoid manifesting with ocular symptoms.^{24,25} A chest CT at the time of the patient's diagnosis showed bilateral hilar and mediastinal adenopathy. However, on follow-up with the pulmonary division she was not felt to have active sarcoid because proptosis resolved and she did not manifest pulmonary symptoms off systemic corticosteroids. She refused follow-up chest imaging. In terms of sarcoid rhinosinusitis, no diagnostic criteria are published; however, it should be in the differential with the coexistence of CRS with at least 2 of the following 3 signs: nasal crusting, anosmia, or epistaxis.²⁶⁻²⁹ The case patient had anosmia only, a common symptom of CRSwNP. Therefore, although she had

ocular sarcoidosis along with AERD (which has not been previously reported), sarcoid rhinosinusitis is not likely the cause of her persistent nasal symptoms. In addition, no reports implicate sarcoidosis as the cause of either nasal polyps or AERD.

Structural disorders

Structural disorders are often unilateral. The nasal septum forms the central support structure for the nose; therefore, deformity of this structure can cause significant symptoms of nasal obstruction.³⁰

A relatively uncommon structural cause of nasal obstruction is mucocoeles, which are caused by obstruction of sinus ostium. They are histologically benign, mucus-containing sacs lined with epithelium. However, mucocoeles slowly expand as they fill with mucus, leading to symptoms of obstruction or worse complications, such as infection or expansion into and destruction of adjacent structures.³¹ Diagnosis is through imaging studies with sinus CT and definitive treatment by surgical decompression into the nose.³²

Other structural causes of nasal obstruction include foreign bodies, adenoid hypertrophy, concha bullosa, and tumors.

TREATMENT OPTIONS

Acute bacterial rhinosinusitis

Although most cases of ARS are viral in origin, treatment of bacterial infection should be strongly considered with symptoms lasting longer than 10 to 14 days or with recrudescence of symptoms after progressive improvement. The most common bacterial pathogens in ABRS are *Streptococcus pneumoniae*, *Haemophilus influenza*, *Moraxella catarrhalis*, *Streptococcus pyogenes*, and *Staphylococcus aureus*.³³ The antibiotics currently approved by the United States Food and Drug Administration for ABRS are amoxicillin-clavulanate, clarithromycin, cefprozil, cefuroxime axetil, loracarbef, levofloxacin, azithromycin, trimethoprim-sulfamethoxazole, and moxifloxacin. Although multiple studies have compared antibiotic choices for adult ABRS, not one was found to be superior.⁵ However, given concerns over bacterial resistance, the Infectious Diseases Society of America no longer recommends the use of macrolides for empiric treatment of ABRS.³³ The Infectious Diseases Society of America recommends amoxicillin-clavulanate as first-line therapy and second-line agents consisting of doxycycline, levofloxacin, and moxifloxacin.³³ Intranasal corticosteroids (INCSs) are beneficial in adult ABRS, whereas other adjunct therapies, such as nasal decongestants and oral antihistamines, show less benefit.⁵ In children with uncomplicated ABRS, amoxicillin is a good first choice, although there are areas where penicillin resistance to common causative organisms is >50%. Other options include amoxicillin-clavulanate or cephalosporins, and for those with beta-lactam allergy, macrolides or trimethoprim-sulfamethoxazole can be used. In the pediatric population INCSs may have a beneficial ancillary role when used in conjunction with antibiotics.⁵

Chronic rhinosinusitis

Because CRS is a chronic inflammatory disease, medical management should be directed at controlling inflammation and treating exacerbations. Daily use of INCSs is the mainstay of therapy for CRS, especially for persons with nasal polyposis. INCSs serve to modify the disease process by decreasing the number of inflammatory cells (eosinophils, T lymphocytes, dendritic cells, and mast cells) through inhibition of their

migration out of the circulation and survival in tissue.³⁴ Because patients with CRSwNP tend to have more difficulty in controlling their disease, higher doses of INCSs are often implemented.³⁵

Although INCSs should be standard medical treatment in CRSwNP, oral corticosteroids are often used for exacerbations of disease because they result in improvement in both objective (polyp size) and subjective (hyposmia score) measures.³⁶ The use of systemic corticosteroids in CRS should be weighed against side effects.

The use of antibiotics in CRS is more controversial. The most common bacterial pathogens in acute exacerbations of CRS are the same as those isolated in ARBS with the addition of *Pseudomonas aeruginosa*.³⁷ No antibiotics for CRS are approved by the Food and Drug Administration; longer courses of the same antibiotics used for ABRS are often used for acute exacerbations of disease in CRS. There are even less data on the use of long-term (prophylactic) antibiotic therapy in CRS. Some studies do show benefit with long-term antibiotics on subjective and objective measures; however, the benefits were not sustained after cessation of antibiotic therapy.³⁸ In addition, the long-term use of antibiotics increases the risk of developing resistant organisms.⁵ In terms of the efficacy of topical antibiotics for CRS, no studies show benefit over saline irrigation.⁵ The use of nasal saline irrigation is common in CRS, and data have indicated that it improves symptoms.^{39,40} Immune deficiency such as common variable immunodeficiency or specific antibody deficiency should be considered in cases of CRS refractory to usual medical therapy.⁴¹ Our patient had normal immune studies. Finally, if medical management fails to control disease, FESS may need to be used. A recent prospective study that compared medical management with surgical management of CRS showed that patients who underwent FESS had greater improvements in quality of life, reduced exposure to antibiotics, and fewer missed days from work or school.⁴² While that study was not randomized and did not find differences in objective measures of sinus disease, it does show that surgery may be necessary when aggressive medical management fails to control disease.

Allergic fungal rhinosinusitis

No definitive guidelines are available on the treatment and management of AFRS. It is generally agreed that the most important step in AFRS treatment is surgical removal of all obstructing allergic mucin and diseased mucosa, because failure to adequately clear disease is associated with greater chance of relapse.⁴³ In addition, the use of oral corticosteroids has been shown to improve clinical outcomes after surgery for AFRS and prolong the time between subsequent surgeries for recurrent disease.⁴⁴ Systemic antifungal medications have not been shown to be effective in AFRS and are not recommended for disease management.^{17,43} The effectiveness of topical sinonasal antifungal therapies for AFRS has not been adequately studied.

Aspirin-exacerbated respiratory disease

Patient education on the identification and avoidance of NSAIDs is a critical first step in treatment of AERD than in other forms of CRS. Alternative safe medications such as acetaminophen and selective COX-2 inhibitors, such as celecoxib, should be recommended.⁵ Leukotriene receptor antagonists (LTRAs), such as montelukast, should be used because they have been shown to improve objective measures (forced expiratory volume at 1 second and peak expiratory flow rate) and subjective

measures (asthma quality of life and rescue bronchodilator use).⁴⁵ Montelukast improved our patient's symptoms; however, no peer-reviewed studies show that LTRAs improve upper airway symptoms in AERD specifically. In fact, studies have shown that the use of LTRAs during aspirin desensitization essentially shifted symptoms from the lower airway (such as bronchospasm) to the upper airway.^{46,47}

Aspirin desensitization therapy has been shown to significantly reduce the number of sinus infections per year, hospitalizations for asthma per year, use of systemic corticosteroids, and numbers of surgeries for sinus disease.⁴⁸ Desensitization can be safely performed in an outpatient setting in persons with well controlled, mild-to-moderately severe asthma, as long as proper safety monitoring and personnel are readily at hand.⁴⁹ Aspirin desensitization seemed to be helpful in our patient.

Because of the extent of disease, at some point, most persons with AERD will require surgical intervention to relieve symptoms and to remove polyp tissue. However, data indicate that surgery may be less effective in AERD, because these patients generally have more surgeries and higher rates of recurrence of both symptoms and polyp disease than persons with aspirin-tolerant CRSwNP.^{5,50} Our patient, unfortunately, falls into this category of CRS with worse outcomes.

SUMMARY

Multiple causes exist for symptoms of nasal obstruction, ranging from mucosal to structural abnormalities. The patient we presented had several unique pathologies occurring simultaneously. She had isolated ocular sarcoidosis, which further yielded a diagnosis of chronic rhinosinusitis during the work-up for sarcoid. She was further classified as having aspirin-exacerbated respiratory disease, given her history of asthma, nasal polyposis, and upper airway symptoms after aspirin ingestion. AERD proved difficult to treat because she had multiple exacerbations that required antibiotics and she refused repeat oral corticosteroids. She showed improvement with aspirin desensitization but continued to show significant polyp burden that will likely require surgical intervention. Aggressive medical management of CRS is necessary to limit exacerbations and the need for surgery and improve quality of life.

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