

Intranasal drug-induced fungal rhinopharyngitis

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Background: Intranasal drug abuse has long been recognized as an etiology of sinonasal pathology. However, the intranasal use of prescription and nonprescription drugs has surpassed the use of illicit drugs, and the pattern of presentation and required therapeutic intervention appears to be different. We report on our experience with these patients, along with a successful treatment algorithm for this disease process.

Methods: Retrospective chart review of 9 consecutive patients who presented with rhinopharyngitis and a history of intranasal opioid and/or acetaminophen abuse, from 2007 to 2010, at a tertiary referral center.

Results: Nine patients were found to have abused intranasal hydrocodone/acetaminophen, oxycodone/acetaminophen, or acetaminophen and were diagnosed with rhinopharyngitis. Sinonasal pain and odynophagia were the most common chief complaints and 8 of 9 patients reported previous antibiotic failures. On endoscopy, all patients exhibited a thick, white, exudative process involving the nasal septum and lateral nasal mucosa. Five of 9 exhibited large septal perforations. Seven of 9 exhibited white, exudative

pharyngitis. Seven of 9 patients had identifiable fungal organisms on culture, including 5 with species of *Candida* and 3 with *Aspergillus*. Two patients grew *Staphylococcus aureus*. Five patients were compliant with follow up. All 5 showed significant improvement in symptoms and examination, following treatment with oral and topical antifungal therapy and nasal irrigations.

Conclusion: Intranasal opioid and acetaminophen abuse is often associated with the development of fungal rhinopharyngitis. Recognizing that this process is primarily fungal in origin is paramount to successful treatment, as most patients respond well to antifungal therapy when compliant with treatment. © 2011 ARS-AAOA, LLC.

Key Words:

acetaminophen; drug abuse; fungal; intranasal; narcotic; nystatin; pharyngitis

How to Cite this Article:

Houlton JJ, Donaldson AM, Zimmer L, Seiden A. Intranasal drug-induced fungal rhinopharyngitis. *Int Forum Allergy Rhinol*, 2011; 00:X-XX

Intranasal drug abuse has long been recognized as a cause of significant sinonasal pathology. Intranasal cocaine use, the most commonly cited offender, has been associated with septal perforation, palatal defects, and saddle-nose deformity.¹⁻⁴ However, the intranasal use of prescription and even nonprescription drugs has surpassed the use of illicit drugs. While similar complications have been reported, the pattern of presentation and required therapeutic intervention appears to be different. Presently, we report on

our experience with patients who have abused intranasal acetaminophen/opioid products.

Over the last 3 years at our institution, 9 patients with a history of intranasal opioid and acetaminophen abuse have presented with severe rhinopharyngitis. Patients present with weeks to months of severe facial pain, odynophagia, and nasal obstruction. A transition from snorting opioid-containing medicines to snorting crushed acetaminophen tablets in order to at least temporarily relieve nasofacial pain is reported. Physical exam generally reveals a thick, white, exudative process involving the nasal mucosa, soft palate, and pharynx. Multiple rounds of antibiotics fail to resolve symptoms.

Complications related to the intranasal abuse of opioid and acetaminophen products have rarely been reported in the literature. An Ovid Medline literature search resulted in 3 pertinent results.⁵⁻⁷ Only 1 of these studies reported an association between intranasal drug abuse and fungal infection.⁶

Presently, we report our experience with fungal rhinopharyngitis associated with intranasal opioid and

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Potential conflict of interest: None provided.

Received: 20 August 2011; Revised: 14 October 2011; Accepted: 5 November 2011

DOI: 10.1002/alr.21001

View this article online at wileyonlinelibrary.com.

TABLE 1. Clinical features of patients with rhinopharyngitis secondary to intranasal drug abuse

Case	Age (years)	Sex	Symptoms	Intranasal drug	Physical findings
1	30	M	Sore throat, dysphagia, odynophagia	Acetaminophen	Excessive nasal crusting, septal perforation, marked exudative pharyngitis
2	40	M	Nasal congestion, nasal pain	Acetaminophen	Nasal crusting, large septal perforation
3	32	F	Nasal pain, nasal obstruction, odynophagia	Oxycodone/acetaminophen; acetaminophen	Saddle nose deformity, subtotal septal perforation, white exudate covering the entire nasal cavity, white exudate covering oropharynx
4	28	M	Nasal pain, nasal congestion	Hydrocodone/acetaminophen; acetaminophen	Septal perforation with crusting white exudate within nasal cavity
5	33	F	Sore throat	Hydrocodone/acetaminophen	No septal perforation, nasal mucosa edema with purulent discharge, oropharynx lined with fibrinous exudate
6	44	M	Nasal pain, nasal congestion	History of snorting pain medications	No septal perforation, right nasal cavity mucosa edematous, left nasal cavity with crusting
7	32	M	Facial pain, nasal pain	Oxycodone/acetaminophen; acetaminophen	No septal perforation, right nasal cavity mucosa edematous with white exudate (only snort drug through right nasal cavity)
8	40	F	Nasal pain, sore throat	Oxycodone/acetaminophen; acetaminophen	No septal perforation, severe necrosis of bilateral inferior turbinates, floor of nasal cavity, and nasopharynx
9	36	F	Dysphagia, odynophagia	Hydrocodone/acetaminophen; acetaminophen	Septal perforation, white exudate on septum and along bilateral inferior turbinates, ulceration of inferior turbinate mucosa, exudative debris along posterior pharynx

acetaminophen abuse. This series represents only the second report to describe this association, and the first to present a treatment regimen for this infectious process.

Materials and methods

Approval was granted by the Institutional Review Board of The University of Cincinnati Academic Health Center. Data was retrospectively reviewed for all consecutive patients diagnosed with fungal rhinosinusitis or fungal rhinopharyngitis, and whose social histories were positive for intranasal drug abuse of any kind. Data was collected from the clinical records of 2 academic otolaryngologists specializing in rhinology at an academic, tertiary referral center from 2007 to 2010. Data collected included salient details of the history and physical examination, demographic data, operative summaries, culture results, treatment interventions, response to therapy, history of drug use, and compliance with medical care.

Results

History

Nine patients were diagnosed with fungal rhinopharyngitis and reported a history of intranasal drug abuse. Median age was 33 years old (range, 28–44 years), and 56% (5/9) were of male gender. In general, patients presented with a history of nasal/facial pain, odynophagia, dyspha-

gia, and nasal obstruction, with or without mucopurulent rhinorrhea. Duration of symptoms ranged from 3 weeks to 6 months. In addition to sinonasal symptoms all patients had a component of pain as part of their chief complaint. Pain was characterized as nasofacial pain, or odynophagia, and was generally described as severe and burning pain. Eight of 9 patients reported failing more than 2 courses of antibiotics prior to presentation. In addition, 2 patients complained of velopharyngeal insufficiency at presentation, and were later found to have palatal erosion on physical exam. Pertinent details of patient presentations are displayed in Table 1.

Eight of 9 patients admitted to actively using intranasal drugs at the time of their first clinic appointment, whereas 1 patient reported previous use but would not expound on details. Of the 8, acetaminophen-containing narcotic pain medicines (either oxycodone/acetaminophen or hydrocodone/acetaminophen) and/or over-the-counter crushed acetaminophen were used. Two patients admitted to hydrocodone/acetaminophen use only, 2 patients used acetaminophen only, while the other 4 used hydrocodone/acetaminophen or oxycodone/acetaminophen along with crushed acetaminophen. During the initial intake, patients generally described euphoria-seeking as their initial motivation for snorting crushed narcotic medications. However, patients commonly described developing nasofacial pain, which was then only relieved by continued intranasal use of narcotic pain medicines, or by snorting



FIGURE 1. Severe presentation of intranasal drug induced rhinosinusitis. White exudate seen along right lateral nasal wall, inferior turbinate, septum, and floor of nasal cavity.

crushed acetaminophen tablets. Eight of 9 patients asked for narcotic pain medications at their initial visit.

Physical exam

On examination, patients were uniformly found to have a thick, white, exudative process, with underlying boggy mucosal edema, involving the nasal septum, inferior turbinates, and lateral nasal mucosa (Fig. 1). Six of 9 (66%) also had large septal perforations, and 2 (22%) patients had severe erosion of the lateral nasal mucosa and turbinates. One (11%) patient had a saddle-nose deformity. The majority of patients had involvement of the oropharynx, with 7 of 9 (78%) having a white, exudative pharyngitis along the posterior pharyngeal wall. Two of these patients also had significant erosion of the soft palate.

Workup

Eight of 9 patients had identifiable organisms on sinus culture. This included 4 patients with *Candida albicans*, 1 patient with *Candida tropicalis*, and 3 patients with unspecified *Aspergillus* species. Two patients with *Candida albicans* also had concomitant *Staphylococcus aureus* grown in culture, as did 1 other patient. Four patients were taken to the operating room for debridement, culture, and nasal biopsy, with culture results included as above. All 4 biopsies showed inflammatory change, numerous fungal elements, and no evidence of vascular invasion or malignancy. No other patients underwent surgical intervention.

Treatment

In general, patients were prescribed fluconazole 100 mg twice daily (BID) for 2 to 3 weeks, 15 mL of nystatin swish and swallow BID for 2 to 3 weeks, and nasal saline sprays or rinses. Three patients were also prescribed itraconazole irrigations. The 3 patients with concomitant *Staphylococcus aureus* were prescribed anti-*Staphylococcus* antibiotics, consistent with antibiotic sensitivities.

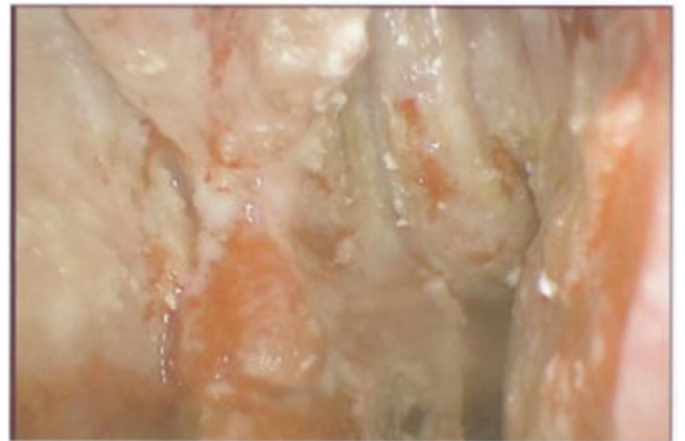


FIGURE 2. Endoscopic view of left nares of a patient with fungal rhinopharyngitis, illustrating white exudative rhinitis with subtotal septal perforation. (A) Exam on initial presentation. (B) Exam after partial response following a 2-week course of antifungal treatment.

Response to treatment

Five patients returned for serial follow up appointments ranging from 2 to 4 clinic visits. All 5 of these patients showed significant improvement in symptoms and resolution of inflammatory/exudative changes on physical examination at 4-week to 6-week follow up appointments. Even after a short course of antifungal treatment physical findings were significantly improved (Fig. 2). One patient, who initially responded to treatment, was treated for a second time 10 months after her initial visit. She reported a relapse in intranasal acetaminophen-product use, and responded well to a second course of antifungal treatment. Four patients did not return after the initial clinic visit.

Discussion

Patients with intranasal drug-induced fungal rhinopharyngitis almost uniformly present with nasofacial pain and odynophagia as their chief complaint. Pain is typically accompanied by symptoms of nasal obstruction and difficulty swallowing. On exam, patients are found to have

a thick, white, exudative inflammation of the nasal mucosa, generally resulting in some degree of necrosis and septal perforation. Most will also have an accompanying exudative pharyngitis. Cultures generally revealed *Candida* or *Aspergillus* species of fungi, which usually responded well to treatment. Contrary to the report by Yewell et al.,⁶ none of our patients in whom histology was obtained demonstrated invasion. This is consistent with our patients' clinical response and is comparable with other noninvasive forms of fungal sinusitis.^{8–10}

In terms of treatment, recognizing that this process is primarily fungal in nature is paramount, as patients typically report multiple failed attempts at nonfungal therapy. We recommend the prescription of both twice-daily oral fluconazole and nystatin swish and swallow. Nasal saline irrigations and an oral topical anesthetic mixture are also prescribed. Twice-daily itraconazole nasal irrigation can be added in recalcitrant or severe cases. Serial in-office nasal debridement may also play an important role in hastening resolution of infection, analogous to the treatment of otitis externa.

When patients present with the prototypical whitish nasopharyngeal exudate and history of intranasal drug abuse, we recommend initiating antifungal therapy without operative biopsy as a reasonable first step. However, given the erosive appearance of the nasal cavity an autoimmune process, such as Wegner's granulomatosis, or other granulomatous process, should remain high on the differential. If patients fail to respond to antifungal therapy we advocate operative nasal debridement and biopsy.

Multiple challenges are posed when treating this patient population. Pain management can be quite challenging, as patients uniformly report severe pain requiring narcotic pain medicines at initial presentation (8/9 in our series). However, by rule, these patients are addicted to intranasal drugs, the very culprit responsible for their sinonasal pain. Therefore, we caution against the prescription of narcotic-containing pills. Distinguishing real pain from drug-seeking behavior can be very difficult and we encourage collaboration with addiction specialists whenever feasible. In our experience, the fungal infection resolves much more rapidly when intranasal drug abuse is ceased. Compliance with treatment can also pose a challenge as follow-up is often inconsistent, and relapses are common. Only 56% of patients in our series returned for a second follow-up appointment.

Our report represents only the second series to describe an association between intranasal opioid and acetaminophen use and fungal rhinopharyngitis. Cocaine, a more frequently studied drug, has been reported to result in nasal inflammation, septal perforation, and mucosal erosion similar to that exhibited in our case series.^{1–4} However,

only acetaminophen and acetaminophen-containing opioid products have been associated with fungal infection.^{5–7,11} This suggests that acetaminophen, opioids, and/or their fillers increase the risk of intranasal fungal infections, rather than the mucosal necrosis itself.

Several theories on the mechanism by which intranasal prescription drugs, including those containing acetaminophen, lead to fungal infections have been entertained. For instance, these medications may cause a localized immunosuppression, which fosters growth of fungal organisms. Name-brand forms of acetaminophen such as Tylenol have several inactive ingredients including cellulose, corn starch, magnesium stearate, and sodium starch.¹² Cellulose has been extensively studied regarding its biodegradation into glucose and the need for enzymes such as cellulase in order for this to happen. Certain *Aspergillus* species have been studied and noted to have an elevated cellulase production. While these studies have generally been performed using cellulose in a culture medium, it is reasonable to suggest that the cellulose found in crushed acetaminophen and acetaminophen containing products may lead to the increased growth of saprophytic fungal organisms.

Definitive conclusions about treatment efficacy are significantly limited due to the study's small number and retrospective nature. We are aware of other physicians who have reported, through personal communications, resolution of symptoms with aggressive nasal irrigation alone. A prospective study comparing nasal saline irrigation to nasal irrigation plus oral fluconazole and nystatin would ultimately be necessary to determine efficacy of fungicidal medications and is encouraged.

As the abuse of prescription narcotic medications continues to increase, and the intranasal route becomes increasingly popular, this condition will be appearing with greater frequency. Patients typically do not volunteer a history of drug use, so the clinician needs to be able to recognize this condition and initiate an effective avenue of treatment.

Conclusion

Intranasal opioid and acetaminophen abuse is associated with the development of fungal rhinopharyngitis. Recognizing that this process is primarily fungal in origin is paramount to successful treatment, as most patients report failure when treated with antibiotics, but respond well to antifungal therapy. Treatment in this patient population is often challenging as patients are frequently noncompliant and often exhibit drug-seeking behavior. We advocate referral to addiction specialists whenever feasible. 

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