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Intranasal Hydrocodone-Acetaminophen Abuse Induced Necrosis of the Nasal Cavity and Pharynx

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Abstract

Objectives—Two million new users will abuse prescription narcotics this year, most commonly hydrocodone. The most commonly prescribed form is hydrocodone-acetaminophen (HA). Many individuals crush the tablets and snort the product to take advantage of the rapid trans mucosal delivery of narcotics. The resultant pathology of intranasal hydrocodone acetaminophen abuse (INHAA) has been described only in a few case studies.

Study Design—Retrospective chart review.

Methods—Two private and one academic otolaryngology practices in Kentucky searched their patient charts for patients with morbidity from intranasal abuse of hydrocodone acetaminophen tablets. We identified thirty-five patients who presented for treatment between 2004 and 2011.

Results—The majority of patients will initially deny the behavior frequently delaying diagnosis. Physical exam findings of white powder covering an underlying nasal mucosal necrosis are characteristic of this condition during active INHAA. Follow up was limited as only 26% returned for follow up care. Patients commonly presented with orofacial-nasal pain (43%) and sino-nasal congestion and discharge (43%). Active necrosis or prior tissue loss was noted in 77% of patients. Fifty-one percent of patients presented with septal perforations, and 26% with palatal perforations. Two cases of invasive fungal sinusitis were clearly documented with one resulting in death.

Conclusions—The vast majority of cases presented with characteristic physical findings that included acute necrosis of soft tissue that can progress to destroy oronasal structures. In the absence of invasive fungal disease, the condition is self-limited after cessation of INHAA and performance of local nasal debridement and nasal hygiene.

Study Design—Chart review, level of evidence: 4

Keywords

Allergy/Rhinology; Nasopharynx; Hydrocodone

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Conflict of Interest: None

Study was presented as a poster to the Triological Society at the 2012 COSM, April 18-22, San Diego, CA.

Introduction

Abuse of prescription pain medication continues to be large problem in today's society. According to the US Department of Health and Human Services, in 2007 an estimated 5.2 million persons used prescription pain relievers non-medically within the past month.[1] As of 2010, it was predicted 2 million new users will abuse prescription narcotics each year, most commonly hydrocodone.[2] Intranasal abuse of drugs such as cocaine and heroin is well described. In our central Kentucky practices, we have seen the emergence of intranasal abuse of orally formulated hydrocodone/acetaminophen (HA) combinations and its toxic sequelae on the upper aerodigestive tract's soft and hard tissues. It has now become far more prevalent since our group first published a case series of this condition in 2002.[3] The small number of case reports that followed began to detail the effects of intranasal hydrocodone-acetaminophen abuse (INHAA).[4-7] These studies point to a more fulminant destructive disease process than that described in other types of nasal drug abuse.[8-11] This behavior is reported with an acute and rapid destruction of the septum and palate, as well as cases that led to invasive fungal rhinosinusitis.[3] We present the first large series of patients presenting with upper aerodigestive tract pathology secondary to INHAA. From analysis of this group of patients, we hope to better characterize the presentation and manifestations of this condition.

Methods

Thirty-five patients were identified across three Otolaryngology practices in central Kentucky from 2004 to 2011. One practice was a solo practitioner, the second a private ENT group practice, and the third a teaching-university group practice. Patients documented to have nasal manifestations of INHAA were retrospectively identified through a variety of mechanisms including physician memory, searches of inpatient logs, and searches of diagnostic billing codes. We then abstracted general demographic information, presenting symptoms, substance abused, duration of the abuse, prior substance abuse history, and past medical history. Pathology reports, microbiology reports, operative reports, and archived endoscopic images were also abstracted from the inpatient and outpatient medical records. Patients were excluded if it was determined a different substance was abused, or if definitive evidence of abuse could not be established.

This study was approved by the University of Kentucky's IRB (protocol #11-0345-p2H).

Results

Thirty-five patients were identified, 22 women (63%) and 13 men (37%). Ninety-one percent were from rural counties in Kentucky. The ICD 9 system is vague in coding this type of nasal pathology. We found this condition was most frequently coded as 478.19 "Other Disease of Nasal Cavity and Sinus," which yielded five hundred patients per year making it impractical in identification. We found the ICD-9 coding scheme for drug abuse frequently missing, in large part due to the ambiguity of history in these patients at initial presentation. The majority of patients will deny INHAA. Some will persist for a period of time with this pretense, even when confronted with direct evidence of pill casings and high levels of HA in their nasal debris. Only nine patients (26%) maintained all follow up appointments, and 22 (63%) never returned for any subsequent follow up care.

Details of INHAA, such as duration of abuse, onset of symptoms and progression of disease were not uniformly documented in the medical records. Four patients (11%) never admitted to nasally abusing pain medications, however their symptoms, physical findings, access to

H-A were so characteristic we included these in our group. Twenty-two patients (63%) were prescribed the medication they were abusing nasally at the time of presentation.

The two most common presenting symptoms (Table 1) were orofacial-nasal pain (43%) and sino-nasal congestion and discharge (43%). Signs and manifestations of INHAA are shown in table 2, and include septal perforations in 51% and palatal perforation in 26%.

Upon exam, frank oronasal tissue necrosis was noted in 27 patients (77%). This was typically covered with a white powdery coating (Figure 1). When necrosis was not noted, the patient appeared to have begun the habit recently and pill debris was uncovered upon exam. A few patients claimed to have ceased INHAA for years, but appeared to have persistent necrosis of the nasal mucosa and break down of the septum and palate. Extracting a reliable detailed history of abuse patterns can be challenging, and we are uncertain if the necrosis is prolonged, or the history of long standing cessation was dubious. In several patients the actual blue pill coatings of the tablets were seen on nasal inspection. Hydrocodone in some cases was isolated from this debris on drug testing. Nasal septum perforation (Figure 2) was noted in 18 patients (51%), with eight (23%) of these patients also co-presenting with a perforation of the hard or soft palate. In one additional case a palatal perforation was noted without an associated septal perforation. Tissue debridement, either in the office or in the operating room, was performed on 14 (40%) patients. The mucosal superficial necrosis was seen in several patients to extend from the nasopharynx into oropharynx typically involving the posterior oropharyngeal wall. One patient who had undergone previous radiation therapy had confluent manifestations that extended onto the supraglottic larynx.

Pathology reports and culture results were examined. Characteristic inflammation and necrosis were uniformly described (Figure 3). Fungal cultures were taken from six patients. Four cultures returned positive for growth, with two of the four patients (6%) being diagnosed both clinically and based on biopsy results with invasive fungal rhinosinusitis (*Aspergillus sp.*). Antifungal therapy was initiated in three of the four cases. Two of the cases resolved with therapy and debridement, the third patient suffered from Hemophagocytic lymphohistiocytosis, a significant immunosuppressive co-morbidity. His disease progressed rapidly in spite of aggressive debridement and antifungal therapy resulting in his demise. The fourth patient resolved without antifungal therapy. Bacterial cultures of the nose were obtained in six patients, three grew *MRSA, two Pseudomonas areugenosa* and one a non-resistant *Staphylococcus Aureus*.

Discussion

Our data reaffirms the destructive nature of INHAA. The majority of patients presented with necrosis of the oronasal mucosa, consistent with prior case reports.[3-7] During periods of active INHAA, this necrosis is easily recognized with characteristic, overlying white, crusty exudate in the nasal cavity that often extends down into the posterior oropharynx (Image 1). Thick, purulent discharge is commonly noted and found under the dried overlying material. The dense involvement of the mucosa leaves one with differential diagnoses including life-threatening conditions such as diphtheria and invasive fungal disease. Getting the patient to admit to abuse is often an arduous task. Clearly, ascertaining any detailed history of INHAA is not possible without cooperation. Since most patients initially deny the behavior, the clinician may need to resort to other investigations to render a diagnosis. The manifestations are characteristic, raising clinical suspicion. Patients who use one nostril exclusively will have unilateral disease which helps to rule out most infectious etiologies. In some cases it is possible to literally visualize crushed pill debris remaining in the nasal cavity, and in some

cases we have used drug analysis of nasal debris to confirm suspicion of IHAA. When confronted with this data, we attain patient cooperation with treatment.

The injury to the mucosa is characteristic, and in many cases the injury extends into the deeper structures. Eighteen (51%) patients developed perforations of the nasal septum, with eight of those developing perforation through the floor of the nose and through the palate, and an additional patient developing an isolated palatal defect. These perforation rates are higher than those of intranasal cocaine, reported between 4% and 11%.[8-11] The rate of septal perforation in INHAA illustrates the significant toxicity of this material upon the mucous membranes. Unlike cocaine, the INHAA mucosal injury frequently extends to involve the nasopharynx, and onto the posterior pharyngeal wall.

The two cases with invasive fungal sinusitis add complexity to understanding this pathogenesis. This is a significantly smaller percentage than Yewell et al, whom noted invasive fungal sinusitis in two of five patients, however selection bias and a small sample size could account for this discrepancy.[3] An unpublished case series reported at the American Rhinologic Surgery meeting in 2011 similarly supported a stronger link between INHAA and fungal infections. A localized immunosuppressive effect may contribute to the acquisition of invasive fungal sinusitis.[3] The concept that chronic opioid abuse has immunosuppressive effects is being validated.[12] Morphine has been shown to have adverse effects on the immune system, and evidence pointing toward opioids acting in concert with HIV-1 proteins to exacerbate immune cell dysfunction and survival exist.[13-15] The chronic irritation and subsequent breakdown of the mucosa combined with a local H-A induced immunosuppression could create an environment for fungal pathogens to invade the local tissues. The need for systemic antifungal therapy in this condition is unclear, and may be considered. The bacterial culture results were taken early in our series. All cases, in which INHAA ceased, improved spontaneously. If the behavior did not change, antibiotic/antifungal therapy was of no benefit. In the later years of our study, with the one noted exception, patients resolved without antibiotic/antifungal therapy. Our study includes one case of invasive fungal sinusitis with the expected typical lethal course in an immune compromised host. In the absence of these co-morbidities, conservative debridement and use of saline irrigation for nasal hygiene has been effective.

Patient education and participation is key. A majority of patients were abusing their own prescription pain medications at the time of presentation. INHAA reportedly provides more immediate pain relief than oral ingestion. Several of our patients with legitimate pain syndromes engaged in this behavior at the suggestion of friends and family, without understanding the possible consequences. This underscores the need for providers to quickly diagnose INHAA. Ideally, the informed participatory patient will cease the behavior. We typically work with their treating physician to alter therapy and discontinue the HA medication.

The management and treatment of a narcotic addict is challenging. The resulting destructive pathology produced by INHAA is painful. As expected, many will unwittingly seek relief by increasing their INHAA exacerbating the disease course. Once diagnosed, pain relief with narcotic management clearly requires caution. Introducing alternative nasal analgesics, such as topical lidocaine is helpful. Debridement of non-vital tissue appears to speed resolution by reducing the bacterial load and allowing effective saline irrigations. We will repair septal or palatal perforations as needed only after full healing and several months of abstinence from INHAA. Until that time we make use of temporary obdurators and silastic septal buttons.

The pathological mechanism of tissue destruction induced by intranasal H-A is not defined. Cocaine abuse similarly causes nasal irritation, crusting, epistaxis, and ultimately tissue necrosis with septal and palatal perforation.[10, 16] Cocaine induces acute vasoconstriction, followed by rebound dilation. The destructive properties of cocaine abuse are thought to be a result of its vasoconstrictive properties, which causes local ischemic injury and inflammation in the oronasal mucosa. Hydrocodone and acetaminophen lack these vasoconstrictive properties. We suspect that high concentrations and local hyperosmotic conditions could be responsible for the tissue necrosis. The well-described condition of pill induced esophageal injury has shown similar mucosal manifestations in the esophagus.[17, 18] When a pill is retained in the esophagus and in contact with the mucosa for a prolonged period frank ulceration and even perforation may occur. A wide variety medications cause this condition. Interestingly, one author describes white overlying exudate over the injured mucosa in several patients, similar to what we see in INHAA.[17] Perhaps the local concentration of acetaminophen is at issue, as hepatotoxic oral doses of acetaminophen can induce necrosis of olfactory mucosa.[19] One of the substances used in pill formulation may also participate in the tissue destruction.

The lack of follow-up, and challenges in attaining a reliable history make it difficult to reach firm conclusions regarding the pathophysiology and efficacy of treatment of the injuries induced by INHAA. The follow up rate for these patients is poor, as seen by both our data and others.[3] This lack of data forces us to present anecdotal observational data with all its limitations and biases. We feel strongly, however, that practitioners need to be aware of this condition that is now prevalent in ours and likely many other populations.

Conclusions

- Diagnosis of INHAA is imperative to instituting effective treatment of the addiction and the sino-nasal disease.
- Oronasal pain with crusty, white exudate overlying necrotic mucosa in the oronasal cavities is highly characteristic of INHAA.
- Abstaining from INHAA in combination with local debridement reverses progression of the disease.
- Our observations do not support a benefit from antifungal/antibiotic therapy.
- Concurrent invasive fungal rhinosinusitis must be considered especially in the immune compromised patient with INHAA mucosal disease.

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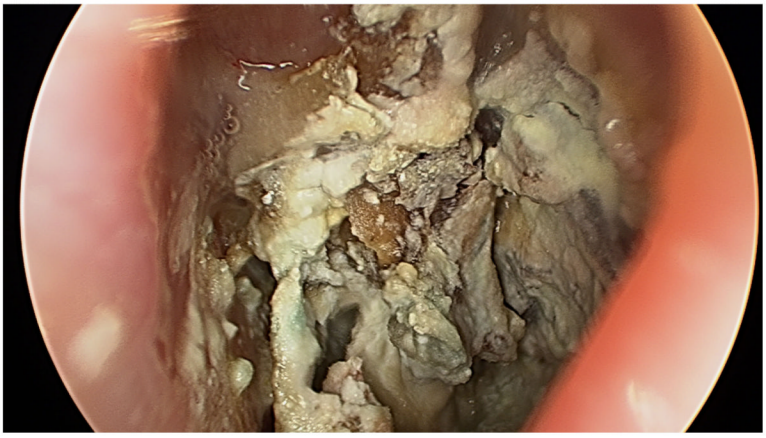

Figure 1.
Acute INHAA nasal manifestations of injury: The characteristic crusty, white exudate is noted overlying the necrotic and ulcerated mucosal surfaces.

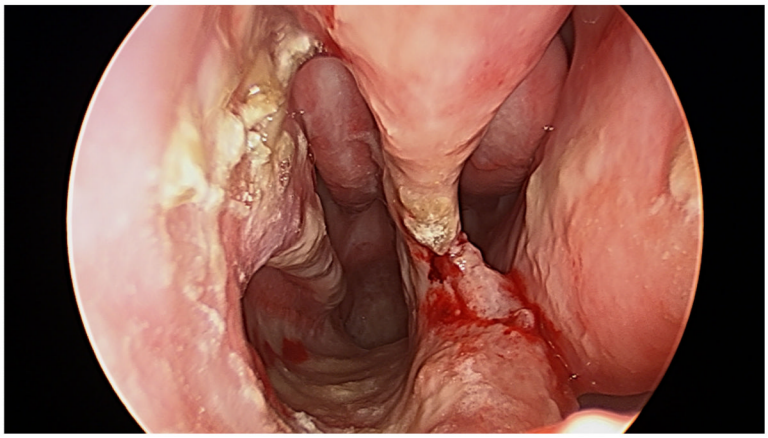

Figure 2.
Near total perforation of the nasal septum, post-debridement: This endoscopic photograph taken within a week of initial debridement and cessation of INHAA demonstrates healing of mucosa and clear cessation of the soft tissue destruction.

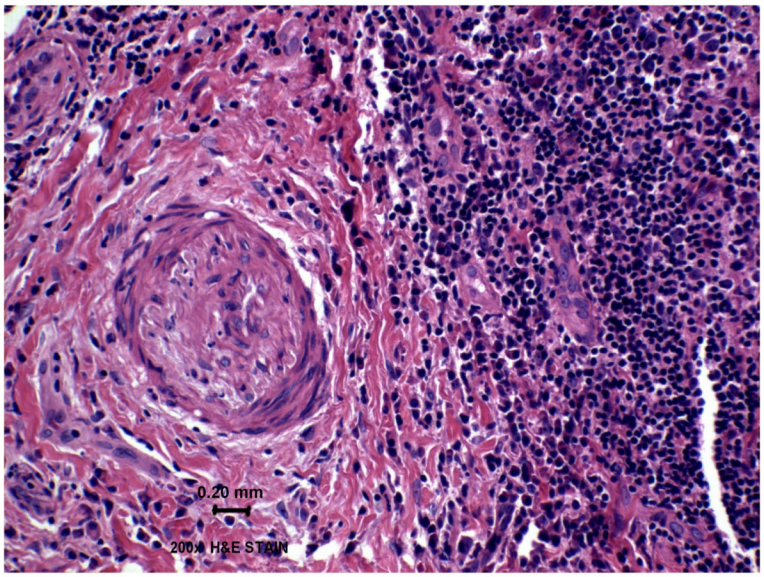

Figure 3.
Biopsy of involved nasal tissue. This high power magnified photomicrograph demonstrates extensive superficial exudates with underlying granulation tissue. The deep tissue on the septum shows extensive fibrous proliferation with a mixed chronic inflammatory cell infiltrate. There is no vasculitis present. There is intimal proliferation of some obliterative vasculopathy. There are scattered fragments of necrotic cartilage and focal osteonecrosis.

Table 1

Presenting symptoms as a percentage of all patients.

Presenting Symptom	N (%)
Orofacial pain	15 (43%)
Sinonasal congestion and/or drainage	15 (43%)
Dysphagia	11 (31%)
Hoarseness/Dysarthria	10 (29%)
Epistaxis	3 (9%)
Otalgia	8 (23%)

Table 2

Presenting physical findings as a percentage of all patients.

Signs of INHAA	N (%)
Mucosal necrosis and crusting	27 (77%)
Septal perforation	18 (51%)
Oropharyngeal ulceration	11 (31%)
Palatal perforation	9 (26%)
Fevers/chills	3 (9%)
Facial swelling	3 (9%)