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Chronic Invasive Fungal Sinusitis Associated with Intranasal Drug Use

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Abstract

Chronic invasive fungal sinusitis (CIFS) is a rare but potentially aggressive form of invasive fungal disease that occurs in immunocompetent patients. We report a case of CIFS in an otherwise healthy young adult associated with intranasal illicit drug abuse. The patient presented with non-healing nasal septal and palatal perforations. Biopsy demonstrated invasive *Aspergillus flavus* requiring surgical debridement and extended intravenous antifungal therapy. Tissue necrosis and ulceration related to intranasal drug use should be recognized as a potential risk factor for invasive fungal sinusitis.

Keywords

invasive fungal sinusitis; chronic granulomatous; invasive; aspergillus; mucor; cocaine; intranasal drug; sinusitis; perforation

INTRODUCTION

Invasive fungal sinusitis is an increasingly prevalent, but still rare infectious disease heralded by progressive tissue destruction, angioinvasion, and generally poor outcomes¹. Unlike acute invasive fungal sinusitis (AIFS), which usually occurs in immunocompromised hosts, CIFS typically presents in otherwise healthy individuals. The disease often progresses slowly over weeks or months, and a lack of obvious predisposing factors can present a diagnostic dilemma and delay needed surgical or medical interventions. Symptoms are often nonspecific and can include nasal obstruction, facial pain, rhinorrhea, headaches, and

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epistaxis. Left untreated, CIFS, like its acute counterpart, can result in proptosis, altered mental status, seizures, and intracranial complications^{2,3}.

The causative organisms in CIFS are saprophytic fungi such as the Zygomycetes (*Mucor*, *Rhizopus*, *Rhizomucor*) and multiple species of *Aspergillus*. These organisms typically inhabit decomposing organic matter and are generally widespread in the airborne environment. They often inhabit the upper and lower respiratory tract in humans and in certain circumstances can invade the sinonasal mucosa and result in aggressive infection and tissue necrosis. CIFS can be separated into granulomatous and non-granulomatous forms, based largely on the presence of soft tissue granulomas with fungal hyphae and multinuclear giant cells on histopathology. Granulomatous CIFS is rare in the United States, and is more commonly observed in Northern Africa and the Middle East⁴⁻⁶. The causative organism in most cases of granulomatous or nongranulomatous CIFS is either *Aspergillus flavus* or *Aspergillus fumigatus*^{4,5}. While AIFS presents primarily in immunocompromised individuals, CIFS presents in immunocompetent individuals and predisposing factors that contribute to its development are poorly understood. Herein, we describe the case of an otherwise healthy, young male who developed CIFS related to a nasal septal and palatal perforation and prior intranasal cocaine use.

CASE REPORT

A 24-year-old Caucasian male presented with intractable nasal and palate pain, and a history of progressive nasal congestion and rhinorrhea for three months. He also complained of worsening dysphagia, dysarthria, and an approximately thirty-pound weight loss. He reported a history of two small palatal erosions that initially developed two years earlier in the setting of intranasal cocaine abuse. His symptoms were fairly stable for more than a year, but a biopsy of the non-healing palatal lesions escalated the erosive process and resulted in progression of his symptoms. His past medical history was negative for immunodeficiency or malignancy, and was otherwise unremarkable. He was evaluated at multiple inpatient and outpatient facilities due to his worsening sinonasal symptoms and facial pain prior to presenting at our institution for further management.

Examination revealed a saddle nose deformity, nasal crusting and rhinorrhea. He had no focal neurologic complaints or related physical exam findings. Nasal endoscopy demonstrated heavy crusting, areas of mucosal necrosis, absent inferior turbinates, and erosion of the middle turbinates and maxillary sinus cavities. The nasal septum was largely absent with circumferential areas of crusting. The erosive process extended through the hard palate with almost complete deficiency of the soft palate. Scattered crusty, yellow-brown debris was noted in the nasal cavity and extending into the nasopharynx and oropharynx. Computed tomography (CT) imaging mirrored the physical exam findings, showing an extensive erosive process involving the palate, nasal cavity, and maxillary sinus without obvious intracranial pathology (Figure 1A). An MRI confirmed a lack of intracranial disease, and again showed extensive tissue loss involving the nasal septum, palate, and paranasal sinuses (Figure 1B).

A bedside biopsy of the palate and nasal septum was performed due to the patient's worsening symptoms and physical exam findings. Initial pathology was concerning for fungal invasion and the patient was subsequently taken to the operating room for a formal endoscopic exam and surgical debridement. This revealed partial absence of the nasal floor due to the large palatal perforation with the endotracheal tube easily visualized intranasally (Figure 2A). The soft palate was almost completely obliterated. Nonviable tissue and diseased mucosa were removed along the nasal floor, nasal septum, and lateral nasal walls until viable, bleeding tissue was encountered (Figure 2B).

Histopathology from the intraoperative debridement and tissue biopsy revealed numerous fungal hyphae within the mucosa, submucosa, and vascular lumen of bone (Figure 3). Also noted was a mixed inflammatory infiltrate with tissue necrosis. Flow cytometry demonstrated a small population of monotypic B cells, thought to be a clonal response to the overlying infectious or inflammatory process, but did not show any evidence of a hematologic malignancy. Hematoxylin and eosin staining was confirmed with Grocott's methenamine silver stain (GMS) and subsequent culture and speciation identified the fungus as *Aspergillus flavus*.

Postoperatively, intravenous amphotericin B was initiated, but this was subsequently changed to voriconazole after fungal speciation. He was subsequently discharged on an indefinite course of oral voriconazole with plans for obturation after resolution of his acute infectious process. He self-discontinued voriconazole approximately six weeks later. Upon evaluation five months after discharge, he denied nasal discharge, drainage, or facial pain, but did have bilateral midface flattening and a persistent saddle nose deformity. Nasal endoscopy showed absence of most intranasal structures with palatal and nasal septal perforations, as previously noted. The nasal mucosa was pink and healthy in appearance with no crusting or tissue necrosis. He was encouraged to pursue palatal prosthesis or obturation, and to consider filler injections to address his midface flattening.

DISCUSSION

CIFS is a rare clinical entity that primarily affects immunocompetent individuals and often presents challenges both in diagnosis and treatment. Previous case reports have associated CIFS with use of topical nasal steroids and chronic sinonasal disease^{2,4}, however, there is a lack of clear consensus regarding putative predisposing factors. Our patient presented with a large septal and palatal perforation and adjacent CIFS due to cocaine abuse. To our knowledge, this represents the first report of invasive fungal sinusitis associated with the intranasal use of illicit drugs.

Intranasal use of cocaine is associated with sinonasal tissue ischemia, palatal and septal perforation, and midline destructive lesions^{7,8}. Chronic use can result in progressive sinonasal symptoms and major complications that include orbital neuropathies, osteomyelitis, and intracranial abscesses⁹⁻¹¹. The exact etiology of such complications is unclear but may be secondary to cocaine-induced vasoconstriction and severe mucosal inflammation that ultimately results in ulceration and tissue necrosis. Non-healing ulcers and

areas of necrosis may increase susceptibility to invasive fungal organisms, which preferentially inhabit decomposing organic matter.

Diagnosis of CIFS, as outlined by deShazo et. al., requires 1) radiologic evidence of chronic rhinosinusitis, and 2) histopathological evidence of fungal hyphae within the sinonasal mucosa, submucosa, blood vessels or bone¹². However, findings on CT or MRI are often nonspecific and timely diagnosis of CIFS is consequently quite difficult. This is evident in the current report, as our patient was evaluated at multiple medical institutions over a three-month period without a diagnosis. The slowly progressive symptoms and destructive process identified on endoscopy ultimately heightened clinical suspicion and led to an accurate diagnosis and prompt treatment.

CIFS is notoriously challenging to treat, with frequent relapses, and often requiring use of oral or intravenous antifungals for several months. Treatment typically consists of surgical debridement and systemic antifungal therapy, most commonly with either amphotericin or voriconazole. Limited published evidence exists for CIFS and approximate survival rates are unknown. Since most patients with CIFS are immunocompetent, their disease is typically reversible with appropriate surgical and medical management, and their overall survival is consequently thought to be higher than patients with AIFS¹. As with AIFS, outcomes often depend on prompt diagnosis. The current report suggests that patients presenting with non-healing sinonasal ulcerations or necrotic septal or palatal perforations may be at increased risk of developing CIFS. A high index of suspicion for invasive fungal disease in patients with a history of intranasal drug use may lead to earlier diagnosis and more prompt surgical and medical management. Early biopsy of nasal septal or palatal perforations, areas of persistent crusting, or ulcerated areas of mucosa may therefore be warranted in this patient population.

CONCLUSIONS

Chronic invasive fungal sinusitis is an indolent, but potentially aggressive infection that typically occurs in immunocompetent individuals. Causative fungal organisms, such as *Aspergillus*, preferentially colonize decomposing or necrotic tissue, and in this case inhabited an ulcerated palatal and septal defect related to long-term intranasal cocaine abuse. Patients with mucosal ulceration or necrosis due to intranasal drug use may be at an increased risk of invasive fungal sinusitis.

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Figure 1.
Coronal non-contrast CT (A) and sagittal T1 MRI (B) showing obliteration of the nasal septum, soft palate and bilateral maxillary cavities.

Figure 2.

Intraoperative nasal endoscopy demonstrating extensive crusting and tissue necrosis (A). After debridement, areas of bleeding, viable tissue are demonstrated with a large palatal and septal defect (B).

Figure 3. Hematoxylin and Eosin staining of palatal biopsy showing abundant fungal hyphae branching at 45° angles, characteristic of *Aspergillus* (500X magnification).