Laryngotracheal mucormycosis: Report of a case

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Abstract

Airway mucormycosis is a deadly opportunistic infection that affects immunocompromised persons, particularly diabetics and those undergoing chemotherapy. Although it is typically a pulmonary or sinonasal infection, mucormycosis can affect the larynx and trachea, with devastating results. We report the case of a 46-year-old man with human immunodeficiency virus infection, hepatitis C infection, neurosyphilis, and recently diagnosed Burkitt lymphoma who presented with dysphonia and stridor after receiving one dose of intrathecal chemotherapy. Flexible laryngoscopy detected the presence of fibrinous material that was obstructing nearly the entire glottis. Surgical debridement revealed a firm mucosal attachment; there was little bleeding when it was removed. After debridement, the patient's dyspnea improved only to recur 2 days later. After an awake tracheotomy, laryngoscopy and bronchoscopy identified necrosis extending from the supraglottic area to the carina tracheae. Biopsies demonstrated hyphal architecture consistent with mucormycosis. Despite continued debridements, the fibrinous material reaccumulated. The patient was placed in hospice care; his airway remained patent, but he died from other causes several weeks after presentation. The management of airway mucormycosis is challenging and complex. Fungal airway infections should be considered in the differential diagnosis of an immunosuppressed patient who presents with dyspnea, dysphonia, and vocal fold immobility. Timely diagnosis and management are critical for a successful outcome, although the prognosis is poor if the infection is widespread, even with the best of efforts.

Introduction

Airway mucormycosis is a rare, deadly opportunistic infection of the upper airway. It is typically found in diabetics and immunocompromised individuals. Only a few cases have been reported in the literature, but the incidence of fungal airway infections may be increasing.[1] Airway mucormycosis usually involves the lungs or the paranasal sinuses. Some of its signs and symptoms, such vocal fold immobility and dyspnea, mimic those of more common illnesses, and these overlapping signs and symptoms can lead to a delay in diagnosis. Because early recognition and intervention are critical to successful management of this disease, a high degree of clinical suspicion should be maintained in susceptible patients.

We describe the case of a patient with infectious and pharmaceutical immunosuppression who developed overwhelming laryngotracheal mucormycosis. This case emphasizes the devastating nature of this disease and the importance of early diagnosis and combined medical and surgical treatment to maximize the chance of survival.

Case report

A 46-year-old black man with human immunodeficiency virus (HIV) infection, hepatitis C infection, neurosyphilis, and recently diagnosed Burkitt lymphoma presented with dysphonia and stridor. A few days earlier, he had been admitted to another hospital for evaluation of acute pancreatitis and psychosis. He had been intubated shortly after presentation in response to his altered mental status.

The patient was subsequently transferred to our institution, where he remained intubated with a 7.5 endotracheal tube for approximately 7 days. After extubation,

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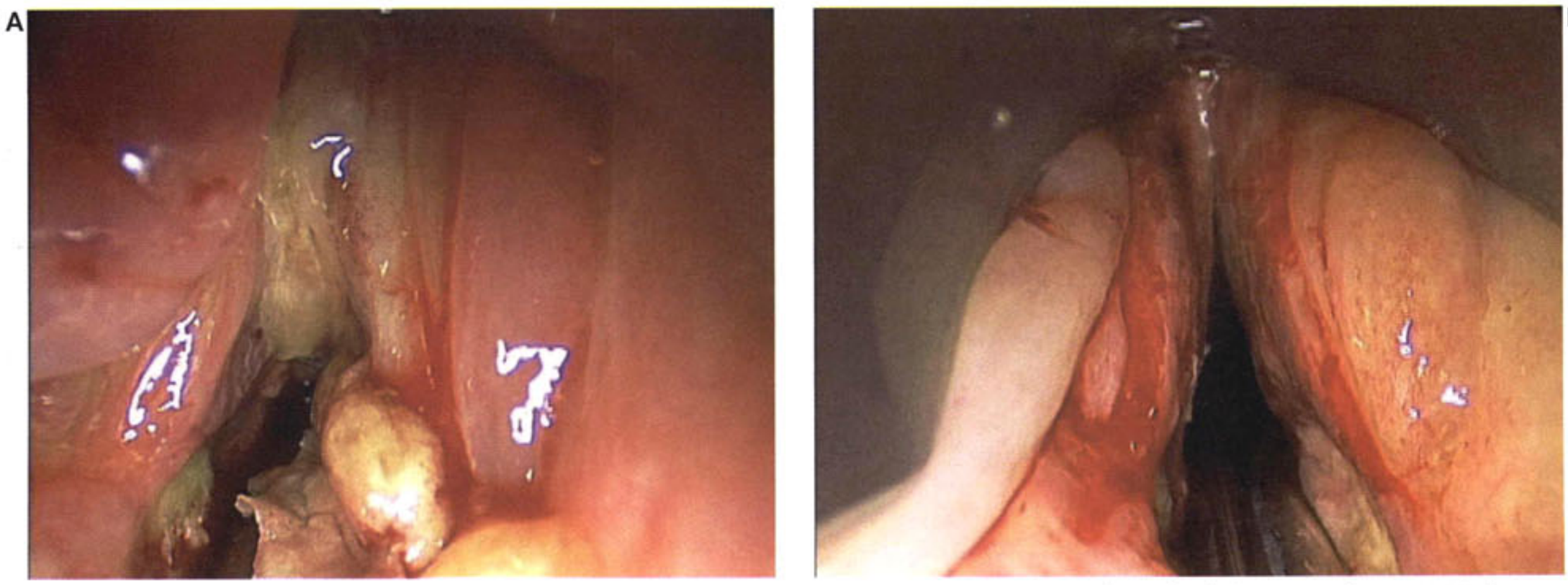

Figure 1. ***A:*** *Direct laryngoscopy shows the fibrinous debris in the entire anterior glottis and much of the supraglottis.* ***B:*** *Following debridement, only minimal bleeding is evident. The endotracheal tube is noted posteriorly.*

his voice was breathy and raspy. The speech-language pathology service was consulted, but before the patient could be evaluated by an otolaryngologist, he left the hospital against medical advice.

The patient returned to the emergency department later that day and was admitted with placement of an Ommaya port. After one dose of intrathecal methotrexate was administered, he developed hyperbilirubinemia, fever, and neutropenia (white blood cell count: 0.1×10^9/L; neutrophils: 0%). He was treated with ceftriaxone for tertiary neurosyphilis, with antivirals (fosamprenavir, abacavir/lamivudine, and ritonavir) for advanced HIV infection, and with an antifungal (fluconazole). Also, filgrastim was prescribed for profound neutropenia.

Shortly thereafter, the patient developed respiratory distress without desaturation. Nebulization with methylprednisolone provided little improvement, and treatment with bilevel positive airway pressure was started. Diphenhydramine and cimetidine were administered to manage subjective tongue swelling that was not evident on physical examination. The patient was transferred to the medical intensive care unit (MICU), and an otolaryngologist was consulted.

The otolaryngologist noted an aphonic patient with biphasic stridor and a markedly increased inspiration-to-expiration ratio. Mild tenderness to laryngeal palpation and normal laryngeal crepitus were present. Nasopharyngolaryngoscopy identified an eschar that was obstructing the anterior two-thirds of the glottis, and there was no discernable abduction or adduction of the true vocal folds.

The patient was taken to the operating room for microdirect laryngoscopy and debridement. Preoperatively, he was advised that a tracheotomy might be required, but he refused consent.

In the operating room, a 4.0 cuffed endotracheal tube was inserted without trauma through the posterior glottis. Firm, fibrinous, yellow material was noted to be obstructing nearly the entire glottis (figure 1, A). After an initial debridement, the material was found to extend from the glottis to the upper trachea. The material was removed and sent for pathologic evaluation and culture. After debridement, only minor bleeding was noted along the pale glottic and subglottic mucosa, even without the use of topical epinephrine (figure 1, B). The arytenoid cartilages were palpated, but due to significant inflammation, no definitive determination could be made regarding mobility. Bronchoscopy found no lesions of the distal trachea or proximal bronchi. At the conclusion of the procedure, the patient was extubated and sent back to the MICU for observation.

Initially, the patient's respiration was much better. However, over the next 2 days, his breathing became progressively labored. A tracheotomy was advised, but he again refused. Instead, an intravenous steroid and humidified oxygen were administered. Finally, as the patient's respiratory status continued to decline, he agreed to undergo an emergency awake tracheotomy. An 8.0 cuffed Shiley tracheotomy tube was inserted and secured uneventfully.

After tracheotomy, direct laryngoscopy and bronchoscopy demonstrated crusting and necrosis from above the glottis to the carina tracheae (figure 2). Extensive biopsies were taken of the vocal fold area, the subglottis, and the trachea; only a little bleeding was noted from the biopsy sites. The initial surgical pathology identi-

fied substantial necrotic tissue with abundant fungal hyphae (figure 3). A Grocott methenamine silver stain and a periodic acid–Schiff (PAS) stain (figure 4) identified fungal organisms. The final culture confirmed invasive mucormycosis.

Eight days after the tracheotomy, the patient's airway became occluded again with necrotic, fibrinous material, and another laryngoscopy and bronchoscopy with debridement of the trachea were performed. Necrosis and crusting were noted to extend to the level of the carina tracheae during this procedure, as well. The patient was placed on micafungin and posaconazole, and he underwent hyperbaric oxygen treatments, but no substantial improvement occurred.

A family meeting was convened, and in view of the patient's overwhelming fungal infection, he was placed in hospice care. He died several weeks later from other causes. In the meantime, he had experienced no recurrence of his symptoms of airway obstruction.

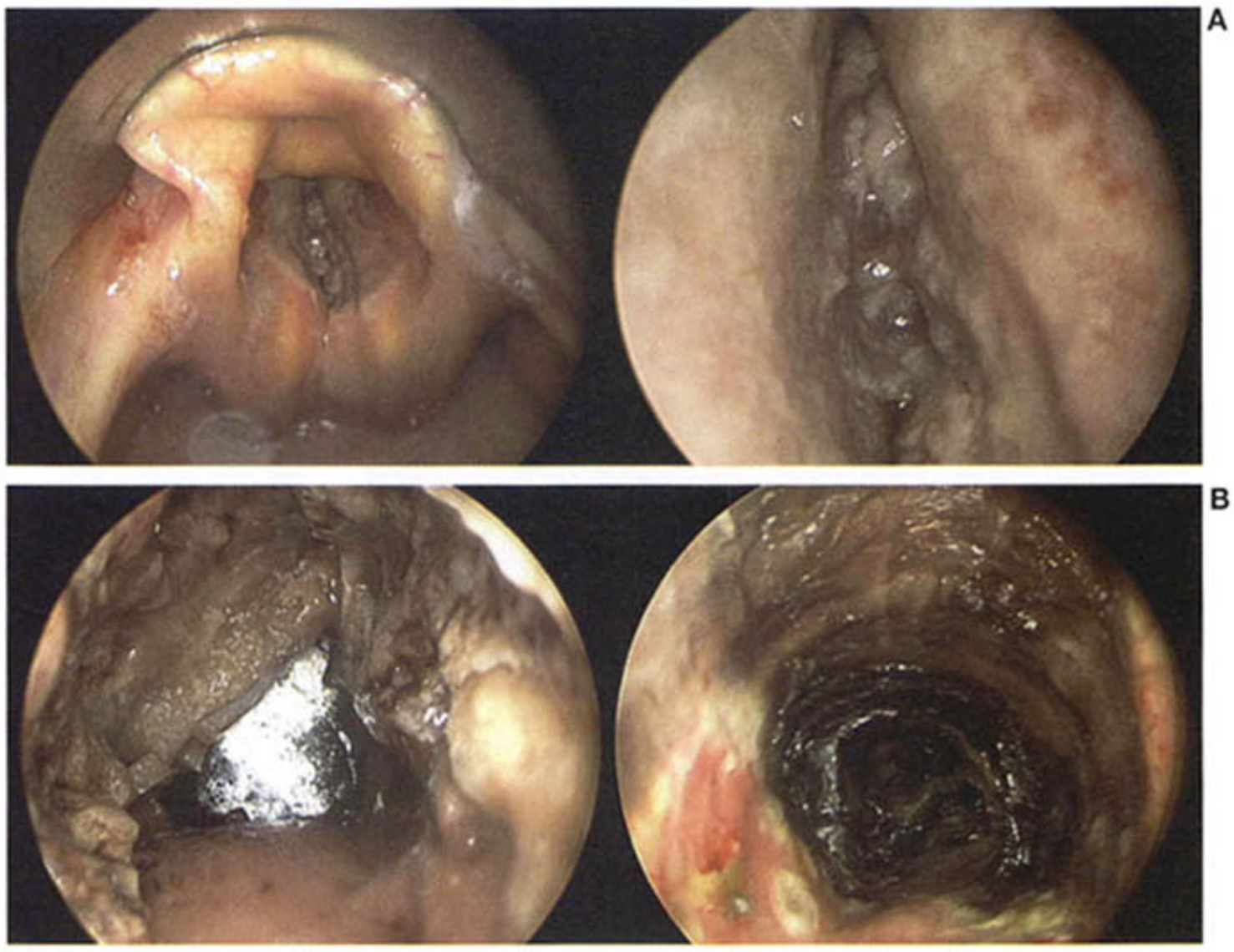

Figure 2. ***A:*** *The larynx is seen in these direct laryngoscopic views 3 days after the initial surgical evaluation. The supraglottis (left) and the glottis (right) are necrotic.* ***B:*** *These images show that the subglottis (left) and the entire trachea (right) are also involved.*

Discussion

Mucormycosis is a fungal infection caused most often by species of *Mucor, Rhizopus, Absidia,* and *Cunninghamella.* While *Aspergillus* spp remain the most common filamentous fungal pathogens of the airway, the incidence of mucormycosis is increasing.[1] Mucormycosis invades the vasculature, leading to embolization and, consequently, ischemia or massive hemorrhage.[2] Mucosa infected with mucormycosis is characteristically black and necrotic appearing. In view of the propensity of mucormycosis for rapid growth and for causing severe morbidity and death, early recognition and treatment are essential.

Airway mucormycosis affects immunocompromised patients, primarily diabetics. In a review of patients with endobronchial mucormycosis, Suresh et al reported that 80 to 85% were diabetic.[3] Challa et al studied 7 patients with pulmonary mucormycosis and found that 6 had diabetes and 1 had Hodgkin lymphoma.[4]

The association between mucormycosis and diabetes may be attributable in part to the acidosis found in uncontrolled diabetes, which promotes mucormycotic growth. In addition, iron is essential for the growth of mucormycosis; as a patient's pH level declines, the ability of transferrin to bind iron decreases, which results in more available free iron.[5] Other immunocompromised states can result in mucormycosis, such as in our patient, who had HIV infection and who was undergoing chemotherapy for Burkitt lymphoma.

Fortunately, upper airway mucormycosis is rare. A

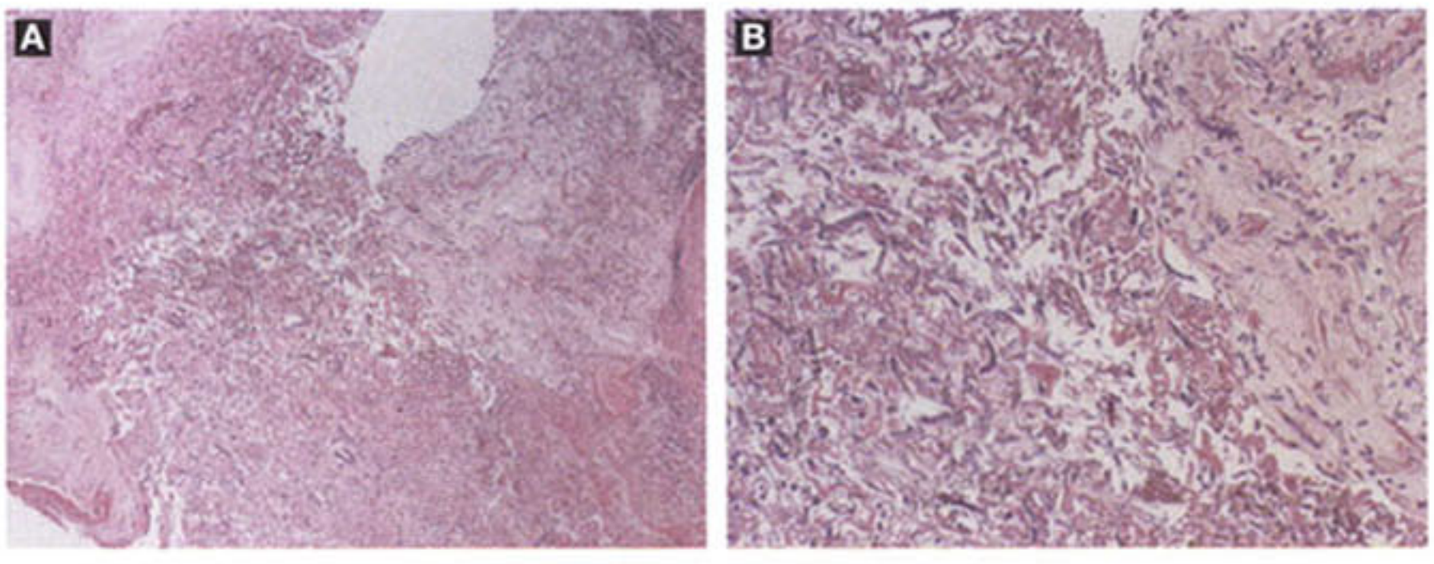

*Figure 3. Images at ×4 (**A**) and ×10 (**B**) magnification show abundant irregular nonseptate hyphae with right-angle branching.* Images courtesy of the Department of Pathology, Drexel University College of Medicine.

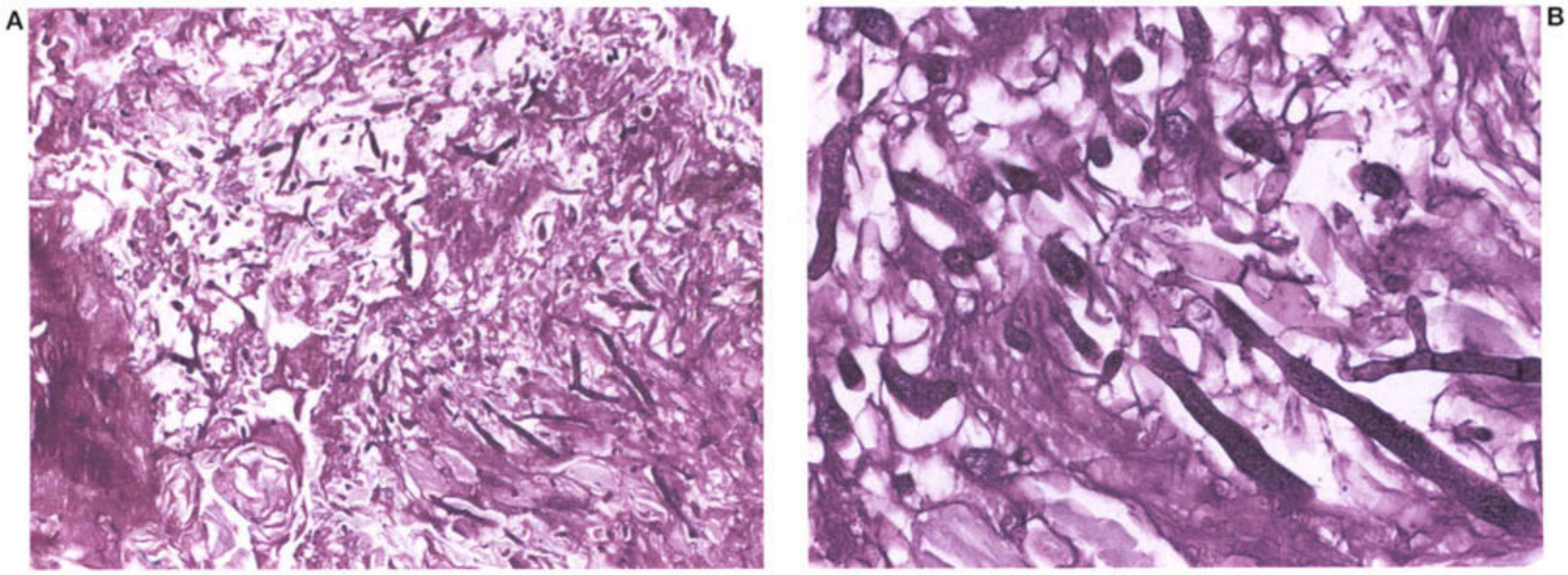

*Figure 4. Images at ×10 (**A**) and ×40 (**B**) magnification show the fungal organisms staining positive with PAS.* Images courtesy of the Department of Pathology, Drexel University College of Medicine.

search of the current literature yielded only 4 additional cases of confirmed laryngeal mucormycosis.[1,6-8] Infection in the airway can be caused by inhaled conidia or by transdermal transmission via spores that penetrate an incompetent skin barrier.[6] Most such patients present with fever, headache, facial pain, dyspnea, and hemoptysis.[7]

Mucormycosis is diagnosed by the identification of organisms on culture or biopsy.[8] In the airway, specimens are obtained via laryngoscopy or bronchoscopy. In the few previously reported cases of upper airway mucormycosis, the most common findings were edema, vocal fold immobility, necrotic ulcers, nodular granulomas, and intraluminal pseudomembranes.[9]

Our patient presented with vocal fold immobility and an eschar that obstructed the anterior two-thirds of the glottis on initial evaluation. Careful biopsies of sufficient amounts of tissue must be obtained to identify characteristic fungal hyphae and necrotic tissue. However, if a biopsy is not performed delicately, its yield can be decreased by crushed tissue.[4] Although our patient's first laryngoscopy revealed only fibrinous debris and pale tissue, the second (after the emergency tracheotomy) yielded more characteristic crusting and necrotic tissue.

The treatment of mucormycosis involves managing the underlying condition, antifungal medication, and surgical debridement.[10] Standard medical therapy consists of parenteral amphotericin B, although posaconazole, an experimental antifungal medicine, has shown promising preliminary results; its use in airway mucormycosis requires further investigation.[10] However, medical treatment alone is inadequate, largely because of poor drug bioavailability at the site of infection due to vasculopathy caused by the fungus and/or underlying disease.[11]

Our patient was treated with both micafungin and posaconazole in an attempt to counter his overwhelming infection. Unfortunately, because of the severity of his immunocompromise, management was not as straightforward as it would have been in an acidotic diabetic.

In a literature review of pulmonary mucormycosis cases, Andrews et al recorded a mortality rate of 11% for patients who received combined medical and surgical therapy vs. 68% for those who underwent medical therapy alone.[12] In addition to surgical debridement, maintenance of a patent airway is critical, and failure to address the issue early can necessitate an emergency tracheotomy.[6] The need for a tracheotomy was conveyed repeatedly to our patient, but he refused to consent until he reached the point that he was barely able to breathe. Our patient's failure to recover completely might have been due to his disease's advanced stage. However, it is interesting that his airway mucormycosis was controlled for several weeks, and he died without symptoms of airway obstruction.

Newer treatment options are being evaluated. Frozen-section–guided debridement has been advocated as an alternative to extensive debridement.[7] In a report of a case of tracheal mucormycosis, Shishir and Brodie wrote that hyperbaric oxygen therapy might have played a role in the early management of tracheal mucormycosis that resolved later.[13] Finally, iron chelation is a novel adjunctive treatment that targets the iron that *Mucor* spp require for growth.[10]

In conclusion, airway mucormycosis is a rare, life-threatening infection associated with an extremely poor prognosis. Laryngotracheal mucormycosis should be

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is highly recommended to minimize the risk of recurrence. Careful follow-up is necessary for early detection should a recurrence arise.

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considered in immunocompromised patients, including nondiabetics, who present with airway distress, vocal fold hypomobility, or necrotic mucosa. Our case illustrates the need for early recognition, prompt airway intervention, and combined medical and surgical treatment to maximize the chance of airway control and patient survival.

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