

Invasive Fungal Infection of the Maxilla Following Dental Extractions in a Patient with Chronic Obstructive Pulmonary Disease

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ABSTRACT

We report on a 74-year-old male patient with chronic obstructive pulmonary disease (COPD) who developed an invasive fungal disease of the facial bones after several teeth were extracted. He had recently suffered an exacerbation of COPD, treated with a course of corticosteroid therapy.

Mucormycosis is an opportunistic fungal pathogen that has the ability to cause significant morbidity and frequently mortality in the susceptible patient. An overview of this class of pathogens and the history, examination findings (clinical and radiographic), pathogenesis and medical-surgical treatment of mucormycosis is presented.

MeSH Key Words: maxillary diseases/complications; mucormycosis/complications; mucormycosis/drug therapy; pulmonary disease, chronic obstructive

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Dentists are seeing a growing number of medically compromised patients in their practices.^{1,2} The lifespan of patients is increasing and access to medical care for elderly patients has improved; thus, more patients are surviving long-term with significant medical problems. These patients present with systemic disease involving multiple organ systems. They may be taking many medications and using other medical therapies. Today, this group of patients survives much longer than they would have even 10–15 years ago. The ability to identify patients whose overall health status may not allow them to tolerate surgical or dental manipulation very well is important to avoid the clinical outcome reported here.

Invasive fungal infections (mycoses) are uncommon, but when they occur, they are devastating to patients. These infections are

opportunistic — they occur when organisms to which we are frequently exposed gain entry to the body due to a decrease in host defenses or through an invasive portal, such as a dental extraction.

Mucormycosis is a saprophytic aerobic fungus commonly found in our environment, for example, in bread moulds or decaying vegetation. This organism is frequently found to colonize the oral mucosa, nasal mucosa, paranasal sinuses and pharyngeal mucosa of asymptomatic patients.^{3,4} These fungi do not usually cause disease in healthy people with intact immune systems, but patients with a number of conditions can be predisposed to the development of invasive fungal disease. These conditions include diabetes mellitus, renal failure, malignancies, intravenous drug abuse, malnutrition states, as well as immunosuppression and corticosteroid therapy.^{5,6}

Invasive fungal diseases that are not recognized early or are treated inadequately are among the most acutely fatal infections known.

Case Report

A 74-year-old man was referred to the Mayo Clinic's division of oral and maxillofacial surgery for evaluation of a progressive nonhealing wound of the left maxilla. He had recently suffered an exacerbation of his chronic obstructive pulmonary disease (COPD), which was managed with intravenous corticosteroid therapy. The patient went on to develop pneumonia, which was successfully managed with antibiotic therapy, and he was discharged from the hospital doing well. At the time of his discharge, he was on a tapering regimen of oral steroids.

Approximately 1 month after discharge from hospital, he presented to his dentist for evaluation of several loose teeth in the left maxilla. This was thought to be due to progression of his baseline periodontal condition. Teeth 11 through 15 displayed Class II mobility and were painful. Simple extractions were carried out, without flap reflection or osseous surgery.

The patient's postextraction course was protracted. He returned a number of times for evaluation of wound healing. At these appointments, exposed alveolar bone was noted in the area of the extractions. Over a number of weeks, and despite local wound care and antibiotics, the tissues did not heal and the patient began to develop mobility in his right maxillary dentition. He was referred to an oral and maxillofacial surgeon, who noted exposed bone on the left side, moderate mobility of the right maxillary dentition as well as softening of the bone of the hard palate. He was subsequently referred to the Mayo Clinic's division of oral and maxillofacial surgery.

The patient's medical history included severe COPD. His medications included montelukast, albuterol, fluticasone propionate/salmeterol xinafoate, tiotropium bromide and amoxicillin/clavulanate. He had completed a tapering regimen of oral steroids just before his left maxillary surgery.

Oral examination showed exposure of the entire left maxillary alveolus, with necrotic bone and purulent drainage from the wound margins. The palatal tissues were edematous (Fig. 1) and the maxilla was mobile to the level of the pyriform rims. Nasopharyngoscopy revealed yellow



Figure 1: Photograph of nonhealing left maxillary postsurgical wound.

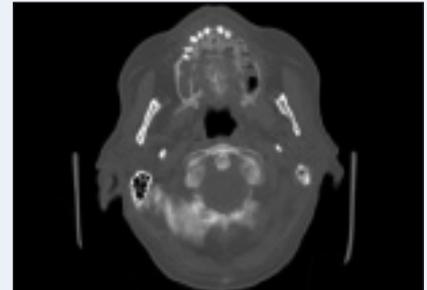


Figure 2: Axial computed tomography scan at the level of the hard palate showing the generalized lytic process in the maxilla, with fluid in the right maxillary sinus and an air-fluid interface in the left.



Figure 3: Intraoperative photo showing general destruction and mobility of the maxilla.

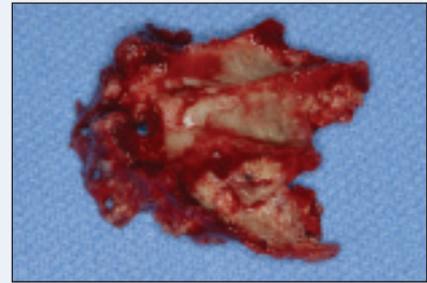


Figure 4: Superior view of surgical specimen.

crusting of the anterior nasal septum, as well as purulent discharge from the maxillary ostia into the middle meatus.

Tomographic imaging revealed postsurgical changes in the left maxilla. The right maxillary bone was somewhat radiolucent; it was difficult to identify the contours of the lamina durae and sinus floor on the right side. At this point, the differential diagnosis included invasive fungal infection, osteomyelitis, necrotizing stomatitis and vasculitis or vascular compromise, with a presumptive diagnosis of invasive fungal infection. A computed tomography scan showed generalized involvement of the maxilla by a lytic, destructive bony process (Fig. 2).

A biopsy specimen revealed polymicrobial osteomyelitis with an underlying fungal component. The patient was taken to the operating room, where the maxilla was found to be necrotic and mobile; it was therefore removed (Figs. 3 and 4). Involvement of the inferior zygomas, nasal septum and pterygoid plates was noted. All necrotic tissue was resected back to viable-appearing bone, and the wound was irrigated and closed. Histopathologic examination revealed nonviable bone and numerous fungal hyphae consistent with *Mucor* species. Bacterial cultures grew *Pseudomonas aeruginosa*, *Haemophilus*

influenzae, *H. parainfluenzae* and *Klebsiella pneumoniae*. At this point, the definitive diagnosis was invasive mucormycosis infection, with a superimposed polymicrobial osteomyelitis.

The patient was treated with liposomal amphotericin B, a potent intravenous antifungal medication. He received intravenous cefepime for the osteomyelitis. His maxillary wound healed well, although large defects in the maxillary sinuses persisted as bilateral oral–antral fistulae. Unfortunately, he developed renal failure due to the antifungal therapy, and his overall course was complicated by an inability to ingest an adequate diet, requiring insertion of a feeding tube. Aggressive medical management, renal dialysis and nutritional support were instituted with the patient in the intensive care unit. Ultimately, his respiratory system was further compromised due to pneumonia, and the patient expired due to cardiopulmonary arrest 43 days after his surgical treatment.

Discussion

Mucormycosis is a fungal infection due to organisms in the order Mucorales. These organisms belong to the general class zygomycetes, which are ubiquitous. They can be found in decaying vegetation, soil and decaying food (for example bread mould). These organisms can occasionally be cultured from noninfected individuals.

Mucormycosis can have multiple clinical presentations. The most common is the rhinocerebral form, involving the nose, paranasal sinuses, orbits and central nervous system. Others include cutaneous, gastrointestinal, pulmonary and disseminated forms. The rhinocerebral form has been subclassified into rhinomaxillary and rhinocerebralorbital by some.⁷

Rhinocerebral mucormycosis typically begins with hyphal invasion of the paranasal sinuses or the oronasal cavity of a susceptible host. Early symptoms may include perinasal paresthesias, cellulitis, periorbital edema, rhinorrhea and nasal crusting. These features are quickly superseded by eschar formation and necrosis of the naso-facial region.⁸ Advancing infection can quickly result in cavernous sinus thrombosis, carotid artery or jugular vein thrombosis (Lemierre Syndrome) and death.

The diagnosis is based on history, clinical examination, diagnostic radiography and biopsy. Debridement of non-viable necrotic tissue has been the mainstay of treatment over the years and remains so today. With the advent of potent antifungal medications, a combination of surgery and medication has provided better outcomes. Overall aggressive medical support of these critically ill patients also improves chances for survival.^{9,10}

Amphotericin B was developed in the 1950s. Before that, invasive fungal infection was a uniformly fatal disease.

Hyperbaric oxygen therapy has also been used to treat mucormycosis. The high oxygen concentrations achieved

in infected tissue may decrease tissue hypoxia and acidosis, thereby reducing the ability of the fungus to proliferate.^{9,11,12}

Conclusions

Mucormycosis is an aggressive, frequently fatal invasive fungal infection that can develop in patients with a number of predisposing conditions. In the susceptible patient, it can be triggered by minor surgical wounds, such as dental extractions. Expedient diagnosis, systemic amphotericin B therapy, aggressive surgical debridement and optimal medical management are critical for patient survival.

This case reinforces the concept that simple procedures such as dental extractions can cause catastrophic complications in susceptible patients. All dental professionals will encounter patients whose general health is tenuous and easily perturbed. It is important to understand how our treatments can affect these patients. We must remain vigilant in our efforts to follow patients after we perform procedures to be certain that appropriate healing occurs. Knowledge of potentially devastating complications can help to prevent the unfortunate consequences described here. In this case, more timely referral to a surgeon may have allowed this patient's fungal disease to be discovered and treated at an earlier stage, thereby avoiding aggressive, in-patient surgical management, with the associated morbidity and, in this case, ultimate mortality of the patient. ✦

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