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CASE REPORT

Invasive Mucormycosis Causing Rhino-orbital Cellulitis

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INTRODUCTION

Mucormycosis manifests in a variety of different clinical presentations in humans, particularly in immunocompromised patients and those with diabetes mellitus.[1] The agents of mucormycosis are common in the environment and can be found on decaying vegetation and in the soil.[2] All humans have ample exposure to these fungi during day-to-day activities. The fact that mucormycosis is a rare human infection reflects the effectiveness of the intact human immune system. This is supported by the finding that almost all human infections, due to the agents of mucormycosis, occur in the presence of some underlying compromising condition.

We report a case of devastating rhino-orbital mucormycosis in a patient with uncontrolled diabetes resulting in exenteration of the left eye. Prognosis is poor for patients with brain, cavernous sinus, or carotid involvement.[3-5] Hence, it is important to make an early diagnosis and initiate appropriate treatment, along with strict glycemic control in diabetics, to decrease morbidity and mortality.

CASE REPORT

A 67-year-old male with stage IV chronic kidney disease, sleep apnea, coronary artery disease status post coronary artery bypass graft, and uncontrolled diabetes mellitus presented to an outside hospital with headache, nasal congestion, diplopia, and photophobia. The patient had invasive fungal sinusitis and underwent endoscopic sinus surgery and debridement. Cultures grew Rhizopus. The patient was transferred to our hospital after he became blind in the left eye (reportedly the night prior to transfer) for further aggressive management with endoscopic sinus surgery for debridement of invasive fungal sinusitis.

On exam, the patient had proptosis of the left eye. He had left afferent pupillary defect, severely restricted gaze, and decreased sensation in all branches of the trigeminal nerve. Labs were significant for hemoglobin of 9.2 g/dl, a white blood count of 13.5 K/µl, BUN of 62 mg/dl, creatinine of 2.05 mg/dl, and glucose of 323 mg/dl.

Maxillofacial computed tomography (CT) showed interval left maxillary antrectomy with improvement in maxillary sinusitis, progression in left ethmoid, frontal and bilateral sphenoid sinusitis, and development of post-septal fat stranding with asymmetric prominence of optic nerve consistent with orbital (post-septal) cellulitis.

Ophthalmology was consulted and the patient underwent left medial orbital exploration and radical orbital exenteration. Pathology showed involvement of middle turbinate, inferior orbital nerve, orbital floor bone, and orbital contents with fungal organisms with vascular invasion consistent with Mucor (Figure 1).

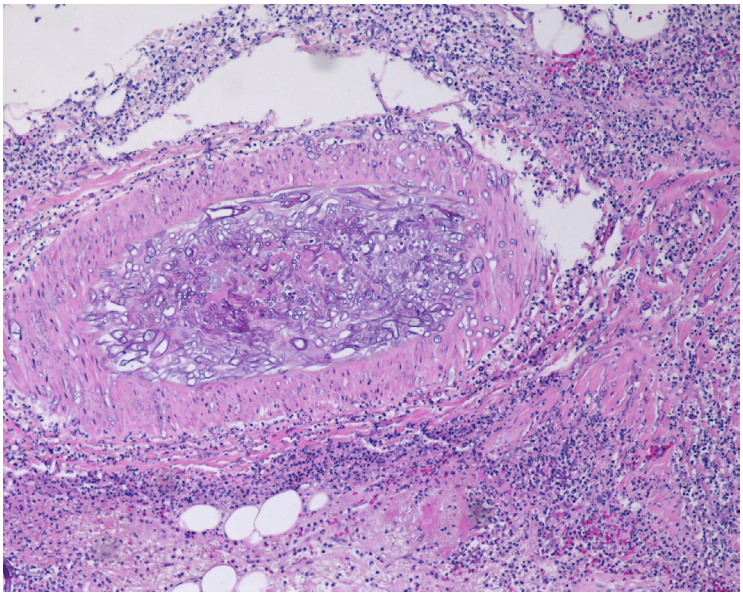

Figure 1. Left orbit enucleation specimen showing fungal organisms with vascular invasion consistent with Mucor.

The patient was started on piperacillin and tazobactam, micafungin sodium, and amphotericin B; oral posaconazole was added later. Strict glycemic control was targeted and achieved throughout the hospital course. Piperacillin and tazobactam was discontinued on discharge. The patient was discharged to a skilled nursing facility [SNF] and advised to continue IV amphotericin and micafungin sodium, to complete a total of four weeks, and oral posaconazole indefinitely. He did well while he was on IV antifungals; once the duration of IV antifungals ended, he rapidly deteriorated and eventually passed away at the SNF.

DISCUSSION

Mucormycosis can manifest as devastating rhino-orbital-cerebral (ROC) and pulmonary infections in immunocompromised patients and in diabetics.[1] The genera common in humans are Rhizopus, Mucor, and Rhizomucor. The hyphae are broad, irregularly branched, and have rare septations. Rhizopus organisms have an enzyme, ketone reductase, which allows them to thrive in high glucose, acidic conditions. ROC and pulmonary mucormycosis are acquired by inhalation of spores. Infection usually begins in the nasal turbinates or alveoli.[6]

The agents of mucormycosis are angioinvasive; infarction of infected tissues is a hallmark of invasive disease.[7] Predisposing conditions are diabetes mellitus, particularly with diabetic ketoacidosis, glucocorticoid use, hematologic malignancies, hematopoietic stem cell/solid organ transplantation, deferoxamine, iron overload, AIDS, IV drug use, trauma/burns and malnutrition. ROC mucormycosis presents with fever, nasal ulceration/necrosis, periorbital/facial swelling, decreased vision, ophthalmoplegia, sinusitis, and headache. Signs of orbital involvement are periorbital edema, proptosis, and blindness. Facial numbness results from infarction of sensory branches of trigeminal nerve. The spread of infection from the ethmoid sinus to the frontal lobe results in obtundation. Spread from the sphenoid sinuses to cavernous sinus can result in cranial nerve palsies, thrombosis of the sinus, and involvement of carotid artery.

ROC mucormycosis should be suspected in patients with diabetes mellitus and metabolic acidosis who present with sinusitis, altered mentation, and infarcted tissue in the nose/palate.[2] The diagnosis of mucormycosis relies upon the identification of organisms in tissue by histopathology with culture confirmation. However, culture often yields no growth and histopathologic identification of an organism with a structure typical of Mucorales may provide the only evidence of infection. A clinician must think of this entity in the appropriate clinical setting and pursue invasive testing to establish a diagnosis as early as possible. The presence of the characteristic hyphae in a clinical specimen provides a presumptive diagnosis that should prompt further evaluation.

Further evaluation includes imaging of the head with either CT or magnetic resonance imaging (MRI) to look for sinus involvement and evaluate contiguous structures, such as the eyes and brain.[8] Treatment of mucormycosis includes surgical debridement and antifungal therapy.[9] IV amphotericin B is the drug of choice for initial therapy.[10] Lipid formulation of amphotericin B is preferred over amphotericin B deoxycholate to deliver a high dose with less nephrotoxicity. The usual duration of treatment with IV amphotericin B is several weeks, until a favorable clinical response is achieved and at that point can be switched to posaconazole.

Posaconazole is used as step-down therapy for patients who have responded to amphotericin B. Posaconazole also can be used as salvage therapy for patients who do not respond or cannot tolerate amphotericin B. For salvage therapy, the decision to use oral or intravenous posaconazole depends on how ill the patient is, whether an initial course of amphotericin B was administered, and whether the patient had a functioning gastrointestinal tract. When switching to oral posaconazole, delayed-release formulation (300 mg every 12 hours on the first day, then 300 mg once daily) is favored.[11] Therapy with posaconazole should continue until there is clinical resolution of the signs and symptoms of infection, as well as resolution of radiographic signs of active disease which often takes months. Isavuconazole, available in both an IV and an oral formulation, can be used if the patient cannot tolerate posaconazole.

Echinocandins [Micafungin] have no in vitro activity against the agents of mucormycosis,[12-14] but Rhizopus oryzae, the most common cause of mucormycosis, expresses the target enzyme for echinocandins, suggesting that these agents may have clinical utility.[15]

Mortality from ROC mucormycosis ranges from 25% to 62%.[16] Factors associated with death are delayed diagnosis, presence of hemiparesis/hemiplegia, bilateral sinus involvement, leukemia, renal disease, and deferoxamine use.[17] Prognosis is poor for patients with brain, cavernous sinus, or carotid involvement.

CONCLUSION

ROC mucormycosis is an invasive disease with high mortality. Despite early diagnosis and aggressive combined surgical and medical therapy, the prognosis for recovery from mucormycosis is poor. Bilateral sinus involvement is one of the poor prognostic indicators. Our patient had bilateral sphenoid sinus involvement. Hence, being cognizant of the clinical manifestations and presentation is important for an early diagnosis and initiating appropriate treatment at the earliest is crucial to decrease morbidity and mortality.

REFERENCES

[1] Kauffman CA, Malani AN. Zygomycosis: An emerging fungal infection with new options for management. Curr Infect Dis Rep 2007; 9(6):435-440. PMID: 17999877.
[2] Cox GM. Mucormycosis (zygomycosis). http://www.uptodate.com/contents/mucormycosis-zygomycosis?source=machineLearning&search=mucormycosis&selectedTitle=1~69&sectionRank=1&anchor=H18#H18. Accessed March 3, 2016.
[3] Strasser MD, Kennedy RJ, Adam RD. Rhino cerebral mucormycosis. Therapy with amphotericin B lipid complex. Arch Intern Med 1996; 156(3):337-339. PMID: 8572846.
[4] Weprin BE, Hall WA, Goodman J, Adams GL. Long-term survival in rhinocerebral mucormycosis. Case report. J Neurosurg 1998; 88(3):570-575. PMID: 9488314.
[5] Shah PD, Peters KR, Reuman PD. Recovery from rhinocerebral mucormycosis with carotid artery occlusion: A pediatric case and review of the literature. Pediatr Infect Dis J 1997; 16(1):68-71. PMID: 9002105.
[6] Ferguson BJ. Mucormycosis of the nose and paranasal sinuses. Otolaryngol Clin North Am 2000; 33(2):349-365. PMID: 10736409.
[7] Greenberg RN, Scott LJ, Vaughn HH, Ribes JA. Zygomycosis (mucormycosis): Emerging clinical importance and new treatments. Curr Opin Infect Dis 2004; 17(6):517-525. PMID: 15640705.
[8] Saltoğlu N, Tasova Y, Zorludemir S, Dűndar IH. Rhinocerebral zygomycosis treated with liposomal amphotericin B and surgery. Mycoses 1998; 41(1-2):45-49. PMID: 9610133.
[9] Spellberg B, Walsh TJ, Kontoyiannis DP, Edwards Jr J, Ibrahim AS. Recent advances in the management of mucormycosis: From bench to bedside. Clin Infect Dis 2009; 48(12):1743-1751. PMID: 19435437.
[10] McCarthy M, Rosengart A, Schuetz AN, Kontoyiannis DP, Walsh TJ. Mold infections of the central nervous system. N Engl J Med 2014; 371(2):150-160. PMID: 25006721.
[11] Noxafil (posaconazole). Highlights of prescribing information. https://www.merck.com/product/usa/pi_circulars/n/noxafil/noxafil_pi.pdf. Accessed on March 18, 2014.

[12] Espinel-Ingroff A. Comparison of in vitro activities of the new triazole SCH56592 and the echinocandins MK-0991 (L-743,872) and LY303366 against opportunistic filamentous and dimorphic fungi and yeasts. J Clin Microbiol 1998; 36(10):2950-2956. PMID: 9738049.
[13] Pfaller MA, Marco F, Messer SA, Jones RN. In vitro activity of two echinocandin derivatives, LY303366 and MK-0991 (L-743,792), against clinical isolates of Aspergillus, Fusarium, Rhizopus, and other filamentous fungi. Diagn Microbiol Infect Dis 1998; 30(4):251-254. PMID: 9582584.
[14] Del Poeta M, Schell WA, Perfect JR. In vitro antifungal activity of pneumocandin L-743,872 against a variety of clinically important molds. Antimicrob Agents Chemother 1997; 41(8):1835-1836. PMID: 9257774.
[15] Ibrahim AS, Bowman JC, Avanessian V, et al. Caspofungin inhibits Rhizopus oryzae 1,3-beta-D-glucan synthase, lowers burden in brain measured by quantitative PCR, and improves survival at a low but not a high dose during murine disseminated zygomycosis. Antimicrob Agents Chemother 2005; 49(2):721-727. PMID: 15673756.
[16] Roden MM, Zaoutis TE, Buchanan WL, et al. Epidemiology and outcome of zygomycosis: A review of 929 reported cases. Clin Infect Dis 2005; 41(5):634-653. PMID: 16080086.
[17] Yohai RA, Bullock JD, Aziz AA, Markert RJ. Survival factors in rhino-orbital-cerebral mucormycosis. Surv Opththalmol 1994; 39(1):3-22. PMID: 7974189.

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