Rhino-orbital mucormycosis usually leads to acutely fatal fungal infections in immunocompromised patients through central nervous system invasion or vascular thrombosis. Historically, untreated orbital mucormycosis has a survival rate of 24%, but the recent combination of surgical debridement and amphotericin B has improved patient survival to 85%.

Ophthalmologists are often involved in making medical and surgical decisions in these complex cases; therefore, it is important to be aware of advances in the management of this disorder. We describe herein a case of rhino-orbital mucormycosis and cavernous sinus and internal carotid thrombosis treated with posaconazole after the failure of initial treatment with surgical debridement and amphotericin B.

Report of a Case. A 7-year-old girl with poorly controlled diabetes was seen at a nearby hospital for a 2-day history of left eyelid swelling and pain. After 2 days of treatment with intravenous ceftriaxone sodium and vancomycin hydrochloride, restricted left eye movements and bitemporal diplopia developed, and her vision declined to 20/100 OS.

On transfer to our institution, the vision in her left eye was 20/150 with periorbital edema, 3 mm of relative proptosis, and a 5-mm dilated and poorly reactive pupil. We found no evidence of an afferent pupillary defect, but she exhibited almost complete ophthalmoplegia. A computed axial tomographic scan showed inflammation in the left ethmoid and sphenoid sinuses extending into the orbit. She had a white blood cell (WBC) count of 8900/µL. After a tentative diagnosis of rhino-orbital mucormycosis, she underwent surgical debridement of the paranasal sinuses and we began treatment with liposomal amphotericin B, 15 mg/kg per day. The sinus biopsy specimen showed fungal elements that were morphologically consistent with Zygomycetes, later identified by fungal culture as Mucor species.

During the next 5 days, despite 3 further debridements and placement of an intraorbital catheter for local amphotericin B administration, her vision declined to hand motions, she developed an afferent pupillary defect, and her WBC count increased to 12 000/µL. A magnetic resonance image showed worsening of the orbital infection and a new left cavernous sinus and internal carotid artery inflammation and thrombosis (Figure). We then instituted therapy of interferon gamma, 40 µg/m² three times per week; daily hyperbaric oxygen; and heparin sodium. Further progression of the cavernous sinus and internal carotid artery thrombosis was noted on a magnetic resonance image on day 7, and this was confirmed with computed tomographic angiography. Subsequently, oral posaconazole, 200 mg 3 times a day, was added because the Mucor species isolate had a lower minimum inhibitory concentration (MIC) to posaconazole (MIC, 0.125 µg/mL) compared with amphotericin B (MIC, 0.25 µg/mL).

Serial magnetic resonance imaging studies after day 21 showed stabilization of the orbital and sinus infection and of the thrombosis while treatment with liposomal amphotericin B was continued.

Figure. Magnetic resonance imaging (T1 images with contrast enhancement) axial (A) and coronal (B) views of the skull and brain at the level of the orbits, cavernous sinuses, and base of the brain. Enhancement of the left cavernous sinus and the diminished flow void of the internal carotid artery (white arrow) are evident compared with the normal right cavernous sinus and internal carotid artery (black arrow).
amphotericin B, posaconazole, interferon gamma, hyperbaric oxygen, and heparin was continued. Her examination results gradually improved during the next 3 weeks, and she was discharged on a regimen of liposomal amphotericin B, posaconazole, and heparin.

After 12 months of this therapy, we found no evidence of active infection (her WBC count was 4900/µL) or progression of the cavernous sinus and internal carotid artery thrombosis. Her vision improved to 20/60 OS, and she experienced near-complete resolution of the ophthalmoplegia.

Comment. Previous reports of orbital mucormycosis have shown survival rates of 85% after a combination of surgical debridement and systemic amphotericin B. Morbidity can be significant secondary to advanced infection and vascular thrombosis within the central nervous system. Our patient initially underwent multiple surgical debridements and treatment with local and systemic amphotericin B, with no improvement. She showed persistent signs of orbital compromise and a rising WBC count and developed a cavernous sinus and internal carotid artery thrombosis. After our patient was started on therapy of posaconazole in conjunction with amphotericin B, interferon gamma, and heparin, and an insulin drip to tightly control her blood glucose levels, she showed clinical improvement.

We chose to use posaconazole because of in vitro study results, its low MIC, and our patient’s declining medical status. Posaconazole acts primarily as a cytochrome P-450 3A4 inhibitor and in vitro has a lower MIC against Zygomycetes than conventional antifungals. Limited clinical data are available on the use of posaconazole in treating mucormycosis. We are unaware of its reported use in treating another case of orbital mucormycosis, but its use has shown improvement in 71% of patients with other invasive zygomycosis infections refractory to amphotericin B or itraconazole.

Ophthalmologists should be aware of advances in the management of orbital mucormycosis, so that medical and surgical interventions are appropriately used in treating the disease. We were able to effectively treat a case of rhino-orbital mucormycosis associated with a cavernous sinus and internal carotid artery thrombosis with surgery and the administration of posaconazole, amphotericin B, interferon gamma, and heparin. Because most patients show clinical improvement with surgical debulking and amphotericin B therapy, we cannot precisely determine the efficacy of posaconazole in the setting of the concurrent treatment modalities. Interferon gamma, a proinflammatory cytokine, up-regulates the immune system against fungi by activating polymorphonuclear leukocytes, monocytes, and macrophages. Interferon gamma has been used as adjunctive therapy to treat fungal infections in other immuno-compromised disease states, and anticoagulation is believed to be important in preventing secondary sequelae such as stroke. Future in vivo studies may better elucidate the clinical efficacy of the azole class of antifungals in the therapy of invasive Zygomycetes infections.

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