Rapidly progressive bilateral optic nerve and retinal infarctions due to rhinocerebral mucormycosis and pseudoephedrine use

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Rhinocerebral mucormycosis is a life-threatening fungal disease due to *Rhizopus* or *Mucor* species. Infection typically occurs in patients who are immunocompromised or have poorly controlled diabetes.¹ The classical syndrome consists of a rapidly progressive sinusitis, periorbital edema and cellulitis, ophthalmoplegia, and unilateral visual loss.^{1–3} We report rapidly progressive bilateral visual loss from mucormycosis due to bilateral optic nerve and retinal infarction in a patient with diabetes.¹

Case report

A 62-year-old woman with poorly controlled type 2 diabetes mellitus and hypothyroidism developed decreased visual perception in the left eye and ipsilateral facial numbness in the setting of diabetic ketoacidosis and recent sinusitis, prompting presentation to the emergency department. Notably, the patient took 8 tablets of pseudoephedrine the day before presentation. Her initial examination was remarkable for left eye periorbital edema, proptosis, and complete ophthalmoplegia with reduced light perception. She had decreased sensation in the left ophthalmic and maxillary divisions of the trigeminal nerve and left facial nerve weakness in a peripheral pattern. Initial brain MRI demonstrated only bilateral proptosis. Rhinoscopic examination showed only mild bilateral ethmoid sinusitis with no evidence of invasive fungal disease. Despite absent findings, there was a concern for invasive fungal sinusitis, and empiric antifungal treatment was initiated. Lumbar puncture on hospital day 2 showed 320 white blood cells per mm³, 41 red blood cells per mm³, protein of 96 mg/dL, glucose of 202 mg/dL, and negative fungal culture. Within 24 hours, there was clinical progression to absent light perception bilaterally with loss of pupillary light reflex as well as complete ophthalmoplegia. Fundoscopic examination revealed bilateral central retinal artery occlusions. Repeat brain MRI showed new restricted diffusion in the bilateral optic nerves, worsened proptosis, infiltration of the intraconal and extraconal fat bilaterally, and major pansinus inflammatory mucosal thickening (figure 1). There was no evidence of sinus venous thrombosis on dedicated venogram. On hospital day 4, intraoperative debridement revealed nonseptated fungal hyphae consistent with *Rhizopus* species with associated necrosis and vascular invasion (figure 2).

Notably, methicillin-susceptible *Staphylococcus aureus* was detected in an initial blood culture, but CSF and serum cultures were negative. Despite surgical debridement, IV amphotericin B and micafungin, and aggressive glycemic control, her clinical condition deteriorated.

Practical Implications

Consider mucormycosis in any patient presenting with rapidly progressive unilateral or bilateral visual loss and ophthalmoplegia despite normal MRI, especially in the setting of pseudoephedrine use.

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Figure 1 Bilateral optic nerve infarcts due to rhinocerebral mucormycosis

(A–D) Apparent diffusion coefficient and diffusion-weighted imaging sequences 24 hours after clinical worsening reveal new bilateral optic nerve infarctions (arrows). (E, F) Axial and coronal T1 postcontrast orbital fat saturation sequences after 24 hours of clinical worsening show infiltration of the intraconal and extraconal fat bilaterally, proptosis, and pansinus inflammatory mucosal thickening.

She declined repeat aggressive debridement surgery and was transitioned to comfort measures only.

DISCUSSION

We report a case of rhinocerebral mucormycosis causing bilateral optic nerve and retinal infarctions leading to bilateral visual loss, proptosis, and ophthalmoplegia. Rhinocerebral mucormycosis is a rapidly progressive and often fatal complication with a propensity to cause vascular occlusion, thrombosis, and infarction in patients with diabetes or those who are immunocompromised.^{1,2}

Figure 2 Histopathology of angioinvasive rhinocerebral mucormycosis from right nasal cavity debridement

Hematoxylin and eosin stain (40× magnification) showing (A) fungal organisms with ribbon-like hyphae within inflamed and necrotic tissue (arrow) and (B) angioinvasion of fungal organisms within blood vessels (arrow).

The fungus typically gains access through the nose via inhalation and is deposited in the nasal turbinates and paranasal sinuses.¹ From the ethmoid sinus, the organisms can spread to the orbit, extraocular muscles, ophthalmic artery, and optic nerve.¹ The brain may be subsequently seeded via invasion of the ethmoidal and orbital veins, which drain into the cavernous sinus.¹

Patients with rhinocerebral mucormycosis often develop nonspecific symptoms such as headache, fever, malaise, and sinusitis followed by periorbital edema and cellulitis, proptosis, ophthalmoplegia, and vision loss.^{1–3} Although usually only one eye is involved, bilateral eye involvement may occur.⁴ In this case, *Rhizopus* affected the ophthalmic arteries and their branches, resulting in combined retinal and optic nerve infarctions and blindness.

Imaging often reveals an aggressive sinonasal and orbital inflammatory process with evidence of periorbital muscle inflammation. The sphenoid sinus, cavernous sinus, carotid artery, and skull base may also be involved. As in our case, diffusion-weighted imaging sequences may reveal optic nerve or cerebral infarctions.^{3,5} However, despite clinical symptoms, initial imaging may be normal; a high clinical suspicion must be retained in patients with typical features of rhinocerebral mucormycosis.¹

Treatment of rhinocerebral mucormycosis requires a multidisciplinary approach that relies on prompt institution of antifungal therapy, control of the underlying predisposing condition, and, when possible, surgical debridement.^{1,2} Despite early treatment, progression of disease often occurs and mortality is high.^{1–3}

In our case, we speculate that the large quantity of pseudoephedrine may have caused vasospasm in the setting of angioinvasive disease. In addition, pseudoephedrine formulations typically contain high amounts of iron, which stimulates growth and enhances the virulence of *Rhizopus*.⁶ Although not standard of care, iron chelation therapy has been used in the treatment of mucormycosis.⁷

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AUTHOR CONTRIBUTIONS

Alexander E. Merkler conceived and designed the study, analyzed and interpreted the data, and drafted and revised the manuscript for intellectual content. Isha Duggal designed the study, analyzed and interpreted the data, and drafted and revised the manuscript for intellectual content. Urlike Kaunzner analyzed and interpreted the data and revised the article critically for important intellectual content. Carolina B. Maciel analyzed and interpreted the data and revised the article critically for important intellectual content. Alexandra M. Miller analyzed and interpreted the data and revised the article critically for important intellectual content. Theresa Scognamiglio analyzed and interpreted the data and revised the manuscript for intellectual content. Marc J. Dinkin conceived and designed the study, analyzed and interpreted the data, and drafted and revised the manuscript for intellectual content.

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