Rhinocerebral Mucormycosis in an HIV/AIDS Patient without Diabetes: A Case Report

Yu Zhao, MD*, Maike Blaya, MD, Adriana Rosero, MD

Abstract—Mucorales is an invasive and angiotrophic fungus, which may cause a life-threatening infection. Mucorale-related infections lead to significant vascular changes including thrombosis, arteritis and aneurysm formation. Those infections occur primarily in diabetics and immunocompromised individuals. The incidence of Mucorales in HIV/AIDS patients is low because it relatively preserves neutrophil function. In this report, we describe a case of rhinocerebral mucormycosis with the presentation of isolated abducens nerve palsy, which was caused by a mucormycotic aneurysm in the internal carotid artery at the intracavernous sinus. The patient suffered from HIV/AIDS but not diabetes mellitus. This is the first report in the literature on an isolated abducen nerve palsy caused by mucormycosis-induced intracavernous carotid aneurysm.

Keywords — abducens nerve palsy, HIV/AIDS, mucormycosis.

I. INTRODUCTION

Mucormycosis is an infection caused by Mucorales, under the category of Zygomycota fungi.¹ ² ³ It includes the diseases caused by any members of Mucorales, not just Mucor. The most common causative form is the Rhizopus species.⁴ Zygomycosis is commonly used interchangeably with mucormycosis in literature. Mucorales are distributed worldwide, and are present in soil, decomposing vegetation, and can be seen as flora in the respiratory and digestive tracts of healthy humans.⁵ ⁶ ⁷

Mucormycosis is the third most common cause of fungal infections in humans after candidiasis and aspergillosis.³ Mucormycosis is a fulminant invasive infection that affects preferably immunocompromised individuals, particularly uncontrolled diabetics and recipients of solid organ transplant. Rhinocerebral mucormycosis is the most common form of mucormycosis.⁶ ⁷ ⁸ However, it has not been seen in the literature that an intracavernous mucormycotic carotid aneurysm in an HIV/AIDS patient without diabetes causing isolated abducens palsy.

II. CASE REPORT

A 33-year-old man presented with horizontal diplopia for two days. He had a history of HIV/AIDS. He was on HAART therapy and his CD4 count was 111. He had recently been diagnosed with sinusitis.

The patient has a complicated neurological history. He had a history of cerebellar toxoplasmosis requiring ventriculo-peritoneal (VP) shunt placement for hydrocephalus and tonsillar herniation. He suffered an intracranial hemorrhage and left hemiparesis related to the VP shunt placement and the shunt had subsequently been removed. He received an effective toxoplasmosis treatment.

On neurological examination, he was found to have left-gaze related binocular horizontal diplopia with limited abduction in the left eye. He had normal visual acuity. No proptosis, ptosis, lid swelling, facial asymmetry, or other cranial nerve abnormalities were noticed. His pupils were equal in size and reaction to light. Brain computerized tomography (CT) showed a worsening chronic paranasal sinusitis without hydrocephalus (Figure A), as compared to a brain CT taken three weeks previously (Figure A1). Brain magnetic resonance imaging (MRI) showed extensive skull base and posterior sinus devitalization with peripheral enhancement (Figure B, C), which was a new finding not seen on an MRI obtained 2 months previously (Figure B1 and C1). These results suggested an ongoing inflammatory process. MRI angiogram (MRA) showed a saccular aneurysm of the cavernous segment of the left internal carotid artery (ICA) (Figure D and E). CT of the maxillofacial sinus disclosed a lytic lesion in the base of the central skull (Figure F). An endonasal tissue biopsy was performed and showed Mucor zygomycetes.

Endovascular aneurysm repair was attempted but was not successful because the patient developed multiple transient ischemic attacks during the procedure. The debridement was prematurely aborted due to the fragility of the giant mycotic aneurysm with maximum dimension measured as 17 x 9 mm. The patient was treated aggressively with liposomal Amphotericin B intravenously. Unfortunately, he had developed acute kidney failure on day 7; at that time the Amphotericin B dose was adjusted and Micafungin was added. Follow up MRI (Figure G) on day 13 showed further progression of the infection in the skull base. In a follow up 6 months later he demonstrated overall improvement while his left abducens palsy remained and a new finding of left postganglionic Horner's syndrome (mild left ptosis, miosis but without anhidrosis).
III. DISCUSSION

Rhinocerebral mucormycosis is the most common form of mucormycosis, which is most often a life threatening subacute infection that usually deteriorates over days to weeks. Sometimes they may present in a “static” or chronic form lasting months or even years. Mucorales are angiotrophic and have a predilection for the internal elastic lamina of blood vessels, especially the arteries, causing arteritis, thrombosis, aneurysm or pseudoaneurysms. Mucorales can also invade the nerves, fatty tissues, and bones. In general, rhinocerebral mucormycosis starts from the nasal mucosal or paranasal sinus and invades intracranially along perivascular channels or the cribiform plate. Mycotic aneurysms, which accounts for about 2.5-6.2% of intracranial aneurysms, can be caused by bacteria, fungi or viruses although the majority are caused by bacteria and most often Staph aureus in endovascular infection. When fungi are the pathogens causing mycotic aneurysms, aspergillus and candida are most common. Mucormycosis is rare, about 10-50 times less common than candidiasis and aspergillosis. However, the occurrence of mycotic aneurysms at intracavernous ICA by mucormycosis is extremely rare. PubMed and internet literature search disclosed only two single case reports on intracavernous aneurysm caused by mucormycosis: one patient with poorly controlled diabetes mellitus; and another in a status post transsphenoidal surgery. The presenting symptoms of both cases were facial pain and nasal symptoms. Management of mucomycotic ICA aneurysms is a clinical
challenge as these infections are often refractory to medical treatment, and surgical intervention is risky and technically difficult.\textsuperscript{18}

Previous clinical observations indicated that individuals who lack phagocytes or have impaired phagocytic function are at higher risk for mucormycosis, however, patients with HIV/AIDS do not seem to have an increased risk since their neutrophilic functions are relatively intact.\textsuperscript{3,6,7} Rarely, extracranial mucormycosis can be seen in HIV/AIDS\textsuperscript{10-14} patients which may manifest as cutaneous, renal and disseminated forms of mucormycosis.\textsuperscript{8,10-14,16}

Phagocytes engulf and destroy Mucorales by a mechanism of generating oxidative metabolites and the cationic peptides defensins (small cysteine-rich host defense peptides).\textsuperscript{3} The major risk factors that predispose to the development of mucormycosis include: a) diabetic ketoacidosis; b) malignancy; c) solid organ and bone marrow transplantation; d) chronic use of various medicines including corticosteroids, deferoxamine and immunosuppressive drugs; e) intravenous (IV) illegal drug use.\textsuperscript{3,4,7,15}

Early diagnosis of mucormycosis is critical in the management but is often delayed due to the nonspecific symptoms and signs seen at presentation, particularly in patients without diabetes. The presenting symptoms may include fever; nasal ulceration or necrosis; periorbital or facial swelling; decreased vision; ophthalmoplegia; sinusitis; headache; facial pain; decrease in mental status; nasal discharge or stuffiness; corneal anesthesia; orbital cellulitis; proptosis; palatal or gingival necrosis; afferent pupillary defect; facial nerve palsy; periorbital pain; chemosis; epistaxis; facial numbness; diplopia; facial necrosis; stroke; malaise; ptosis; decreased hearing; lacrimation, toothache and earache.\textsuperscript{3,20}

Bearing the long track course intracranially, the abducens nerve is susceptible to injury at multiple locations including the abducens nucleus, the abducens fascicles traversing and exiting thepons, the subarachnoid space, the cavernous sinus, and the orbital apex. Additionally, abducens nerve palsy can also be a false localizing sign in patients with raised intracranial pressure or hydrocephalus.\textsuperscript{21}

Intracavernous ICA aneurysm is a possible cause of abducens nerve palsy.\textsuperscript{22,23,24,25,26,27,28,22,29,30,31} The abducens nerve together with oculomotor, trochlear, and ophthalmic and maxillary branches of the trigeminal nerve, pass through the cavernous sinus. Notably, the abducens nerve is the closest cranial nerve to the ICA in the cavernous sinus. The sympathetic plexus surrounds the carotid artery throughout its entire course;\textsuperscript{23} therefore, when the intracavernous ICA is affected, postganglionic Horner's syndrome (ipsilateral ptosis, miosis without anhidrosis) may occur.\textsuperscript{23,32}

Neuroimaging studies such as brain CT or MRI are useful tools in evaluating vasculature and other tissues non-invasively. CT scan is sensitive to demonstrate mucosal thickening, bone erosion, and necrosis; MRI is superior to CT in resolution and ability to demonstrate intracranial and intraorbital pathologies,\textsuperscript{9,33} Both CTA (CT angiogram), and MRA can delineate the blood vessel involvement but their sensitivity are low in early stages of vascular involvement.\textsuperscript{20} Definitive diagnosis of mucormycosis usually is made based on a tissue biopsy.\textsuperscript{4} A presumptive pathologic diagnosis of mucormycosis can be made by broad ribbon-like, haphazardly branched hyphae, with absence or paucity of hyphal septations.\textsuperscript{4,34}

Treatment for mucormycosis includes surgical/endoscopic debridement, intravenous administration of Amphotericin B, and treatment of underlying medical conditions. Amphotericin B frequently causes nephrotoxicity, which may limit its use.\textsuperscript{3} The lipid formulation tends to be better tolerated.\textsuperscript{35,36} Echinocandins (a class of antifungal drugs that inhibit glucan synthesis of cell wall, such as Micafungin) have also been used in some cases; these drugs have more favorable toxicity profiles than Amphotericin B and some retrospective reviews demonstrated improved outcomes as compared to Amphotericin B monotherapy. However, a large-scale clinical trial is still necessary to determine the benefit.\textsuperscript{36} Roden and colleagues reported a study of 929 cases of zygomycosis. The survival rate in this series was obvious: 3% for untreated patients, 61% for Amphotericin B monotherapy, 57% for surgery only, and 70% for patients treated with both Amphotericin B and surgery.\textsuperscript{15} A small series of 14 cases published by Camara-Lemarroy also demonstrated a significant mortality of 50% in rhinocerebral mucormycosis.\textsuperscript{37}

In our case, the possible risk factors for mucormycosis were HIV/AIDS and low CD4 counts. Our patient did not have other commonly recognized risk factors, such as diabetes, organ transplantation, immunosuppressants or IV illegal drug use.\textsuperscript{16,18,39} However, detailed chart review disclosed that our patient had transient mild neutropenia to 1.5 x 10\textsuperscript{3} /L two months previously: 2 days before his toxoplasmosis treatment and 2 days during his toxoplasmosis treatment. The relationship between the existence of this short period of mild neutropenia and the occurrence of his mucormycosis remained unclear.

Mycotic intracavernous carotid aneurysm caused by mucormycosis in HIV/AIDS has not been seen in the literature. Our observation with the findings of neuroimaging studies (Figure B, D, E) and pathologic confirmation adds information into literature in this regard, which may help widen our thoughts and improve clinical performance. Even though mucormycosis is rare in HIV/AIDS patients, cases may be in increase due to the improvement in health care with HAART therapy and prolonged survival in HIV patients.\textsuperscript{8,9,38}

IV. SUMMARY

Isolated abducens nerve palsy can be an early presenting symptom of mucormycosis seen in an HIV/AIDS patient in whom it may be caused by an intracavernous ICA mycotic aneurysm due to Mucor. Early diagnosis and prompt treatment may lead to a more favorable outcome.

V. ACKNOWLEDGMENTS

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References


Questions (please choose one single answer):

1. Which is the most common clinical manifestations of mucormycosis
   A. Cutaneous mucormycosis
   B. Disseminated mucormycosis
   C. Renal mucormycosis
   D. Rhinocerebral mucormycosis

2. Which is the most common infection that causes mycotic aneurysm:
   A. Aspergillus
   B. Staph Aureus
   C. Candida
   D. Mucormycosis
   E. Staph epidermidis

3. Mucormycosis diagnosis is made based on
   A. Tissue culture
   B. Serum antibody
   C. Nasal secretion study
   D. Tissue biopsy
   E. CT/MRI