

Recurrent Stroke and Fatal Ruptured Mycotic Aneurysm Caused by Invasive *Aspergillus fumigatus* Infection

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ABSTRACT

Introduction: *Aspergillus* species are ubiquitous fungi that may cause invasive infection, particularly in immunocompromised patients. Invasive aspergillosis most commonly affects the lungs but can also disseminate to the central nervous system (CNS). Manifestations of CNS aspergillosis include abscesses and, rarely, mycotic aneurysm leading to subarachnoid hemorrhage (SAH).

Case Presentation: A 48-year-old man undergoing treatment for squamous cell cancer of the larynx with chemotherapy and steroids presented with dysarthria and weakness. He was found to have both lung and CNS infection secondary to *Aspergillus* species. While receiving intravenous antifungal treatment after biopsy-proven *Aspergillus* infection, he developed a fatal SAH caused by a mycotic aneurysm.

Discussion: Intracranial mycotic aneurysms are uncommon. However, mycotic aneurysm leading to a fatal SAH is a well-documented sequela of CNS aspergillosis. Mortality rates for CNS aspergillosis are extremely high.

Conclusion: In immunosuppressed patients with neutropenia or using chronic steroids who have concurrent pulmonary and CNS infection, there should be a low threshold to treat empirically for fungal infections prior to confirmation of diagnosis.

INTRODUCTION

Aspergillus spores are regularly inhaled from soil or decaying vegetation. While *Aspergillus* infections occur throughout the United States, Wisconsin has among the highest number of overall cases.¹ In an immunocompetent host, these spores rarely cause infection, but in patients with neutropenia or other immunosuppression, lung infection can occur. Dissemination

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via bloodstream can affect virtually any organ, including the skin, eyes, liver, kidneys, bone, and brain.²

CASE REPORT

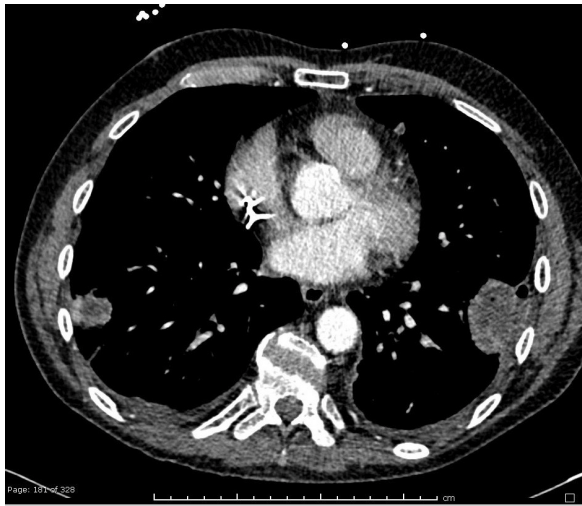
A 48-year-old man presented to the hospital after coworkers noticed dysarthria with left-sided weakness. He was reportedly driving on the wrong side of the road the previous day. His past medical history was notable for head and neck squamous cell cancer, and he had completed 3 weeks of cisplatin and radiation treatment. He was taking oral dexamethasone daily for soft tissue facial edema and was on trimethoprim/sulfamethoxazole for *Pneumocystis* prophylaxis. He had been discharged from another hospital 3 days prior to presentation with *Pseudomonas aeruginosa* pneumonia, diagnosed via spu-

tum culture and chest x-ray.

Physical exam was notable for an ill-appearing drowsy male with mild left-sided weakness. Computed tomography (CT) chest showed numerous new solid and cavitary lesions throughout both lungs, the largest of which measured 5 cm in the right hilum and 4.6 cm in the left lower lung (Figure 1).

Initial brain magnetic resonance imaging (MRI) showed multiple ring-enhancing abscesses throughout the bilateral hemispheres and his cerebellum. The patient was empirically started on vancomycin, cefepime, and metronidazole. On hospital day 4, he developed acute aphasia and new transient right-sided weakness. Repeat brain MRI with magnetic resonance angiography (MRA) showed stable diffuse abscesses with a new infarct in the left thalamus without intracranial aneurysm. The patient was started on

Figure 1. Chest CT Showing Cavitory Lesions



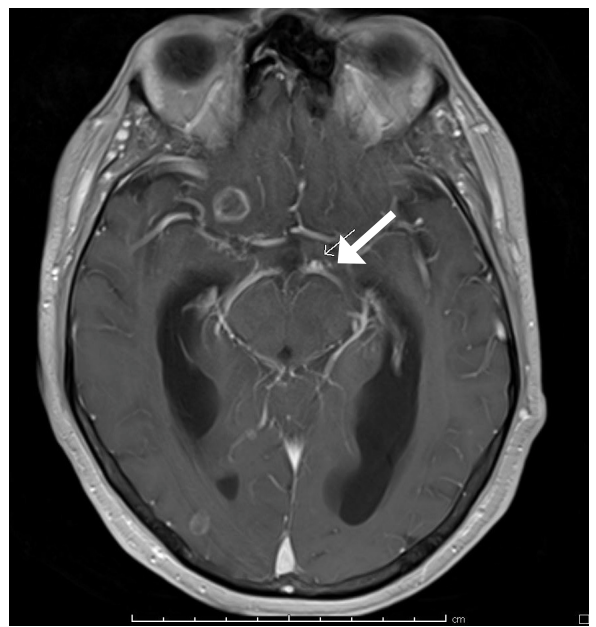
The left-sided cavitary lesion contains gas and a rim of necrosis, also known as the "halo sign."

Figure 2. Computed Tomography Head



Arrow points to subarachnoid blood in the basal cisterns.

Figure 3. Brain Magnetic Resonance Angiography



Arrow points to mycotic aneurysm.

intravenous amphotericin B to broadly cover possible fungal infections, including mucormycosis. Neurosurgery consultation recommended pulmonary biopsy rather than brain biopsy due to the higher risks of the latter intervention. The biopsy of one of the pulmonary nodules grew *Aspergillus fumigatus*.

After the biopsy results returned positive for *Aspergillus* on hospital day 8, intravenous micafungin and voriconazole were started. He continued to be intermittently somnolent throughout his hospital course. On hospital day 12, medical emergency was called as the patient was unresponsive and apneic. His pupils were dilated and nonreactive to light. Emergent head CT showed acute subarachnoid hemorrhage (SAH) with moderate hydrocephalus. (Figure 2). MRA of the brain showed enlarging abscesses with a 2 mm mycotic aneurysm in the posterior cerebral artery, consistent with the location of his SAH (Figure 3).

After a family care conference with the neurosurgery team, family decided to pursue comfort care and the patient died 3 days later.

DISCUSSION

Due in part to an increasing number of patients receiving immunosuppression, *Aspergillus* infections are becoming more prevalent. Both the number of hospitalizations and deaths from *Aspergillus* infection have increased greatly over the past 20 years.³

Aspergillus infection typically starts in the lung or sinuses due to inhalation of spores and can spread either contiguously or disseminate via the bloodstream. Central nervous system (CNS) aspergillosis due to abscess formation presents with variable symptoms, including mental status changes, headaches, or more acute presentations such as stroke or seizure.^{4,5}

Once invasive *Aspergillus* disseminates to the brain, the mor-

talidity rate increases from 58% to 88%.⁶ Mycotic aneurysm leading to SAH is a particularly devastating event in CNS *Aspergillus* infection. Intracranial mycotic aneurysms are uncommon in general but are a known sequela of CNS aspergillosis. Thirty-three patients with intracranial mycotic aneurysms due to *Aspergillus*

have been reported in the literature from 1990 to 2005.⁷ This is certainly underdiagnosed, as a review of 92 cases of CNS aspergillosis showed that only 56% of cases were diagnosed during life.⁸

Mycotic aneurysm is a focal abnormal dilation of an artery due to infection. Sir William Osler first used this term in 1885 to describe an aneurysm caused by bacterial endocarditis. The term “mycotic” was applied because of the resemblance of the aneurysm to fungal vegetation. Mycotic, however, is a misnomer as most mycotic aneurysms are bacterial.⁹

The main treatment for mycotic aneurysm involves antimicrobial therapy, open neurosurgery, endovascular approach, and/or a combination of them. Given the lack of randomized controlled trials, there are no definitive guidelines to direct clinical decision-making. Overall management depends on whether the aneurysm has ruptured, the aneurysm characteristics, and the patient’s overall health status. In those without high surgical risk, endovascular or surgical treatment is advised given the risk of rupture.¹⁰ To date, there are no trials comparing endovascular versus neurosurgical approach; however, endovascular is becoming more popular. In a retrospective review of patients with intracranial mycotic aneurysm (mostly from infective endocarditis) in the *American Journal of Neuroradiology (AJNR)*, overall mortality was lower in the intervention group (13%) versus those who received antibiotics alone (40%).¹¹

Patients deemed too high risk for surgery should undergo antimicrobial treatment for at least 4 to 6 weeks followed by repeat angiography. In the *AJNR* study, of the 22 patients treated with antibiotics alone, 64% had resolution of their mycotic aneurysm, although this was limited by a small sample size and variable angiographic follow-up.¹¹ It should be noted that this study had only 1 patient with a mycotic aneurysm caused by *Aspergillus*.

CONCLUSION

In immunosuppressed patients who have concurrent pulmonary and CNS findings, there should be a high suspicion for *Aspergillus* infection and a low threshold to treat empirically prior to confirmation of diagnosis. Despite antimicrobial treatment, CNS aspergillosis mortality remains high. Neurosurgery consultation is necessary in patients with mycotic aneurysm, as endovascular or neurosurgical repair can be effective in those without high surgical risk.

Funding/Support: None declared.

Financial Disclosures: None declared.

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