

Scedosporium brain abscess in an individual with Crohn's disease on chronic immunosuppression

Jean Liew, Jia Luo, Graeme Forrest, Adam Obley

ABSTRACT

Introduction: *Scedosporium* species are ubiquitous molds found in the environment that are uncommon pathogens in humans. Infections usually occur in immunosuppressed hosts. *Scedosporium* infection of the central nervous system is an even rarer manifestation that has mostly been described in transplant recipients and in cases of near-drowning. **Case Report:** We present a case of an elderly man with a history of Crohn's disease on moderate immunosuppressive therapy, who presented with subacute progressive encephalopathy and was found to have a rim-enhancing lesion in the left frontal lobe. Cultures from biopsy of the lesion grew *Scedosporium apiospermum*. Although the patient was appropriately treated with voriconazole, he eventually succumbed to complications of his illness. **Conclusion:** This case highlights that *Scedosporium*, an increasingly recognized opportunistic pathogen, should be considered in the differential of rim-enhancing brain

lesions, even in patients with lesser degrees of immunosuppression. Clinical suspicion and early diagnosis is critical because *Scedosporium* species are resistant to many antifungal agents including amphotericin B, but may respond to voriconazole.

Keywords: Brain abscess, Crohn's disease, Fungal infection, Immunosuppression, Opportunistic infection

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INTRODUCTION

Scedosporium apiospermum, a ubiquitous mold commonly found in the soil, is an emerging cause of infectious disease in humans [1]. In immunocompetent individuals, *S. apiospermum* is usually limited to cutaneous infections such as mycetoma. Invasive or disseminated infections are more often seen in the immunocompromised, especially those with prolonged neutropenia following solid organ or hematopoietic stem cell transplants [2–3]. *Scedosporium* central nervous system (CNS) infections may also be seen in transplant recipients, but are more common in immunocompetent individuals who have received a massive inoculation, such as in cases of near-drowning in fresh water [4].

Mortality for CNS scedosporiosis ranges from 55–70%, as reported in case report; this was in spite of surgical intervention having been performed in the majority of cases [2–6]. We present a case of a man on chronic immunosuppression for Crohn’s disease, who was found to have CNS scedosporiosis.

CASE REPORT

A 77-year-old Caucasian male with Crohn’s disease, with multiple bowel resections and maintained on budesonide, azulfidine, and azathioprine, presented to his gastroenterology clinic with confusion of one week’s duration. This change in mentation was in the setting of diffuse weakness and poor oral intake over a longer period of time. He had been in his usual state of health (albeit with a chronic baseline of 10–20 bowel movements daily due to Crohn’s disease) until a month prior, when he was admitted to an outside hospital and treated for mucocutaneous candidiasis. Prior to that, he had also received two weeks of oral prednisone 20 mg daily with a taper. His past medical history was significant for compensated cirrhosis secondary to non-alcoholic steatohepatitis, coronary artery disease, paroxysmal atrial fibrillation, diabetes mellitus, and chronic obstructive pulmonary disease. He had an 80 pack-year smoking history, but otherwise did not have a history of heavy alcohol or illicit drug use. He had no significant history of recent travel, and resided in suburban Oregon with his wife.

Upon admission he was afebrile with vital signs within the normal limits. On examination, he appeared well-nourished and nontoxic, alert but oriented only to self, and unable to follow simple commands. There were neither meningismus nor focal neurological signs. Basic laboratory studies were unremarkable, and urinalysis and urine drug screen were both negative. A chest X-ray did not demonstrate any consolidations. A non-contrast head CT showed a lesion in the left frontal lobe, which was further characterized on MRI scan as a rim-enhancing 1.3 cm mass with associated vasogenic edema (Figure 1).

Empiric antibacterial and antiviral coverage was initiated with intravenous cefepime, metronidazole, and acyclovir. The infectious disease service was consulted. The differential for the patient’s solitary rim-enhancing brain mass was divided into broad categories of infectious and malignant causes. The initial workup encompassed testing for viral (Herpes, Varicella, Epstein Barr, Cytomegalovirus, JC virus); bacterial (meningitis, infectious endocarditis with septic emboli, syphilis); fungal (endemic mycoses, *Cryptococcus*); and parasitic (*Toxoplasma*, *Strongyloides*) etiologies. The initial evaluation, including lumbar puncture, transthoracic echocardiogram, and axial imaging of the chest, abdomen, and pelvis, was subsequently found to be non-diagnostic for these etiologies. Neurosurgery was consulted and a brain biopsy of the lesion was

performed. Fungal stains revealed irregularly branching septate hyphal forms, suggestive of, but not specific for, *Aspergillus*. The culture grew mold suspicious for *Scedosporium*, later speciated by combined phenotypic characterization and DNA sequencing as the species *apiospermum* (Figures 2 and 3).

Intravenous voriconazole was started and the patient had initial improvement of his mental status to the point that he was able to follow simple commands and answer questions appropriately. However, after two weeks of antifungal therapy there was concern for toxicity with a rising total bilirubin and the development of hallucinations and visual changes, prompting a decrease in voriconazole dose. The patient’s course was further complicated by intractable large volume diarrhea secondary to untreated Crohn’s disease while immunosuppression was held in the setting of active infection. He also developed perirectal abscesses and was found to have portal venous thrombosis and a subdural hematoma at the site of the biopsy. A diverting colostomy was considered in order to alleviate the deleterious effects of his stool output, but he was felt to be a poor surgical candidate owing to his anasarca and poor functional status. Despite nearly six weeks of voriconazole, he experienced worsening of his mental status. Multidisciplinary care conferences were held and it was felt that he would unlikely improve with a longer course of antifungal treatment. A trial of intravenous corticosteroids failed to improve his stool output. After further discussions with his family regarding his poor prognosis, they made the decision to pursue comfort measures only. He died on hospital day-49.

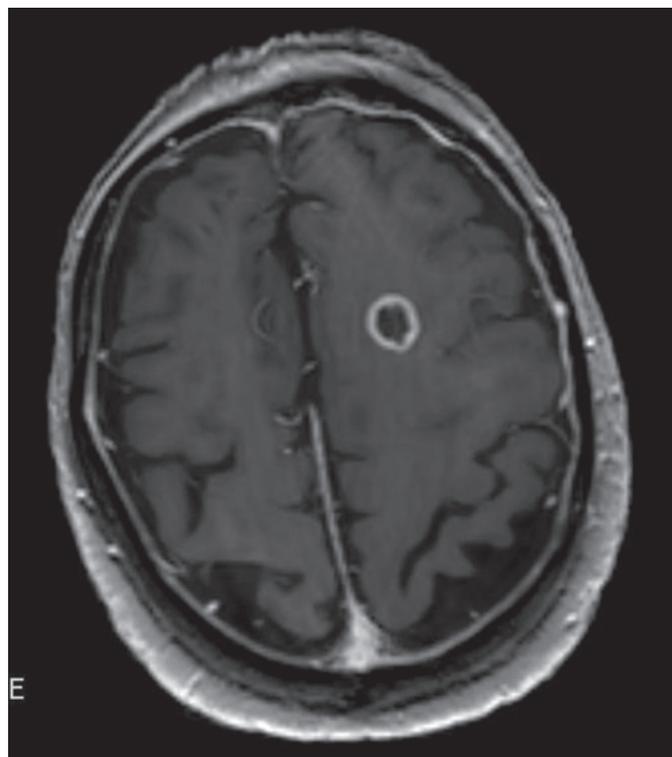


Figure 1: MRI scan of the brain: A 1.3 cm rim-enhancing lesion is seen in the left frontal lobe with surrounding vasogenic edema.

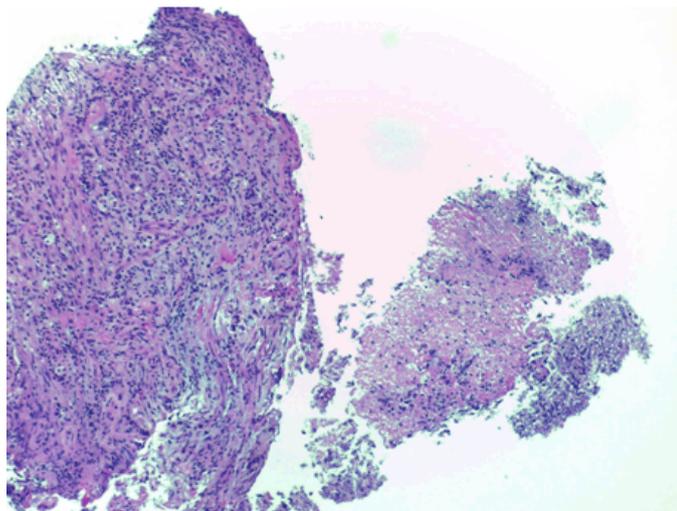


Figure 2: Brain biopsy: Hematoxylin and eosin stain of tissue demonstrates inflammation with infiltration of polymorphonuclear cells and necrosis of brain tissue.

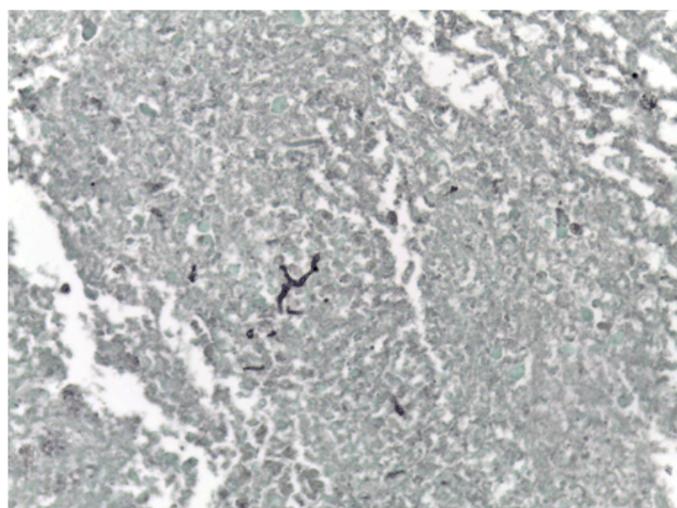


Figure 3: Brain biopsy: Grocott methenamine silver fungal stain of tissue biopsied from the left frontal lobe lesion. Septate hyphae are seen within the abscess.

DISCUSSION

Scedosporium apiospermum is a ubiquitous mold found in the soil. It was originally thought to be the asexual form of *Pseudallescheria boydii* – and earlier reports were classified under this nomenclature – but *Scedosporium* was later reclassified as a distinct genus [1, 2]. *Scedosporium* causes opportunistic infections in transplant recipients who are maintained on immunosuppressive therapy; in this population, pulmonary infections are the most common, occurring in 64% of solid organ transplant recipients in one study [3]. Central nervous system manifestations are less common, usually occurring in the profoundly immunosuppressed or in near-drowning victims.

The presenting symptoms for an infectious brain abscess are nonspecific and may include headache, fever, and altered mental status. Neuroimaging (usually CT scan followed by MRI scan) is indicated when brain abscess is suspected. The differential for rim-enhancing brain lesions found on imaging should include bacterial, Mycobacterial, fungal, and parasitic causes, as well as non-infectious etiologies [7]. Fungal causes of CNS infection include *Aspergillus*, *Fusarium*, *Scedosporium*, Mucorales, and dematiaceous molds [8].

Risk factors for CNS infection should be taken into account, and a higher degree of suspicion for fungal etiologies is warranted if the patient is immunocompromised. Most of the reported cases of CNS scedosporiosis in literature are of individuals who were made more susceptible to infection by either their degree of immunosuppressive therapy or by the large inoculum directly delivered to the CNS. Some reports describe invasive Scedosporiosis in individuals on more moderate immunosuppression, as our patient was; Muñoz et al. reported disseminated scedosporiosis in a woman with asthma maintained on systemic corticosteroids, while Caggiano et al. reported CNS scedosporiosis in a woman on chronic corticosteroids for the treatment of idiopathic pulmonary fibrosis [9–10]. CNS scedosporiosis in a man with silicosis who was not otherwise immunosuppressed has also been described [11].

Since lumbar puncture yields a diagnosis in only one-fourth of patients with infectious brain abscess, stereotactic aspiration or biopsy of the lesion by neurosurgery is usually necessary to determine the causative organism [7]. Fungal elements may be appreciated by Gomori methenamine silver stain, or periodic acid Schiff stain. However, *Scedosporium* species can be difficult to differentiate from *Aspergillus* because of their similar morphology of branching septate hyphae. *Scedosporium* has right rather than acute angle hyphae, as well as ovoid conidia. For fungal abscesses, isolation in culture from the aspirate or biopsy becomes even more important for diagnosis so that further testing may be performed. Polymerase chain reaction (PCR) can confirm a diagnosis of *Scedosporium* [1, 8]. In our case, the molecular confirmation of the speciation was paramount, as a related species, *S. prolificans*, is known to be resistant to most available antifungal [2].

The choice of antifungal agent in CNS scedosporiosis is important, as various case series have shown that it is invariably resistant to amphotericin B and fluconazole. Variable results have been obtained from miconazole and itraconazole, and both agents have poor CNS penetration. The best available evidence suggests that voriconazole is the optimal agent for both *Aspergillus* and *Scedosporium* species, while amphotericin B has no activity against the latter. Voriconazole also achieves high levels in the CNS, making it the best option for fungal brain abscesses [1, 3, 5–6]. Another azole antifungal, posaconazole, has also been reported to have similar efficacy against CNS scedosporiosis [6].

In our case, treatment failure was likely due to the patient's underlying medical conditions and general debility. However, this is not a significant departure from the outcomes reported in literature. In one study of 80 transplant recipients with scedosporiosis, there was a 58% mortality rate, although receipt of voriconazole was associated with a trend towards increased survival [2]. In another retrospective study of 27 transplant recipients with scedosporiosis, the six month mortality rate was 55%, despite 91% of patients having received voriconazole during the course of treatment. It must be noted that all survivors in the second study had all received voriconazole [3].

CONCLUSION

We present a case of central nervous system scedosporiosis in a male on chronic low-grade immunosuppression for Crohn's disease. Although this presentation is rare outside of highly immunosuppressed transplant patients, it is prudent to keep this on the differential for a fungal brain abscess. Surgical intervention and early initiation of voriconazole are essential for treatment, although mortality remains high.

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Author Contributions

Jean Liew – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Jia Luo – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Graeme Forrest – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Adam Obley – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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