CASE REPORT

Antifungal therapy and surgical drainage for the treatment of a cerebral abscess caused by *Scedosporium apiospermum* in a renal transplant patient - a case report [version 1; peer review: 1 approved, 1 approved with reservations]

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Abstract

Scedosporium apiospermum, the asexual form of *Pseudallescheria boydii*, is a filamentous, opportunistic fungus which can be found in environmental sources all over the world. It is a human pathogen mostly associated with lung, bone and joint infections and less frequently with infections of the central nervous system (CNS). The latter is generally related to the patient's immune state, and occurs most frequently in immunocompromised patients. We present the case of a 64-year-old male patient with a background of chronic kidney failure secondary to nephroangiosclerosis and a renal transplantation who presented with left-sided hemiplegia and dysarthria. A brain MRI revealed a hyperintense lesion with ring enhancement at the right paramedian posterior frontal subcortical area with an associated vasogenic edema. A stereotactic biopsy of the lesion revealed the presence of *S. apiospermum*. The patient received a combined therapy of voriconazole and terbinafine with surgical drainage, which led to temporarily clinical and radiological improvement.

Keywords

Scedosporium apiospermum, *Pseudallescheria boydii*, cerebral abscess, kidney transplant

Open Peer Review

Approval Status

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1. Corrado Girmenia , Sapienza University of Rome, Rome, Italy		
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Any reports and responses or comments on the article can be found at the end of the article.		

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Introduction

Scedosporium apiospermum is a filamentous fungus causing a rare but serious opportunistic infection. It is the asexual form of *Pseudallescheria boydii* and is found in many environmental sources including soil and fresh water, but most commonly in stagnant or contaminated water¹. The infection may be acquired by inhaling the microorganism or after traumatic inoculation through the skin². The sites of infection include the lungs, sinuses, bones, skin, joints and notoriously, the central nervous system (CNS)³. *S. apiospermum* can infect the CNS of both healthy⁴ and immunocompromised hosts. Cerebral abscess is the most common clinical manifestation of *S. apiospermum* brain infections, although cases of meningitis and, less frequently, ventriculitis have also been reported⁵. Brain abscesses may be found as one or multiple lesions⁶. The overall mortality rate of patients infected with this pathogen is higher than 70%⁷. Solid organ transplant and its associated immunosuppression are important risk factors for infections with *Scedosporium* species⁸. Here we present a case of CNS infection caused by *S. apiospermum* in a patient who had received a kidney transplant and was treated with dual antifungal therapy and surgical drainage. The patient initially responded well to the therapy.

Clinical case

A 64 year-old male patient underwent deceased-donor kidney transplantation following a chronic kidney failure secondary to nephroangiosclerosis. The past medical history was significant for hypertension, hyperlipidemia, peripheral vascular disease, chronic anemia and deep venous thrombosis of right lower extremity. Family history was significant for cardiomyopathy in one brother and diabetes in another. The immunosuppressive medication consisted of tacrolimus 3 mg every 12 hours, prednisone 20 mg daily and mycophenolate mofetil 500 mg every 12 hours. Seventeen days after transplantation, he presented left-sided hemiplegia and dysarthria. A brain MRI was performed, which revealed a hyperintense lesion with ring enhancement at the right paramedian posterior frontal subcortical area with an associated vasogenic edema (Figure 1).

A stereotactic biopsy was performed and tissue examination revealed the presence of a filamentous fungus that was identified as *S. apiospermum* (Figure 2). The sample was also cultured in Sabouraud's dextrose agar medium at 25°C for a period of 14 days (Figure 3), the culture turned a dark brown color.

The patient started a treatment with voriconazole (6 mg/Kg po q12h for two days, then 4 mg/Kg q12h VO) and terbinafine (250 mg po daily) and subsequently was subjected to surgical drainage by craniotomy in order to remove the infected tissue.

The patient was on terbinafine for 4 months and continued to be on voriconazole for almost a year. At a follow up visit he showed significant recovery from the left-sided palsy and also an absence of dysarthria. The brain MRI follow-up images showed an improvement in the brain lesion.

Unfortunately, 8 months later the patient clinical course was complicated and he eventually died of problems unrelated to fungal CNS disease.

Figure 1. Brain MRI T2-weighted image. A hyperintense lesion with ring enhancement at the right paramedian posterior frontal subcortical area with an associated vasogenic edema is shown.

Figure 2. Microscopic examination of *S. apiospermum* (from culture). Methylene blue staining showing the morphology of *S. apiospermum*: unicellular microconidia attached to filaments by conidiophores (original magnification 400×).

Figure 3. *S. apiospermum* culture in Sabouraud's dextrose agar medium. The culture grew in Sabouraud's dextrose agar medium at 25°C and turned a dark brown color on the 14th day.

Discussion

Solid organ transplant recipients are highly susceptible to invasive fungal infections⁹.

During the last few decades there has been a marked increase in the number of immunocompromised patients who have suffered *Scedosporium* infections, the most frequent cases being infections of the CNS¹⁰.

Solid organ transplant patients are susceptible to invasive fungal infections as their immunity might be compromised due to the use of immunosuppressant drugs¹¹. Therefore *S. apiospermum* should be considered in the differential diagnosis of immunocompromised patients presenting with a brain abscess¹².

Within the nervous system, abscesses may be located in brain hemispheres, the cerebellum, the brain stem or the spinal cord, where they may cause alterations of consciousness levels, signs of meningeal irritation or focal neurological deficits¹³.

If not adequately treated, fungal brain abscesses in immunocompromised patients often result in poor prognosis. The diagnosis of an invasive fungal infection such as *S. apiospermum* is based on the combination of histopathological, microbiological and clinical findings¹⁴. As the clinical and histopathological presentations of *S. apiospermum* infections are similar to those of other fungi such as *Aspergillus* and *Fusarium* spp., a culture is necessary for accurate diagnosis. Furthermore, while most species of *Aspergillus* (except for *Aspergillus terreus*) are sensitive to amphotericin, *S. apiospermum* is usually resistant¹⁵. In addition, PCR techniques are important to diagnose as well as to distinguish between different species¹⁶.

There are many treatment options described in the literature, but there is an ongoing controversy over which treatment is most suitable

for *S. apiospermum* infections. Voriconazole has emerged as a possible treatment option, since it shows high activity against several species of fungi, including *S. apiospermum*¹⁷. Several reports have shown the successful use of voriconazole synergistically combined with terbinafine against *S. apiospermum*¹⁸ and *S. prolificans*. Furthermore, many authors recommend the surgical drainage of brain abscesses caused by *S. apiospermum*¹⁹. Therefore, a combined antifungal therapy along with an aggressive surgical approach is recommended for therapeutic success²⁰.

Conclusion

S. apiospermum infection of the CNS is a rare but it is an extremely serious medical condition. Immediate diagnosis in the event of brain abscess in an immunocompromised patient is crucial and the choice of a suitable medical treatment is a priority. Despite the aggressive surgical treatment and the appropriate anti-fungal therapy used, mortality rates continue to be high.

Consent

Written informed consent for publication of clinical details and clinical images was obtained from the patient's family.

Author contributions

MIG, PES and JPC contributed to the design of the study. All the authors contributed to writing the manuscript and agreed to the final contents.

Competing interests

No competing interests were disclosed.

Grant information

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Emmanuel Roilides

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This is an interesting rare case of brain abscess due to *Scedosporium apiospermum* in a kidney transplant immunocompromised patient, indeed relatively early (17 days) post-transplantation. The report reads nicely and the Discussion is thoughtful. However, there are a few points that the authors should take into consideration:

1. Have the authors performed an antifungal susceptibility testing? In addition, any molecular identification? It is *apiospermum* complex now.
2. Please, add ESCMID Guidelines for rare fungi as a reference. This is a document that should be definitely cited and used in clinical practice. Tortorano AM *et al.* Clin Microbiol Infect. 2014 Apr;20 Suppl 3:27-46.
3. Page 2. VO should be po

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 03 June 2014

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Corrado Girmenia

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This is an interesting case report of an unusual fungal infection in an immunocompromised patient. The methodology in the diagnostic approach and the description of the case are both adequate.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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