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Case Report

Scedosporium apiospermum BRAIN ABSCESS SUCCESSFULLY TREATED WITH VORICONAZOLE AND SURGERY

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Abstract- *Scedosporium apiospermum* is a filamentous fungus found in soil and stagnant water. It is an emerging pathogen and treatment-resistant opportunistic fungus. Here we describe a brain abscess caused by this emerging pathogen, which was successfully treated by surgery and voriconazole therapy.

Keywords- *Scedosporium apiospermum, Brain Abscess, Voriconazole*

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Introduction

Scedosporium species are increasingly reported as opportunistic fungal infections but can also act as primary pathogens. *Scedosporium* infections are commonly seen in severely immunosuppressed individuals with hematological malignancies and transplant recipients but cases are reported even from immunocompetent individuals sustaining major trauma or near-drowning events are also at risk [1-3]. Disseminated disease is more common in immunocompromised patients with involvement of the lungs, brain, skin and heart whilst infections related to trauma or near-drowning events typically result in focal bone/joint and soft tissue, and lung and/or central nervous system (CNS) disease, respectively [1-5].

Scedosporium apiospermum (*S. apiospermum*) is a ubiquitous saprophytic filamentous fungus present in soil, sewage, and polluted waters [6]. Infections caused by this organism occur in the paranasal sinuses, lungs, skin, soft tissue, central nervous system, and bones. Disseminated disease is also common with usually hematogenous dissemination [7, 8]. It is an emerging pathogen associated with the increased use of glucocorticosteroids, immunosuppressive therapy, and chemotherapy [7, 9]. *S. apiospermum* is considered a major cause of non-Aspergillus mold infections in organ transplant recipients and cystic fibrosis patients [7, 10]. Prompt laboratory diagnosis by culture is important because *S. apiospermum* can be misidentified as other molds with different resistance profiles, such as *Aspergillus* species (spp) [7].

Case Report

A 48-year-old lady presented with a short history of headache, difficulty of speech and right hemiplegia, which was insidious in onset and rapidly progressive. She was a diabetic and had a history of left ear discharge about a month before presentation which was managed at a local health care facility. On examination, she was drowsy but arousable, dysphasic, and had right hemiplegia. There were no signs of meningeal irritation and no active ear discharge. Her hematological investigations revealed hemoglobin of 8.5 gm/dl, with a leucocyte count of 4870/cumm (64% polymorphs, 26% lymphocytes, 2% eosinophils and 8% monocytes). Platelet count was 1.28 lakhs/cumm. Random blood sugars were 345 mg/dl and HBa1c was 10.8, Urine ketone bodies were negative.

Serological status was non-reactive for HIV, Hepatitis B and HCV. Spiral CT acquisition of the whole brain was performed using a 128-detector Row Multislice CT scanner. Multiple hypodense lesions with subtle thin-walled peripheral iso-hyperdense rim were seen in the left temporal lobe, left inferior frontal lobe, left corona radiata, left external capsuloganglionic region with surrounding edema. Few of them appeared to be coalescent, the largest measuring 39x25 mm.

She underwent a left frontotemporal craniotomy and following durotomy the abscess wall was noted on the surface of the middle and inferior temporal gyrus and the wall was dissected and excised. The abscess was filled with thick greenish pus.

Gram stain of the pus showed plenty of polymorphs and no organisms. Genexpert and Zeihl Neelsen stain for Acid-fast bacilli were negative. The potassium hydroxide mount of the pus revealed plenty of branching filamentous hyphal structures suggesting fungal etiology.

Aerobic and anaerobic bacterial cultures resulted in no bacterial growth. Fungal culture was put up on SDA (Sabouraud's Dextrose Agar) at 30°C.

Fungal growth was initially observed after 72-96 h as whitish-gray colonies. After 5-7 days of culture, the colonies became grey white with wooly texture. On the reverse side of the plates, the color of the colonies was dark with brownish-black zones in the center. Lactophenol cotton blue preparation of these colonies showed the conidial structures of *Scedosporium apiospermum*; the conidiophores contained conidiogenous cells producing conidia.

For further identification, the plates were sent for MALDITOF MS (Matrix-associated laser desorption ionization-time of flight mass spectroscopy), which resulted in *Scedosporium apiospermum* with 99% confidence intervals.

She made an uneventful recovery and her post-operative CT showed residual abscesses in the centrum semiovale region. Her speech and motor power in the right upper and lower limbs improved. Chronic suppurative otitis media (CSOM) could be the predisposing factor in our patient. The patient was started on voriconazole 200mg twice daily and showed a good response with serial imaging showing a reduction in the size of the residual lesion. She was continued on oral voriconazole for a total duration of 3 months. She also made a full neurological recovery at the last follow-up.

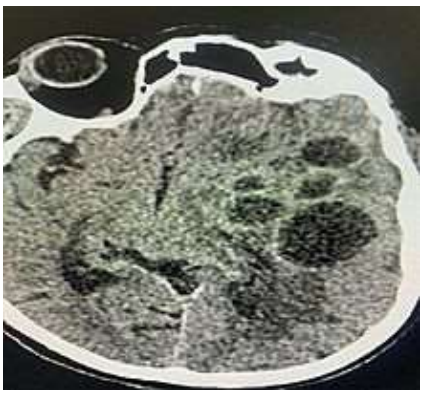

Fig-1 CT brain showing multiple thin-walled hypo-dense lesions with peripheral iso-dense rim at left sub-thalamus and temporal region with surrounding edema causing midline shift to right.

Fig-2A Whitish gray fungal colonies on Sabouraud's Dextrose Agar

Fig-2B Lactophenol cotton blue preparation of these colonies showed the conidial structures of *Scedosporium apiospermum*; the conidiophores contained conidiogenous cells producing conidia.

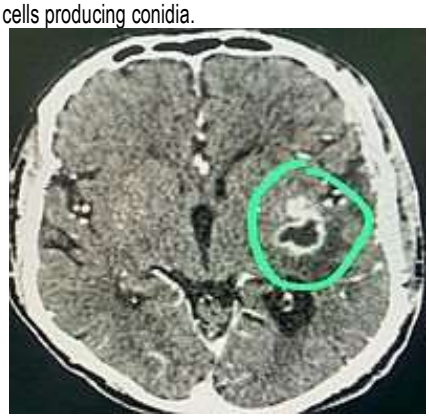

Fig-3 CT Brain showing ring enhancing lesions with surrounding edema at left capsuloganglionic region. Decrease in size and edema noted as compared to previous CT

Discussion

S. apiospermum is a saprophyte with worldwide distribution, found in soil, polluted water and sewage, cattle and poultry manure, and coastal waters. Mycetoma of the foot is a common clinical manifestation seen due to this organism [11]. It involves the CNS in 50% of invasive disease cases, with brain abscess being the main pathology with or without associated meningitis [11,12]. The respiratory tract is thought to be the major portal of entry for invasive disease, either by the inhalation of conidia or aspiration of polluted water, with hematogenous spread to other organs. However, dissemination may also occur from other primary sites of infection, or from direct inoculation, for example penetrating injury or surgery [13].

The clinical spectrum of infection in immunocompetent hosts includes keratitis, endophthalmitis, otitis, sinusitis, central nervous system infections, osteoarticular and soft tissue infections and pneumonia after near drowning [14,15,16]. In patients with severe immunosuppression, deep-seated infections can involve any organ with a predilection for skin, sinuses, lungs and central nervous system [17,18]. The diagnosis of *Scedosporium* infection is often difficult, because clinical features, histopathology and radiological features are like those of *Aspergillus, Fusarium* and other relatively common hyaline hyphomycetes.

Scedosporium apiospermum is a difficult organism to treat in the CNS. It often demonstrates resistance to many of the commonly available antifungal agents, including amphotericin B, itraconazole, and ketoconazole. These antifungal agents have poor penetration into the CNS [19].

Currently, Voriconazole is considered a first-line agent for the treatment of invasive infections caused by Scedosporium apiospermum. [20] Voriconazole has good blood-brain barrier penetration. Of the available triazoles, voriconazole has the most potent in vitro activity against *S. apiospermum*, with MIC values from 0.03 to 1 mg/ml [13,21]. Posaconazole has good in vitro activity (MIC 0.5–2 mg/ml), however, clinical data is lacking [13,21,22]. Other antifungals have demonstrated less promising results. Amphotericin B has weak in vitro activity against *S. apiospermum* with an MIC of 1–16 mg/ml, and when used as monotherapy for CNS infection had a mortality rate of 87.5% in 16 reported cases [23]. There is limited clinical experience with echinocandins which have highly variable activity against Scedosporium sp. (MIC 0.2–16 mg/ml for caspofungin and anidulofungin) [22].

Antifungal therapy combined with surgery is generally considered important for successful treatment of invasive *S. apiospermum* infection. A significant difference in the mortality of patients with *S. apiospermum* CNS infection has been documented in those treated with antifungals alone (74%) and those treated with antifungals in addition to surgical debridement (31%) [23].

Conclusion

The clinical improvement of our patient after surgery combined with voriconazole therapy was remarkable. Based on this experience, we would like to recommend voriconazole as the drug of choice for the management of CNS infections with *S. apiospermum*.

Application of research: Diagnosis and treatment of *Scedosporium* brain abscess

Research Category: Mycology

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Study area / Sample Collection: KIMS Hospital, Kondapur, Hyderabad

Strain name: *Scedosporium apiospermum*

Conflict of Interest: None declared

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.
Ethical Committee Approval Number: Nil

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