Case Report

Time versus tissue: Timely identification of Scedosporium Rhinosinusitis in a post-COVID-19 case by MALDI-TOF MS leading to successful management

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ABSTRACT

COVID-19 (Coronavirus Disease 2019), illness with associated comorbidities and corticosteroid therapy makes the host immunocompromised and prone to opportunistic microbial infections. As the world continues to struggle with the pandemic of COVID-19, an increase in cases of opportunistic fungal infections have been reported from all over the world during the second wave of COVID-19 like aspergillosis, mucormycosis, and candidiasis. Scedosporium apiospermum is an emerging pathogen that is usually associated with mycetoma, pulmonary infection, and central nervous infections. It has been rarely associated with fungal rhinosinusitis (FRS). In this study, a rare case of FRS caused by S.apiospermum in an immunocompromised post-Covid-19 diabetic woman is reported.

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Scedosporium species are ubiquitous, filamentous fungi commonly isolated from soil, polluted water bodies, and sewage. The genus Scedosporium consists of two medically important species Scedosporium apiospermum and Scedosporium prolificans.1 Recent molecular studies have shown that Scedosporium is a species complex comprising of five distinct groups, which are S. auranticum, Pseudoallescheria minitispora, S. dehoogii, S. apiospermum, and Pseudoallescheria boydii, the last group consisting of four subgroups which are P. boydii, P. angusta, P. ellipoidea, and P. fusoidae. Also, S. prolificans is now renamed as Lomentospora prolificans.2

Scedosporiasis represents a broad spectrum of clinical diseases caused by agents of the genus Scedosporium. Infections

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Case report

A 64-year-old female patient, a known case of diabetes mellitus and hypertension was admitted to a local regional hospital with a provisional diagnosis of post-COVID viral pneumonia. During her stay in the hospital, she developed right-sided facial swelling, facial pain, and right-side headache. Computed tomography was done which showed inflammatory mucosal thickening in bilateral maxillary sinuses and sphenoid sinuses. Soft tissue swelling with fat stranding in the right maxillary, frontonasal and infraorbital region along with blockage of right osteomeatal complex was seen. However, no erosion was seen along the walls of paranasal sinuses (PNS).

Histopathological examination revealed fungal elements suggestive of *Aspergillus* spp. The patient was managed as a case of acute invasive fungal sinusitis. She underwent bilateral functional endoscopic sinus surgery (FESS), was put on injection amphotericin B, and was subsequently discharged. However, the patient had persisting symptoms along with swelling of the right side of the face for which she reported to our hospital. On ENT (ear, nose, and throat) examination post-FESS changes were seen. After examination in the oral and maxillofacial surgery (OMFS) OPD, multiple draining sinuses were observed in the alveolar mucosa of the maxilla Fig (1a, b) along with boggy swelling of the alveolar and palatal mucosa. Patient consent was obtained for images and inclusion in the study.

A pus sample from the draining sinuses and a necrotic bone sample from the right maxillary alveolus was sent to our lab for KOH mount, fungal stain, and culture. No fungal elements were seen on KOH and fungal stain (Grocott’s methenamine silver stain) on the pus sample. But KOH mount and fungal stain (GMS) from necrotic bone showed hyaline septate hyphae with acute angle branching (Fig. 3a) (Fig. 3b). The culture was done on sabouraud dextrose agar (SDA) at room temperature. Fungal growth was initially observed after 72 h as whitish-grey coloured colonies with cottony texture. Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) was performed to identify the isolate. It identified the fungus as *Scedosporium apiospermum* with a score of 99.9% within 15 min (Fig. 3f). After 6–7 days of culture, colonies became greyish-brown in the center and grey–white at the periphery with a fluffy texture. The reverse side was orange in color (Fig. 3e). LPCB mount done from slide culture showed clavate to ovoid conidia which we rounded above with truncate bases. Conidia were elongated, simple, or branched conidiophores, and few were seen laterally over hyphae. It also shows septate hyphae with acute angle branching (Fig. 3c and d). The colony morphology of *Aspergillus* can vary with different species. Usually, colonies are velvety, have a floccose texture, and are pigmented on front and reverse. Colonies grow at very rapid growth and mature in three to four days. On microscopy, it has long conidiophores with uniseriate to biseriate heads bearing conidia which varies with different species. Colony morphology and microscopic features of *Pseudoallescheria boydii* and *Scedosporium apiospermum* are quite similar so to differentiate between them we need molecular techniques.

Before the lab reports were out, the patient was thought to be a case of mucormycosis and was empirically started on

![Fig. 1 – a: Boggy swelling in anterior maxilla involving the palatal mucosa with active draining abscess. b: Grade II tooth mobility present with respect to 11, 12, 13, 21, 22, and 23. c: Post-op follow up after three months.](image-url)
injection amphotericin B (150 mg/kg). However, based on the lab reports, the injection of amphotericin B was stopped and the patient was managed with surgical debridement and antifungal treatment, which included syrup posaconazole (400 mg BD). Repeat computed tomography was carried out to find out the extent of invasion. It depicted bony destruction of the maxillary alveolus, maxilla, and hard palate along with changes suggesting the involvement of maxillary, ethmoidal, and sphenoidal sinus (Fig. 2a, b and c). The patient underwent repeat FESS for endoscopic clearance of the ethmoidal and sphenoidal sinuses followed by sequestrectomy, surgical debridement, and partial bilateral maxillectomy by the OMFS team. Patient was put on injectable antibiotics (injection Magnex (1.5 g/day), injection Flagyl (500 mg/TDS), injection Targocid (400 mg/TDS) and syrup posaconazole (400 mg BD) for three months.

The patient responded well to injectable antibiotics and antifungals. The patient was discharged after one week. The patient came for review after two weeks subsequently and was found to be stable and responding well to treatment. On further follow-up, post-op healing was satisfactory with no evidence of recurrence (Fig. 1c).

**Discussion**

*Scedosporium* is a species of fungus classified in the phylum Ascomycota. Mostly it is associated with eumycetoma. Sinus and CNS infections by *Scedosporium apiospermum* are not so common. Most of the reports of *S. apiospermum* sinusitis have involved the maxillary sinuses, with a few instances of the ethmoidal, frontal, and sphenoid sinus involvement. In our case report, patient has presented with maxillary sinusitis which remains the most common involved sinus as per the literature. The source of the infection could be explained by understanding the epidemiology of *Scedosporium* species. Agricultural areas, as well as playgrounds and soils in urban surroundings, are found to be densely colonized with *Scedosporium* species.

*Scedosporium* species has got similar clinical as well as histopathological presentation as that of *Aspergillus*, so usually, it gets misdiagnosed as *Aspergillus*. Both appear as septate hyaline hyphae with acute angle branching on histopathological examination. A reporting pathologist needs to correlate the histopathology findings with microbiological diagnosis as an erroneous assumption of *Aspergillus* infection could lead to ineffective therapy with antifungal, and hence poor outcome. Colony morphology on culture and sporulation by culture can help in differentiating *Aspergillus* species and *Scedosporium* species infection; however, it can also sometimes lead to confusion. Hence, accurate identification of clinical isolates at the species level becomes of utmost importance as these species differ in their antifungal susceptibility pattern. Matrix-assisted laser desorption ionization-time-of-flight mass spectrometry (MALDI-TOF/MS) can be used for fast and accurate diagnosis of the species from the clinical isolate. Species identification can be done by macroscopic and microscopic examination of the colonies but it should be always confirmed by molecular methods such as fungal PCR, genus/species-specific multiplex PCR. In our case, we used MALDI-TOF/MS and phenotypic methods to establish the diagnosis.

Fungal sinusitis due to *Scedosporium apiospermum* has rarely been reported. In COVID -19 pandemic, mostly the isolates which have been reported are *Aspergillus* spp, *Candida* spp, and *Mucor* spp. In our study, patient has shown improvement after treatment with surgical debridement and antifungal treatment with posaconazole, and this is further strengthened by a study done on the treatment of *Scedosporium apiospermum* in a case of brain abscess. However, due to the scarcity of data and the potential publication bias, no solid recommendations can be provided for the therapy of *Scedosporium* infection. In vitro and in vivo data shows that *S. apiospermum* is resistant to amphotericin B and flucytosine.
and demonstrates variable susceptibility to itraconazole, voriconazole, posaconazole and micafungin. This case enlightens us to consider rare fungal infections as a differential diagnosis in a post-COVID-19 patient with an immunocompromised state. This case also highlights the importance of culture for fungal isolation over histopathological examination and the role of MALDI-TOF/MS in identification up to species level. Prompt diagnosis and early treatment are imperative in such patients for a better prognosis. This study brings out the role of Posaconazole in the treatment of fungal rhinosinusitis (FRS).

Disclosure of competing interest

The authors have none to declare.

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Fig. 3 – a: KOH mount with LPCB stain showing irregular branching with septate hyaline hyphae. b: Grocott’s methenamine silver (GMS) stain showing acute branching in hyaline septate hyphae (x400). c: LPCB mount of Scedosporium apiospermum from slide culture showing clavate to oval conidia which are rounded above with truncate bases. Conidia are born on elongated, simple, or branched conidiophores and few are seen laterally over hyphae. Conidia having truncated base (x400). d: LPCB mount of slide culture showing acute angle branching of the hyphae (black arrow) (x400). e: Sabourauds dextrose agar (SDA) with white- to brown-colored growth seen with cottony texture after seven days of incubation. f: Fungal isolate from culture was identified as Scedosporium apiospermum to the accuracy of 99.9% by MALDI-TOF/MS.

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