Schizophyllum commune maxillary sinusitis in an immunocompromised patient: A case report

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ABSTRACT

Schizophyllum commune is a basidiomycotic fungus that grows ubiquitously on trees and rotting wood. Human infections caused by it are of diverse presentation but are very rare. We present a case of sinusitis caused by S. commune in a 58-year-old female patient with post-COVID-19 infection along with a history of allergic rhinitis and diabetes mellitus type 2. Computed tomography scan findings established the clinical diagnosis of fungal maxillary sinusitis which was confirmed with culture report and polymerase chain reaction followed by sequencing. The patient underwent functional endoscopic sinus surgery. She was treated empirically with itraconazole after surgical excision.

Key words: Schizophyllum commune, Sinusitis, COVID-19, Sequencing, Antifungal susceptibility testing

Schizophyllum commune is a filamentous fungus of phylum Basidiomycota and family Schizophyllaceae which colonizes diverse trees and rotting wood globally [1]. Since the first reported case of S. commune as a human pathogen in 1950 by Klingman; until recently, it was thought to be a rare cause of human disease [2]. Although human diseases are reported rarely, it is an emerging fungal pathogen, causing an array of allergic and invasive clinical manifestations both in immunocompetent and immunocompromised individuals [2]. However, because of difficult definitive identification and lack of familiarity with its pathogenicity, infections caused by S. commune are probably underreported in India.

Here, we describe a case of sinusitis caused by S. commune in a 58-year-old immunocompromised patient with post-COVID-19 infection.

CASE REPORT

A 58-year-old female presented with nasal obstruction and purulent nasal discharge from the left side for one week. It was associated with cough, cold, and headache. She had an episode of cerebral infarction 2 years back following which, she had developed right-sided hemiplegia and was bedridden since then. She was a known case of allergic rhinitis. She was on oral antihyperglycemic drugs for diabetes mellitus type 2 for the past 8 years. She had a history of COVID-19 infection one month before for which she was hospitalized for 10 days and was treated with dexamethasone, remdesivir, azithromycin, and low-molecular-weight heparin for 5 days.

On examination, the patient was breathless with shallow respiration, respiratory rate 34/min with SpO2 of 90% at room air, afebrile, pulse rate 110/min, and blood pressure 100/60 mmHg. Local examination revealed inflammation of the mucosa, bilateral nasal obstruction, hypertrophy of the left inferior and central turbinates, and pain at palpation over the maxillary and frontal regions. Examination of the head and neck revealed no significant finding.

Laboratory investigations revealed hemoglobin of 10.3 g/dl, white blood cell count of 17,800/mm³ with 6.7% eosinophils, and a high level of serum immunoglobulin E, 179 IU/mL (0–100 IU/mL). Hemoglobin A1C levels were found to be 7.8%. X-ray chest was normal. A non-enhanced computed tomography scan of the paranasal sinuses revealed homogenous soft-tissue opacification in the left maxillary sinus including left ostiomeatal complex, left ethmoid sinus, and left half of the sphenoid sinus (Fig. 1a and 1b). There was associated rarefaction and erosion of medial/nasal wall maxillary sinus and maxillary bone including an incisive canal (Fig. 2a and 2b). These findings were suggestive of invasive fungal sinusitis in a patient with a history of COVID-19 infection.
The left-sided functional endoscopic sinus surgery was done with the opening of the left maxillary sinus. The thick mucus material removed from the right maxillary sinus was sent for fungal culture, as well as, for aerobic and anaerobic bacterial culture. Direct microscopy with Calcofluor white stain of the mucus material showed the presence of fluorescence hyphae (Fig. 3a). About 20% KOH preparation showed the presence of septate hyphae (Fig. 3b). Culture at 27°C and 37°C on Sabouraud’s dextrose agar containing gentamicin yielded a rapidly growing, white to pale buff, densely woolly fungus with a pale yellow-brown reverse in 3 days (Fig. 4). It produced a strong unpleasant odor at 37°C. No fungal growth was seen on cycloheximide-containing medium. No bacterial growth was observed under aerobic or anaerobic conditions. No conidia or sporangiospores were seen in microscopic examination. Septate, narrow, and wide-angled both branched hyphal filaments with clamp connections and without spicules were seen (Fig. 5a and b). The macroscopic examination did not reveal structures such as fruiting bodies even after 1 month of incubation.

The grown fungus could not be identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDITOF MS)(bioMérieux, France). Molecular identification of the isolate was done by panfungal DNA polymerase chain reaction (PCR) and sequencing of amplified products. The PCR sequencing targets multicopy genes, the ribosomal DNA (rDNA), genes (18S, 28S, and 5.8S), and the intervening internal transcribed spacer (ITS) regions (ITS1 and ITS2). DNA was extracted. The amplified and purified product was sequenced on 3500 DX Analyzer (Thermo Fisher Scientific, Massachusetts, USA). The sequences were then run through GenBank Basic Local Alignment Search Tool (BLAST) searches (http://www.ncbi.nlm.nih.gov/BLAST/Blast.cgi) for species identification. BLAST searches confirmed the isolate as S. commune with 99.64% identity (GenBank accession no. MK647986.1) of ITS1, ITS2, 5.8S gene, and rRNA gene. Antifungal susceptibility testing (AFST) by broth microdilution method (BMD) was done, however, it gave inconclusive results. The patient was treated empirically with itraconazole given 200 mg/day for 21 days after surgical excision. Follow-up on day 30 post-surgical excision showed no swelling and recurrence. The patient was lost to follow-up then after.

**DISCUSSION**

*S. commune* has been implicated in the etiology of onychomycosis, while at the other, it is recognized as the etiological agent of a variety of hypersensitivity disorders, such as allergic sinusitis, bronchopulmonary mycoses, bronchial mucoid impaction, and chronic eosinophilic pneumonia, and of invasive infections, such as fatal disseminated infections involving the lungs, orbit, and brain [3,4]. Globally, most reported cases are of bronchopulmonary infections and sinusitis, consistent with airborne transmission of...
basidiospores. Depending on several underlying factors such as host immune status, deviated nasal septum, corticosteroid therapy, and duration of exposure to spores, the infection may remain localized or become disseminated [5]. To the best of our knowledge, the first case of sinusitis by *S. commune* in India was reported by Swain *et al.* in 2011 in an immunocompetent patient [6]. Few cases of sinusitis due to *S. commune* were documented by Premamalini *et al.*, Verma *et al.*, and Gupta *et al.* [1,7,8]. Chaudhary *et al.* had reported *S. commune* as the etiological agent of allergic bronchopulmonary mycosis and pulmonary fungal ball [3]. Fungal keratitis due to *S. commune* had been described by Reddy *et al.* [4].

Distinctive spicules, clamp connections, and basidiocarp are the key characteristic features for the identification of dikaryotic isolate of *S. commune*. However, these are not exhibited by many strains of *S. commune* isolated from human specimens [3]. The isolate from our patient displayed clamp connections but no fruiting bodies were seen even after a longer incubation. Earlier, the use of a mating test was suggested, where a monokaryotic strain is dikaryotized which further could result in a fruiting body. However, it is cumbersome with prolonged incubation and thus not easily suitable for routine mycology diagnostic laboratory [9]. MALDI TOF MS (bioMérieux, France) was unable to identify *S. commune* in our case. However, studies by Cavaonna *et al.* and Michel *et al.* could successfully identify it using MALDI TOF MS (Bruker Daltonics GmbH, Bremen, Germany) [5,10]. In the present case report, gene sequencing of the ITS region and D1/D2 regions of the 26S rDNA was used for accurate identification of *S. commune*. In accordance with our findings, sequence-based identification was used and reported in a few cases [4,8,9,11,12]. Given the excellent specificity of this technique, sequencing has become the gold standard for fungal identification. Accurate identification is important considering the invasive nature of *S. commune*. Buzina *et al.* suggested that in case of white, cottony, rapidly growing fungal culture obtained from the clinical sample and without a distinct microscopic feature for clear identification, the possibility of *S. commune* should be considered, and simultaneously, it may be confirmed by molecular techniques [13].

The optimal approach to the management and utility of the azoles in treating *S. commune* infections remains unclear. Varied response to oral itraconazole and topical steroids has been reported [6,9]. Monotherapy with amphotericin B was reported to be effective [12,14]. Voriconazole monotherapy was reported by Michel *et al.* [10]. In sinusitis or invasive disease, surgical drainage or debridement and antifungal therapy would seem to be the approach of choice. The type, dose, and duration of antifungal therapy remain uncertain [1,9]. Low minimum inhibitory concentrations range were reported by Chaudhary *et al.*, Kim *et al.*, and Gonzalez *et al.* for amphotericin B, echinocandins, and azoles [3,12,15]. However, further AFST by BMD with a greater number of *S. commune* isolates is indicated for a more efficacious antifungal therapy for this emerging fungal pathogen.

**CONCLUSION**

*S. commune* is an emerging pathogen. Each case should be documented elaborately to aid clinicians and microbiologists. Considering its invasive nature, accurate and timely diagnosis with molecular diagnostic methods along with antifungal susceptibility data are important to prevent chronicity of illness, local or systemic complications, and non-specific treatment to the patient.

**REFERENCES**


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