



Short Communication

# Allergic fungal sinusitis caused by *Schizophyllum commune*



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## KEYWORDS

Sinonasal infection;  
Surgery;  
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**Abstract** A case of allergic fungal sinusitis (AFS) due to *Schizophyllum commune* was reported. The pathogen was identified using molecular bioanalysis. The patient underwent the functional endoscopic sinus surgery followed by the radical maxillary sinusotomy with canine fossa trephine. This case suggested that complete surgery allowed optimal disease clearance for AFS caused by *Schizophyllum commune*.

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## Introduction

Allergic fungal sinusitis (AFS) was first reported by Millar et al<sup>1</sup> in 1981 and named by Katzenstein et al<sup>2</sup> in 1983 who proposed the diagnostic criteria of eosinophilia, the presence of Charcot-Leyden crystals and *Aspergillus* hyphae. However, subsequent reports demonstrated that AFS could

be caused by fungi other than *Aspergillus*. The Bent and Kuhn diagnostic criteria became the standard for diagnosis of the disease, including the following major criteria: (1) characteristic computed tomography (CT) findings of chronic paranasal sinusitis, (2) nasal polyposis, (3) allergic mucin, (4) identification of fungi in the paranasal sinus contents without fungal invasion of the tissue and (5) type I allergy confirmed by history, positive skin tests or serology.<sup>3</sup>

The basidiomycete fungus *Schizophyllum commune* is a rare cause of mycotic disease. *Schizophyllum commune* is often misdiagnosed to *Aspergillus* sp, as the histopathological findings are similar and the fungus is difficult to identify in culture when atypical fungal populations are present.<sup>4</sup> We present a case of AFS associated with *Schizophyllum commune*.

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A 56-year-old woman presented to the Department of Otolaryngology, Sun Yat-sen Hospital, Sun Yat-sen University, Guangzhou, China in March, 2008. She complained of a predominantly left-sided nasal obstruction accompanied by malodorous, thick, mucopurulent rhinorrhea, mild swelling and pain in the left cheek for 3 months. There was no bloody rhinorrhea, fever, headache, or toothache. Patient denied past medical and surgical histories were unremarkable without preexisting asthma or other allergic diseases. Cigarette smoking and illicit drug using were negative. No potential risk factors such as diabetes mellitus, immunodeficiency, or previous facial trauma were determined. She was given an antibiotic and antihistamine for one month with minimal improvement.

Physical examination revealed mild non-tender swelling of the left cheek. Eye movement was normal and there was no exophthalmos. Anterior rhinoscopy showed mucopurulent discharge in the left nasal cavity. Endoscopic examination found thick, greasy secretions at the left middle meatus and swelling of left middle and inferior turbinates. There were no polyps and other neoplasm in the nasal cavity and meatus. The dental examination showed no infectious sites.

Laboratory investigations showed an increased peripheral blood eosinophil count ( $1 \times 10^9/\text{ml}$ , 0.154). Total serum IgE (sIgE) was 565 IU/ml, which was significantly elevated (reference range: 0–100 IU/ml). sIgE to *Penicillium*, *Cladosporium*, *Aspergillus* was grade 1 (reference range:  $\leq$  grade 1). IgA, IgM, IgG, C4 and C3 levels were within normal limits.

A CT scan of sinuses revealed opacification of the left maxillary sinus without bony erosion or calcification (Fig. 1).

**The 1st operation:** An endonasal endoscopic surgery was undertaken. The mucosa of left middle meatus was found edematous. After cutting the uncinata process, the ostium of left maxillary sinus was expanded. The sinus was completely filled with thick, viscous, yellow secretions. The

mucosa was noted to be with apparent polypoid edema. The secretion was removed and the polypoid mucosa was kept. The maxillary cavity was irrigated with normal saline and then filled with budesonide inhalation suspension (Pulmicort Respules). Merocel was placed into left middle meatus and removed 24 h later.

The secretion and maxillary mucosa samples were sent to pathology and microbiology. Microscopic examination of the tissue showed eosinophil accumulation in specimen without fungal organisms. Fungal culture failed to detect colonizations.

**Post-operative management and follow-up:** Within the 1st week after surgery, the patient was prescribed with systemic antibiotics (intravenous cefamandole 2 g every 12 h for 3 days followed by oral cefuroxime 250 mg every 12 h for 4 days). Topical corticosteroid (Budesonide aqueous nasal spray 64  $\mu\text{g}/\text{nostril}$  twice daily) and saline irrigation at 500 ml/time once daily were started after nasal packing removal.

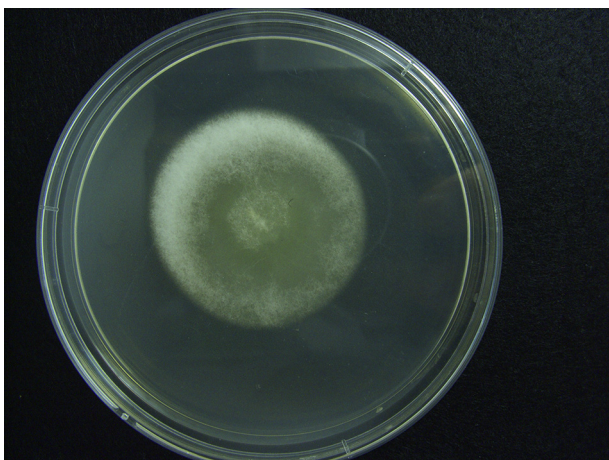
Weekly endoscopic monitoring was used to assess the patient postoperatively. In the first month, the left maxillary sinus was filled with thick, viscous, yellow secretions and mucosa was edematous as seen intraoperatively. Pathological examination showed inflammatory tissue with eosinophilic mucin and fungal hyphae. The hyphae were septated microscopically. Mucus culture was positive for fungal colonization but unable to identify the microorganism. Samples were sent for molecular analysis that detected *Schizophyllum commune*. In the 2nd month, the maxillary sinus was irrigated using Amphotericin B once daily (5 mg of Amphotericin B dissolved in 250 ml of sterile water). A course of systemic corticosteroid, prednisolone, was commenced at a dose of 30 mg/day for 2 weeks, then tapered to 5 mg/day, at which patient was maintained up to 6 month postoperatively. By then, the maxillary secretion was decreased and became thin. But the polypoid edema continued to be observed at the maxillary mucosa.

**The 2nd operation and post-operative management:** The patient refused conservative, topical treatment and opted for radical surgery. Therefore, 8 months after the first surgery, the patient underwent radical maxillary sinusotomy using the canine fossa trephine (CFT) technique. All the diseased mucosa and mucus were cleared but the mucosa lining the ostium was preserved. Pathology report showed chronic inflammation with granuloma formation and eosinophilic infiltration. The patient was continued on nasal spray of topical corticosteroid and saline irrigation for 3 months. Again, monthly endoscopy was performed. Two months after radical surgery, the maxillary cavity became epithelialized and patient reported resolution of symptoms. Topical corticosteroid was continued and the patient was followed for 60 months without recurrence.

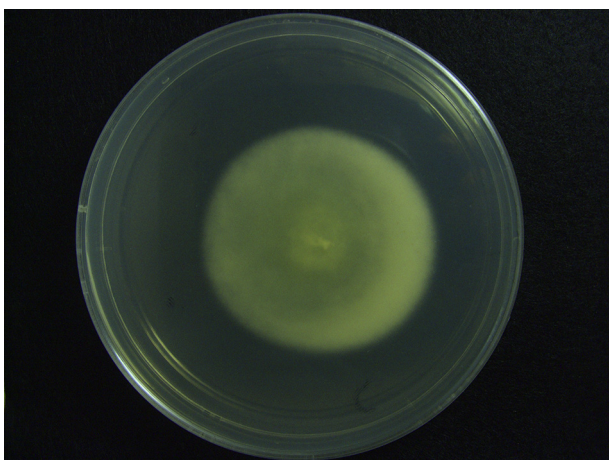
**Mycological studies:** The contents of the paranasal sinuses were cultured on Sabouraud dextrose agar (SDA) at 27 °C. After 7 days, the fungal colony grew fast and its aerial mycelium is white and cotton-like (Fig. 2). The back of the fungal colony was light-yellow after turning over the culture plate (Fig. 3). Microscopic detection of the fungus (staining with lactophenol-cotton blue solution) showed transparent and septate hypha with short projection at the septum (Fig. 4). Since the isolate was difficult to identify, the culture was sent for molecular biology exam.



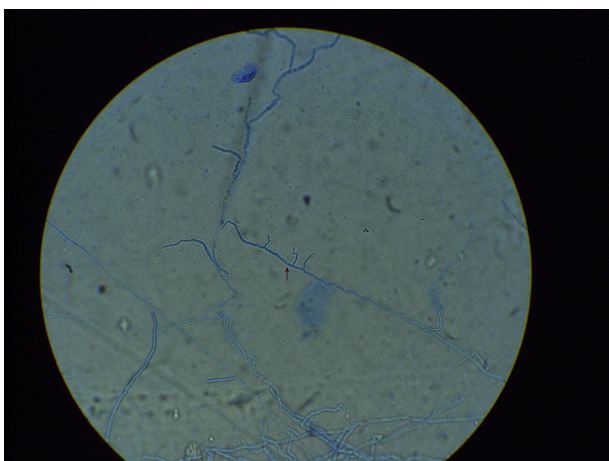
**Fig. 1** Axial CT showed the left maxillary sinus was filled with opaque, without bony erosion or calcification.



**Fig. 2** Fungal culture, the right side, the fungal colony grew fast and its aerial mycelium is white and cotton-like.



**Fig. 3** Fungal culture, the reverse side, the back of the fungal colony was light-yellow after turning over the culture plate.



**Fig. 4** Microscopic detection, staining with lactophenol-cotton blue solution, the black arrow showed the short projection at the septum.

**Molecular biology:** The fungus was isolated and saved at the Centre of Clinical Fungus Research, Sun Yat-sen Memorial Hospital, Sun Yat-sen University (Num: SUMS0427). The fungus was cultured on SDA for 7 days at 27 °C. Some hyphae were put into a mortar box and grinded with liquid nitrogen, then transferred to Homogenizer Tubes (Omega). Genomic DNA was then extracted by using the Omega Fungal DNA Kit (D3390-00). PCR was performed with universal fungus-specific primers for ITS rDNA-ITS4 and ITS5 (ITS: 5'-TCCTCCGCTTATTGATATGC-3', ITS:5'-GGAAGTAAAA GTCGTAACA AGG-3'). The total volume for PCR was 50 µl, which included 25 µl for Premix Taq Version2.0 (TaKaRa Code:D331A), 2 µl for template, 21 µl for sterile bidistilled water and 1 µl for each primer. Reaction condition included: pre-denaturation at 94 °C for 4 min; denaturation at 94 °C for 30 s, annealing at 55 °C for 30 s; extension at 72 °C for 1 min, 35 cycles totally; final extension at 72 °C for 10 min. And the amplicon was purified and sequenced by Invitrogen Life Technologies Corporation, Shanghai. The amplicon was 581 bp and the sequence was as the following:

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TGATTTGAGGTCaAGTCAAAAGTTAGCGCACAAAGTCGCTAG
TCTCAGTCAAGAGACGGTTAGAAGCAGACTCCTATTGAAACTG
ACTAGGTCAGCCCCGAGATGGTCAACGACGTAGAAATTATCAC
ATCGGAGACGCGATCCCGCAAGGGAAAATCCGCTAATACATTTA
AGAGGAGCTGGCTCCGTTAGGCTCCAGCAGACCTCCACTTCC
AAGCCACTCTCGAGACCGAAGTCAAAAGAGGGTTGATGGTAT
TTAATGACACTCAAACAGGCATGCCCTCGGAATACCAAAGGG
CGCAAGGTGCGTTCAAAGATTCGATGATTCACTGAATTCTGC
AATTCACATTACTTATCGCATTTCGCTGCGTTCCTTCATCGATG
CGAGAGCCAAGAGATCCGTTGTCGAAAGTTGTATTAACTTTTT
AGGGTCTGTCAAGACCATGATTACATTCGTTAACATACTTTAA
GGTGTGAGGTAGACGTAGTCAACCGCCGCCCGTGAAGGCTT
TGGGACTACATAAGGTGCACAGGATCAGAACAAAGATGAAGT
GTTTGATTCGTTAATGATCCTTCCGCAGGC.

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The fungus was identified by using the BLAST program ([www.ncbi.nlm.nih.gov/BLAST](http://www.ncbi.nlm.nih.gov/BLAST)). The result showed that SUMS0427 (Accession No.: GQ358924.1) matched with *Schizophyllum commune* (AB369909.1) in GenBank. The 581bp-nucleotide sequence showed 99% homology with the reference sequence.

## Discussion

AFS constitutes 5%–7% of all cases of chronic rhinosinusitis that require surgery.<sup>5</sup> Most series were from medical centers in the southern United States.<sup>6</sup> Allergic fungal sinusitis is not a common disease in China. The patient in this report had nearly all of the typical characteristics of AFS raised by Bent and Kuhn. It is believed that AFS is a type I-mediated allergic reaction. The majority are associated with the members of the ascomycota or the basidiomycota, and *Calvatia*, *Coprinus*, *Ganoderma*, *Pleurotus* and *Psilocybe* are the most prominent genera of the basidiomycota.<sup>7</sup> *Schizophyllum commune* also belongs to the basidiomycota and is worldwide growing on various trees, decaying wood and mushrooms that was reported in more than 10 series of AFS over the last 25 years according to pubmed.<sup>8–22</sup>

Since the fungi for AFS are in the highly viscous mucin, it is often difficult to isolate them by simply inoculating a

portion of the paranasal sinus contents on agar and incubating. Maybe it was the failure reason for the first-time fungal culture for our case. Ponikau et al<sup>23</sup> reported that it became easy to detect fungi if an enzyme, dithiothreitol, was employed to degrade the mucin at first.

Clark et al<sup>12</sup> described the first case of AFS associated with *Schizophyllum commune*. The fungus was identified on the basis of its morphology and minute peg-like outgrowths from vegetative hyphae and clamp connections. Sigler et al<sup>24</sup> thought that the mycological diagnosis of *Schizophyllum commune* is easy to make when hyphae bearing spicules or clamp connections are present. Identification of *Schizophyllum commune* is difficult in case of monokaryotic isolate because it is devoid of clamp connections. It was the first time to find this fungus in our mycology lab and we did molecular biology exam to identify it.

AFS is considered as a special type of chronic rhinosinusitis and the primary treatment for AFS is surgery. Functional endoscopic sinus surgery (FESS) is the gold standard surgical treatment for chronic rhinosinusitis. Although this case was localized in maxillary sinus, it had severely polypoid edema and was rich in eosinophilic mucus. According to the "Grading and management of the diseased maxillary sinus" proposed by Seiberling et al,<sup>25</sup> our case was Grade 3 belonging to severely diseased maxillary sinusitis. We had cleared the mucus and kept the polypoid mucosa according to the role of FESS during the first operation and used antifungal irrigation after surgery, and it had no effect. We thought that maybe there was mucus left among the polyps which cannot be seen and cleared by FESS. In patients with severe nasal polyposis with complete opacification of the sinus and eosinophilic mucosa, it is proposed that complete removal of all gross disease will decrease the risk recurrence for the residual eosinophilic mucus will continue to stimulate the immune system leading to recurrence.<sup>26</sup> The best approach to the severely diseased sinus is still controversial. Jankowski et al support the use of "nasalization" for patients with severe nasal polyposis.<sup>27</sup> Seiberling et al<sup>25</sup> performed canine fossa trephine for severely diseased maxillary sinus (clearing entirely all polyps and disease and leaving only a thin layer of mucosa). We also adopted canine fossa trephine to clear all the diseased mucosa in maxillary sinus totally during the second operation and it kept in remission for one-year follow-up.

The optimal medical therapy for AFS has not been determined. Systemic steroids are the mainstay of therapy in ABPA. However, steroids have multiple side effects and their use is controversial. It has been suggested that patients with recurrent AFS should have receive systemic corticosteroids after extensive debridement of all affected sinuses. After 2 weeks this is gradually reduced to alternate day therapy at lower doses.<sup>28</sup> The eventual aim is for maintenance inhaled corticosteroid therapy. Topical intranasal steroid sprays have minimal side effects and are used routinely in the postoperative management of AFS. However, the duration and effectiveness of steroid sprays in AFS has not been proven scientifically. The role of antifungal therapy in treatment of AFS is unclear. Since AFS is thought to be an allergic disease caused by an extrinsic fungal antigen rather than a true infection, systemic antifungals should be ineffective. Topical antifungal agent irrigation may

reduce the fungal load and hence decrease antigenic stimuli.

From our case, we found that the complete surgery was the most important and topical steroids after surgery was necessary and effective.

## Conclusion

We have shown a case of AFS due to *Schizophyllum commune* which was rare case in China according to the publishing reports. It was a different fungus which may be identified by molecular biology. Complete surgery is primary for it and topical steroids were also necessary.

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