CASE REPORT

Pulmonary *Schizophyllum Commune* Infection Developing Mucoid Impaction of the Bronchi

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A 54-year-old woman was admitted for cough, sputum, and an abnormal chest X-ray shadow. Bronchoscopy showed mucoid impaction of the bronchi (MIB\(^†\)). Histopathologic evidence of mucous plugs was consistent with one component of allergic bronchopulmonary mycosis. *Schizophyllum commune* (*S. commune*) was identified. Two attempts at removal of the mucous plugs were unsuccessful. Itraconazole was then administered, and the mucous plugs disappeared. There are few reports of MIB due to *S. commune*; we herein report a case of MIB due to *S. commune* infection.

INTRODUCTION

Mucoid impaction of the bronchi (MIB) is an uncommon condition indicating segmental and subsegmental bronchi characterized by the dilatation and filling of bronchi with characteristic thick mucoid material. MIB is believed to occur most commonly as a manifestation of a hypersensitivity state in bronchial asthma or in association with allergic bronchopulmonary mycosis (ABPM). In this report, we describe a patient in whom *Schizophyllum commune* (*S. commune*) caused MIB, which improved with itraconazole (ITCZ) administration. *S. commune* is a basidiomycetes fungus found throughout Japan, commonly in dry logs, dead wood, and fallen trees. *S. commune* is considered edible in Peru or Thailand; however, in Japan, it recently has been identified as a causative agent of MIB and ABPM. There are limited reports of pulmonary involvement due to *S. commune*, and we believe the case is worth reporting.

CASE

A 54-year-old woman was referred to Saitama Cardiovascular and Respiratory Center in August 2000 for investigation of...
A cough, sputum, and an abnormal chest X-ray shadow. The cough and sputum had developed in December 1999 and had not improved. The patient had no relevant personal or family history. Physical examination did not reveal any abnormalities, including wheezes.

Chest X-ray showed bilateral, hilar band-like shadows (Figure 1a). Computed tomography (CT) of the chest showed mucous plugs in both B3 bronchi and consolidation (indicating atelectasis) in the peripheral part of the mucous plugs (Figure 1b,c). Pulmonary function tests did not indicate bronchial asthma. Laboratory tests showed a white blood cell count of 3,400/mm³, with 9.5 percent eosinophils (323/µl). Radioimmunosorbent test showed the IgE concentration to be within normal limits, and results of radioallergosorbent test for specific IgE antibodies against *Aspergillus*, *Cladosporium*, *Candida*, and *Cryptococcus* were all negative. No inflammatory reactions, assessed by the C-reactive protein level and erythrocyte sedimentation rate, were observed. Bronchoscopy disclosed thick white mucous plugs in both B3 bronchi (Figure 2a,b) that could not be removed by forceps and suctioning. Removal was attempted again on another day but failed. Higher magnification of the mucous plug sample showed numerous eosinophils (Figure 3a). Grocott staining of the mucous plug sample showed mold with a fragmented appearance (Figure 3b). Transbronchial lung biopsy specimens showed infiltration of eosinophils in the wall of the right upper lobe bronchus. From the third to tenth day after cultivation, cultures of the mucous plugs, bronchial aspirates, and sputum samples yielded the same mycelial colonies, which were white and had a felt-
like, fluffy appearance on Sabouraud dextrose agar plates (Figure 4a); however, no other pathogenic microorganisms were isolated. A methane-like odor was observed. With regard to form, there were narrow and thin walls approximately 1.5 mm in width, as well as wide and thick walls approximately 2.5 mm in width, with separate hyphae but no clamp connection. Considering the feature of colonies, form, odor, and the two types of hyphae in the colony, we hypothesized that it was a monokaryotic strain of *S. commune*. We consulted the Chiba University Research Center for Pathogenic Fungi and Microbial Toxicoises for identification of the fungus. Mating tests were performed [1,2,3]. The clinical isolate was inoculated onto plates opposite each tester monokaryotic strain of *S. commune*, wherein it was dikaryotized and a fruit body was formed at the point of contact (Figure 4b). When co-cultured with a dikaryotic strain, it was dikaryotized and produced basidiocarps. From the foregoing, this fungus was identified as a monokaryotic mycelium of *S. commune*. At a later time, the presence of *S. commune* in the patient’s garden was confirmed (Figure 6).

ABPM, as well as ABPA (allergic bronchopulmonary aspergillosis), usually is
diagnosed on the basis of Rosenberg’s seven primary criteria [4]: (1) episodic bronchial obstruction (asthma); (2) peripheral blood eosinophilia; (3) immediate scratch test reactivity to *Aspergillus* antigen; (4) precipitating antibodies to *Aspergillus* antigen; (5) elevated serum IgE concentrations; (6) history of pulmonary infiltrates (transient or fixed); and (7) central bronchiectasis. The diagnosis of ABPM is considered likely if the first six criteria were present, and the presence of all seven made the diagnosis certain. The present case satisfied only two (the second and the sixth criteria) of seven criteria (neither the third nor the fourth criteria were investigated because of methodological limitation), and diagnosis of ABPM cannot be established. We diagnosed the patient as MIB due to *S. commune* infection.

Complete removal of the mucous plugs by bronchoscopy was attempted twice unsuccessfully, and the patient was treated with ITCZ for three months, beginning in September 2000. The cough improved and sputum diminished, and in December 2000, bronchoscopy disclosed that the mucous plugs had disappeared. Bronchoscopy was repeated in July 2001, January 2002, and 2003, and there has been no recurrence of the mucous plugs (Figure 5) or symptoms. The patient has been followed up on an out-

**Figure 5.** Bronchoscopy showed a patent bronchial lumen after administration of itraconazole 200 mg daily.

**Figure 6.** A photomicrograph shows that *Schizophyllum commune* was found on a tree in the patient’s garden.
DISCUSSION

We encountered a case of MIB due to *S. commune* infection. ITCZ was administered, and the mucous plugs disappeared.

MIB occurs commonly in association with ABPM, and it is known that there is clinical overlap between MIB and ABPM [5,6,7]. ABPM/MIB is considered to be the result of an immunologic inflammatory reaction in the bronchi and the surrounding parenchyma in response to antigens (fungi) growing in mucous plugs in the airways. The major causative agents of ABPM/MIB are *Aspergillus fumigatus* and other *Aspergillus* spp (Allergic bronchopulmonary aspergillosis; ABPA); reports of ABPM/MIB due to *S. commune* are limited. The reasons we speculate are as follows: (1) its pathogenic significance is not well understood; and (2) isolation and identification of *S. commune* is difficult [8]. It is not easy to identify this fungus only by using pathological samples or smears. This fungus appears in a clavate form in smears, and it is difficult to discriminate morphologically from filamentous fungi such as *Aspergillus* spp. Indeed, in some previous cases, *S. commune* was morphologically misidentified as *Aspergillus* [2,9,10]. Kamei and colleagues reported that 12 percent of undetermined pathologic fungi obtained in clinical specimens were *S. commune* and urged consideration of its pathogenic significance [8]. Therefore, it is possible that the frequency of ABPM/MIB due to *S. commune* has been underestimated. The presence of *S. commune* infection should be investigated in case of ABPM/MIB in which the antibody against *Aspergillus fumigatus* is negative or *Aspergillus fumigatus* is not detected in the sputum or in specimens obtained in the airway.

The present case was diagnosed clinically as MIB, not ABPM. Katzenstein noted pathologically that MIB or bronchocentric granulomatosis with eosinophil infiltration into the tissue strongly suggests ABPM or ABPA, and the diagnosis is established when fungal hyphae are recognized in the mucous plug [11]. The present case was histologically characterized by numerous eosinophils, Charcot’s-Leiden crystals, hyphae in the mucous plugs, and infiltration of eosinophils in the wall of the right upper lobe bronchus; thus, the present case can be diagnosed as ABPM histologically. However, in most cases, the diagnosis of ABPM not due to *Aspergillus* was clinically based

Table 1. Previous Reports of Lung Infection of *Schizophyllum commune*

| Ref | Author | Age | Sex | Diagnosis | Treatment |
|-----|--------|-----|-----|-----------|-----------|
| 1994 | 8 Kamei | 57 | F | ABPM | ITCZ |
| 1996 | 4 Sigler | 53 | F | fungus ball | Lobectomy |
| 1996 | 9 Rihs | 58 | M | lung abscess | AMPH, FLCZ, ITCZ |
| 1996 | 3 Ammitani | 67 | F | MIB | Bronchial toilet |
| 1996 | 10 Tomita | 72 | F | ABPM | AMPH, ITCZ |
| 1997 | 11 Ikushima | 53 | F | ABPM | AMPH, steroid |
| 1997 | 6 Yamaschima | 44 | F | ABPM | AMPH, steroid |
| 2001 | 12 Ito | 51 | F | MIB | ITCZ |
| 2002 | 13 Yamazaki | 79 | F | ABPM | steroid |
| 2003 | 14 Kawano | 27 | F | ABPM | steroid |
| 2003 | 14 Kawano | 33 | F | ABPM | steroid |
| 2007 present case | Ishiguro | 54 | F | MIB | ITCZ |

ABPM: Allergic bronchopulmonary mycosis; ITCZ: Itraconazole; AMPH: amphotericin B; FLCZ: fluconazole; MIB: mucoid impaction of the bronchi.
on Rosenberg’s criteria as well as ABPA. In the present case, although peripheral blood eosinophilia was found, allergic component including elevated serum IgE concentration and bronchial asthma was not found. In addition, there were some criteria that could not be investigated because of methodological limitation. In such cases, Rosenberg’s criteria should not be applied. There are other diagnostic criteria for ABPA used in the United Kingdom [12], including asthma, pulmonary eosinophilia (fleeting shadow on the chest radiograph in association with a peripheral blood or airway eosinophilia), and a positive immediate skin prick test to *A. fumigatus*; however, the criteria also were not satisfied (the third criterion could not investigated), so this case clinically cannot be diagnosed as ABPM.

Reports of pulmonary involvement due to *S. commune* are limited. To our knowledge, 13 cases (including the present case) have been reported (Table 1). Among the 13 were seven cases of ABPM, one of a fungus ball, one of a lung abscess, and four of mucoid impaction (including the present case). Patients were predominantly female (female: male, 12:1), and 11 of 13 patients were over 40 years of age. The reason for the predominance of middle-aged female patients remains unknown. In addition, seven of the patients had bronchial asthma (53.8 percent). Kamei and colleagues reported eight cases of ABPM due to *S. commune*, only 30 percent of which were accompanied by bronchial asthma, and they suggested that the frequency of bronchial asthma may be lower in ABPM due to *S. commune* than in ABPA [8]. A greater number of reported cases is necessary to clarify this matter.

Kamei and colleagues postulated that underlying diseases of the lower respiratory tract such as old tuberculosis, bronchial asthma, and malignancy often exist in the patients with ABPM due to *S. commune*, but noted there are patients without any underlying disorder [8]. Therefore, *S. commune* infection can develop in any patient, with or without underlying diseases. In the present case, the patient had no underlying disease.

There are no reports that *S. commune* infection develops more frequently in individuals in any specific environment or job such as mushroom culture, in which causative fungi are easily inhaled. In the present case, however, *S. commune* was growing in the garden at the patient’s house.

MIB has been treated effectively by repeated bronchoscopic drainage [1], washing with Amphotericin B, and bronchoscopic suctioning [3,9,15]. In this case, however, two attempts to remove the mucous plug were unsuccessful. Subsequent administration of ITCZ 200 mg daily resulted in symptomatic relief and disappearance of the mucous plugs.

ABPM/MIB is a state formed when pathogens and biological immune responses become entangled in a complex way. The allergic aspect of ABPM/MIB has been stressed, and steroid therapy generally is used for allergic aspect of ABPM/MIB [19-21]; however, an infectious aspect has recently been recognized on the basis of the effectiveness of antifungal therapy for ABPA [10,22] and histopathologic findings [23]. The present case improved with ITCZ administration without steroid therapy, which may indicate that the infectious aspect was more likely than the allergic aspect in this case. However, the histological findings of the mucous plugs characterized by numerous eosinophils, Charcot’s-Leiden crystals, and infiltration of eosinophils in the wall of the right upper lobe bronchus strongly suggested allergic background. It is possible ITCZ reduced *S. commune*, an allergic antigen, which resulted in attenuated allergic reaction; therefore, an allergic aspect should have co-existed. It is therefore difficult to differentiate clearly infection from allergic reaction.

Kamei reported a recurrence after a period of improvement with itraconazole 50-100 mg daily [1]; thus, long-term follow-up is necessary.

In summary, we report a case of MIB due to *S. commune* infection. The most frequent causative fungus of ABPM is known to be *Aspergillus fumigatus*; however, *S. commune* should be added to the differential
diagnosis in case of MIB, especially if mold is found in the specimen with no evidence of *Aspergillus fumigatus*. An antifungal agent may be useful in the treatment of MIB due to *S. commune*.

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