

## CASE STUDY

# Polypoid bronchial lesions due to *Scedosporium apiospermum* in a patient with *Mycobacterium avium* complex pulmonary disease

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**ABSTRACT:** A 69 yr old female was hospitalized for further examination of abnormal shadows on chest radiographs. She had a history of tuberculous pleurisy, rheumatoid arthritis and gold-induced interstitial pneumonia. On admission she still suffered from rheumatoid arthritis. A chest computed tomography scan on admission showed clusters of small nodules in subpleural regions of both lungs combined with bronchiectasis. *Mycobacterium avium* complex was cultured repeatedly from the sputum. Bronchoscopic examination disclosed white-yellow polypoid lesions in the orifice of the left B<sup>4</sup> bronchus. Cultures of the brushing specimen of the polypoid lesions and bronchial aspirates from the B<sup>4</sup> bronchus yielded smoky-grey mycelial colonies that were later identified as *Scedosporium apiospermum*. It was concluded that the polypoid bronchial lesions due to *Scedosporium apiospermum* were formed in the pre-existing dilated bronchus caused by *Mycobacterium avium* complex pulmonary disease.

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*Scedosporium apiospermum*, the asexual stage of the fungus *Pseudoallescheria boydii*, exists saprophytically in soil, sewage and polluted streams with a worldwide distribution. Host factors such as systemic and local impaired host defences are considered to determine whether *S. apiospermum* infection occurs and how invasive it will be [1]. Lung involvement caused by *S. apiospermum* ranges from colonization including fungus ball formation to necrotizing pneumonia. This study reports a case of polypoid bronchial lesions caused by *S. apiospermum* in a patient with *Mycobacterium avium* complex (MAC) pulmonary disease. To our knowledge, there have been no reports of such lesions due to *S. apiospermum*.

### Case report

A 69 yr old housewife was admitted to our hospital in November 1995, for further examination of abnormal shadows on chest radiographs. She had a history of tuberculous pleurisy at the age of 16 yrs. She had been suffering from rheumatoid arthritis for 20 yrs. Interstitial pneumonia due to gold used for rheumatoid arthritis occurred at the age of 53 yrs and was improved by discontinuation of the drug. She underwent surgical procedures for joint replacement of the right hip joint at the age of 61 yrs and both knee joints at the age of 66 yrs. She had taken bucillamine since she was 61 yrs old and methylprednisolone (4 mg·day<sup>-1</sup>) since the age of 68 yrs. She had never smok-

ed. She did not have any history of heavy exposure to any kind of dust. Two years before admission to the hospital, chest radiographs demonstrated small nodular shadows in the right middle lung field. One month before admission, chest radiographs showed the worsening of small nodular shadows in bilateral middle lung fields and the thickening of bronchial walls. She had never complained of any respiratory symptoms, including cough and sputum.

On admission, physical examinations revealed inspiratory fine crackles in the lower back. Peripheral lymph nodes were not palpable. Her fingers had severe deformities due to rheumatoid arthritis. Her blood pressure was 124/74 mmHg. Results of laboratory examinations were as follows: haematocrit, 35.4%; white cell count, 6,200·mm<sup>-2</sup>, with 67% neutrophils, 20.4% lymphocytes, 8.3% monocytes and 3.9% eosinophils; and CD3+ cells, CD4+ cells and CD8+ cells were 88.8%, 72.4% and 14.8%, respectively. The blastogenic response to phytohaemagglutinin was normal. C-Reactive protein was 1.73 mg·dL<sup>-1</sup> and rheumatoid factor test was positive. Serum immunoglobulin (Ig)G, IgA, IgM and IgE levels were normal. The precipitating antibodies to *Aspergillus* spp. and antigen of cryptococcus were negative. *Candida* antigen was slightly elevated. The tuberculin skin test was negative. Chest radiographs (fig. 1) and a computed tomography (CT) scan on admission showed clusters of small nodules in the subpleural regions of both lungs, combined with bronchiectasis, especially in the right middle lobe and left lingula bronchi.



Fig. 1. – Posteroanterior view of the chest radiograph, showing evidence of multiple small nodules combined with the thickness of bronchial walls in bilateral middle lung fields.

The first bronchoscopy performed on the eighth hospital day disclosed two white-yellow polypoid lesions in the orifice of the left B<sup>4</sup> bronchus (fig. 2). These polypoid lesions were immobile and the bronchial mucosa around the lesions did not macroscopically show any inflammatory changes. No other abnormal findings were demonstrated in other bronchi by bronchoscopy. The CT scan

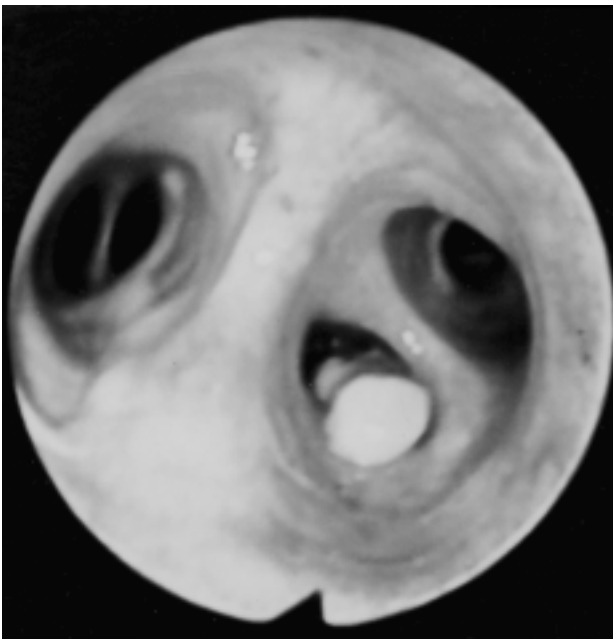


Fig. 2. – The bronchoscopy disclosed two white-yellow polypoid lesions in the orifice of the left B<sup>4</sup> bronchus.

showed a protrusion which corresponded to the polypoid lesions in the lumen of the left B<sup>4</sup> bronchus, but no invasiveness towards the surrounding lung tissues was shown (fig. 3). Cytological studies of the brushing specimens of the polypoid lesions revealed hyphae resembling *Aspergillus* spp. Cultures of the brushing specimens and bronchial aspirates yielded smoky-grey mycelial colonies on Sabraud's dextrose agar plates. Microscopic examinations of the mycelial colonies from cultures showed hyaline branching septate hyphae with unicellular pale brown ovoid conidia developing either singly or in clusters on short conidiophores (fig. 4). Cleistothecium was not formed by culture on agar. The organism was identified as *S. apiospermum* on the basis of the above microscopic features. No other pathogenic micro-organisms were isolated from these samples and the patient was diagnosed as having pseudoallescheriasis. On the 15th hospital day, bronchoscopy was performed again and bronchial washing of the right B<sup>4</sup> bronchus was performed with 50 mL sterilized saline. *Mycobacterium avium* was demonstrated by rapid identification using polymerase chain reaction (PCR) (Amplifire™, F. Hottmann, La Roche Ltd., Basel, Switzerland) in the bronchial washing specimen and MAC was also cultured from the same sample. In addition, a four-week culture of sputa repeatedly yielded MAC. Although she had a history of tuberculous pleurisy, rheumatoid arthritis and gold-induced interstitial pneumonia, *M. tuberculosis* was not cultured from any specimen and chest radiographs and CT scan on admission did not reveal recurrence of interstitial lung diseases and pleural diseases. Therefore, the diagnosis of bronchial polypoid lesions due to *S. apiospermum* in combination with MAC pulmonary disease was finally established. Methylprednisolone was discontinued and she has since been followed without any worsening on chest radiographs or CT scan for 2 yrs.

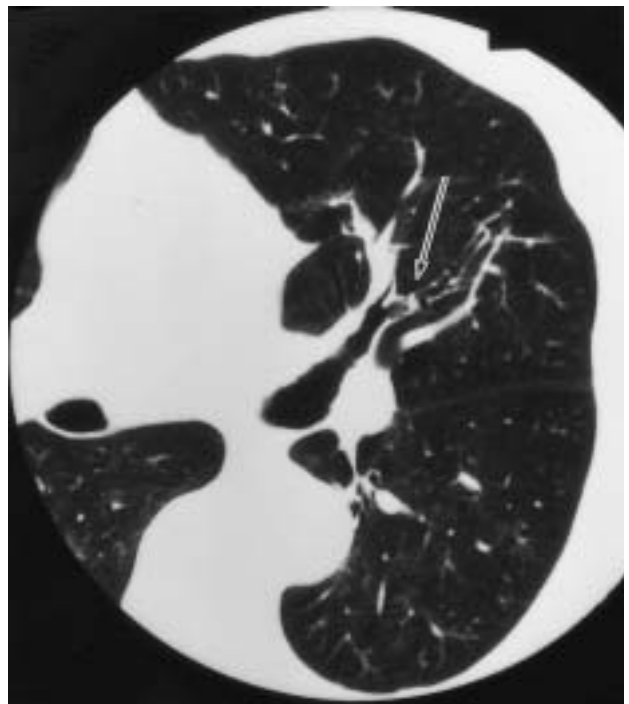


Fig. 3. – Computed tomography scan, demonstrating a protrusion (arrow) which corresponded to the polypoid lesion of the left B<sup>4</sup> bronchus.

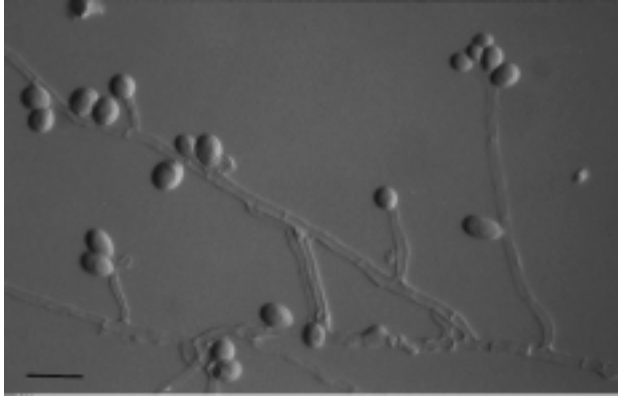


Fig. 4. — Microscopic examinations of a colony from cultures on Sabraud's dextrose agar plates, showing hyaline branching septate hyphae with unicellular pale brown ovoid conidia. (Internal scale bar=25 µm).

### Discussion

*S. apiospermum*, the asexual form of *P. boydii*, has been shown to be a causative agent of mycetoma, a cutaneous and subcutaneous saprophytic lesion usually caused by traumatic implantation of *S. apiospermum* on extremities [1, 2]. Recently, several cases of invasive diseases caused by *S. apiospermum* in immunocompromised hosts with organ transplantation, haematological malignancies or corticosteroid therapy have been reported [3]. The lungs were primarily involved in these patients and dissemination frequently occurred. In immunocompetent patients, a fungus ball (pseudoallescherioma), a common form of pulmonary lesion, occasionally occurs in pre-existing tuberculous cavities, bronchiectasis or pathological air spaces of diverse aetiologies [1]. TRAVIS *et al.* [2] reported patients with pulmonary involvements of whom 87% had a variety of underlying pulmonary diseases and 17% had received corticosteroid therapy. Solitary nodular lesions, pleurisy, and allergic bronchopulmonary fungal disease were reported as atypical pulmonary lesions [1, 4, 5].

MAC pulmonary disease is the most common nontuberculous mycobacterial infection of the lung. Recently, the disease has become prevalent in elderly females without predisposing bronchopulmonary illness. Characteristic CT findings of MAC pulmonary disease are clusters of small nodules in the subpleural regions of the lung in combination with dilated changes of the bronchi [6]. Between 1990 and 1997, 210 patients with MAC pulmonary disease were seen in the author's hospital and a variety of fungi were concurrently isolated from 10 patients: *Aspergillus fumigatus* (6), *Aspergillus niger* (2), *S. apiospermum* (2), *Schizophyllum commune* (1) and *Exophiala dermatitidis* (1) (unpublished data). In a patient who had been treated with rifampin, ethambutol and clarithromycin, both *S. apiospermum* and *A. fumigatus* were isolated from bronchial washing specimens and sputa. To the author's knowledge, there have been no previous reports of a concurrence between mycosis and MAC pulmonary disease. However, a variety of mycosis may develop in patients with MAC pulmonary disease, which is probably associated with impaired local host defences including mucociliary clearance, and some factors derived from fungi and/or MAC may facilitate colonization and lead to infection with both fungi and MAC.

The most effective treatment of pseudoallescheriasis is surgical resection. In the present case, surgical treatment was not performed because of the extensive MAC pulmonary disease. Although the efficacy of antifungal chemotherapy against *S. apiospermum* colonization remains to be evaluated, it has been reported that *S. apiospermum* is more sensitive to azoles, but more resistant to amphotericin B, in contrast to *Aspergillus* spp. [1, 7]. The *in vitro* activities of itraconazole and amphotericin B against the strain of *S. apiospermum* isolated in the present case were examined. The minimal inhibitory concentrations of itraconazole and amphotericin B were 1 µg·mL<sup>-1</sup> and 2 µg·mL<sup>-1</sup>, respectively. RIPPON and CARMICHAEL [4] reported colonization of the bronchi by *S. apiospermum* in a patient receiving steroid therapy in whom the lesions disappeared when steroid therapy was discontinued. In the present case, methylprednisolone was discontinued soon after the definitive diagnosis was obtained. During a 2 yr observation at intervals of 3 months since then, there has been no evidence of worsening. However, careful observation is required to assess prognosis.

Pseudoallescheriasis is an uncommon fungal disease. To the author's knowledge, bronchial polypoid lesions of *Scedosporium apiospermum* arising in the bronchiectasis are very rare, although mycetoma in pre-existing cavities have been reported [1, 2]. Laboratory experiments demonstrated neither neutropenia nor an impairment of cellular immunity. However, the patient's immune defence could not have been entirely normal because of low-dose methylprednisolone therapy. There is a possibility that the history of tuberculous pleurisy and gold-induced interstitial pneumonia damaged the airways and lungs, leading to an impairment of local host defences. Furthermore, dilatation of the bronchi caused by *Mycobacterium avium* complex pulmonary disease may impair the local host defences and enable the fungus to colonize and proliferate. It is necessary to accumulate further such cases to understand the pathophysiology of pseudoallescheriasis combined with *Mycobacterium avium* complex infection.

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