Cavitating Invasive Pulmonary Aspergillosis Visualized and Diagnosed by Ultrathin Bronchoscopy*

Masahide Oki, MD; Hideo Saka, MD, FCCP; Chieko Sako, MD; Shigeru Tanaka, MD; Yoshihiro Kawata, MD; Chiyoe Kitagawa, MD; and Nobuyoshi Minemura, MD

A definitive diagnosis of invasive pulmonary aspergillosis (IPA), which usually occurs in immunocompromised patients, is often difficult. We report two cases of cavitating IPA in a peripheral pulmonary region in patients who were receiving corticosteroids, in whom the cavity was successfully visualized and sampled during ultrathin bronchoscopy. Ultrathin bronchoscopy provides a new option for definitive diagnosis of cavitating IPA.

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Key words: bronchoscopy; cavity; invasive pulmonary aspergillosis; transbronchial biopsy; ultrathin bronchoscope

Abbreviations: IPA = invasive pulmonary aspergillosis; TBB = transbronchial biopsy

Invasive pulmonary aspergillosis (IPA), which commonly occurs in immunocompromised patients, is a life-threatening infectious disease. Not only are such patients difficult to treat, the diagnosis is especially difficult. Although bronchoscopic procedures such as BAL and transbronchial biopsy (TBB) have been used to establish the diagnosis of IPA, their diagnostic yield is insufficient.1 The diagnostic yield of TBB is particularly low,2 so its value for the diagnosis of IPA remains controversial.3

Recently, ultrathin bronoscopes offering a smaller outer diameter and higher image quality have been developed. Such a bronchoscope with an outer diameter of 2.8 mm is now commercially available and permits the observation and manipulation of more peripheral bronchi than was previously possible with a standard bronchoscope. The ultrathin bronchoscope has been reported to be a valuable diagnostic tool for peripheral pulmonary lesions.4–6 Although various diseases can be diagnosed histologically using the ultrathin bronchoscope, there is, to our knowledge, no report in the literature about its contribution to the diagnosis of IPA. We herewith report two cases of IPA diagnosed in patients were receiving corticosteroids, in whom the cavity was visualized and sampled during ultrathin bronchoscopy.

Case Reports

Case 1

A 57-year-old man with dermatomyositis was referred for bronchoscopic evaluation of progressive radiographic changes consisting of an enlarging cavity despite antibiotic therapy. For 3 months, he had received prednisolone, 40 to 80 mg/d, and azathioprine, 100 mg/d, for intractable dermatomyositis. Two weeks earlier, he complained of fever, increased cough, purulent sputum, and dyspnea. The chest radiograph showed a cavity with surrounding infiltrates in the upper lobe of the right lung. Sputum cultures grew Pseudomonas aeruginosa and Candida glabrata. The patient had been treated with IV cefozopran and fluconazole for 2 weeks without any clinical improvement.

A CT scan of the chest the day before bronchoscopy revealed a thick wall cavity in the anterior segment of the right upper lobe that had not been present 2 months previously (Fig 1). Bronchoscopic examination using a standard bronchoscope with an external diameter of 6.1 mm (BF-6C240, Olympus, Tokyo, Japan) [Fig 2] was first performed. The bronchoscope reached the segmental bronchus of the right upper lobe and revealed no abnormalities. Then, for peripheral investigation, a 2.8 mm in diameter ultrathin bronchoscope with a 1.2-mm working channel (BF-XP40; Olympus) [Fig 2] was employed. The ultrathin bronchoscope was inserted into the right B3 and advanced through the fifth-generation bronchus under direct observation, and then entered a cavity, as confirmed by fluoroscopy (Fig 3). A whitish intracavitary lesion was seen (Fig 4, left, A). Biopsies using a miniforceps (FB-56D-1; Olympus) and washing were performed with bronchoscopic visualization, and then amphotericin B, 5 mg, was instilled into the cavity through the ultrathin bronchoscope for treatment of a presumptive fungal infection. Biopsy specimens showed septate-branching hyphae suggestive of aspergillosis and cultures of the cavital washing grew Aspergillus fumigatus. Unfortunately, 9 days later the patient suddenly died of cerebral hemorrhage.

Case 2

A 69-year-old man with systemic lupus erythematosus was admitted to the hospital with cough, bloody sputum, fatigue, decreased appetite, and enlarging left lower lobe pulmonary cavity. For 6 months before hospital admission, he had received prednisolone, 20 to 30 mg/d, for systemic lupus erythematoses. Two months earlier, he complained of bloody sputum, and a chest CT showed cavitory infiltrates in the superior segment of the right lower lobe.

A CT scan of the chest the day before bronchoscopy revealed a thick wall cavity in the anterior segment of the right lower lobe that had not been present 3 months previously (Fig 1). Bronchoscopic examination using a standard bronchoscope with an external diameter of 6.1 mm (BF-6C240, Olympus, Tokyo, Japan) [Fig 2] was first performed. The bronchoscope reached the segmental bronchus of the right lower lobe and revealed no abnormalities. Then, for peripheral investigation, a 2.8 mm in diameter ultrathin bronchoscope with a 1.2-mm working channel (BF-XP40; Olympus) [Fig 2] was employed. The ultrathin bronchoscope was inserted into the right B3 and advanced through the fifth-generation bronchus under direct observation, and then entered a cavity, as confirmed by fluoroscopy (Fig 3). A whitish intracavitary lesion was seen (Fig 4, left, A). Biopsies using a miniforceps (FB-56D-1; Olympus) and washing were performed with bronchoscopic visualization, and then amphotericin B, 5 mg, was instilled into the cavity through the ultrathin bronchoscope for treatment of a presumptive fungal infection. Biopsy specimens showed septate-branching hyphae suggestive of aspergillosis and cultures of the cavital washing grew Aspergillus fumigatus. Unfortunately, 9 days later the patient suddenly died of cerebral hemorrhage.

*From the Departments of Respiratory Medicine (Drs. Oki, Saka, Sako, Tanaka, Kawata, and Kitagawa) and Internal Medicine (Dr. Minemura), Nagoya Medical Center, Nagoya, Japan.

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Correspondence to: Masahide Oki, MD, Department of Respiratory Medicine, Nagoya Medical Center, 4-1-1 Sannomaru, Naka-ku, Nagoya 460-0001, Japan; e-mail: Masahideo@aol.com

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the left lower lobe (Fig 5, left). Sputum cultures showed *A. flavus*. Clinical deterioration with an enlarging cavity had occurred despite antibiotic treatments including itraconazole (Fig 5, right).

Bronchoscopic examination was performed using a 2.8-mm ultrathin bronchoscope (BF-XP260F; Olympus), which could be inserted into the seventh-generation bronchus under direct vision and then advanced into the cavity. A yellowish white intracavitary lesion was noted (Fig 4, right, B). Biopsies and washing were

**Figure 1.** Chest CT on the day before bronchoscopy showed a thick wall cavity in the anterior segment of the right upper lobe (right) that had not been present 2 months previously (left).

**Figure 2.** A comparison of bronchoscopes. *Left:* a standard bronchoscope with an external diameter of 6.1 mm and a working channel of 2.0 mm (BF-6C240; Olympus); *right:* an ultrathin bronchoscope with an external diameter of 2.8 mm and a working channel of 1.2 mm (BF-XP40; Olympus).
performed under ultrathin bronchoscopic visualization. Histologic examination of biopsy specimens showed septate-branching hyphae, and cultures of the cavital washing grew *Aspergillus fumigatus*. IV amphotericin B was administered at a total dose of 2,000 mg, and the patient showed clinical improvement with resolution of the extracavitary and intracavitary infiltrates but persistence of a thin wall cavity.

**DISCUSSION**

IPA occurs mainly in severely immunocompromised patients, particularly those with prolonged severe granuloctopenia. Although the incidence is relatively uncommon, mildly immunocompromised patients, such as those receiving corticosteroids similar to our cases, can also acquire IPA. Palmer et al. reported six patients with lung disease receiving corticosteroids who acquired IPA, and they indicated that IPA should be included in the differential diagnosis when pneumonia and cavitory infiltrates occur in such patients.

Although the diagnosis of IPA is often admittedly difficult, when compatible clinical and radiographic findings are supported by the presence of positive culture results for *Aspergillus* species from respiratory secretions, it is highly likely that the patient has IPA. BAL during bronchoscopy has proved helpful in diagnosing IPA. In one review article, it was reported that the diagnostic sensitivity of BAL was 43% in histologically proven IPA. However, the reported diagnostic sensitivity of BAL for IPA appears to vary with the investigator. Saito et al. reported that BAL was diagnostic for pulmonary aspergillosis in none of nine patients with leukemia. Most specific diagnoses for pulmonary aspergillosis were established solely from autopsy, so BAL was reportedly useless in most cases. Moreover, the specificity of BAL for IPA is good, but it may be difficult to exactly distinguish infection from colonization.

The definitive diagnosis of IPA requires histopathologic demonstration of septate acute branching hyphae with positive culture results for *Aspergillus*. TBB is a safe and established bronchoscopic method in the histopathologic diagnosis of pulmonary infections in immunocompromised patients. As for diagnosing IPA, however, the diagnostic sensitivity of TBB has been reported to be quite low. Some authors advocate the use of invasive surgical procedures for the diagnosis and treatment of IPA. In our case 2, the clinical and radiologic progress was relatively less acute, and the immunosuppression was mild, so it might be categorized as subacute IPA. However, a

![Figure 3. Tip of the ultrathin bronchoscope shown entering a cavity.](image)

![Figure 4. Ultrathin bronchoscopic views of the lung cavity. A whitish intracavitary lesion caused by *A. flavus* was seen in case 1 (left, A), and a yellowish white lesion caused by *A. fumigatus* was seen in case 2 (right, B).](image)
precise distinction has not been made between IPA and other chronic forms of Aspergillus, such as subacute IPA or chronic necrotizing pulmonary aspergillosis. Moreover, the diagnostic yield of TBB for chronic cavitary pulmonary aspergillosis has also been reported to be quite low.16

A commercially available ultrathin bronchoscope with an external diameter of 2.8 mm has been used as a diagnostic4–6 and therapeutic tool17 in the peripheral airways. It can reach the peripheral area of the lung and occasionally even the visceral pleura.18 Nevertheless, the closer the ultrathin bronchoscope is brought to the peripheral bronchi, the poorer the visibility is. Soft peripheral bronchi, which easily collapse under bronchoscopic suction, and bronchial secretions obstruct the visibility. However, a cavitary lesion in the peripheral area of the lung may be a good indication for ultrathin bronchoscopy. Once the tip of the ultrathin bronchoscope enters the cavity through a small bronchus, the range of vision becomes broad. Biopsy of a lesion with bronchoscopic visualization should result in higher diagnostic yield. Moreover, a biopsy with direct visualization using miniforceps may decrease the risks of bleeding.

Visualization of intracavitary lesions during bronchoscopy in patients with pulmonary aspergillosis, mostly aspergilloma, which is characterized by mycelial growth in a preexisting lung cavity and usually has a good prognosis without any treatments, has been rarely reported.19–21 However, there may be only a limited number of cases in which the diameter of the bronchus leading to the cavity is relatively large. In our case 1, a conventional bronchoscope could reach no farther than the segmental bronchus. Our results indicate an ultrathin bronchoscope can enter a cavity more frequently than a conventional bronchoscope. In some cases, it appears that ultrathin bronchoscopy can be useful in the diagnosis of cavitating IPA. Further studies are needed to elucidate in more detail its utility for the diagnosis of IPA.

**REFERENCES**

8 Karam GH, Griffin FM. Invasive pulmonary aspergillosis in

**Figure 5.** A cavity in the superior segment of the left lower lobe shows enlargement (right) compared to 2 months previously (left).
nonimmunocompromised, nonneutropenic hosts. Rev Infect Dis 1986; 8:357–363

Closure of a Bronchopleural Fistula Using Bronchoscopic Placement of an Endobronchial Valve Designed for the Treatment of Emphysema*

J. Scott Ferguson, MD, FCCP; Kimberly Sprenger, BSN; and Timothy Van Natta, MD

Pneumothoraces are sometimes complicated by a persistent air leak or bronchopleural fistula requiring prolonged chest tube drainage. Non-surgical treatment of persistent bronchopleural fistulas is often performed in patients who are poor surgical candidates, but the ideal method of closure is not known. Here we report closure of a persistent distal bronchopleural fistula using a one-way endobronchial valve designed for the treatment of emphysema. (CHEST 2006; 129:479–481)

Key words: bronchial fistula; bronchoscopy; pneumothorax

Abbreviations: BPF = bronchopleural fistula; RML = right middle lobe

Pneumothoraces are sometimes complicated by a persistent air leak or bronchopleural fistula (BPF) requiring prolonged chest tube drainage. It is generally recommended that surgical treatment be undertaken when possible. However, many patients are very poor surgical candidates. In this article, we report the successful closure of a prolonged air leak with a one-way endobronchial valve originally designed for the palliative treatment of emphysema.

CASE REPORT

A 63-year-old man with widely metastatic breast cancer was admitted for sudden onset of severe dyspnea 8 days after thoracoscopic placement of an indwelling cuffed pleural catheter. A large hydropneumothorax was discovered, and the indwelling catheter was connected to suction, relieving the pneumothorax. A chest tube was then placed and connected to a water-seal device. A large air leak was noted with each exhalation and continued for the next 9 days. A new chest tube was placed, but the air leak continued.

The etiology of the pneumothorax was not certain but was assumed to be a delayed complication of the thoracoscopy, as opposed to necrosis and breakdown of a metastatic focus of tumor. A thin-section, multidetector CT scan of the chest revealed multiple metastases, hydropneumothorax, and airspace disease of the lower lobes. No radiographic evidence of BPF was present.

Surgical correction with plication of the offending lobe was considered but judged to be risky given that the patient’s pulmonary reserve was limited due to the metastatic disease. Endoscopic therapies with glue, gel foam, and coiling were considered but were judged to have a low likelihood of success based on the endoscopist’s previous experience with these methods in other patients. Therefore, these techniques of BPF closure were not attempted in this patient.

One-way endobronchial valves for the treatment of emphysema became available in the United States last year as part of a national clinical trial. We thought placement of an endobronchial valve that would allow escape of air from the offending segment or lobe, but

*From Carver College of Medicine, Departments of Internal Medicine (Dr. Ferguson and Ms. Sprenger) and Thoracic and Cardiovascular Surgery (Dr. Van Natta), University of Iowa, Iowa City, IA.
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Correspondence to: J. Scott Ferguson, MD, Department of Internal Medicine, C-33 GH 200, University of Iowa, Iowa City, IA 52242; e-mail: john-s-ferguson@uiowa.edu.