Case Report

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Recent Strategy for Diagnosing Pulmonary Actinomycosis: A Case Report and Literature Review

Robert Shan-Fon Tsai[1], Shew-Meei Sheu[2], Yi-Jen Chen[3], Hsiao-Lun Tseng[3,]*

Pulmonary actinomycosis is a frequently misdiagnosed infectious disease due to the nonspecific findings on clinical examinations. A 57-year-old man who presented with hemoptysis, significant weight loss and shortness of breath came to our chest medicine outpatient department. Chest X-ray and computed tomography revealed heterogeneous consolidation and fibronodular infiltration over the right upper lung field. Based on pathological analysis of the endobronchial ultrasound (EBUS)-guided lung specimen, the patient's initial diagnosis was unclear. The patient still had intermittent episodes of hemoptysis. Repeated chest X-ray showed persistent findings over the right upper lobe. The patient was diagnosed with pulmonary actinomycosis after pathological examination of the lung specimen from surgical resection. We discussed the feasibility of multiple samplings by EBUS and the application of lung biopsy for nucleic acid amplification, which may increase the identification rate of pulmonary actinomycosis.

Key words: pulmonary actinomycosis, endobronchial ultrasound, chest X-ray, computed tomography

Introduction

Pulmonary actinomycosis is a rare and slowly progressive suppurative disease caused by *Actinomyces* species, which are anaerobic Gram-positive bacilli.[1] It is not associated with specific respiratory symptoms and imaging characteristics, leading to frequent misdiagnosis as pulmonary tuberculosis and lung malignancy.[2,3] Patients with pulmonary actinomycosis may present with cough, expectoration, chest pain, hemoptysis, fever, shortness of breath and weight loss.[4,5] Due to poor yields of *Actinomyces* species from the microbial culturing of clinical samples, making an accurate diagnosis and assigning the right antibiotic treatment remain clinical challenges. Through the presentation of a recent case with pulmonary actinomycosis in our department, we aimed at proposing an efficient strategy for diagnosing pulmonary actinomycosis.

Case Report

A 57-year-old man who had been expe-

From the [1]Department of Medicine, Kaohsiung Municipal Ghangshan Hospital, Kaohsiung; [2]Department of Medical Research, Ditmanson Medical Foundation and [3]Division of Pulmonary and Critical Care Medicine, Ditmanson Medical Foundation Chia-Yi Christian Hospital, Chia-Yi, Taiwan.

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* Address reprint request and correspondence to: Hsiao-Lun Tseng, Division of Pulmonary and Critical Care Medicine, Ditmanson Medical Foundation Chia-Yi Christian Hospital, No. 539, Zhongxiao Road, East District, Chia-Yi 60002, Taiwan.
Tel: 05-2765041, E-mail: 04686@cych.org.tw

riencing intermittent blood-tinged sputum for approximately 4 – 5 months visited our chest medicine outpatient department (OPD) on October 4, 2018. Associated symptoms included significant weight loss of ten kilograms in the past five months, fever, night sweats, chest tightness, and shortness of breath on exertion. He had a 40-year history of smoking, drinking alcohol and chewing betel nut but denied any significant medical or surgical history. Physical examination was unremarkable except for minor crackles in the right upper lung field. Laboratory testing showed a normal hemogram (WBC: 8610/μL, Hb: 12.2 g/dL, platelet: 350 × 10^3/μL, segment: 65.9%). A standing chest X-ray revealed consolidation and fibronodular infiltration over the right upper lung field (Fig. 1A). Chest computed tomography (CT) demonstrated irregular heterogeneous consolidation over the right upper lung field (Fig. 1B) as well as enlarged lymph nodes in the right hilar region. The patient's sputum was collected for acid-fast staining and *Mycobacterium tuberculosis* (TB) culture. Based on negative laboratory findings, the patient was preliminarily excluded from having a TB infection. Given the potential diagnosis of progressive bacterial pneumonia, the patient was treated with empirical intravenous antibiotics (cefuroxime, 1.5 g, ivd, q8h) starting on October 5, but his condition did not improve. On October 8, bronchoscopy was arranged to obtain a linear endobronchial ultrasound (EBUS)-guided biopsy and bronchoalveolar lavage (BAL) fluid for microscopic and histologic examinations. Isolated cultures from BAL fluid yielded both Gram-positive and Gram-negative anaerobic microorganisms: *Veillonella* and *Clostridium clostridioforme*. Histopathological analysis of the EBUS-guided biopsy showed dense mixed inflammatory infiltration and focal lymphoid aggregation. Although hemoptysis subsided after hospitalization, repeated chest X-ray showed persistent heterogeneous consolidation over the right upper lobe. We switched intravenous antibiotics from cefuroxime to cefoperazone-sulbactam sodium on October 12, 2018. Due to persistent intermittent episodes of

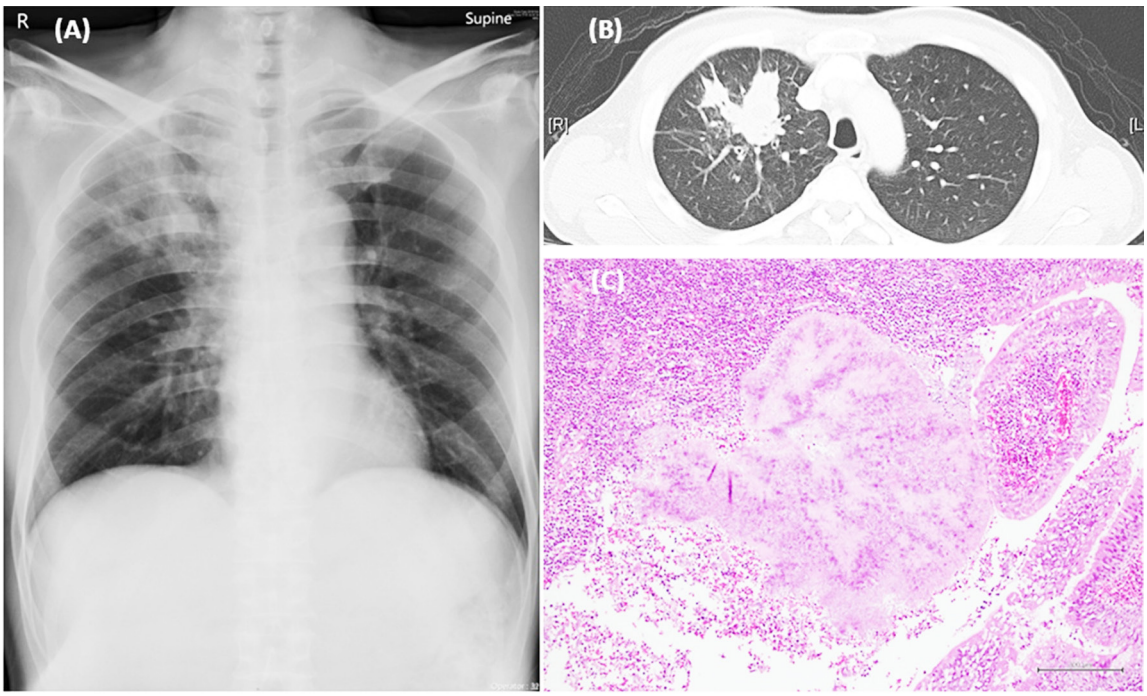

Fig. 1 (A) Chest X-ray revealed some fibronodular density over the right upper lung site. (B) Computed tomography (CT) showed irregular heterogeneous consolidation over the right upper lung site. (C) Lung tissue obtained from the surgical resection was stained with hematoxylin and eosin. Histopathology showed dense chronic inflammatory infiltration and filamentous bacterial clumps.

hemoptysis, we consulted a chest surgeon who recommended video-assisted pulmonary surgical resection of the right upper lobe lesion, which was performed on October 17, 2018. Resection margin of the lung showed dilated bronchioles with pus and tiny yellowish granules. Histopathological examination showed dilated bronchi and bronchioles accompanied by dense chronic inflammatory infiltration and destruction of the muscle layer. Besides, the lumens of the bronchi and bronchioles contained filamentous bacterial clumps, which were morphologically compatible with those of *Actinomyces* species (Fig. 1C). We prescribed amoxicillin (1 g, po, qid) for treatment. He was successfully discharged on October 27. Oral antibiotics were continued for three months. He was followed at our OPD four times. His chest radiograph was normal.

Discussion

Because the clinical and radiological findings of pulmonary actinomycosis are ambiguous, diagnosis is difficult without a positive culture of *Actinomyces* species.[5,6] Numerous radiographic terminologies, including air meniscus, "ball-in-hole" appearance, consolidation, chronic alveolar infiltration, abscess formation, cavitation, pulmonary fibrosis, hilar lymphadenopathy, and pleural effusion, have been used to describe the signs of pulmonary actinomycosis.[5-9] Nevertheless, these radiographic signs may also indicate other pulmonary diseases, including chronic pneumonitis, pulmonary tuberculosis, fungal infection, and lung malignancy.[2,3] A definitive diagnosis is made by a positive culture of *Actinomyces*, but the bacterium requires a critical anaerobic culture condition for growth. A presumptive diagnosis is often made by the histological feature of sulfur granules or actinomycetes filaments. However, biopsy taken by bronchoscopy might not be sensitive enough to yield a disease diagnosis, leading to a high percentage of patients (42.8%) who are diagnosed after surgery.[4]

Flexible bronchoscopy and EBUS are frequently adopted to biopsy suspected actinomycotic lesions; Nakamura et al. performed flexible bronchoscopy twice to obtain a biopsy with a mass of bacteria in the specimen center.[6] Caballero Vázquez et al. obtained a sample that was useful for diagnosis through EBUS instead of flexible bronchoscophy.[9] In our study, we performed EBUS once. Histopathological examination of our specimen and the culture from the BAL fluid both yielded negative results for *Actinomyces*. Fujita et al. identified their pathogen by molecular detection of their endobronchial biopsy specimen only after a third fiberoptic bronchoscopy.[8] These reports indicate that it is possible to maximize the success of identifying the pathogen by frequently repeating the flexible bronchoscopy or EBUS procedures.

When neither microbiological culture nor cytological features can be used to identify *Actinomyces*, the application of nucleic acid amplification techniques (NAAT) can be an alternative method to accelerate the diagnosis of pulmonary actinomycosis.[10] PCR amplification and DNA sequencing of 16S ribosomal RNA (rRNA) are especially useful when the quantity of tissue sample is limited. Fujita et al. utilized molecular techniques to successfully identify *Actinomyces graevenitzii* from the lung biopsy specimen of a 69-year-old patient who presented with unresolved organizing pneumonia after being treated with antibiotics for two months.[8] The advantage of NAAT is that it allows rapid and accurate diagnosis even when conventional tests are negative and the availability of specimens is limited.

Surgery is usually required to exclude lung cancer and confirm the histopathological diagnosis of *Actinomyces* infection. Zhang et al. demonstrated that up to 42.8% of cases were diagnosed only after surgical resection, and only 20% were confirmed by flexible bronchoscopy in their study.[4] Not only can the

surgical approach help in making the correct diagnosis but it can also control severe hemoptysis. Nevertheless, although we recommend surgical resection, a repeated EBUS procedure remains a valuable approach to confirming the diagnosis of pulmonary actinomycosis without recourse to surgery.

Penicillin G is the standard treatment regimen for pulmonary actinomycosis. High-dose penicillin G (18 – 24 million units daily) can be given intravenously for 2 – 6 weeks, followed by oral penicillin or amoxicillin for 6 – 12 months.[4] Our patient received oral amoxicillin for three months without evidence of recurrence, supporting the feasibility of a short antibiotic treatment course for patients after surgical treatment of the disease.

Conclusion

On encountering patients with unresolved lung lesions and intermittent hemoptysis, clinicians should consider the possibility of pulmonary actinomycosis. Repeating EBUS-guided sampling combined with molecular analysis can be helpful in the diagnosis of pulmonary actinomycosis.

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