Case Report

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Acute mediastinitis associated with tracheobronchial tuberculosis and aspergillosis: a case report and literature review

Chao-nan Liang, Hong-wen Zhao, Jian Kang, Gang Hou and Yan Yin

Abstract

Acute mediastinitis (AM) is a rare but life-threatening disease. Here, we report a case of AM secondary to endobronchial tuberculosis (EBTB) and pseudomembranous *Aspergillus* tracheobronchitis (PMATB) co-infection. EBTB was confirmed by tissue culture for *Mycobacterium tuberculosis* and GeneXpert MTB/RIF (Cepheid, Sunnyvale, CA, USA) detection (simultaneous detection of *M. tuberculosis* and resistance to rifampin) using endobronchial biopsies; PMATB was confirmed by histopathology. Even with antibiotic treatment and systemic support treatment, the patient died of massive hemoptysis on day 10 after admission. When immunocompromised hosts have AM, especially with central airway involvement, EBTB and aspergillosis should be considered potential causes. Bronchoscopy is helpful for rapid diagnosis and administering precise treatment.

Keywords

Bronchoscopy, interventional pulmonology, co-infection, *Mycobacterium tuberculosis*, endobronchial tuberculosis, *Aspergillus* tracheobronchitis

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Introduction

Acute mediastinitis (AM) is a rare but life-threatening disease with a mortality rate of up to 80%.[1] In general, esophageal rupture and postoperative complications are the most common causes of AM.[2] Tracheal perforation, direct extension of an infection from the lungs, and descending infection

Department of Pulmonary and Critical Care Medicine, First Hospital of China Medical University, Shenyang, Liaoning, China

Corresponding authors:
Yan Yin and Gang Hou, Department of Pulmonary and Critical Care Medicine, First Hospital of China Medical University, No. 155 Nanjing North Street, Shenyang 110001, Liaoning, China.
Emails: yinyan1b@126.com; hougangcmu@163.com

from the neck are also common causes of AM.[3] Overall, the bacteriologic findings in mediastinitis secondary to extension of an infection from head and neck sources indicate polymicrobial infections. Tuberculosis and fungal infections, such as histoplasmosis and aspergillosis, are the most common infections in chronic mediastinitis[4,5] but rarely cause AM. Rapid and accurate confirmation of pathogens is crucial to determining both the treatment and prognosis of AM. Here, we report a case of tracheobronchial tuberculosis (TBTB) and pseudomembranous *Aspergillus* tracheobronchitis (PMATB) co-infection presenting as AM in a female with uncontrolled diabetes mellitus (DM). Optimal management of combined TB and DM is important but challenging in terms of achieving good disease outcomes and avoiding toxicity, drug interactions, and other issues.[6,7] Although we confirmed the pathogens and administered antibiotics in a timely manner, we could not rescue the patient. To the best of our knowledge, such a case has not been reported in the literature.

Case report

This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Written informed consent to use the patient's information and images for publication was provided by a relative of the patient.

A 63-year-old female patient was admitted due to dyspnea and productive cough that had lasted for 6 days. The patient was febrile, and her highest temperature was 38.6°C. She had been diagnosed with type 2 DM, hypertension, and coronary heart disease six years prior and had uncontrolled hyperglycemia and hypertension. On admission, her vital signs were as follows: temperature, 35.5°C; respiration rate, 20 breaths/minute; pulse, 108 beats/minute; and blood pressure, 256/113 mmHg. Blood gas analysis showed type I respiratory failure (pH, 7.44; $PaCO_2$, 34 mmHg; PaO_2, 52 mmHg; and SpO_2, 88%). Laboratory data revealed a white blood cell count of 18.31×10^9/L, a neutrophil count of 17.27×10^9/L, a C-reactive protein level of 123.1 mg/L, a procalcitonin level of 0.61 ng/mL (0–0.05 ng/mL), an immunoglobulin E level of 332 IU/mL (0.00–100.00 IU/mL), a glucose level of 17.91 mmol/L, and a plasma glycosylated hemoglobin level of 14.90%. The level of (1,3)-β-D-glucan was normal. Liver and renal functions were normal. The human immunodeficiency virus antibody test was negative. Sputum smears were positive for gram-positive cocci, Gram-negative bacilli, and fungal spores but negative for *Mycobacterium tuberculosis* (MTB).

High-resolution computed tomography (CT) revealed stenosis of the right main bronchus, infiltrative and patchy shadows in the bilateral lungs, atelectasis of the right middle lobe, bilateral pleural effusion, pericardial effusion, increased attenuation of mediastinal fat, localized mediastinal fluid, free gas bubbles in the mediastinum, and mediastinal lymph node enlargement (Figure 1a–f).

Initial empirical antibiotic therapy included meropenem (1.0 g, q8h, iv) and moxifloxacin (400 mg, qd, iv). We controlled the patient's blood glucose and blood pressure to acceptable levels. To further evaluate the tracheobronchial lesion, we performed a bronchoscopy, which revealed stenosis of the lower segment of the trachea and bilateral main bronchi, which were covered with yellowish-white mucus and secretions (Figure 1g–i). Eight biopsies were obtained using forceps, one for bacterial culture, one for fungal culture, one for tuberculous bacteria culture (BACTEC MGIT 960 System; Becton Dickinson, Oxford, UK), one for GeneXpert MTB/RIF (Cepheid, Sunnyvale, CA, USA) detection,

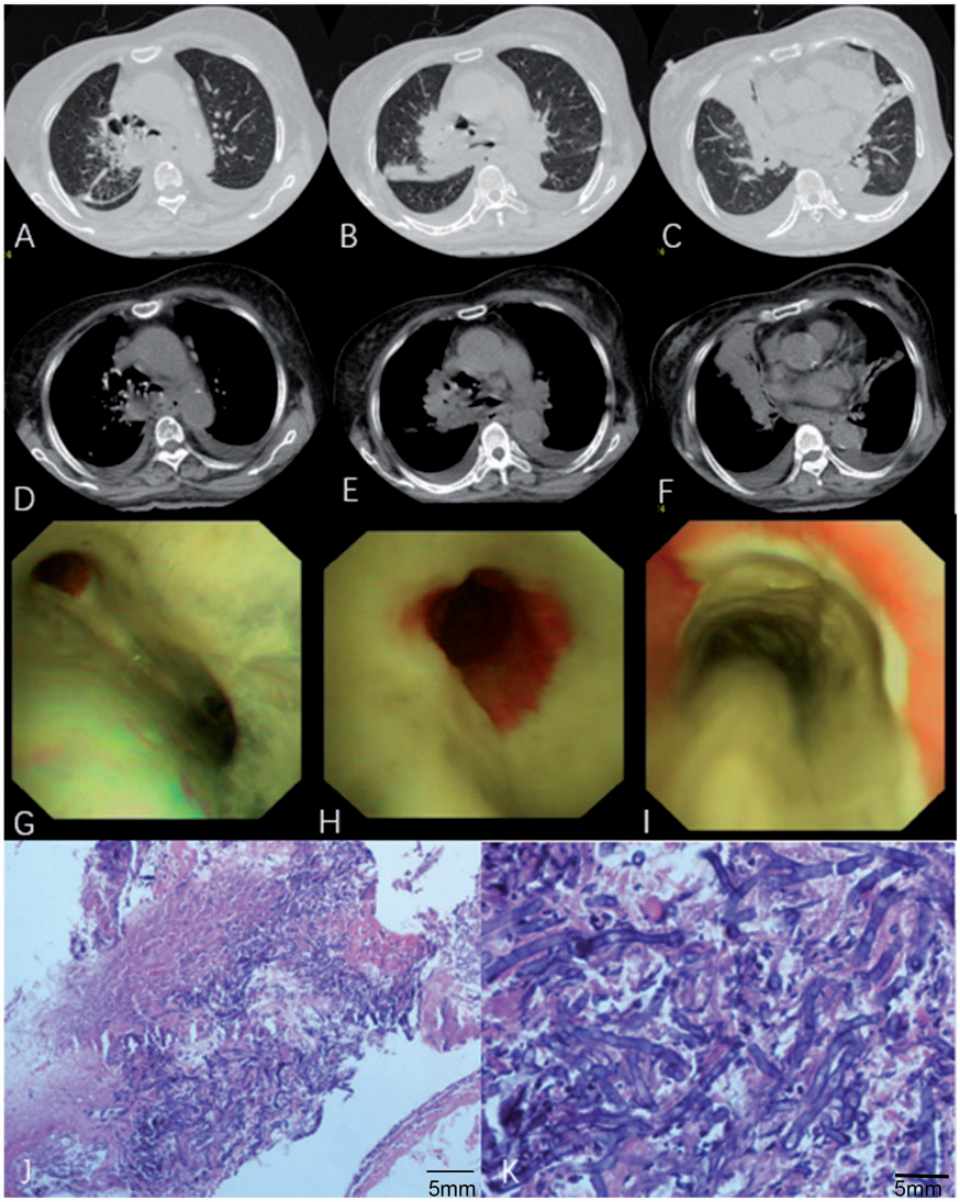

Figure 1. The details of chest computed tomography (CT), bronchoscopy, and pathology. Panels a–f: Chest CT revealed the fullness of the mediastinum and increased attenuation of mediastinal fat, localized mediastinal fluid, free gas bubbles in the mediastinum, and mediastinal lymph node enlargement (d, e, f). Panels show inflammatory infiltration of the bilateral lungs, especially in the right middle lobe (a–f), atelectasis of the right middle lobe (c, f), bilateral pleural effusion, and pericardial effusion. Panels g to i reveal diffusive pseudomembranous tracheobronchitis of the trachea and right and left bronchus. Panels J and K show hematoxylin and eosin staining of the biopsy of membrane of the right bronchus (j: 100×, k: 400×), which revealed septate and branching fungal hyphae, consistent with the features of *Aspergillus,* and some underlying necrotic lung tissue.

and four for pathological examination. Histopathology of the samples suggested hyphae typical of *Aspergillus* with necrotic and inflammatory cell infiltration (Figure 1j, k). GeneXpert MTB/RIF detection confirmed the existence of MTB (MTB detected at a high level, with no rifampicin resistance detected) and tissue culture was positive for MTB. Because of the policy regarding MTB control and treatment, the patient had to be transferred to a hospital specializing in patients with tuberculosis. Thus, on day 6 after admission to our hospital, the patient was transferred to a hospital for systemic treatment, including anti-tuberculosis and anti-fungal therapy. Anti-tuberculosis treatment was initiated orally with isoniazid 300 mg/day, rifampicin 450 mg/day, ethambutol 750 mg/day, and pyrazinamide 500 mg tid; anti-aspergillosis treatment was initiated with voriconazole (4 mg/kg, q12h). Unfortunately, the patient's condition deteriorated rapidly, and she died suddenly from massive hemoptysis on day 4 after transfer from our hospital.

Discussion and conclusion

AM is rare and associated with a high mortality if not treated in a timely manner. Chills, high fever, tachycardia, and sepsis are common clinical symptoms of AM,[2] but they are nonspecific. CT findings are very important for recognizing AM, including increased attenuation of mediastinal fat, localized mediastinal fluid, free gas bubbles in the mediastinum, mediastinal lymph node enlargement, pleural and/or pericardial effusion and lung infiltrate.[3] In our case, we observed mediastinal fat attenuation, free gas bubbles in the mediastinum, and pericardial and pleural effusion, which are typical radiologic manifestations of AM.

Rapid confirmation of pathogens is crucial in AM. Bronchial biopsy, which is a relatively safe and noninvasive technique, can quickly provide high-quality tissue samples when the infection involves the central airways. The GeneXpert MTB/RIF assay is an innovative tool for rapidly diagnosing TBTB and rifampicin resistance.[8] In our case, we performed bronchial biopsy and identified MTB using the GeneXpert MTB/RIF assay on the same day, but the MTB-positive tissue culture result was not reported until 4 days after the patient had died.

Tracheal fistulae caused by TBTB have been reported, and anti-tuberculosis therapy has proven to be effective.[9] Of note, tracheal fistulae are an uncommon complication of *Aspergillus* tracheobronchitis (ATB).[10] The AM in our patient might have been caused by a tracheobronchial mediastinal fistula due to TBTB or PMATB, but we could not confirm the position of the fistula because of the existence of a pseudomembrane. Involvement of the full tracheobronchial layer in ATB that may lead to mediastinitis has been identified as a poor prognostic factor in previous study.[11] Bronchoscopy in our patient showed the lower segment of the trachea, carina, the left mainstem bronchus, right mainstem bronchus and the bronchus intermedius were covered with yellowish-white mucus and secretions, and both the right mainstem bronchus and the bronchus intermedius were narrowed, consistent with the bronchoscopic manifestations of TBTB and PMATB. *Aspergillus* can colonize the airways of patients with underlying lung disease, such as tuberculosis, but the patient in this case died of massive hemoptysis. This was indirect evidence of AM caused by *Aspergillus* because invasive *Aspergillus* infections can lead to vascular invasion and infarction, which can then result in transmural necrosis.[12] Diabetes mellitus is a moderate-to-strong risk factor for the development of TBTB and ATB. Moreover, treatment failure and death are more frequent in diabetic patients.[13] Reversal of

predisposing factors, such as hyperglycemia, is crucial for the treatment of invasive fungal infections.

In conclusion, when AM occurs in an immunocompromised host, especially with central airway involvement, endobronchial tuberculosis and aspergillosis should be considered potential causes. Bronchoscopy should be performed in a timely manner to facilitate a rapid definite diagnosis and administration of precise treatment.

Author contributions

GH and YY made substantial contributions to the conception or design of the work. All authors contributed to the acquisition of data for the work. GH, C-NL and H-WZ helped to collect the data of the case. YY and C-NL wrote the manuscript. GH, YY, and JK interpreted data. GH performed the bronchoscopy. All authors revised the paper critically for important intellectual content and approved the final version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of conflicting interest

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ORCID iD

Gang Hou https://orcid.org/0000-0003-3438-1764

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