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

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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
from the neck are also common causes of
AM. Overall, the bacteriologic findings in
mediastinitis secondary to extension of an
infection from head and neck sources indi-
cate polymicrobial infections. Tuberculosis
and fungal infections, such as histoplasmo-
sis and aspergillosis, are the most common
infections in chronic mediastinitis but
rarely cause AM. Rapid and accurate con-
firmation of pathogens is crucial to deter-
mining both the treatment and prognosis
of AM. Here, we report a case of tracheo-
bronchial tuberculosis (TBTB) and pseudo-
membranous *Aspergillus* tracheobronchitis
(PMATB) co-infection presenting as AM
in a female with uncontrolled diabetes mel-
itus (DM). Optimal management of com-
bined TB and DM is important but
challenging in terms of achieving good dis-
ease outcomes and avoiding toxicity, drug
interactions, and other issues. Although
we confirmed the pathogens and adminis-
tered 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 publi-
cation was provided by a relative of
the patient.

A 63-year-old female patient was admit-
ted 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 uncon-
trolled 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; PaCO₂, 34 mmHg; PaO₂,
52 mmHg; and SpO₂, 88%). Laboratory
data revealed a white blood cell count
of 18.31 × 10⁹/L, a neutrophil count of
17.27 × 10⁹/L, a C-reactive protein level
of 0.61 ng/mL (0–0.05 ng/mL), an immunoglob-
ulin 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 con-
trolled the patient’s blood glucose and
blood pressure to acceptable levels. To fur-
ther 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, 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. 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 TTB and rifampicin resistance. 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 TTB have been reported, and anti-tuberculosis therapy has proven to be effective. Of note, tracheal fistulae are an uncommon complication of *Aspergillus* tracheobronchitis (ATB). The AM in our patient might have been caused by a tracheobronchial mediastinal fistula due to TTB 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. 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 TTB 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. Diabetes mellitus is a moderate-to-strong risk factor for the development of TTB and ATB. Moreover, treatment failure and death are more frequent in diabetic patients. 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.

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