A 37-Year-Old Woman Presenting With Hemoptysis, Dyspnea and Fever

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CASE PRESENTATION: A 37-year-old woman presented to the ED in Singapore with a 6-month history of chronic cough and dyspnea that was associated with small volume hemoptysis, night sweats and occasional fever. Of note, she had no sick contacts or recent travel. Systemic review revealed no loss of weight or appetite and no autoimmune features. She had no other medical history and was a lifelong nonsmoker and was not an alcoholic.

Physical Examination Findings
On admission, she was febrile at 38.7°C with a heart rate of 134 beats/min, a BP of 129/74 mm Hg, respiratory rate of 16 breaths/min, and a pulse oxygen saturation of 88% on room air that improved to 95% with Fio2 50% via an air-entrainment mask. Examination of the chest was remarkable for reduced air entry and crepitations over the right basal hemithorax. There was no elevated jugular venous pressure, pedal edema, or cervical lymphadenopathy.

Diagnostic Studies
Chest radiogram showed a right lower zone opacification with a clear right-sided heart border and mediastinal shift to the right (Fig 1). Laboratory investigations revealed anemia with a hemoglobin level of 8.8 g/dL and normal renal function. Inflammatory markers were bland with a WBC count of 10.6 10^3/μL, C-reactive protein level of 10.5 mg/L (reference range, < 3.0 mg/L), and procalcitonin level of 0.07 μg/L (reference range, 0.0 to 0.5 μg/L). Arterial blood gas performed on Fio2 50% reported Pao2 of 73.3 mm Hg. Her retroviral screen was negative, and her hemoglobin A1c was 5.7%. Autoimmune screen was nonyielding. Sputum Gram stain results were negative; the respiratory virus polymerase chain reaction (PCR) was positive for rhinovirus.

CT scan of the thorax revealed a dense consolidation of the right lower lobe with gas pockets and marked mucus plugging of the airways. No discrete endobronchial lesion or narrowing of the right lower lobe bronchus was

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seen. Of note, there were diffuse, patchy areas of ground-glass consolidation and tree-in-bud opacities with small mediastinal lymph nodes. There was no cervical lymphadenopathy or bony destruction (Figs 2, 3). Her sputum and peripheral blood bacterial cultures also returned negative.

What is the diagnosis?
**Diagnosis:** Necrotizing pneumonia secondary to pulmonary TB

**Discussion**

Necrotizing pneumonia is a severe form of community-acquired pneumonia on the extreme end of the pneumonia severity spectrum between lung abscess and pulmonary gangrene. It is characterized by development of necrosis within consolidated lung tissue, which often leads to the formation of multiple cavities and gas pockets. It is associated with high morbidity and mortality rates. Common causes of necrotizing pneumonia described in literature include *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Klebsiella pneumoniae*. Mycobacterium TB complex (MTC) remains a rare cause of necrotizing pneumonia in the adult population, with only one other described case in current literature.

The pathophysiologic evidence behind MTC necrotizing pneumonia is postulated to be a cell-mediated delayed-type hypersensitivity reaction to tuberculoprotein that results in an inflammatory cytokine response that leads to pulmonary vascular thrombosis and arteritis, which eventually leads to necrosis and multiple small cavity formation.

Incidence of necrotizing pneumonia caused by MTC is higher in children than in adult patients because of a more developed T-cell-mediated adaptive immune system in the latter group. Establishment of national Bacillus Calmette-Guérin vaccination schemes have also reduced the incidence of severe TB infections, such as disseminated TB and TB meningitis.

Viral co-infections (namely, influenza) have been shown to increase host susceptibility to bacterial infections and propel the development of necrotizing pneumonia.

Clinical differentiation of MTC necrotizing pneumonia from the other bacterial causes is difficult because there is no pathognomonic feature for either. Radiologic features of tree-in-bud opacities can suggest MTC infection but includes other differentials such as aspiration, viral, or other bacterial infection. Imaging pattern of patchy bronchiectasis with tree-in-bud opacities in a random small-airway pattern has a higher prediction rate for mycobacterium infection. MTC PCR testing or acid-fast bacilli (AFB) cultures can help to differentiate between MTC from nontuberculous mycobacterium. A high degree of suspicion and a thorough review that includes the epidemiologic evidence and immune constitution of the patient are also pertinent in clinching the correct diagnosis.

Management of necrotizing pneumonia caused by MTC encompasses a three-pronged approach: treatment of the disease, transmission reduction, and prevention of drug resistance. This involves prompt initiation of multidrug anti-TB therapy while ensuring compliance to treatment and early consideration of surgical intervention.

Multidrug antituberculous therapy has two phases: initiation and continuation. Initiation typically includes a four-drug regimen of bacteriostatic (ethambutol) and bactericidal drugs with sterilizing activity (rifampicin, isoniazid, pyrazinamide) for 2 months. Continuation phase includes a two-drug regimen with bactericidal and sterilizing activity (rifampicin, isoniazid) with an aim to eliminate slow intermittent growers or dormant MTC under anaerobic conditions. No guidelines are available regarding the duration of therapy in MTC necrotizing pneumonia. However, expert opinion suggests a prolonged duration of therapy of 9 months, depending on the patient’s clinical progress.

Surgery is usually required in cases refractory to antimicrobial treatment or with progression to pulmonary gangrene, because antimicrobial delivery to the affected lung is compromised because of poorly perfused tissue. Therefore, in cases of antimicrobial failure despite compliance to culture-directed treatment, early surgical intervention coupled with continuation of antimicrobial therapy should be considered.

Compliance to treatment via direct observed therapy should also be enforced to prevent the emergence of drug-resistant MTC. Infection control measures such as physical segregation and isolation are used while the patient’s condition is still infectious because of public health implications.

MTC necrotizing pneumonia is an uncommon disease. Accurate and prompt diagnosis is important because of the downstream implications of public health concerns and different antimicrobial cover. Thorough clinical review coupled with early microbiologic AFB analysis is essential in obtaining an accurate diagnosis. Early surgical intervention should always be considered in patients with necrotizing MTC pneumonia because of
the nature of the disease, especially if there is paucity of clinical improvement despite culture-directed multidrug antimicrobial therapy.

**Clinical Course**

Despite broad-spectrum antibiotic therapy, the patient experienced worsening respiratory distress and hypoxemia that required endotracheal intubation and positive pressure ventilation.

Bronchoscopy performed at bedside revealed a fresh blood clot in the right bronchus intermedius with no active bleeding seen. Because of concerns of dislodging the blood clot, no attempts were made at distal inspection. Endotracheal specimens were dispatched for AFB analysis in light of the endemic history and radiologic findings.

Her endotracheal AFB smears subsequently returned positive 1+, and MTC was confirmed on PCR, establishing a diagnosis of MTC necrotizing pneumonia. The patient was started on four-drug antituberculous therapy that consisted of rifampicin, isoniazid, ethambutol and pyrazinamide. Her hemoptysis and hypoxemia resolved, and extubation was successful. She was discharged well on days 3 and 5 of her antituberculous therapy, respectively.

**Clinical Pearls**

1. TB necrotizing pneumonia can occur even in healthy, immunocompetent hosts. It is described more commonly in children than in adults.

2. In an endemic country, Mycobacterium TB as the causative agent should be considered in all patients presenting with necrotizing pneumonia.

3. Prompt initiation of appropriate antituberculous therapy is the mainstay of treatment of TB necrotizing pneumonia. Expert opinion suggests a prolonged duration of therapy.

4. Surgery should be considered in refractory cases because of impaired antimicrobial delivery that is a consequence of impaired perfusion in pulmonary gangrene.

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**Suggested Readings**


