

Ventilator-dependent pulmonary nocardiosis in a patient with chronic obstructive pulmonary disease

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ABSTRACT

Nocardiosis is a rare infectious disease entity that mostly affects the lungs, brain, or skin of immunocompromised individuals. Recent reports of pulmonary nocardiosis (PN) in patients with chronic obstructive pulmonary disease (COPD) as the only risk factor suggest a possible association between nocardiosis and COPD. Herein, we present a case of ventilator-dependent PN in a patient with a moderate degree of COPD. A high level of suspicion for PN should be maintained when encountered with COPD patients complaining of symptoms of pneumonia and excessive thirst.

KEY WORDS: Acute respiratory failure, chronic obstructive pulmonary disease, pulmonary nocardiosis, ventilator

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INTRODUCTION

Nocardia is aerobic Gram-positive bacteria that can cause opportunistic infections through direct inhalation in the lungs, brain, and skin of immunocompromised individuals.^[1,2] Due to its inherent inoculation pathway, 90% of nocardiosis involves the pulmonary system.^[1] Pulmonary nocardiosis (PN) has been reported to occur mostly in the following populations: HIV patients, lymphoreticular cancer patients, transplant recipients, alcoholics, and diabetics. Disseminated nocardiosis has been reported to even mimic a metastatic malignancy in the immunosuppressed.^[3] However, 4 cases of PN in patients with chronic obstructive pulmonary disease (COPD) as the only risk factors have been reported, suggesting a close association for PN and COPD.^[4] Underlying pulmonary disease was the second most common predisposing condition for the development of PN in one cohort of patients.^[5] The potential mechanism behind this association is the recurrent or persistent bacterial infection in the respiratory system and long-term exposure

to steroid therapy. Recurrent bouts of pulmonary infection can impair ciliary motility and damage the epithelial layer. The resultant dysfunction of protective mechanisms in the airway may facilitate the infection process by Nocardia.^[2]

In the United States, approximately, 500–1000 cases of PN are reported annually. The mortality from PN is about 38.7%, whereas the mortality rate reaches 100% for nocardiosis involving the central nervous system (CNS). If the CNS is not involved, disseminated nocardiosis has a mortality rate of 64%.^[6] Herein, we report a case of PN that led to acute respiratory failure complicated by Type II myocardial infarction and pulmonary embolism in a patient with COPD on systemic steroid therapy.

CASE REPORT

A 65-year-old woman presented with a 3-day duration of worsening confusion, dyspnea, chest pain, wheezing, and cough with yellow and blood-tinged sputum. These

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symptoms were accompanied by intermittent high fever, excessive thirst, polyuria, diarrhea, and anorexia. Significant medical history included moderate degree of COPD managed with inhaled albuterol 2.5 mg PRN and tiotropium bromide 18 mcg. Her blood pressure, heart rate, respiration rate, temperature, and oxygen saturation at room air were 190/114 mmHg, 149/min, 40/min, 37.4°C, and 64%. Her white blood cell and lactic acid levels were elevated at $13.6 \times 10^9/L$ (70% granulocytes) and 21.3 mg/dL, respectively. Her sodium level was found to be low at 128 mmol/L. Arterial blood gas showed hypoxemic respiratory failure (pH 7.21, CO_2 43.0 mmHg, O_2 57.6 mmHg, HCO_3 18.8 mmol/L, and O_2 saturation 85.8%). She was expeditiously placed on 2 L of oxygen, but she continued to complain of worsening dyspnea and desaturated to 84%. In light of rapidly progressing hypoxemic respiratory failure, she was intubated and placed on mechanical ventilation. For acute management of her tachycardia and hypertension, metoprolol was given.

Chest X-ray revealed multilobar pneumonia [Figure 1]. Computed tomography (CT) of her chest revealed extensive consolidating pneumonia throughout the lung field bilaterally. This finding was most extensive in the lower lung fields, but there was considerable ground glass infiltrate in the right upper lobe and to a lesser extent, the left upper lobe [Figure 2]. She was started on vancomycin, cefepime, and methylprednisolone for empirical treatment. Her sputum culture grew *Nocardia asteroides*. The diagnosis of nocardiosis prompted the medical team to obtain a CT of her brain, which showed no signs of abscess or infection. Based on the result from the culture, antibiotic regimen was switched to piperacillin/tazobactam, sulfamethoxazole/trimethoprim, and azithromycin; however, the patient did not show any improvement on the combinative antibiotic therapy. A third antibiotic regimen with levofloxacin, ampicillin-sulbactam, meropenem, and sulfamethoxazole/trimethoprim was tried for a week without success. The fourth combinative antibiotic therapy consisted of vancomycin, imipenem, metronidazole, and sulfamethoxazole/trimethoprim, also with no success.

Due to lack of improvement, further investigation with bronchoscopy and video-assisted thoracoscopy (VAT) was performed. Bronchoscopy showed an inflamed airway with thin frothy secretions, mainly from the right hemithorax. Bronchoalveolar lavage showed nonspecific acute inflammation and blood. VAT of the right lung showed patchy infiltrates of all 3 lobes, the lower lobe most prominently. A modest amount of serous pleural effusion was also noted. Lung biopsy revealed acute fibrinous and organizing pneumonia [Figure 3] consistent with the diagnosis of multifocal necrotizing pneumonia, and a large thickened vessel with an organizing fibrin thrombus [Figure 4]. Overall, the lung was described as bobby and friable.

Following the investigation, the patient was treated with imipenem, metronidazole, and sulfamethoxazole/trimethoprim. Three days later, amikacin was added. Over

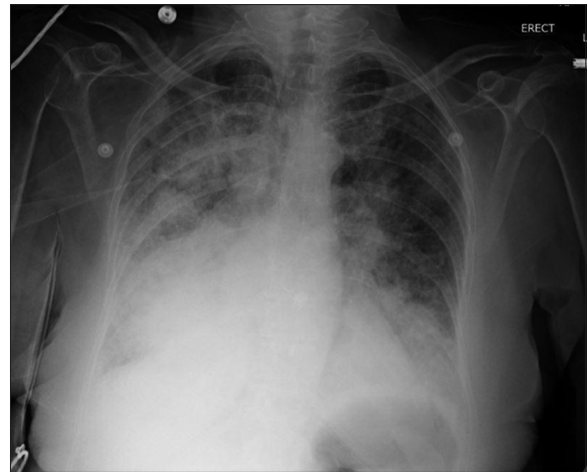


Figure 1: Roentgenogram of chest demonstrating multilobar pneumonia

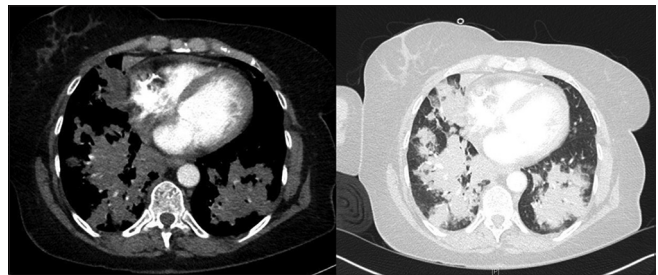


Figure 2: Computerized tomography of chest visualizing extensive consolidating pneumonia throughout the lung field bilaterally

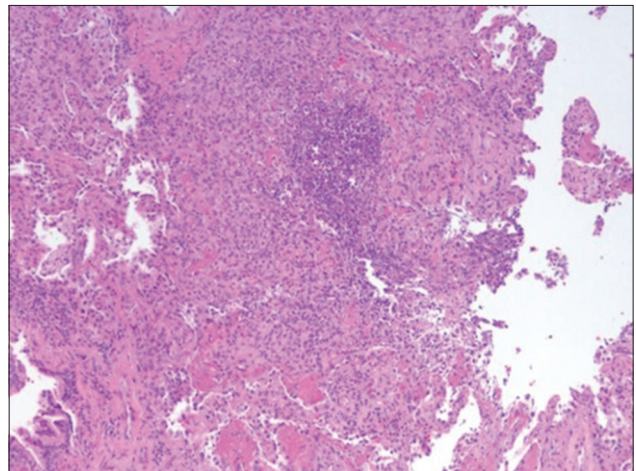


Figure 3: Lung biopsy (H and E, $\times 10$ power) showing a large blue sheet of predominantly neutrophilic active pneumonia, and organizing pneumonia consisting of amorphous pink fibrin bands in alveolar spaces

a 1 month period, the patient clinically improved. Repeat blood and sputum cultures were negative for *Nocardia*. Despite this, three attempted extubations were unsuccessful, and the patient remained ventilator-dependent. A tracheal tube was placed on her 31st day on the ventilator to prevent vocal cord damage and tracheal stricture. The patient failed a swallowing test after tracheal tube placement and subsequently had a percutaneous endoscopic gastrostomy tube inserted for feeding purposes.

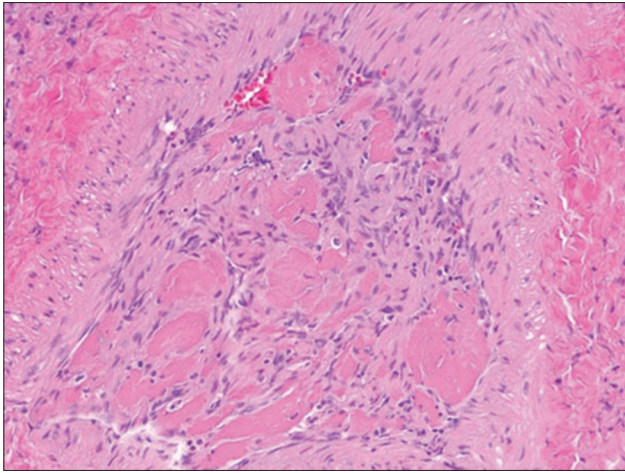


Figure 4: Lung biopsy (H and E, $\times 20$ power) showing a large thickened blood vessel with organizing fibrin thrombus

During her admission, she developed a non-ST elevation myocardial infarction, possibly from demand ischemia. Coronary angiography was deferred due to the severe infection. The patient was started on 6 weeks of clopidogrel. Other cardiovascular conditions included DVT of her right arm resulting in a pulmonary embolism [Figure 5]. She was started on a heparin drip, and later bridged to warfarin. Another complication was persistent hyponatremia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH). Throughout admission, her sodium level fluctuated from 120 to 131 mmol/L. She was treated with tolvaptan, furosemide, fluid restriction, and sodium chloride tablets. At the time of discharge, her sodium level was at 130 mmol/L.

Two days before the patient's discharge, her WBC was still elevated at $17.2 \times 10^9/L$, thus her antibiotic regimen was changed to linezolid, tobramycin, and sulfamethoxazole/trimethoprim. On the 60th day of hospitalization, she was discharged to a long-term acute care facility with a peripherally inserted central catheter for continuous antibiotic therapy. The patient expired 9 months following discharge due to failure to thrive.

DISCUSSION

Clinical presentation of PN is nonspecific and can resemble acute exacerbation of COPD. Common symptoms include chest pain, coughing, sputum production, dyspnea, fatigue, and loss of appetite.^[5] Common, nonspecific radiographic findings include infiltrates, cavitation, pleural effusion, or bony erosion.^[2] The diagnosis of PN can be challenging due to the rarity of the disease entity, radiographic pleomorphism, and lack of pathognomonic clinical signs or serologic markers. Only isolation of the organism through smears or culture is diagnostic.^[7] Nocardia species grow on aerobic media over 5–21 days, and can exhibit acid-fast characteristics. Sensitivity of cultures from sputum and bronchoalveolar lavage are approximately 90% and 100%, respectively.^[2] This slow method greatly delays the

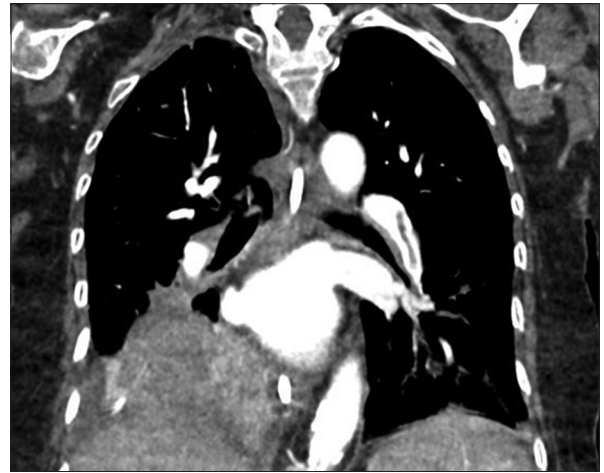


Figure 5: Computerized tomography of chest showing pulmonary embolism

diagnostic process. Improvements on current diagnostic methods are urgently needed.

Following a diagnosis of PN, it is critical to start treatment immediately because about 50% of untreated PN can spread to other parts of the body through the blood or lymphatic systems.^[7] Treatment of PN consists of systematic antibiotic therapy. Sulfonamide-based antibiotics, such as trimethoprim-sulfamethoxazole, are the first line of treatment. For patients with sulfa allergies or nocardiosis refractory to sulfonamide-based regimen, the following alternative treatment options may be adopted: minocycline, doxycycline, amoxicilline-clavulanate, carbapenem, amikacin, cefuroxime, ceftriaxone, clarithromycin, ofloxacin, linezolid, and inhaled aminoglycoside. The recommended treatment duration is 3–12 months.^[2,8]

SIADH is a known complication from PN, but the treatment of nocardiosis and fluid restriction typically resolves hyponatremia.^[9] Proper electrolyte balance is critical to improving patient outcomes.

The lesson to learn here is that clinicians should be aware of the association between PN and structural lung disease such as COPD, cystic fibrosis, and bronchiectasis. Broader awareness of this association would help reduce misdiagnosis and decrease the mortality rate from PN. Immunocompromised patients on long-term steroid therapy are also very vulnerable to PN.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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