

Pulmonary nocardiosis revisited: A case series

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ABSTRACT

Pulmonary nocardiosis is a rising bacterial infection, with a high propensity for misdiagnosis. On account of a paucity of prospective studies, there is limited understanding on various aspects of its diagnosis and treatment. We present three patients with pulmonary nocardiosis, with emphasis on the predisposing factors, variable disease course, and treatment issues. There is a need to understand the basis of these discrepancies so as to rationalize the management of this potentially fatal infection.

KEY WORDS: Infection, nocardiosis, pulmonary

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INTRODUCTION

Pulmonary nocardiosis is a major cause of morbidity and mortality in immunocompromised patients. Lack of suspicion, non-specific clinicoradiological presentation (often mimicking tuberculosis and fungal infections), diagnostic intricacies, and lack of systematic reporting are the probable reasons that have hindered the true estimation of its incidence, worldwide.^[1] We present a case series of three patients of pulmonary nocardiosis, who had different clinicoradiological presentations and also responded differently to treatment. Difficulties in their management have been discussed in light of the available literature that may help in improving disease management. In view of the rising incidence of cancer, organ transplant surgeries, and use of parenteral steroids, *Nocardia* is likely to attain a higher place among the causes of pulmonary infections.

CASE REPORTS

Case 1

A 50-year-old female presented with complaints of breathlessness at rest, cough, and right-sided chest

pain since 15 days. Breathlessness was present since five years, for which she was on inhaled steroids and bronchodilators. She had completed successful anti-tubercular treatment (ATT) eight years ago and was again advised ATT for her current condition. On examination, she was tachypneic, with decreased intensity of breath sounds over the right hemithorax, and bilateral expiratory wheeze. Hematological investigations revealed leukocytosis and neutrophilia and the values of the arterial blood gases showed type II respiratory failure. On a chest radiograph, there was right-sided non-homogenous opacity involving all zones with air-fluid levels and left lung mid-zone infiltrates [Figure 1a]. An empirical antibiotic, cefoperazone plus sulbactam, was started along with supportive treatment. A sputum examination was negative for *tubercle bacilli*. However, it revealed weak, acid-fast, filamentous bacilli resembling *Nocardia* spp. Bronchoalveolar lavage (BAL) also yielded the growth of *Nocardia* spp. [Figure 1b]. Considering the disease severity, the patient was started on two drugs, co-trimoxazole (dose 40 mg/kg/day of sulfamethoxazole) and amikacin (sensitive to *Nocardia* spp.). Contrast-enhanced computed tomography (CECT) of the thorax showed right lower lobe and left lingular necrotizing consolidation, with loculated hydropneumothorax [Figure 1c]. Right-sided intercostal tube drainage was done which improved the patient's dyspnea. Amikacin was replaced with linezolid on the fifteenth day. The patient gradually responded to antibiotics. At the end of the fifth week, the patient developed pancytopenia, due to which, cotrimoxazole and linezolid were replaced with doxycycline. Ensuring persistent improvement, the patient was discharged on the same drug. She successfully completed seven months of

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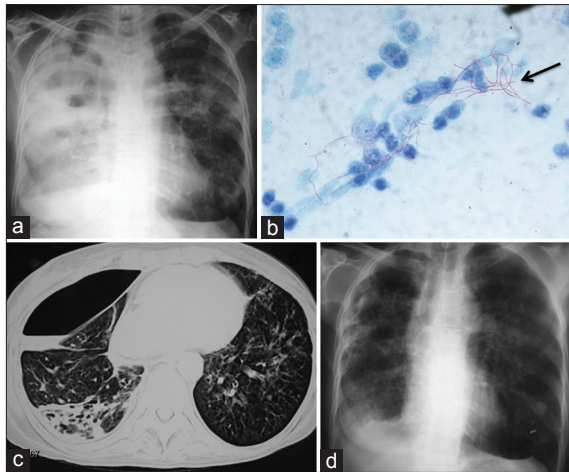


Figure 1: (a) X-ray chest, PA view, showing non-homogenous opacity involving all zones on the right side and in the left para-hilar region; (b) Photomicrograph showing *Nocardia* species (black arrow) stained with modified Ziehl Neelsen stain (under $\times 100$); (c) Axial cut section CT thorax showing a right-sided, loculated, hydropneumothorax and basilar necrotizing consolidation; (d) X-ray chest PA view, showing clearing of shadows with residual fibrotic scarring over the left lung field

antibiotics with negative serial cultures and satisfactory clinico-radiological improvement [Figure 1d].

Case 2

A 72-year-old male, presented with a three-month history of progressive shortness of breath and productive cough. He had a 120-pack-year history of smoking tobacco in the form of 'bidis' (Indian cigarette). He had been on multiple courses of oral steroids for recurrent breathlessness, present for over five years. The blood picture showed a normal leukocyte count. CECT of the chest showed areas of necrotizing consolidation with a few cavitating nodules involving the upper lobe on both sides, with a background of emphysema [Figure 2]. On suspicion of pneumonia/tuberculosis, the sputum was subjected to microbiological tests and cytology, which was inconclusive. However, BAL showed the growth of *Nocardia* spp. The patient was started on antibiotics, cotrimoxazole and linezolid (600 mg b.i.d.), along with oral steroids. Cotrimoxazole was replaced with doxycycline due to severe gastric disturbances and leukopenia. The patients showed gradual clinical improvement. He was discharged on doxycycline and linezolid. However, he got readmitted after 12 days in Emergency with complaints of loose stools and deranged consciousness. He had severe electrolyte imbalance, hyponatremia (Serum Na^+ : 111meq/l), and hypokalemia (Serum K^+ : 1.7meq/l), and died due to sudden cardiac arrest.

Case 3

A 42-year-old male smoker presented with cough, increased breathlessness, and high-grade fever since 20 days. The patient had been self-medicating with oral steroids for the last three years due to persistent breathlessness. On auscultation, bronchial breath sounds were heard in the right interscapular region. The leukocyte count was mildly

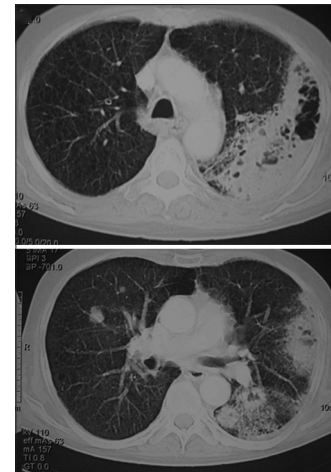


Figure 2: Two axial cut sections of the CT thorax, with contrast showing patchy areas of necrotizing consolidation and few cavitating nodules

raised at 12,600/ μl . The X-ray chest PA view and CECT thorax showed bilateral mass-like consolidations with air bronchograms [Figure 3a and b]. On suspicion for lung carcinoma/pneumonia, BAL was performed, which showed the growth of *Nocardia* spp. Cotrimoxazole (40mg/kg/day of sulfamethoxazole) and injection Ceftriaxone 3 g/day were started and the steroids were continued in tapering doses. The patient showed gradual improvement in symptoms. Ceftriaxone was stopped after three weeks. The patient completed six months of treatment with marked clinico-radiological improvement [Figure 3c].

DISCUSSION

Nocardiosis is caused by the aerobic, gram-positive filamentous bacteria of genus *Nocardia*.^[2] A majority of the *Nocardia* species responsible for respiratory and disseminated nocardiosis have been re-grouped as the "*Nocardia asteroides* complex".^[3] This change in the *Nocardia* nomenclature has affected proper disease estimation and understanding. The existing literature from India is no better and merely consists of case series^[4] and a few case reports.^[5,6]

Lungs are the most common site of involvement and are affected in 70% of all cases of Nocardiosis.^[7] The Central Nervous System (CNS), skin, and disseminated disease are other presentations, the likelihood of which depends on the individual's immune status, time to diagnosis, and virulence of the *Nocardia* species. All three patients in our series had isolated pulmonary involvement, as dictated by the absence of extrapulmonary symptoms. Pulmonary nocardiosis usually affects patients with leukemia, human immunodeficiency virus (HIV) infection, organ transplantation, diabetes, or patients receiving prolonged corticosteroids.^[8,9] However, it has also been seen in patients without a definable predisposing condition.^[1,9,10] Although unlikely, COPD has been found as a predisposing factor in 23-70% of pulmonary nocardiosis.^[9,11] All patients in the series also had underlying airway disease consistent

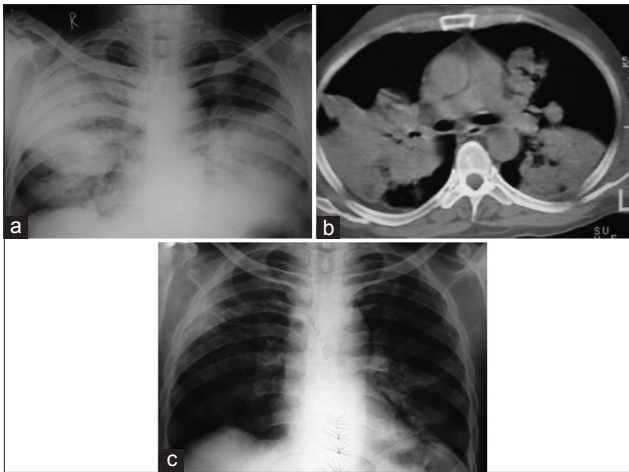


Figure 3: (a) X-ray chest, PA view, showing homogenous opacity involving all zones over the right hemithorax, as well as, over the mid and lower zones on the left side; (b) Axial section of the CT thorax below the carina showing three areas of mass-like consolidations, involving the bilateral hemithorax; (c) X-ray chest, PA view, showing marked resolution of the opacities with residual fibrosis

with chronic obstructive pulmonary disease (COPD) and two of them had a history of prolonged steroid intake. However, it may be difficult to quantify the relative contribution of each factor in predisposing the disease.

Pulmonary nocardiosis may present as an acute, subacute or chronic disease, with remissions and exacerbations. Symptoms include fever, cough, breathlessness, hemoptysis, and weight loss, which are often attributed to tuberculosis or community-acquired pneumonia. Apart from these, nocardiosis may also mimic fungal pneumonia, anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis and lung cancer. Imaging studies are not of much help in reaching the diagnosis. Nodules, necrotizing consolidation, cavities, and mass shadows are some of its varied but non-specific presentations.^[12] One patient in our series had a mass shadow mimicking carcinoma and the other two had non-specific consolidations.

Isolation and identification of the organism from the clinical specimens form the backbone for diagnosis of pulmonary nocardiosis. Requirement for invasive sampling (BAL, biopsy), a slow growth, and varying degrees of acid fastness of the bacteria cause a hindrance to the microbiological confirmation. Typically, *Nocardia* are weak, acid-fast organisms, visualized by a modified Ziehl-Neelsen stain, using 1% sulfuric acid (instead of 20%, which is used for *tubercle bacilli*).^[13] Hence, the laboratory should always be notified about its suspicion so as to optimize recovery. Moreover, isolation of the organism should be interpreted under the light of a relevant clinical background, as bacteria can also be isolated from colonized airways of apparently healthy individuals, like bronchiectasis.^[14] In the present series, *Nocardia* was isolated from the BAL of all patients with suggestive symptoms. Species

identification could not be done in our patients because of a lack of the requisite infrastructure. Once confirmed, the extra-pulmonary spread of disease should be explored, if clinically indicated.

Owing to the paucity of prospective trials, there is a lack of standard treatment guidelines for pulmonary nocardiosis. In view of the difference in virulence and *in vitro* drug susceptibility of bacterial subtypes, the treatment needs to be individualized. Trimethoprim-sulfamethoxazole is the most common drug combination used, in a dose of 25-50 mg/kg per day of sulfamethoxazole, in divided doses. Amikacin, imipenem, ceftriaxone, minocycline, levofloxacin, linezolid, and amoxicillin-clavulanic acid are the alternate drugs that have activity against *Nocardia*. A combination of two drugs has been used in our patients. This is sometimes recommended in sick patients, during the initial period. Usually, the treatment is recommended for a total duration of six to twelve months, which may be prolonged in immunocompromised patients.^[15] Two patients in our series were treated successfully with six and seven months of treatment, respectively, while one died during the course of treatment.

The burden of pulmonary nocardiosis seems to be highly underestimated. The disease should always be considered in the differential diagnosis of pneumonia, not only in the immunocompromised, but also in the immunocompetent, especially when they are not responding to the standard therapy. In tuberculosis endemic countries like India, nocardiosis should always be excluded among patients not responding to anti-tubercular treatment. Early recognition and appropriate individualized treatment is the key to a successful outcome.

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