Case Report

Primary pulmonary nocardiosis by *Nocardia brasiliensis*: A case report and review of Indian literature

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Abstract

Infection by *Nocardia brasiliensis* is usually localized to the skin but can rarely spread to the lung, brain, or multiple sites particularly in the immunocompromised hosts. Moreover, primary systemic involvement without cutaneous disease is an extremely rare case. In the current study, we present a case of primary pulmonary nocardiosis caused by a multi-drug resistant *N brasiliensis* along with a review of the cases reported from India.

Keywords: India, nocardiosis, *Nocardia brasiliensis*, pulmonary

Introduction

Pulmonary infections, despite being the leading infectious cause of hospitalization and death worldwide, are often misdiagnosed, mistreated, and underestimated. Diagnosis is usually made by clinical features (history and physical examination) and chest imaging. Establishing a microbial etiology is necessary where unusual or drug-resistant pathogens are suspected in patients with immunocompromised states or in patients who are not responding to empirical antimicrobial agents. Culture and susceptibility data enable pathogen-directed therapy and show trends in antimicrobial resistance.[1]

Nocardiosis is an uncommon pulmonary infection and is only kept as differential in cases of nonresolving pneumonia in patients with compromised cell-mediated innate immunity. The majority of cases of pulmonary nocardiosis are caused by *Nocardia asteroides* and the drug of choice is cotrimoxazole.[2,3] We recently had the opportunity of observing a patient with acute fatal pulmonary nocardiosis caused by a multi-drug resistant *N brasiliensis*.

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Case Description

A 65-year-old gentleman was admitted with high-grade fever, productive cough, and rapidly progressive dyspnea for 7 days in a medical intensive care unit.

Six years ago the patient was diagnosed with chronic obstructive pulmonary disease (COPD) and pulmonary tuberculosis (PTB) and had received antituberculosis treatment for 6 months. Currently, he was on inhaled corticosteroids and bronchodilators for COPD. He had no history of diabetes mellitus (DM) and use of systemic steroids or chronic alcohol consumption. He was an ex-smoker and was a farmer by occupation.

On admission, the patient had tachypnea with respiratory rate 30 breaths per min and oxygen saturation of 88% while breathing in ambient air. Lung auscultation revealed bilateral diffuse crackles and rhonchi. A provisional diagnosis of acute exacerbation of COPD with community-acquired pneumonia or suspected PTB

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relapse was made and the patient was started on intravenous antibiotics (ceftriaxone, amikacin, and ofloxacin), high flow oxygen, nebulization with bronchodilators, and intravenous hydrocortisone.

Laboratory investigations showed leukocytosis (11.4 × 10^9/l), high erythrocyte sedimentation rate (80 mm/h), and normal liver and renal function tests. A chest X-ray (CXR) showed diffuse bilateral airspace opacities with right upper lobe fibrosis. Blood glucose levels were normal and an HIV serology was nonreactive.

Sputum examination showed gram-positive beaded, branching, thin filamentous bacteria resembling *Nocardia spp*. The bacterium was acid-fast on modified (1%) Ziehl-Neelsen (ZN) stain [Figure 1]. Sputum specimen was cultured on nutrient agar and blood agar and after 72 h of incubation white dry colonies with rough surface were seen [Figure 2 a and b]. Gram and ZN staining of these colonies revealed bacteria resembling *Nocardia spp*. The bacterium was identified as *N brasiliensis* by standard biochemical tests. Antibiotic susceptibility testing by disc diffusion method showed that the isolate was susceptible to amikacin, ceftriaxone, doxycycline, chlorpheniramine, and imipenem but resistant to cotrimoxazole and aztreonam [Figure 3].

Initially, cotrimoxazole was started after sputum microscopy examination but later it was changed to imipenem after antimicrobial susceptibility results. Despite this, the patient developed rapidly progressive respiratory failure and septic shock and could not be revived.

Discussion

Pulmonary nocardiosis is typically regarded as an uncommon opportunistic infection which causes high mortality. Dysfunction of cell-mediated immunity is a major predisposing factor and patients with uncontrolled DM, HIV, malignancy, organ or stem cell transplant, alcoholism, and long-term use of immunosuppressive agents (e.g. steroids) are particularly at risk.[2,4,5]

Pulmonary nocardiosis usually has a subacute (weeks to months) or chronic (months to years) presentation and may mimic tuberculosis or lung cancer. Acute pulmonary infection (days) is usually fulminant and is commoner in immuno-suppressed individuals. Clinical features are nonspecific and a constellation of fever, cough, dyspnea, chest pain, anorexia, or weight loss. As pulmonary nocardiosis is a great mimicker, it may have a plethora of radiological findings; common being consolidation, nodules, or lung mass; solitary or multiple; and with or without breakdown or cavitation. For diagnosis, a strong clinical suspicion is needed, and it requires isolation and identification of *Nocardia* from a clinical specimen that is, sputum, broncho-alveolar lavage (BAL), fine needle aspiration, or biopsy.[2,4,5]

N asteroides accounts for up to 90% of the reported cases. *N brasiliensis* is usually limited to cutaneous and lymphocutaneous disease but can rarely spread to produce pulmonary or disseminated disease in immunosuppressed hosts.[2,4,5]

A PubMed/MEDLINE search of literature tracked a total of eight adult Indian patients with a diagnosis of pulmonary nocardiosis by *N brasiliensis* [Table 1].[6-12] Age and sex distribution (mean age 51.66 years; median age 45 years; male preponderance); underlying conditions (common being chronic lung disease and chronic

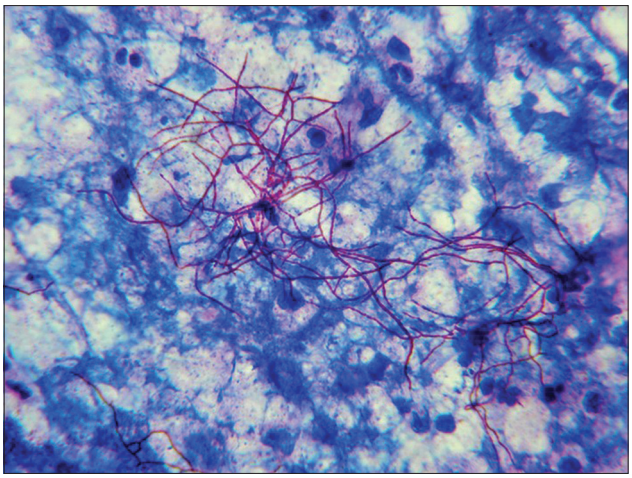

Figure 1: Branching, thin filamentous acid-fast bacteria on modified (1%) ZN stain

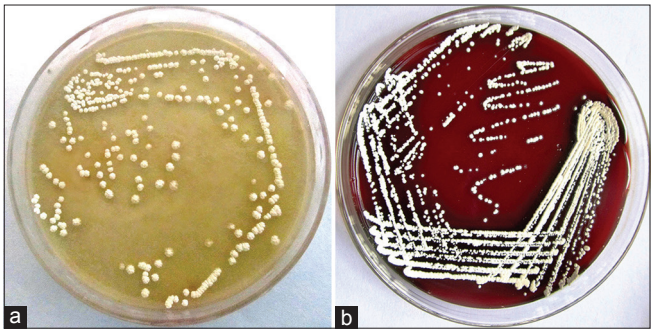

Figure 2: White dry colonies with a rough surface on nutrient agar (a) and blood agar (b)

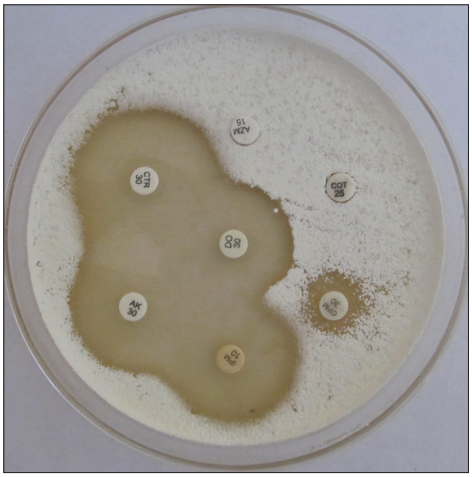

Figure 3: Antibiotic susceptibility testing

Table 1: Review of cases of pulmonary nocardiosis by *N brasiliensis* reported from India

Author/Year	Age (years)/Sex	Predisposing or underlying condition	Clinical presentation	Radiological features	Specimen	Anti-biotic therapy	Outcome	Drug Susceptibility Testing
Wadhwa V *et al.*[4] 2006	42/M	COPD, chronic steroid therapy	Cough, dyspnea, fever for 5 days	CXR: B/L infiltrates and patchy consolidation	Sputum	CTR, AMK, CTZ	Died	S- AMG, CMP. R- COT, ERY, CTR, AMP, CFX.
Shivaprakash MR *et al.*[5] 2007	40/M	Post renal transplant, DM	Right eyelid swelling*, cough, sputum, hemiparesis	CXR: B/L infiltrates; MRI brain: multiple RELs	Pus, BAL, sputum	COT, AMX	Died	S- COT, AMK, CFT, IMP.
Shivaprakash MR *et al.*[5] 2007	45/M	Type 2 DM, steroid therapy	Cough, sputum, dyspnea	CT: consolidation with areas of breakdown and air fluid level	BAL	COT, CFP	Improved	S- COT, AMK, CFT, IMP.
Chawla K *et al.*[6] 2009	52/M	BA, steroid therapy	Dyspnea for 10 days	Pleural effusion	Pleural fluid	COT	Improved	S- COT.
Amatya R *et al.*[7] 2011	26/F	Pregnancy	Cough, dyspnea, right hand swelling and right axillary sinus* for 1 year	CXR: Opacities in left hemithorax and right upper lobe	Sputum, pus and tissue from swelling	COT	Improved	NA
Rawat *et al.*[8] 2011	65/M	COPD	Cough, sputum, fever for 2 months	CXR: right apex consolidation and right lower lobe cavity	Sputum	AMK, CFT	Improved	S- COT, AMG, CMP, TC. R- AMX, AMP, PIP, ERY, CFX.
Khare V *et al.*[9] 2013	85/F	COPD, chronic steroid therapy	Fever, cough, dyspnea for 10 days	CXR: patchy infiltrates in right lung and left hemithorax consolidation	Sputum, endotracheal aspirate	CTR, LFX, COT	Died	S- IMP, AMG. R- COT, ERY, CFX.
Bagali S *et al.*[10] 2016	45/M	Rheumatic heart disease	Cough, sputum, hemoptysis, dyspnea for 1 month	CXR: right pleural effusion and cardiomegaly	Pleural fluid	PIP	Died	NA
Index case	65/M	COPD, previously treated PTB	Fever, cough, dyspnea for 7 days	CXR: B/L air space opacities with right upper lobe fibrosis	Sputum	CTR, AMK, OFX, COT	Died	S- AMK, CTR, TC, CMP, IMP. R- COT, AZT.

*Primary cutaneous nocardiosis Abbreviation: B/L=bilateral, CTR=ceftriaxon, AMK=amikacin, CTZ=ceftazidime, AMG=aminoglycosides, CMP=chlorampenicol, COT=cotrimoxazole, ERY=erythromycin, CTR=ceftriaxone, AMP=ampicillin, CFX=ciprofloxacin, AMX=amoxicillin, CFT=cefotaxim, IMP=imipenem, CT=computed tomography, CFP=cefepime, TC=tetracycline, PIP=piperacillin, LFX=levofloxacin, OFL=oflaxacin, AZT=aztreonam, NA=data not available

steroid use); clinico-radiological features; and mortality (more with acute presentation and cotrimoxazole resistant cases) are similar to overall pulmonary nocardiosis cases. The involvement of the lung is usually thought to occur after transcutaneous inoculation by *N brasiliensis*; however, in the reviewed cases, only two out of nine had primary cutaneous nocardiosis.

In conclusion, inhalation may be the primary route of infection by *N brasiliensis*. Primary care physicians should have awareness of pulmonary nocardiosis as correct and efficient diagnosis is quite challenging. Moreover, cotrimoxazole resistant cases have poor outcomes.

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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Conflict of interest

There is no conflict of interest.

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