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Case Report

Microbiology Section

Thinking beyond Tuberculosis: Pulmonary Nocardiosis by *Nocardia farcinica* in a Patient with Autoimmune Hepatitis

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ABSTRACT

Nocardiosis is a rare but serious infection caused by *Nocardia* species (class Actinobacteria, order Corynebacteriales). *Nocardia* is commonly found in soil, dust and plant material, and the infection primarily affects immunocompromised individuals, most often presenting as Pulmonary Nocardiosis (PN) via inhalation. It requires a prolonged course of antimicrobials and is a significant cause of mortality in such patients. PN is often misdiagnosed as Tuberculosis (TB) due to overlapping features, delaying diagnosis and treatment. This case describes a 44-year-old male, a known case of autoimmune hepatitis on corticosteroid therapy, who presented with clinical and radiological features suggestive of pulmonary TB. Modified Kinyoun staining of pleural fluid showed acid-fast, branched, filamentous bacilli and culture grew yellow, chalky colonies identified as *Nocardia farcinica*. The organism was also isolated on automated and conventional mycobacterial culture media. The patient was successfully treated with cotrimoxazole (double strength). This emphasises the need to include Modified Ziehl-Neelsen (ZN) stain as a rapid screening test to rule out PN and avoid treatment with Antitubercular Therapy (ATT).

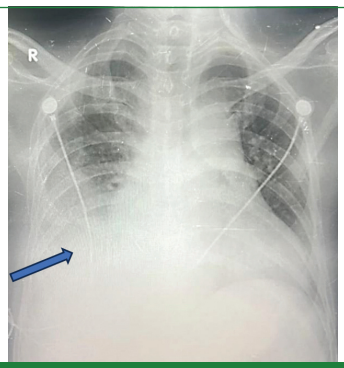
Keywords: Corticosteroids, Immunocompromised, Infection, Modified Ziehl-Neelsen stain, Pleural effusion

CASE REPORT

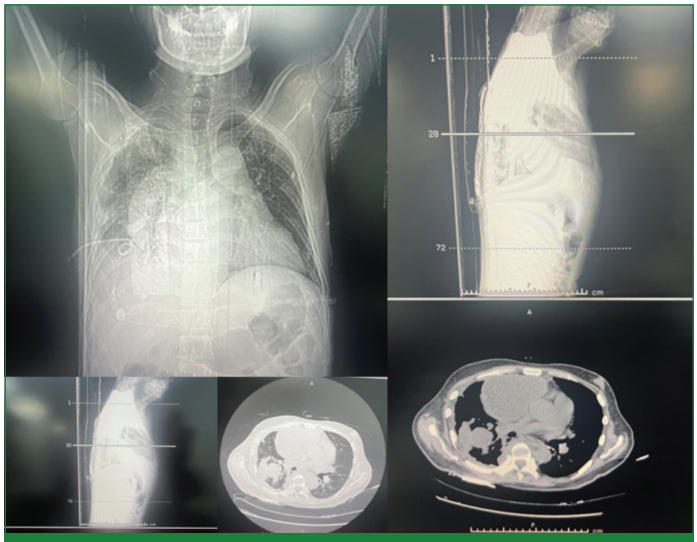
A 44-year-old male presented to the emergency department with shortness of breath for two days, right-sided chest pain for 15 days and a productive cough for one month. He had a history of fever, rash and jaundice diagnosed as autoimmune hepatitis three months earlier and was treated with prednisone and methotrexate. On physical examination, blood pressure was 100/70 mmHg, pulse 82/min and respiratory rate 20/min. Systemic examination showed decreased air entry in the right axillary area, while all other organ systems were unremarkable. Laboratory investigations are summarised in [Table/Fig-1]. Chest X-ray showed right-sided pleural effusion [Table/Fig-2a], and HRCT of the thorax suggested features of pulmonary TB [Table/Fig-2b]. Pleural fluid analysis revealed WBC 49,892 cells/µL (10.4% neutrophils, 89.6% lymphocytes), ADA 71 U/L, and was negative for acid-fast bacilli, malignant cells and Xpert MTB/RIF Ultra. In view of the clinical and radiological diagnosis of TB, he was started on ATT, intravenous fluids, antibiotics, and nutritional support. The symptoms did not resolve after one week of initial therapy. Repeat cultures were sent to the laboratory. Pleural fluid was subjected to modified Kinyoun stain (1000×) and showed acid-fast filamentous bacilli [Table/Fig-3].

S. no.	Lab parameter/Normal value	Value/Result
1.	Haemoglobin (g/dL)/ (14-18.0)	10.3
2.	Total Leukocyte Count (TLC) (/µL)/(4.5 to 11.0×10^3)	31.6×10³
3.	Platelet (/µL)/(150 to 450 x 10^3)	440×10³
4.	PT (sec)/ (10-13.5)/INR	16/1.34
5.	Blood Urea (mg/dL)/ (6-24)/ Serum Creatinine (mg/dL)/(0.6-1.35)	16.6/0.22
6.	Serum Sodium (136-145)/Potassium (3.50-5.10)/Chloride (mmol/L)/ (96-106)	132.3/4/94.9
7.	Bilirubin total (mg/dL)/(0.1-1.2)	11.41
8.	Bilirubin direct (mg/dL)/ (0.0-0.3)	5.9
9.	Bilirubin indirect (mg/dL)/(0.2-0.8)	5.51
10.	Aspartate Amino Transferase (AST) (IU/L)/ (8-48)	86
11.	Alanine amino transferase (ALT) (IU/L)/ (8-48)	86
12.	Albumin (g/dL)/(3.4-5.4)/Globulin (g/dL)/ (2.0-3.5)	2.22/ 3.34
13.	GGT (IU/L)/(5-40)	50
14.	Aerobic blood culture	No bacterial growth after 48 hours of incubation
15.	Aerobic urine culture	No bacterial growth after 48 hours of incubation
16.	Pleural fluid cytology	WBC=49,892 (Neutrophil 10.4, Lymphocyte is 89.6), Negative for malignant cells
17.	Pleural fluid Xpert MTB/RIF Ultra assay	Not detected
18.	Pleural fluid ADA (U/L)/(<40)	71
	Pleural fluid ZN stain	Negative
19.	Pleural fluid gram stain	Branched, beaded, filamentous Gram-positive bacilli
	Pleural fluid Modified-ZN stain	Acid fast filamentous bacilli
20.	Aerobic pleural fluid culture	Rough, dry whitish, tiny colonies which on further incubation yielded yellow, dry, raised, chalky colonies
21.	Chest X-ray	S/O Pleural effusion right-sided
22.	HRCT	Right parenchymal soft-tissue nodule with upper lobe cavity, encysted pleural effusion with bulging of fissures and pleural cavity

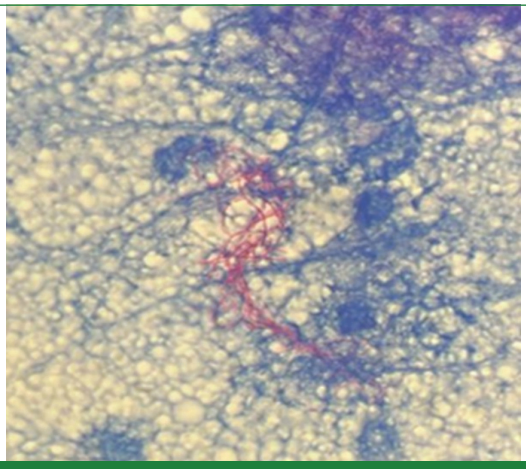
[Table/Fig-1]: Laboratory parameters and tests of the index patient.



[Table/Fig-2a]: Chest X-ray: Suggestive of right-sided pleural effusion (arrow).

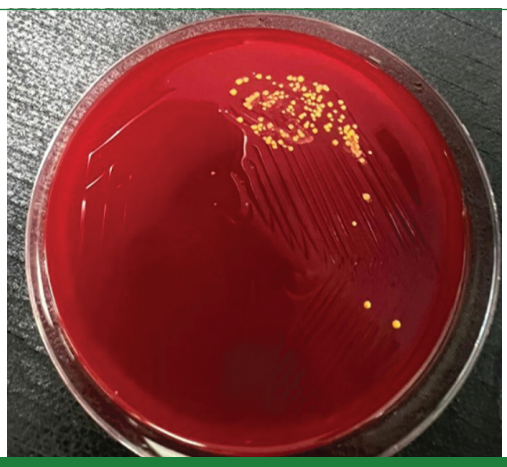


[Table/Fig-2b]: HRCT of chest showing pleural effusion with bulging of fissures.

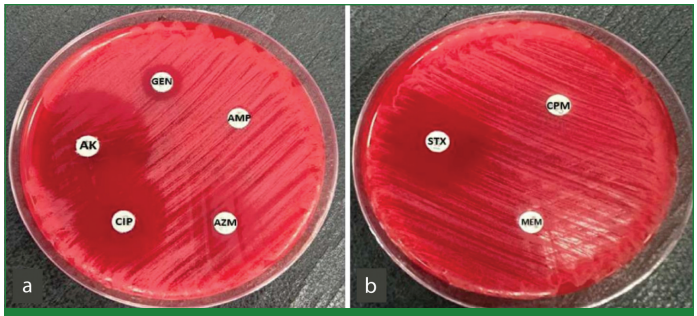


[Table/Fig-3]: Modified Kinyuon stain under 1000x: of colony isolate showing acid-fast bacilli.

Aerobic culture of the pleural fluid sample grew yellow, chalky-textured colonies on blood agar [Table/Fig-4]. Matrix-Assisted Laser Desorption/Ionisation–Time of Flight (MALDI-TOF) identified the isolate as *Nocardia farcinica*. Antimicrobial susceptibility testing by disc diffusion showed susceptibility to amikacin, ciprofloxacin and cotrimoxazole [Table/Fig-5a,b], and was performed using the Kirby–Bauer disk diffusion method on Blood agar plates. Inocula were prepared according to Clinical and Laboratory Standards Institute (CLSI) standard M24-A2 [1,2]. Results were read after 72 hours of culture, using zone-diameters as defined by Lebeaux D et al., [3]. Samples sent for mycobacterial culture on an automated system (MGIT 960; Becton, Dickinson and Company, BD USA) also grew acid-fast bacilli after three days. He was diagnosed with pleuro-pulmonary nocardiosis (PN). ATT was discontinued and he was



[Table/Fig-4]: Blood agar plate showing growth of *Nocardia* isolate.



[Table/Fig-5]: a) Blood agar: showing Antibiotic susceptibility pattern of *Nocardia farcinica*; (AK: Amikacin; GEN:Gentamicin, AMP: Ampicillin; AZM: Azithromycin; CIP: Ciprofloxacin). b) Blood agar: showing Antibiotic susceptibility pattern of *Nocardia farcinica*; (STX: cotrimoxazole, CPM: cefepime, MEM: meropenem).

treated with ciprofloxacin (500 mg oral twice daily), amikacin (500 mg IV once daily), and cotrimoxazole (sulfamethoxazole 800 mg with trimethoprim 160 mg, oral twice daily), and he was discharged. During follow-up one month later, he was clinically improved.

DISCUSSION

Nocardiosis is an uncommon but significant infection caused by various species of the *Nocardia* genus. These bacteria are aerobic, gram-positive, partially acid-fast organisms that are resistant to lysozyme and catalase-positive, with a distinctive beaded, branched appearance [4]. Common species include *Nocardia asteroides*, *N. farcinica, N. nova* and *N. abscessus. Nocardia* species are ubiquitous in the environment, inhabiting soil, dust and both fresh and marine water, where they act as saprophytes decomposing organic matter [4,5]. The most common mode of transmission is inhalation of aerosols containing spores and mycelia, leading to PN. About 60% of *Nocardia* infections occur in immunosuppressed patients. Risk factors include long-term use of oral and inhaled corticosteroids and underlying lung conditions such as Chronic Obstructive Pulmonary Disease (COPD), bronchiectasis and cystic fibrosis [6,7]. Prolonged corticosteroid use is associated with higher mortality (85%) compared with immunocompetent patients (15%) and those not on corticosteroids (20%) [8]. Additional risk factors include Human Immunodeficiency Virus (HIV) infection and monoclonal antibody therapy (e.g., alemtuzumab) in patients with haematologic cancers. The overall prevalence of nocardiosis is unknown due to limited published data. An estimated 500-1,000 cases occur in the USA [9]. *Nocardia farcinica* is reported to account for about 5%-6.7% of nocardial infections in Switzerland and Greece, respectively [10,11]. The proportion of *N. farcinica* among all *Nocardia* infections varies from 19-24.5%, with a high incidence of disseminated disease [5,12].

Clinical presentations include acute, subacute, or chronic infection, often with pneumonia, lung abscess, or cavitary disease leading to effusion and empyema. Common symptoms, such as cough, dyspnea, fever, and weight loss, are non specific and may persist for weeks, complicating diagnosis. In immunocompromised patients, the infection can disseminate to multiple organs, including the central nervous system, increasing morbidity and mortality [13].

Diagnosing PN is challenging due to non specific clinical and radiographic presentations. The gold standard for diagnosis is culture of *Nocardia*; however, it is a slow-growing bacterium. In cases where sputum cultures are inconclusive, invasive diagnostic procedures such as bronchoscopy, needle aspiration, or open-lung biopsy may be necessary to obtain definitive samples (bronchial washings and bronchoalveolar lavage) [14]. *Nocardia* can grow on blood agar and tuberculous culture media after about 3-5 days of incubation. *Nocardia* colonies often present as buff-coloured or pigmented, with a waxy, dry texture or chalky appearance similar to the present case. *Nocardia farcinica* may initially appear raised and moist when young but develop characteristic aerial hyphae as they mature [4].

Reference	Symptoms	Underlying condition	Radiology finding	Diagnostic method	Treatment	Outcome
Present case, 2025	Autoimmune hepatitis on corticosteroids	Fever, cough, dyspnoea	Pleural effusion, infiltrates	MZN stain, culture, MALDI-TOF	Cotrimoxazole, ciprofloxacin, amikacin	Improved
Sudhaharan S et al., 2017, [20]	Fever, SOB, cough, CNS and cutaneous lesions (in disseminated case)	Renal transplant, HIV, immunosuppressed	Cavitating nodules, empyema, pleural effusion	BAL, blood/pus culture, MALDI-TOF	Meropenem, amikacin, colistin, TMP-SMX	Two improved, two died
Gupta N et al., 2020, [21]	Fever, cough with sputum, dyspnoea	Elderly, newly diagnosed diabetic	Diffuse heterogeneous opacities in right upper and bilateral middle/lower zones	Gram stain, Kinyoun stain, culture, MALDI-TOF	Imipenem, linezolid, minocycline	Improved with resolution on X-ray
Aggarwal D et al., 2015, [22]	Breathlessness, cough, chest pain, fever	COPD, prolonged steroid use	Mass lesions, necrotising consolidation, cavitary nodules, hydropneumothorax	BAL, Modified Ziehl-Neelsen (ZN) stain	Cotrimoxazole, amikacin, linezolid, doxycycline	Two recovered, one fatal outcome
Shebeena S et al., 2024, [23]	Cough, expectoration, weight loss	Recurrent respiratory illness, post-TB	Cystic areas, bronchiectasis, patchy consolidation	Sputum and BAL, Modified Ziehl-Neelsen (ZN), molecular ID (16S rRNA)	Cotrimoxazole, ceftriaxone	Recovered with 6 months TMP-SMX
Chan DECY et al., 2020, [24]	Dyspnoea, cough, chest pain, fatigue	Alpha-1 antitrypsin deficiency, long-term steroids	Necrotising pneumonia in right lower lobe	Sputum Gram, Kinyoun stain, MALDI-TOF, PCR	Ceftriaxone, TMP-SMX, amikacin, then imipenem	Improved, discharged on maintenance TMP-SMX

[Table/Fig-6]: Comparative analysis of index case with published literature.
MZN: Modified Ziehl-Neelsen;MALDI-TOF: Matrix-assisted laser desorption/ionisation-time of flight; SOB: Shortness of breath; CNS: Central nervous system; HIV: Human immunodeficiency virus; BAL: Broncho alveolar lavage; TMP-SMX: Trimethoprim/sulfamethoxazole; PCR: Polymerase chain reaction

Nocardia in this current case was also isolated from an automated TB culture system (MGIT-960). In a retrospective study by Hu Y et al., the sensitivities of blood agar culture and MGIT-960 for detection of *Nocardia* were 46.1% and 81.3%, respectively. MALDI-TOF has been thoroughly validated in the literature for its accurate identification of *Nocardia* species [15]. Its ability to provide rapid and precise results makes it a preferred diagnostic tool, especially given the limited use of biochemical tests.

Stains are non specific for *Nocardia*; however, special stains, such as modified Ziehl-Neelsen (mZN) or fluorescent auramine-rhodamine, can aid in the visualisation of *Nocardia* in clinical specimens. It appears as gram-positive beaded filamentous morphology on Gram stain. The mZN stain weakly stains it as acid-fast with a branched filamentous appearance, differentiating it from Actinomyces. Molecular techniques like Polymerase Chain Reaction (PCR) offer rapid identification but are not widely available in all laboratories [14]. Radiographic findings of PN are diverse and non specific, often resembling other pulmonary conditions such as TB, bacterial pneumonia, or malignancies. Typical features include consolidations, nodules, cavitary lesions and pleural effusions, predominantly affecting the upper lobes of the lungs [16].

The standard treatment for PN involves the use of sulfonamides, particularly trimethoprim-sulfamethoxazole (TMP-SMX). Initial treatment typically involves intravenous administration, followed by oral therapy upon clinical improvement. The duration of therapy varies, generally lasting 6-12 months, depending on the severity of the disease and the patient's immune status. Resistance patterns among *Nocardia* species necessitate identification of the specific strain and its antimicrobial susceptibility. *Nocardia farcinica* may exhibit resistance; hence, alternative antibiotics such as amikacin, imipenem, linezolid and minocycline may be used [17,18]. In severe or disseminated cases, combination therapy is recommended with TMP-SMX and amikacin or imipenem. Surgical intervention may be necessary for abscess drainage or resection of necrotic tissue in certain cases [19].

A comparative analysis of this reported case with recently published literature on PN in immunocompromised individuals has been summarised in [Table/Fig-6] [20-24]. Common clinical features include fever, cough and radiological findings often mimicking TB. Diagnostic approaches ranged from bronchial washings to histopathology; the presented case uniquely combined mZN staining and culture with MALDI-TOF for rapid species identification. Treatment regimens were largely sulfonamide-based, though alternative antibiotics such as linezolid or imipenem were used depending on susceptibility. This case, along with the comparative overview, underscores the importance of considering PN in the differential diagnosis of chronic pulmonary infections, especially in TB-endemic regions and highlights the value of early suspicion, species-level diagnosis and tailored therapy in improving outcomes.

CONCLUSION(S)

This case highlights the diagnostic challenge of PN in immunocompromised individuals, particularly when radiological features mimic TB. Misdiagnosis can lead to inappropriate initiation of ATT and delays in appropriate management. Early identification through modified ZN staining and confirmation by culture and MALDI-TOF is critical. The successful outcome following targeted therapy emphasises the need for high clinical suspicion in atypical presentations. Routine consideration of *Nocardia* in differential diagnosis can significantly improve prognosis, especially in patients receiving long-term corticosteroids.

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