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Case report

Cavitary lesion from pulmonary nocardiosis in non-immunocompromised patients with chronic lung disease: A report of three cases

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ABSTRACT

Pulmonary nocardiosis commonly presents with respiratory symptoms resembling those observed in community-acquired pneumonia caused by other agents. *Nocardia* was previously considered to primarily affect immunocompromised populations, particularly transplant patients. However, recent studies have indicated a rise in the incidence of pulmonary nocardiosis among non-immunocompromised patients. In this report, we present the cases of three non-immunocompromised patients with pulmonary nocardiosis with a subacute clinical presentation who showed cavitation on chest computed tomography. Our reports emphasize the potential diagnostic clues documented in the literature that may help pulmonary nocardiosis diagnostic investigations. The development of a high index of suspicion for pulmonary nocardiosis remains crucial.

Key words: pulmonary nocardiosis, non-immunocompromised, community-acquired pneumonia, cavitary lesion

INTRODUCTION

Nocardiosis is a rare but potentially fatal infection that can be difficult to treat. Although a disseminated *Nocardia* infection can impact various organs, the respiratory system is the most prevalent site of infection since the respiratory tract is the bacteria's main transmission pathway [1]. Nocardiosis is a relatively rare cause of community-acquired pneumonia (CAP), and, notably, over a third of patients with this disease are not immunocompromised [1,2]. Chronic lung disease is an increasingly recognized risk factor for *Nocardia* infection [2–5]. This report describes three clinical cases of adult non-immunocompromised chronic lung disease patients with pulmonary nocardiosis presenting as CAP with subacute symptoms. These patients were observed at Cho Ray Hospital in southern Viet Nam.

CASE PRESENTATION

Case 1

A 60-year-old male patient with type 2 diabetes and well-controlled chronic obstructive pulmonary disease (COPD) on two puffs of budesonide/formoterol (160/4.5 mcg) twice daily was admitted to the hospital due to shortness of breath, pleuritic left chest pain, and green sputum cough that started two weeks prior to hospitalization. At the time of admission to Cho Ray Hospital, the patient's vital signs were normal, and respiratory failure was absent. A clinical examination found no localized skin lesions or neurological signs; however, the lungs demonstrated sporadic crackles on auscultation. The patient was negative for human immunodeficiency virus (HIV) antibodies. The laboratory analysis revealed a C-reactive protein (CRP) level of 61 mg/l, a white blood cell (WBC) count of 17.71 G/L, and a neutrophil percentage of 95%. Blood cultures were not initially performed, and sputum cultures did not reveal any pathogens. The chest computed tomography (CT) showed bilateral patchy ground-glass opacities in the lungs and a cavitary nodule 2.5 cm in size with an even border in the left upper lobe adjacent to the chest wall, which was suspected to be malignant (as shown in **Figure 1**). Consequently, the patient underwent bronchoscopy, during which yellow, viscous sputum was observed exuding from the left lobe (as shown in Figure 2A). Bronchoalveolar lavage fluid (BALF) acid-fast bacillus (AFB), fungal culture, and Xpert MTB/RIF test results were all negative, as were the tuberculosis polymerase chain reaction (PCR) assay results. After three days, *Nocardia beijingensis* was discovered in the BALF using the Matrix Assisted Laser Desorption Ionization–Time of Flight (MALDI–TOF) technique; however, the antibiotic susceptibility pattern could

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not be determined. The transbronchial lung biopsy specimen analysis revealed no malignant cells. The therapy was altered from intravenous cefoperazone and ciprofloxacin (which yielded no improvement) to trimethoprim–sulfamethoxazole (TMP–SMX) after the pathogen was identified as *Nocardia beijingensis*; a six-month oral course was prescribed after ruling out pathogen-associated brain abscesses via CT. The patient showed no evidence of recurrence after one year of follow-up.

Case 2

A 62-year-old male patient with a 30 pack-year smoking history presented with a 15-day history of purulent cough, left chest pain, fever, and dyspnea. Initial treatment at a lower-level hospital included a combination of intravenous meropenem, moxifloxacin, and oral fluconazole. Unfortunately, the patient developed severe respiratory failure after three days of treatment, forcing transfer to Cho Ray Hospital. The patient's vital signs on arrival were as follows: blood pressure of 130/80 mmHg, pulse rate of 80 beats per minute, and oxygen administration through a cannula at a rate of 6 liters per minute to maintain SpO_2 of 94%. The patient had no skin lesions or specific neurological impairments on clinical examination; however, tachypnea, accessory respiratory muscle usage, pyrexia, and bilateral lung crackles were recorded. The initial laboratory analysis showed a WBC count of 7.75 G/L, a neutrophil percentage of 82.7%, negative HIV antibody test results, a CRP level of 157 mg/L, and negative sputum and blood bacterial cultures. The patient's fever and respiratory failure persisted after six days of therapy with intravenous imipenem, linezolid, and oral fluconazole. Chest CT revealed two cavitary lesions. The first lesion, measuring 4.6 cm in diameter, was located in the S1 and S2 segments of the left lung. The second lesion, with maximum dimensions of 9 cm and 6 cm in diameter, was in the lower left lobe. The second lesion contained dense fluid that showed signs of necrosis or an abscess. The CT also demonstrated bronchiectasis, emphysema, and calcification, primarily in the upper lobes of the lungs (as shown in **Figure 2**). During the bronchoscopy, a significant volume of purulent sputum from the left segment S6 was discovered (as shown in **Figure 3B**). In the microbiological analysis of the BALF, the AFB, fungal culture, Xpert MTB/RIF, and tuberculosis PCR test results were all negative. *Nocardia otitidiscaviarum* was discovered on further investigation of the BALF by MALDI-TOF MS. Hence, the patient's antibiotic regimen was modified to include oral TMP–SMX in addition to intravenous meropenem and amikacin despite an unavailable antibiotic susceptibility pattern. No lesions were observed on brain CT, and the patient received ongoing therapy for an additional 14 days, resulting in improvements in fever and respiratory failure. A subsequent six-month oral course of TMP–SMX was prescribed, during which the patient remained asymptomatic and did not experience infection recurrence.

Case 3

A 65-year-old male patient with a medical history of untreated COPD was hospitalized at Cho Ray Hospital after experiencing a persistent fever and productive cough for ten days before admission. The patient's blood pressure was 140/80 mmHg, his heart rate was 106 beats per minute, and his oxygen saturation was 96% when breathing room air. No skin lesions or localized neurological deficits were observed during the clinical examination; however, both lung fields had crackles. Upon examination, the patient's test results showed elevated levels of CRP at 110 mg/L, a WBC count of 9.15 G/L, and a neutrophil percentage of 94.7%. HIV antibody testing yielded negative results. Additionally, arterial blood gas analysis recorded a PaO_2 of 78 mmHg, $PaCO_2$ of 46.1 mmHg, and HCO_3 of 21.4 mmHg. A chest x-ray revealed diffuse alveolar damage affecting both lung fields, accompanied by multilobar cavitation (as shown in **Figure 4**). The chest CT demonstrated multiple lung consolidations containing dense fluid with cavitating features suggestive of necrosis or abscesses. The largest of these cavities, with maximum dimensions of 8 cm and 6 cm in diameter, was located in the right lower lobe. Additionally, bilateral patchy ground-glass opacifications were present in the lungs, and signs of emphysema were also observed (as shown in **Figure 5**). The patient's initial treatment regimen consisted of intravenous administration of cefoperazone/sulbactam, levofloxacin, and clindamycin. The blood cultures were negative for bacteria. After three days of treatment, sputum cultures were assessed by MALDI–TOF, revealing *Nocarida* sp. as the causative agent. Accordingly, the patient's antibiotic therapy was modified to include meropenem, amikacin, and TMP–SMX. The patient's condition deteriorated after five days despite treatment with antibiotics specifically targeting *Nocardia*, with increasing respiratory failure despite the lack of COPD symptom exacerbation. A bronchoscopy revealed purulent sputum in both lungs (as shown in **Figure 2C**). BALF specimens were assessed by AFB, fungal culture, Xpert

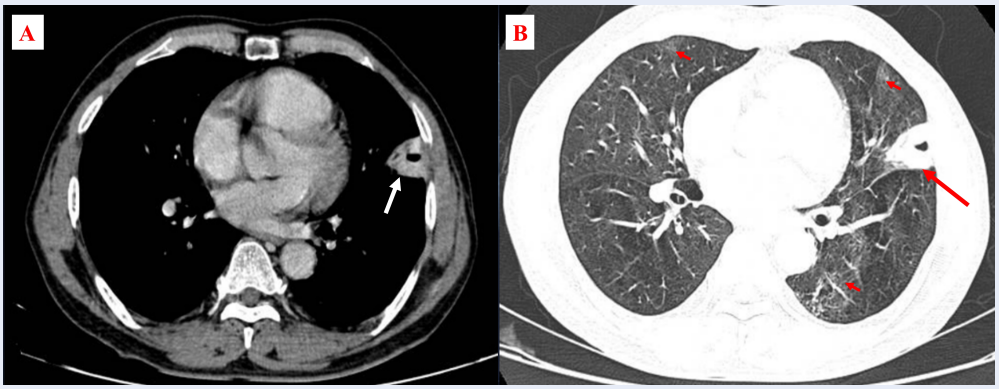

Figure 1: **Chest computed tomography in case 1**. **A** showed the presence of a cavitary nodule measuring 2.5 cm in size with an even border located in the left upper lobe, adjacent to the chest wall and suspicious of malignancy (white arrow). **B** showed the presence of patchy ground-glass opacities bilaterally in the lungs (red arrowhead) and a cavitary nodule (red arrow).

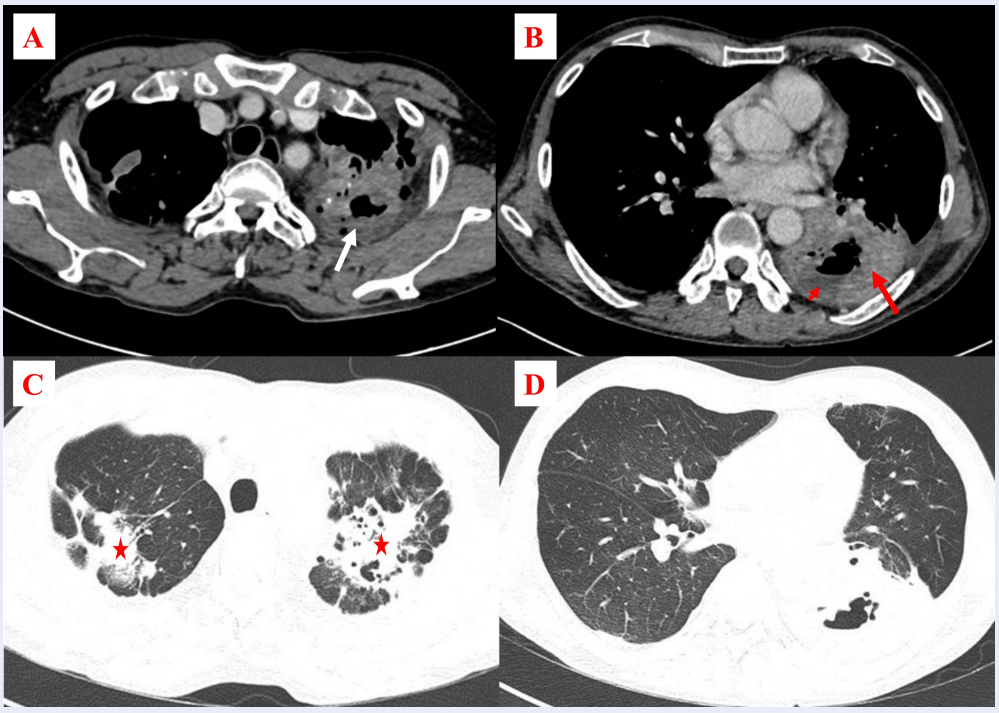

Figure 2: **Chest computed tomography in case 2**. **A** showed a cavitary lesion measuring 4.6 cm in diameter, was positioned within S1 and S2 of the left lung (white arrow). **B** showed the second lesion, with the maximum dimensions in terms of its two axes, is 9 cm and 6 cm in diameter, and was identified in the lower left lobe (red arrow). The second lesion had a dense fluid that showed signs of necrosis or an abscess (arrowhead). **C** demonstrated bronchiectasis, emphysema, and calcification, primarily localized in the upper lobes of the lungs (red star).

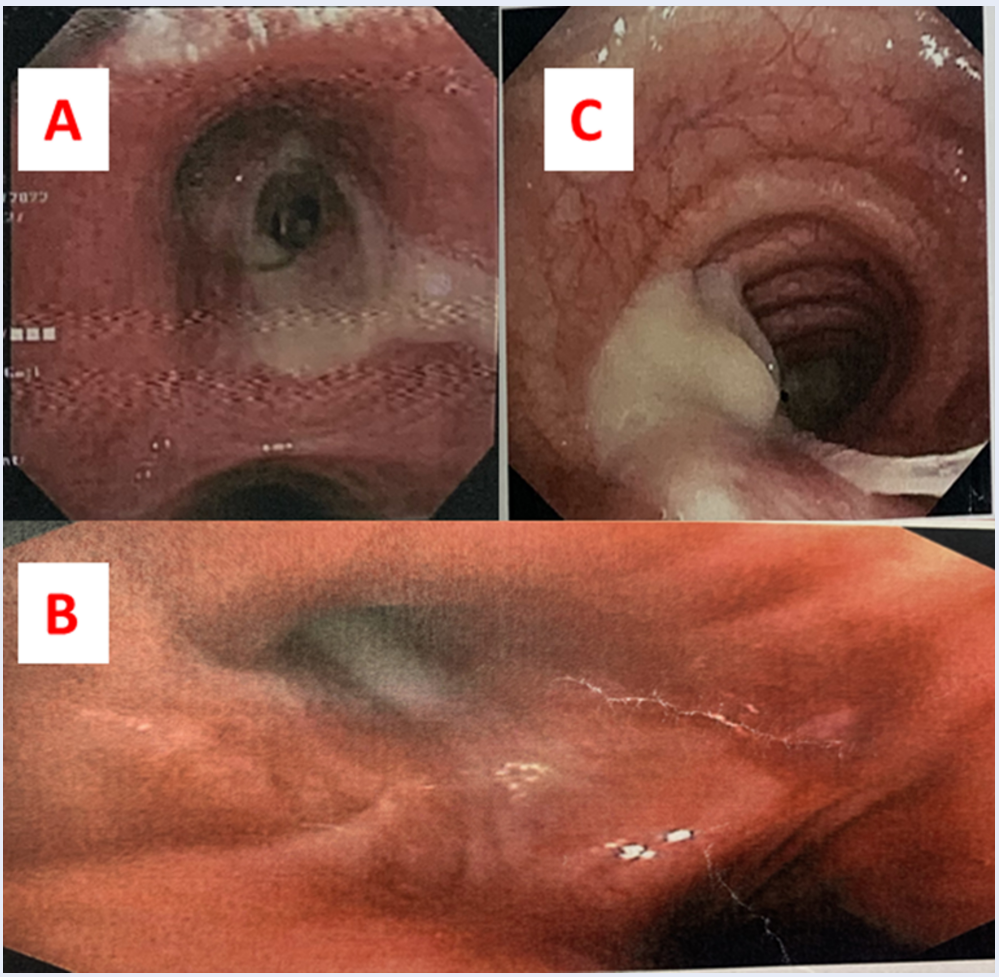

Figure 3: **Bronchoscopy appearance of there cases**. All cases showed yellow, viscous sputum on flexible bronchoscopy. **A**: Case 1. **B**: Case 2. **C**: Case 3.

MTB/RIF, and tuberculosis PCR assays, all yielding negative results. However, microbiological testing revealed multidrug-resistant *Acinetobacter baumannii*. Imipenem, TMP–SMX, and colistin were administered; however, the patient's condition quickly deteriorated, resulting in respiratory failure and death.

DISCUSSION

Prompt and accurate diagnosis of the causative agent is crucial for successfully managing nocardiosis. Pulmonary nocardiosis should be considered as a potential diagnosis in patients with chronic lung disease presenting with cavitary lesions on imaging and negative results for tuberculosis. When a patient with CAP does not respond sufficiently to initial broad-spectrum antibiotic therapy, clinicians should consider investigating for less common pathogens, such as *Nocardia*. While examining the patient's immunodeficiency status is essential, it is not mandatory for diagnosing nocardiosis. In the context of the three clinical cases we observed, identifying *Nocardia* was crucial in guiding treatment decisions, resulting in favorable outcomes for the first two patients. Co-infection with multidrug-resistant *Acinetobacter baumannii* may have contributed to disease progression and eventual mortality in the third patient.

Pulmonary nocardiosis can present with acute, subacute, or chronic symptoms, but subacute manifestations are more common. In a study of 51 transplant recipients, Hemmersbach revealed that pulmonary nocardiosis diagnosis is frequently delayed by one month from the onset of symptoms[6]. Similarly, Martínez reported a median time to diagnosis of 42 days in a report describing 31 patients with pulmonary nocardiosis[7]. Symptoms of *Nocardia* infection can be comparable to those observed with CAP

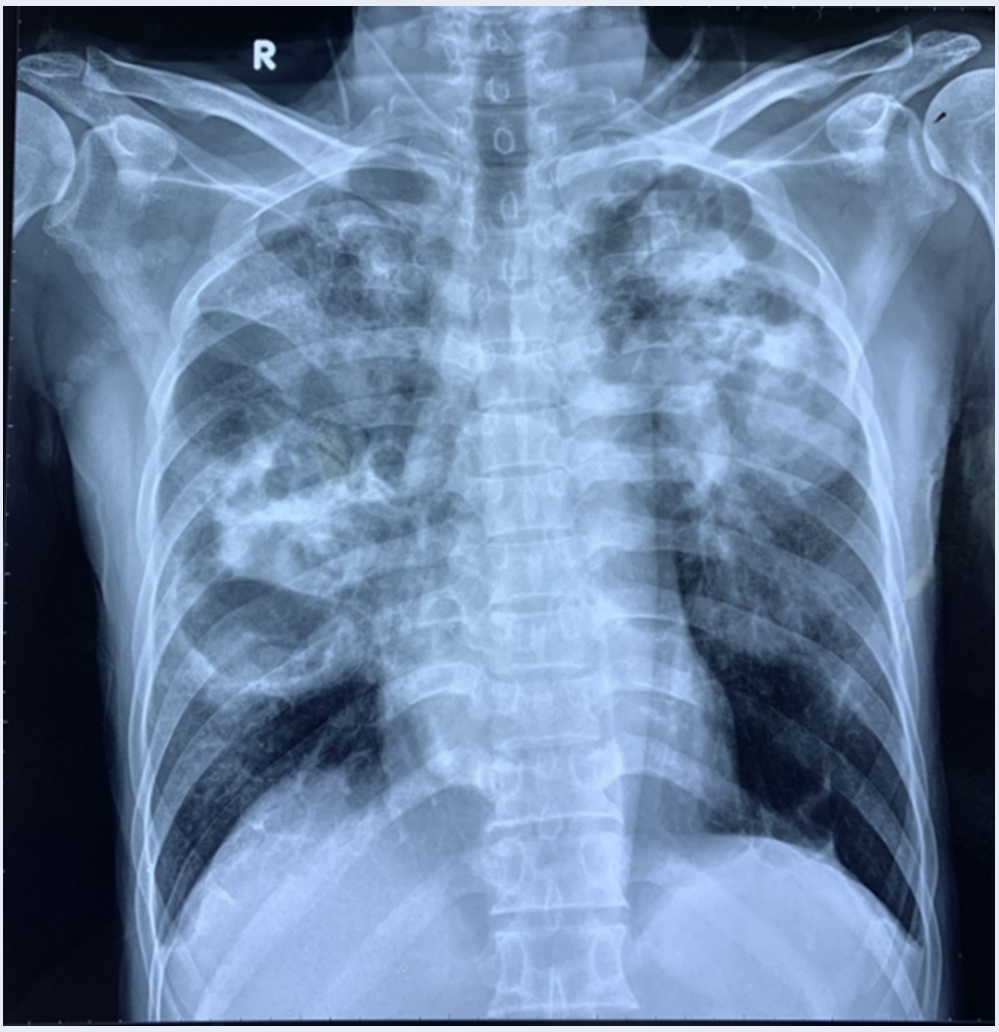

Figure 4: **Chest x-ray in case 3**. Chest x-ray revealed diffuse alveolar damage affecting both lung fields, accompanied by multilobar cavitation.

caused by other agents[8], such as shortness of breath, a dry or productive cough, hemoptysis, fever, weight loss, and weakness[8,9]. The three patients in our study had symptoms for 10 to 15 days prior to admission, which is in line with the typical subacute presentation of pulmonary nocardiosis.

Pulmonary nocardiosis is characterized by various chest CT imaging patterns, including single or multiple nodular lesions with regular borders, diffuse consolidation, interstitial infiltrates, pleural effusions, or cavitary lesions[9,10]. Kevin studied 53 patients with pulmonary nocardiosis and found that homogeneous consolidation was the most common lesion, observed in 64.2% of cases, followed by nodular lesions (56.6%) and nodular or mass lesions with cavitation (40%–60%)[11]. Baoliang reported 9 cases of pulmonary nocardiosis and found that consolidation and nodule/mass were the most typical findings[12]. All three patients reported here presented cavitation, and two-thirds exhibited diffuse consolidations. Hence, physicians should consider *Nocardia* as a potential causative organism when CAP imaging findings reveal cavitation and the patient's tuberculosis test results are negative. The differential diagnosis should include pulmonary tuberculosis, aspergillus infection, and lung cancer[8]. Providing relevant clinical information to the Microbiology Department is important for accurately identifying *Nocardia* bacteria. Reports indicate that the growth of *Nocardia* on culture media, such as blood agar, chocolate agar, buffered charcoal-yeast extract (BCYE) agar, and sabouraud agar, can take from 1 to 2 weeks[1,9].

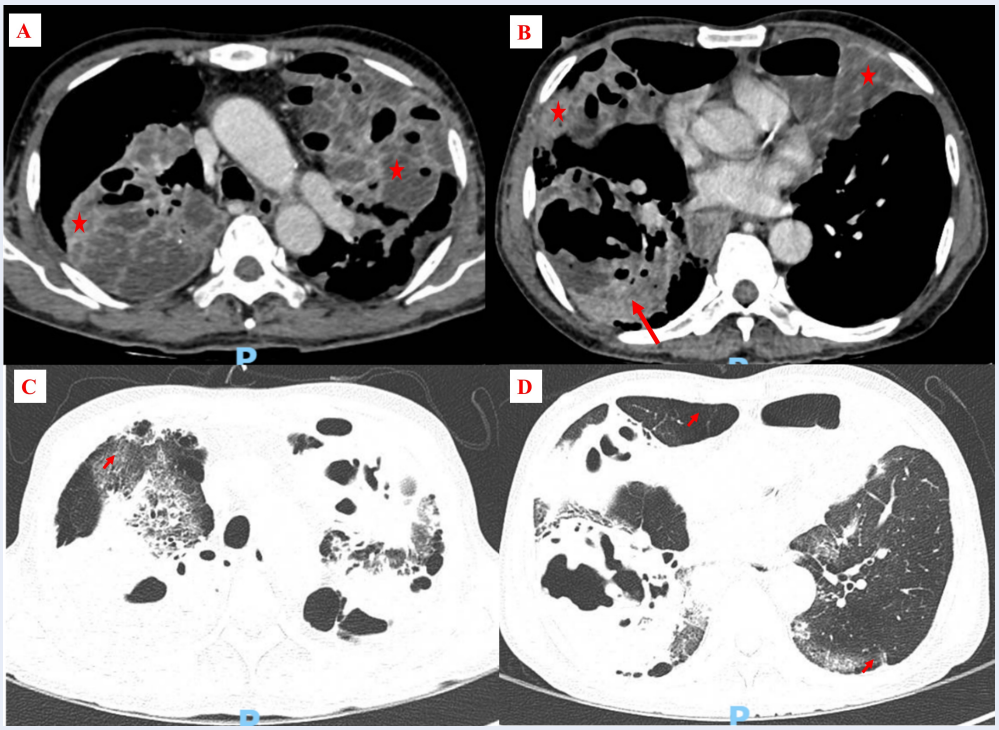

Figure 5: **Chest computed tomography in case 3**. The chest computed tomography demonstrated multiple lung consolidations, containing fluid density with cavitating features suggestive of necrosis or abscesses (red star) (**A** and **B**). The largest of these cavities, with maximum dimensions of 8 cm and 6 cm in diameter, was located in the right lower lobe (red arrow) (**B**). Patchy ground-glass opacifications were present bilaterally in the lungs, and signs of emphysema were also observed (**C** and **D**).

Additionally, the MALDI–TOF MS method should be used for bacterial identification in suspected cases of pulmonary nocardiosis due to its ability to accurately identify the majority of commonly encountered *Nocardia* species [1,9].

Non-immunocompromised patients account for approximately one-third of nocardiosis cases [1]. The definition of immunodeficiency differs among studies; however, our report utilized the definition of immunodeficiency in the Treatment of Community-Acquired Pneumonia in Immunocompromised Adults guidelines of the American College of Chest Physicians, issued in 2020 [13]. Although all three patients in our report were not immunocompromised, they shared the common feature of chronic lung disease, particularly COPD, with one case prescribed inhaled corticosteroids. Many studies have linked chronic lung conditions, such as cystic fibrosis, bronchiectasis, chronic bronchitis, asthma, sarcoidosis, and COPD, to pulmonary nocardiosis. These conditions may account for 21.6% to 39.7% of nocardiosis patients [7,8,14–16]. Furthermore, pulmonary nocardiosis presenting as an exacerbation of chronic pulmonary disease has been reported [17]. Thus, chronic lung disease may be a risk factor for *Nocardia* infection. Specifically, case series and reports have indicated that COPD is commonly considered an isolated risk factor for pulmonary nocardiosis, even in immunocompetent patients [18]. Catellana *et al.* described pulmonary nocardiosis in an immunocompetent patient with COPD who had never undergone systemic or inhaled steroid therapy and did not have a respiratory failure or comorbidities leading to immunodepression [18].

TMP–SMX is the cornerstone treatment for nocardiosis, either as monotherapy or as part of an antibiotic combination regimen. Although no consensus exists on managing nocardiosis, several regimens have been proposed [1,9,18]. In the first clinical case presented in our report, we utilized TMP–SMX monotherapy for non-severe pulmonary nocardiosis for six months and achieved favorable outcomes. We initially administered intravenous antibiotics for two weeks to the second patient, who was diagnosed with isolated pulmonary nocardiosis with respiratory failure. Subsequently, we switched to oral TMP–SMX for 6 months,

resulting in positive outcomes. As most strains of *Nocardia* remain susceptible to TMP–SMX, it is a viable option for empiric treatment in resource-limited healthcare facilities[19].

CONCLUSIONS

While *Nocardia* is an uncommon etiology of community-acquired pneumonia, patients with subacute symptoms, cavitary lesions on imaging, and underlying chronic lung disease should raise suspicion for *Nocardia* infection. Trimethoprim–sulfamethoxazole can be considered an empirical therapy for non-severe cases of pulmonary nocardiosis.

ABBREVIATIONS

CAP: Community-acquired pneumonia, **COPD**: Chronic obstructive pulmonary disease**HIV**: Human immunodeficiency virus, **CRP**: C-reactive protein, **WBC**: White blood cell, **CT**: Computed tomography, **AFB**: Acid-fast bacillus, **PCR**: Polymerase chain reaction, **BALF**: Bronchoalveolar lavage fluid, **MALDI-TOF**: Matrix assisted laser desorption ionization-time of flight, **TMP-SMX**: trimethoprim-sulfamethoxazole.

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AUTHOR'S CONTRIBUTIONS

NDK, LTV, NHL, TNN: Conceptualization, Methodology, Writing original draft preparation; NDK, TNN: Visualization, Methodology, Software; LTV, NHL: Data curation; NDK, LTV, NHL, TNN: Validation, Investigation; LTV: Supervision. All authors read and approved the final manuscript.

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AVAILABILITY OF DATA AND MATERIALS

None.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was conducted in accordance with the amended Declaration of Helsinki. The institutional review board approved the study, and all participants provided written informed consent.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for publication of this Case series and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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