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CASE REPORT

Nocardia cyriacigeorgica Infection in a COPD Patient

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SUMMARY

Background: **Pulmonary infections caused by *Nocardia spp*. exhibit diverse clinical manifestations. However, the clinical manifestations and imaging examinations of the disease lack specificity, leading to an increased misdiagnosis rate. Therefore, the etiological diagnosis is crucial for the confirmation of this disease. *Nocardia cyriacigeorgica* is an aerobic, weak acid-fast, Gram-positive opportunistic pathogen characterized by slow growth.**
Methods: **In March 2024, a sputum specimen was sent for examination by the Department of Respiratory and Critical Care Medicine. The appearance was yellow purulent sputum, and no obvious "sulfur particles" were found. Gram staining of sputum revealed numerous Gram-positive bacilli with 90° branching and even tangled filamentous forms, and weak acid-fast staining was positive. Under aerobic conditions at a constant temperature of 37°C, we observed slow-growing colonies that were white, dry, and wrinkled on blood agar.**
Results: **We used MALDI-TOF MS for identification, and by comparing the mass spectrum peaks of the isolate with the known mass spectrum peaks in the database (MS-IVD database version 3.0), the result was *Nocardia cyriacigeorgica* with 99.9% confidence. The patient was started on empiric antibiotic therapy with piperacillin-tazobactam (4.5 g, q 8 hour), along with supportive measures such as nebulized treatments, cough suppressants, bronchodilators, oxygen therapy, and gastric acid suppression. Due to the patient's acute exacerbation of chronic obstructive pulmonary disease (COPD), accompanied by multiple underlying diseases such as heart failure, chronic bronchitis, and gastrointestinal bleeding, the clinical focus was mainly on improving the main symptoms. The patient was kept under observation for Nocardia infection and did not receive targeted treatment.**
Conclusions: **Through the review of this case and related literature, close cooperation between clinicians, laboratory departments, and imaging departments is essential in the diagnosis and treatment of this atypical pulmonary infection. Therefore, it is necessary that we analyze the laboratory diagnosis of this case to enhance the understanding of the disease and increase the actual positive rate.**
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KEYWORDS

Nocardia cyriacigeorgica, pulmonary infection, sputum culture, weak acid-fast, case report

INTRODUCTION

Pulmonary nocardiosis is a suppurative or granulomatous disease of the lung caused by *Nocardia species* (*Nocardia spp.*), accounting for 70% of all nocardiosis cases [1]. With the widespread application of mass spectrometry identification technology, these bacteria have been continuously identified. Concurrently, following the increase in patients with underlying diseases

and impaired immune function, the incidence rate of the disease has shown a rising trend in recent years. Pulmonary nocardiosis caused by Nocardia infection exhibits diverse clinical manifestations and lacks specificity in imaging examinations [2]. Delayed diagnosis and treatment can lead to an increased mortality rate [3]. The key to diagnosing the disease is etiological evidence. The pathogenic bacterium of pulmonary nocardiosis is *Nocardia cyriacigeorgica*, which is relatively rare in previous reports. In light of this, we reported a case of pulmonary nocardiosis in March 2024 by the Department of Respiratory and Critical Care Medicine at The First Affiliated Hospital of Guilin Medical University and reviewed the domestic and international literature to improve the diagnosis and treatment of pulmonary nocardiosis.

CASE REPORT

An 80-year-old Chinese man with a 20-year history of chronic obstructive pulmonary disease (COPD) had been receiving long-term home oxygen therapy. Two weeks ago, the patient developed severe symptoms of cough, expectoration, and worsening shortness of breath for no apparent reason. He was subsequently admitted to a local hospital, where he was diagnosed with an acute exacerbation of COPD. The patient received treatments including anti-infection and cough and expectoration reduction, resulting in alleviation of symptoms. At one-week prior to admission, the patient's symptoms further aggravated, including difficulty in expectorating sputum and the development of edema in both lower limbs. Subsequently, he was referred to our hospital for further evaluation on March 15, 2024. His medical history including hypertension, hyperlipidemia, coronary disease, diabetes, etc. was negative.

On physical examination, the patient was not febrile (36.5℃). His heart rate was 119 beats per minute, blood pressure 115/70 mm Hg, respiratory rate 24 breaths per minute. Since clinical symptoms of acute exacerbation of COPD, he had received 2 L/minute O_2 via nasal cannula to maintain SpO2 ≥ 80%. Respiratory system examination showed a barrel chest, widened intercostal spaces, hyperresonant percussion notes bilaterally, decreased breath sounds, and bilateral coarse crackles in both lungs.

The blood test showed an elevated white blood cell count of 10.95 x 10^9/L, an increased neutrophil percentage of 87%, an elevated high-sensitivity C-reactive protein of 87.6 mg/L, and an elevated IL-6 of 49.4 pg/mL. The B-type natriuretic peptide was 4,350 pg/mL (reference range: 0 - 125 pg/mL). Arterial blood gas analysis with the patient receiving 2 L/minute of oxygen via nasal cannula showed hypoxemia (pH = 7.49, pO_2 = 49 mmHg, pCO_2 = 33 mmHg, HCO_3^- = 26.3 mmol/L, SaO_2 = 83.7%). Renal function was within the normal range, and tests for tuberculosis antibodies, serum IgM for nine respiratory pathogens, and quantitative detection of 1-3-β-D glucan were all negative.

The patient presented with significant dyspnea, and a bedside chest radiograph (Figure 1) showed bilateral lung infiltrates and a nodule in the left upper lung field, suggesting the need for a chest CT scan. The patient also had emphysema in both lungs with localized bullae formation, as well as small bilateral pleural effusions. The patient was initially diagnosed with acute exacerbation of COPD, type I respiratory failure, cor pulmonale, and heart failure. The patient was started on empiric antibiotic therapy with piperacillin-tazobactam (4.5 g, q 8 hours), along with supportive measures such as nebulized treatments, cough suppressants, bronchodilators, oxygen therapy, and gastric acid suppression.

We conducted further microbiological examination. The submitted sputum specimen appeared as yellow purulent sputum, without obvious “sulfur granule”-like materials (Figure 2A). Direct microscopic examination of the smear using gram staining revealed numerous Gram-positive, filamentous, branching bacilli, with some hyphae branching at 90 degrees and exhibiting variable staining (Figure 2B), initially suggestive of an actinomycosis infection. Subsequent acid-fast staining of the smear showed negative, but the modified acid-fast staining revealed distinct red-stained, clustered filamentous structures (Figure 2C - D), further suggesting a Nocardia infection. After 48 hours of culture, the specimen showed slow-growing, dry, wrinkled, grayish-white colonies on the blood agar (Figure 2E), which were suspected to be the causative organism. Ultimately, we used MALDI-TOF MS for identification, and by comparing the mass spectrum peaks of the isolate with the known mass spectrum peaks in the database (MS-IVD database version 3.0), the result was *Nocardia cyriacigeorgica* with 99.9% confidence. During the hospitalization, the patient developed gastrointestinal bleeding (stool test showed positive for occult blood by immunoassay, and 3+ by chemical method on March 17, 2024), so vasoactive medications were used to maintain blood pressure, along with acid-suppressing medications for hemostasis, and blood transfusions as supportive care. By April 3rd, the patient’s respiratory symptoms and daily activities had improved, and his condition was relatively stable. The patient has been discharged from the hospital.

DISCUSSION

Nocardia spp. are aerobic actinomycetes that exhibit variable Gram staining and weakly acid-fast characteristics. They are widely distributed in dust, soil, polluted water, and decaying vegetation [4]. The inhalation of fungal fragments is the primary mode of *Nocardia spp.* transmission, which commonly causes pulmonary infections. It can also enter the human body through damaged skin or the digestive tract [5]. Pulmonary nocardiosis is an opportunistic infection primarily affecting the lungs, and it typically occurs in patients with underlying

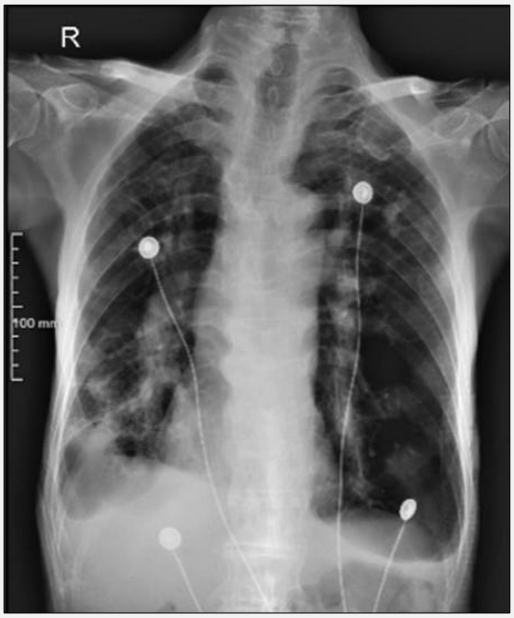

Figure 1. Chest X-ray examination.

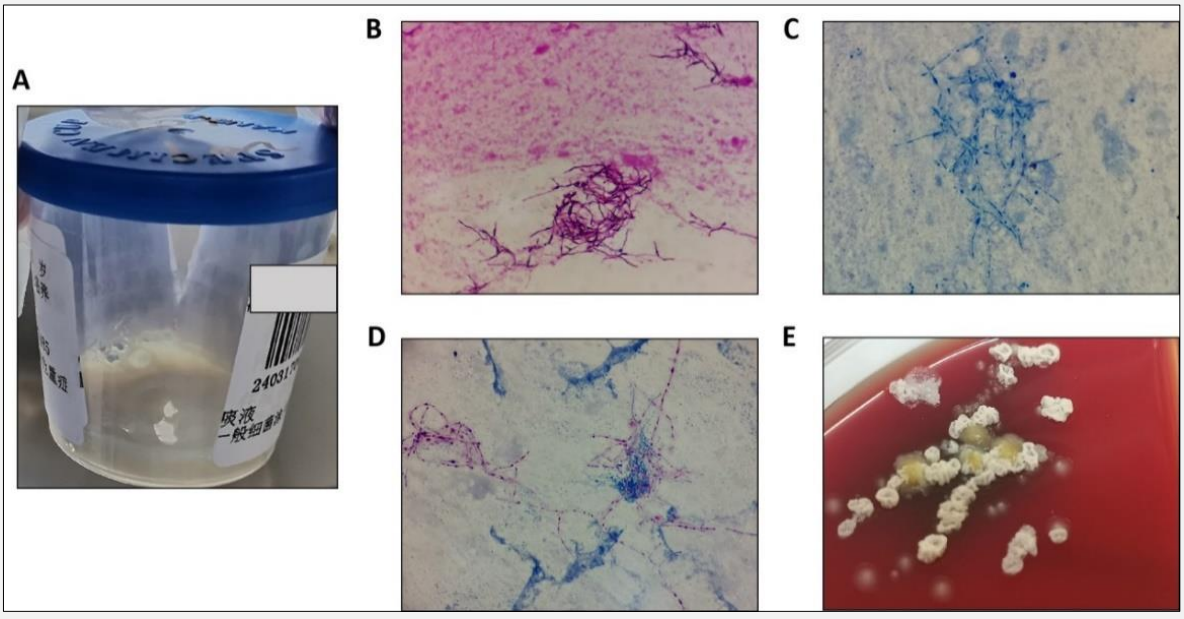

Figure 2. Sputum specimen status, smear, and cultured colony morphology.

(A) Initial state of the sputum specimen. (B) Gram-stained sputum smear (oil, 100 x). (C) Acid-fast stained sputum smear (oil, 100 x). (D) Weakly acid-fast stained sputum smear (oil, 100 x). (E) Colony morphology on blood agar after 48 hours of sputum culture.

diseases and compromised or deficient immune function [6], such as COPD, bronchiectasis, long-term steroid use, and HIV infection [7]. The patient in this case report had acute exacerbation of COPD and multiple underlying conditions, including heart failure, chronic bronchitis, and gastrointestinal bleeding. The clinical approach focused on managing the primary symptoms, with a watchful waiting approach to the Nocardia infection without targeted treatment.

Microbiological culture is the gold standard method for diagnosis of nocardiosis, but *Nocardia spp.* grow slowly, typically requiring more than 2 days, and even 4 - 6 weeks [8]. However, the *Nocardia cyriacigeorgica* isolated in this case grew relatively faster compared to other *Nocardia spp.*, with distinct colonies visible on the original blood agar after 48 hours. Meanwhile, direct smear staining of the specimen can provide important information for identifying slow-growing pathogens, and 77% - 90% of cases can be diagnosed through sputum specimen analysis [9]. In this case, we performed Gram staining of the smear prior to sputum culture, which revealed the typical morphology suspicious for Nocardia, and we also conducted the modified acid-fast staining examination. As reported in the relevant literature, prolonging the sputum culture duration can significantly reduce the missed diagnosis rate of *Nocardia spp.* Conducting comprehensive examinations, such as bronchoscopic lavage fluid and lung tissue specimens can maximize the positive culture rate for *Nocardia spp.* [10]. Given that the *Nocardia spp.* are an opportunistic pathogen, the detection of them in sputum or blood samples may indicate colonization, transient infection, or contamination. For immunocompromised patients, the positive Nocardia result in sputum culture is typically considered an infection, requiring antimicrobial treatment. However, for immunocompetent patients, even if *Nocardia spp.* are detected in sputum samples but without obvious signs of infection, close monitoring should be performed, and treatment may not be immediately necessary [11].

CLSI M24A recommends the broth microdilution method for antimicrobial susceptibility testing of *Nocardia spp.*. According to the literature, amikacin, amoxicillin/clavulanic acid, cefotaxime, ciprofloxacin, clarithromycin, imipenem, linezolid, minocycline, moxifloxacin, trimethoprim-sulfamethoxazole, tobramycin, cefpodoxime, cefotaxime, and doxycycline have reported breakpoints for antimicrobial susceptibility of *Nocardia cyriacigeorgica* [12]. Due to the limitations of the specific culture media and instruments required for manual antimicrobial susceptibility testing, our laboratory is temporarily unable to perform antimicrobial susceptibility testing for *Nocardia cyriacigeorgica*.

For pulmonary nocardiosis, clinicians need to use combination therapy with trimethoprim-sulfamethoxazole as the mainstay, avoid monotherapy, and select appropriate antibiotics while considering factors such as the patient's indications, allergies, and liver and kidney function. For severe patients awaiting antimicrobial susceptibility results, empiric multi-drug therapy is recommended, typically including broad-spectrum antibiotics such as carbapenems (imipenem or meropenem), trimethoprim-sulfamethoxazole, amikacin, linezolid, or parenteral cephalosporins (e.g., cefotaxime, cefotaxime) [13].

CONCLUSION

Based on this case report, close collaboration between clinicians, the laboratory, and the radiology department is essential for diagnosing and treating atypical pulmonary infections. The case also prompts us to reflect that, since only one sputum sample was cultured in this case, the possibility of contamination cannot be excluded. Therefore, we proactively communicated with the clinicians and recommended repeated specimen collection. Additionally, we need to enhance our own skills in radiographic interpretation and clinical reasoning to improve the actual positivity rate.

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Ethical Approval:
Written informed consent for the publication of this case report, images, and all information was obtained from the patient. A copy of the written consent is available for review by the editor of this journal upon request.

Declarations of Interest:
All authors declare to have no conflict of interest.

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