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A Case Report of Disseminated Nocardiosis

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Abstract: *Objective:* To summarize the clinical characteristics and treatment plan for a case of disseminated nocardiosis. *Methods:* The study summarized the clinical characteristics and treatment plan for a case of disseminated nocardiosis. *Results:* The primary symptoms of the patient included high fever and multiple enlarged lymph nodes. Chest computed tomography revealed a shadow of nodules in the upper lobe of the left lung, multiple nodules, and pleural effusion in both lungs. Additionally, bilateral blood cultures indicated the presence of *Nocardia terpenica*. The final diagnosis was disseminated *Nocardia sp.* infection. Upon admission, anti-infective treatment was initiated with sulfamethoxazole and linezolid. *Conclusion:* In patients with normal immune function, disseminated nocardiosis may present as high fever with lymph node enlargement, necessitating differentiation from lymphoma. This study reports on the diagnosis and treatment plan of a case of disseminated nocardiosis to enhance understanding and clinical management of this disease.

Keywords: *Nocardia terpenica*; Disseminated nocardiosis; Pulmonary infection; Septicemia; Case report

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1. Clinical data

A 50-year-old man was admitted to the hospital with complaints of general fatigue lasting over 10 days and a fever persisting for 4 days. He was admitted to the Respiratory Department on May 4, 2020. More than 10 days prior to admission, the patient experienced fatigue without any apparent cause. Four days before admission, he developed repeated high fevers, with the highest temperature reaching 39°C, but no cough, expectoration, chest tightness, shortness of breath, or other discomfort was reported. One day before admission, laboratory tests revealed a leukocyte count of 12.44×10^9/L, an absolute neutrophil count of 11.32×10^9/L, an absolute lymphocyte count of 0.40×10^9/L, a hypersensitive C-reactive protein level of 273.62 mg/L, and a procalcitonin level of 2.74 ng/mL. Chest computed tomography (CT) showed inflammation in both lungs. Left lung nodules were evaluated, and neoplastic lesions were investigated, along with a small amount of bilateral pleural effusion and incomplete expansion. Abdominal CT revealed bilateral renal exudation, effusion in the left colonic sulcus, and inflammatory changes near the left ureter (**Figure 1**). The patient denied any history of chronic disease. He worked as a farmer and had a 20-pack-year smoking history but no history of alcohol use.

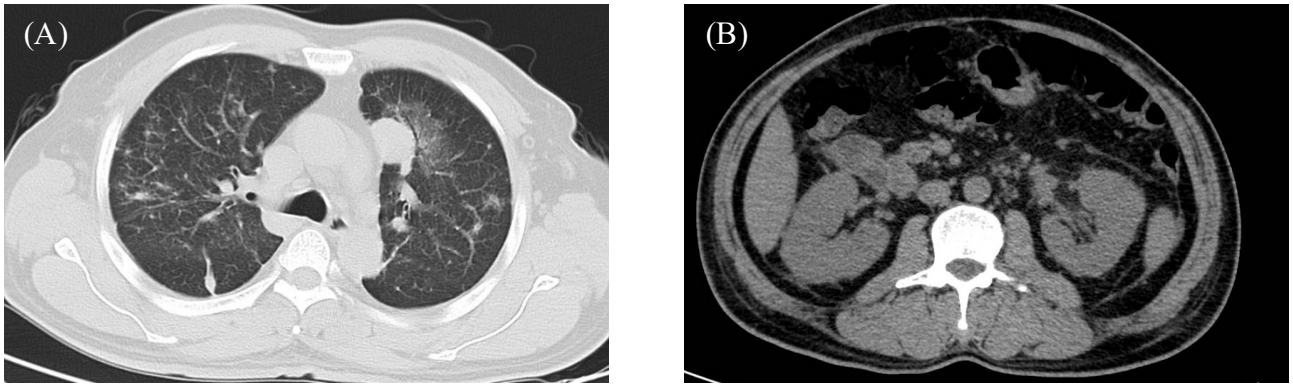

Figure 1. (A) Chest CT showing patchy blurred shadows and multiple small nodular shadows in both lungs. A nodule approximately 25 mm in diameter was observed near the mediastinum of the left upper lung without distinct spiculations. Small bilateral pleural effusions and adjacent lung parenchyma were noted. The trachea and main bronchial branches were patent, and no enlarged lymph nodes were found in the bilateral hilum or mediastinum. **(B)** Abdominal CT showing bilateral perirenal exudation, thickened fascia, slight effusion in the left paracolonic groove, slight dilation of the left ureter's upper segment, peripheral exudation, and slight effusion in the pelvic cavity

Upon admission, physical examination showed a temperature of 38.7°C, a pulse rate of 96 beats per minute, a respiratory rate of 22 breaths per minute, and a blood pressure of 116/72 mmHg. The patient was alert and responsive. Moist rales were present in both lungs, scattered rash was observed across the body, and multiple cord-like swollen lymph nodes were palpable under the neck and in the armpits.

(1) Admission diagnosis: Fever; suspected lung infection. Evaluation of lung nodule characteristics was pending.

(2) Treatment: Upon admission, the patient's condition was monitored closely. Routine blood analysis indicated the following: white blood cell count, 10.65×10^9/L; neutrophil percentage, 89.90%; creatinine, 162 μmol/L; eGFR, 42.08 mL/(min·1.73 m²); hypersensitivity C-reactive protein, 287.36 mg/L; procalcitonin, 2.74 ng/mL; interleukin 6, 156.1 pg/mL; erythrocyte sedimentation rate, 80 mm/h; complement C3, 0.46 g/L; and complement C4, 0.06 g/L. Lymphocyte subset analysis revealed $CD3^+$ $CD4^+/CD3^+$ CD8: 17.70%; absolute $CD3^+$ $CD8^+$: 275.50 cells/μL; absolute $CD3^+$ $CD4^+$: 98.93 cells/μL; and absolute $CD3^-$ $CD19^+$: 65.86 cells/μL. A syphilis test, including reagin titers, returned positive results: syphilis serum reagin titer, 1:256; specific syphilis antibodies, 21.41. Results for G test, GM test, respiratory virus panel, influenza virus antigen, mycoplasma pneumoniae IgM, TORCH, tuberculosis immune assay, enterovirus nucleic acid, and multiple tumor markers were within normal ranges. Spinal lymph node ultrasound detected involvement of the bilateral cervical, left supraclavicular, and bilateral axillary regions. Echocardiography showed slightly elevated pulmonary artery pressure (PASP = 36 mmHg). The patient's high fever persisted, and pleural fluid and urine cultures were negative, as were initial blood cultures. Bronchoscopic biopsy of the lung tissue revealed chronic inflammation, widening of the alveolar septa, fibrosis, and an increase in tissue cells within alveolar spaces. Immunohistochemistry was positive for TTF-1, CD68, and CK7, while special staining for acid-fast bacilli, PAS, and silver was negative (**Figure 2**). A lymphoma diagnosis was not excluded, given the patient's high fever and multiple swollen lymph nodes.

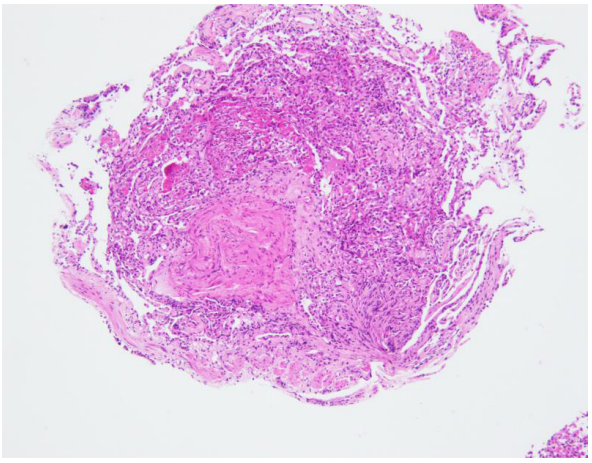

Figure 2. Left upper lung tissue biopsy revealed chronic inflammation in bronchial mucosa and lung tissue, widening of some alveolar septa, fibrosis, increased cellularity in alveolar spaces, and mild alveolar epithelial hyperplasia without signs of suppurative pathology

On May 11, PET-CT indicated high metabolic activity in multiple lymph nodes. Metabolic activity was elevated in soft tissue shadows in the left upper lobe and across both lungs. Increased spleen volume and metabolic activity, localized metabolic activity in the left kidney, and increased systemic bone marrow metabolism were noted (**Figure 3**). No abnormal phenotypic cells were found on bone marrow flow cytometry, and a bone marrow smear showed significant hyperplasia with diverse lymphocytes.

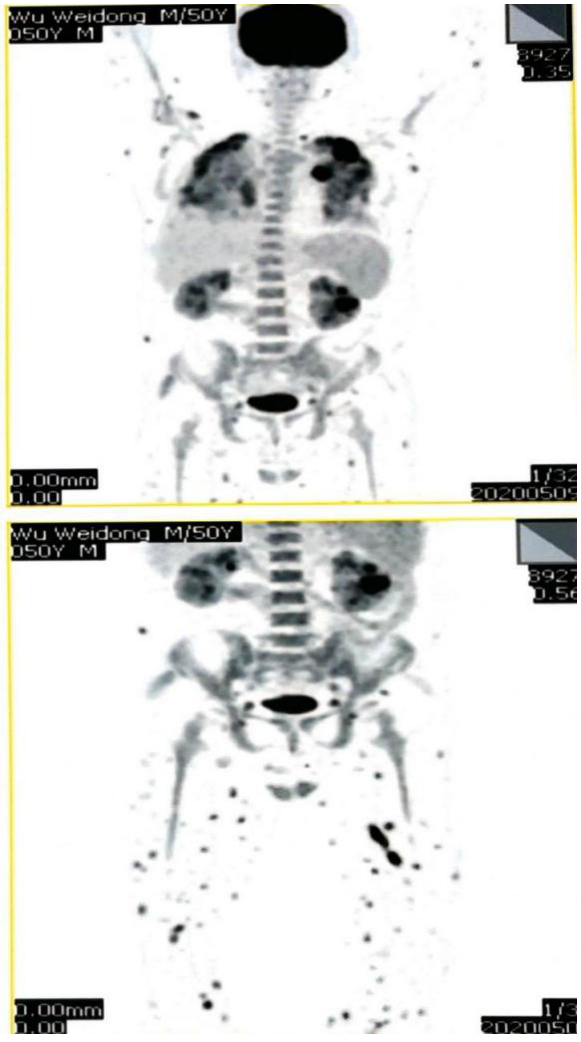

Figure 3. PET-CT findings: Elevated metabolic activity in multiple lymph nodes, soft tissue shadows in the left upper lobe, and multiple areas in both lungs. Diffuse metabolic activity was seen in the spleen, left kidney, muscle spaces, subcutaneous tissues, and bone marrow

Empirical treatment with moxifloxacin (400 mg daily) was started after admission, but the patient's fever persisted. On May 6, linezolid (600 mg every 12 hours) and oral valacyclovir (0.3 g twice daily) were added. Despite treatment, high fevers and multiple painless swollen lymph nodes persisted. Differential diagnoses included lymphoma, sarcoidosis, and carcinomatous lymphangitis, although sepsis and infective endocarditis could not be ruled out. Benzathine penicillin (2.4 million units, divided into two gluteal injections) was given for secondary syphilis on May 8. Body temperature normalized on May 9, and subsequent blood cultures were negative. By May 15, blood cultures grew *Nocardia sp.*, confirming disseminated nocardiosis. Treatment included oral sulfamethoxazole (0.96 g four times daily, adjusted for renal function). Sputum Gram staining showed 90° branching, long filamentous Gram-positive bacteria (**Figure 4**).

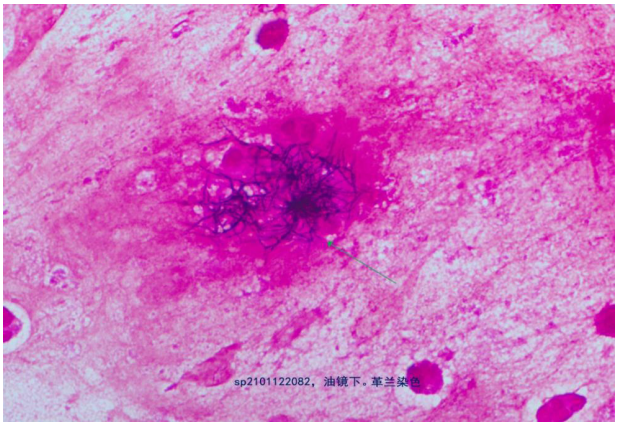

Figure 4. Gram staining (1,000×): Clusters of 90° branching, long filamentous Gram-positive bacteria

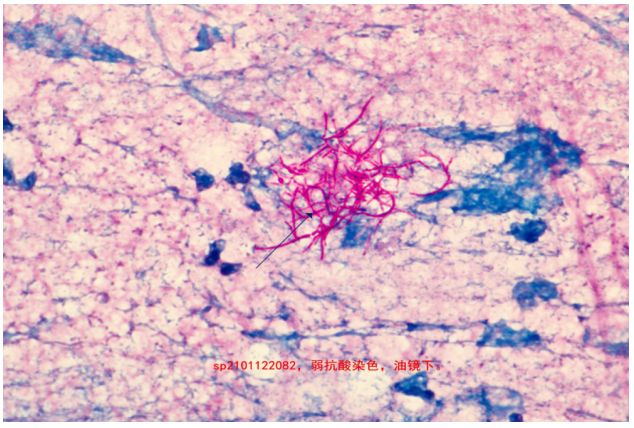

Figure 5. Weak acid-fast staining (1,000×) revealed clustered, positive mycobacteria

Weak acid-fast staining was positive, with a 1,000-fold microscopic aggregation and positive mycobacteria (**Figure 5**). 16S rRNA sequencing identified the bacteria as *Nocardia terpenica*. After a 5-day culture of transferred blood plates, the colonies appeared drier and milky with wrinkled surfaces and emitted a soil odor (**Figure 6**). Bilateral blood cultures confirmed *Nocardia terpenica* (positive time: 71.7 hours left, 87.2 hours right) and were negative for mycobacteria.

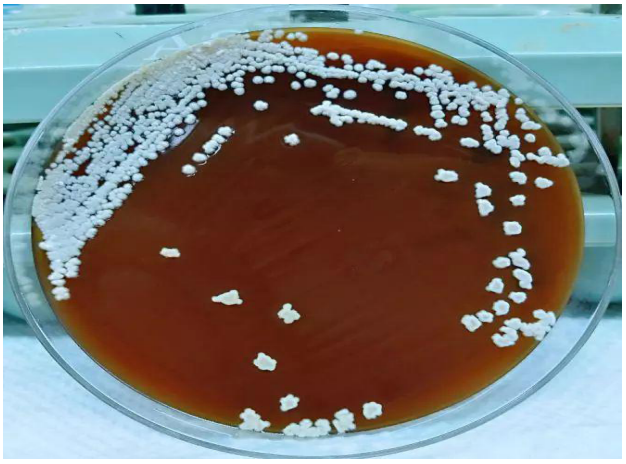

Figure 6. After 5 days of culture on transferred blood plates, the colonies appeared drier, milky white, with wrinkled folds on the surface and an earthy odor

The broth microdilution method recommended by the Clinical and Laboratory Standards Institute was used. The Thermo Fly reagent results showed the following minimum inhibitory concentrations (MIC): compound sulfamethoxazole: 20 mg/mL; imipenem: ≤ 2 mg/mL; TCana: ≤ 1 mg/mL; linezolid: ≤ 1 mg/mL; moxifloxacin: 1 mg/mL; clarithromycin: ≤ 0.06 mg/mL; tobramycin: ≤ 1 mg/mL; ciprofloxacin: 2 mg/mL; doxycycline: 1 mg/mL; minocycline: 4 mg/mL; cefepime: 32 mg/mL; ceftriaxone: 64 mg/mL; and amoxicillin: > 64 mg/mL (**Table 1**). Sulfamethoxazole, linezolid, and moxifloxacin were sensitive with no adjustments needed. C-reactive protein levels decreased significantly; however, multiple lymph nodes remained enlarged. Consequently, a lymph node puncture biopsy was recommended to rule out lymphoma. However, due to the risk of infection spread, lymph node needle biopsy was temporarily deferred. The patient was discharged following stabilized infection control, with follow-up PET-CT and potential lymph node biopsy if necessary.

Table 1. Susceptibility testing using Thermo Fly reagent (sample no.: 2005051033)

Antibiotic	Result	Method	Drug sensitivity
Compound sulfamethoxazole	20	MIC	S
Imipenem	≤ 2	MIC	S
Butylamine kanamycin	≤ 1	MIC	S
Linezolid	≤ 1	MIC	S
Moxifloxacin	1	MIC	S
Clarithromycin	≤ 0.06	MIC	S
Nebcin	≤ 1	MIC	S
Ciprofloxacin	2	MIC	I
Doxycycline	1	MIC	I
Minocycline	4	MIC	I
Cefepime	32	MIC	R
Ceftriaxone	64	MIC	R
Amoxicillin	> 64	MIC	R

After discharge, moxifloxacin was replaced with oral moxifloxacin 0.4 g, sulfamethoxazole 0.96 g every 8 hours, and linezolid 600 mg every 12 hours. Side effects included nausea, vomiting, and swelling of the right foot. Linezolid was discontinued, moxifloxacin was stopped on June 19, and sulfamethoxazole was adjusted to 0.96 g twice daily as maintenance therapy. Three months post-discharge, chest CT showed absorption of the left upper lobe nodules and bilateral pleural effusion (**Figure 7**). A PET-CT review on June 8 showed no systemic signs of malignancy or lymphoma, with lymph node biopsy indicating reactive hyperplasia. In December 2024, a bone marrow examination revealed BCR/ABL P210 positivity, leading to a diagnosis of chronic myeloid leukemia in the chronic stage.

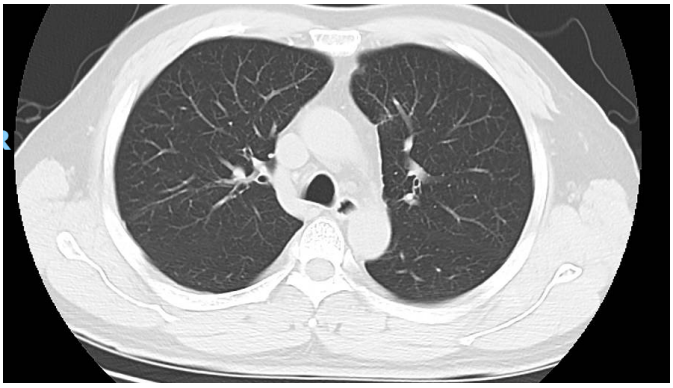

Figure 7. Chest CT re-examined on August 30, 2020, showed a tiny nodule approximately 1 mm in diameter in the anterior segment of the right upper lobe and lateral basal segment of the lower lobe, similar to previous imaging. A small fiber-like shadow was observed in the left upper lung, similar to earlier findings. A few cord-like structures were visible under the pleura of the left lower lobe. No pleural effusion was detected in either thoracic cavity. On the right side of the upper mediastinal trachea, a capsular bright shadow was noted, similar to previous imaging.

2. Discussion

Nocardia terpenica is an aerobic, filamentous, beaded, Gram-positive bacterium with weak acid-fast staining. This species is widely found in the environment, particularly in soil, organic matter, and water. Individuals may become infected through respiratory inhalation or contact with damaged skin, and infections are more common in those with immune deficiencies or immunosuppression. *N. farcinica* and *N. cyriacigeorgica* are the most common species in China [1,2]. First reported in Japan in 2007, *Nocardia terpenica* has been rarely isolated from clinical specimens [3] and accounts for only 2.2% of the known Nocardia species in China, primarily distributed along the southeast coast [2]. Disseminated nocardiosis is an infection involving non-contiguous organs, with Nocardia species being isolated and cultured from multiple sites or blood samples [4]. The case fatality rate for *Nocardia* infection is between 15.8% and 24.5% [5], with disseminated nocardiosis exhibiting a higher mortality rate and poor prognosis [6,7]. Although *Nocardia* infection can occur at any site, it most commonly affects the lungs, followed by the skin, brain, and other areas [4,8]. Chest CT is useful in diagnosing and assessing the severity of pulmonary nocardiosis, with possible CT findings including lobe consolidation, isolated or multiple nodules, peribronchial consolidation, and centrilobular nodules. The presence of cavities and pleural effusion is associated with disseminated pulmonary nocardiosis, and CT findings of multinodular consolidation are linked to a poor prognosis [5].

In this study, the patient was a middle-aged man with an acute presentation, high fever, multiple red rashes, and painless enlargement of multiple lymph nodes as the primary clinical symptoms. Chest imaging, including abdominal CT and PET-CT, indicated multiple nodules in both lungs, exudation from the upper ureter of both kidneys, and increased metabolism in the left lung nodules and lymph nodes. Bilateral blood cultures confirmed *Nocardia terpenica*, suggesting hematogenous dissemination and sepsis involving systemic organs. This study emphasizes that sulfamethoxazole remains the first-line treatment for *Nocardia* infections. This compound has long been the cornerstone of *Nocardia* treatment [1,2,8]. For cases resistant to trimethoprim-sulfamethoxazole or involving disseminated or severe infection, a combination of sulfamethoxazole with amikacin, imipenem, or a third-generation cephalosporin is recommended [9,10]. Immunocompetent patients with

pulmonary or non-central nocardiosis are advised to undergo treatment for 6 to 12 months [11]. In this case, the patient had disseminated *Nocardia* infection and was empirically treated with sulfamethoxazole, linezolid, and moxifloxacin. The patient was discharged after his temperature normalized and continued on sequential oral treatment with sulfamethoxazole, linezolid, and moxifloxacin. Follow-up chest CT revealed significant lesion absorption, leading to the discontinuation of moxifloxacin and linezolid while sulfamethoxazole was maintained as a maintenance therapy. The patient also presented with high fever and systemic lymphadenopathy, raising concerns for lymphoma. A post-discharge PET-CT showed no signs of lymphoma, and lymph node biopsy indicated reactive hyperplasia, suggesting that lymphadenopathy was related to disseminated nocardiosis. Clinical manifestations of disseminated nocardiosis are non-specific and may include cough, expectoration, fever, and other symptoms, complicating differentiation from other bacterial infections or tumors. Due to the low detection rate, cases are often misdiagnosed, missed, or diagnosed late, leading to disease progression. Clinicians should improve awareness of this condition and ensure thorough re-examination in suspected cases, with close collaboration with microbiology labs. Additionally, extending culture time and increasing detection efforts can help facilitate earlier diagnosis and treatment.

Disclosure statement

The authors declare no conflict of interest.

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