A rare case of pulmonary nocardiosis comorbid with Sjogren’s syndrome

Yumeng Peng | Xiaoyan Dong | Yongze Zhu | Huoyang Lv | Yumei Ge

1 Center of Clinical Laboratory Medicine, the Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College, Zhejiang, China
2 Bengbu Medical College, Anhui, China
3 The Second Medical College, Zhejiang Chinese Medical University, Zhejiang, China

Correspondence
Yumei Ge, Center of Clinical Laboratory Medicine, the Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College, Zhejiang 310014, China. Email: 11218070@zju.edu.cn

Funding information
This study was financially supported by grants from the National Natural Science Foundation of China (81802021), a grant from the Zhejiang Medical and Health Science and Technology Project of China (2023KY022, 2019KY013), Zhejiang Provincial Natural Science Fund (LY20H200008), and a grant from the Research Initiation Fund of Zhejiang People's Hospital in China (ZRY2018B004)

Abstract
Background: Nocardia is an opportunistic pathogen, which occurs in patients with autoimmune diseases and immune dysfunction, and can cause bacteremia and other life-threatening complications. The clinical manifestations of Nocardia pneumonia are similar to tuberculous and other clinical common bacterial pneumonia, but its antibacterial treatments are different and detection methods are unique, which may lead patients to suffer for many years due to clinical misdiagnosis and missed diagnosis.
Methods: Imaging and laboratory examinations were performed for preliminary diagnosis, and next-generation sequencing was used to identify the exact species type of Nocardia in the bronchoalveolar lavage fluid (BALF) of the patient.
Results: Imaging and laboratory parameters preliminarily implied that the patient was infected with Nocardia with Sjogren's syndrome (SS), and NGS showed that the strain was N. terpenica.
Conclusions: Accurate etiological diagnosis and corresponding antibiotics are key to improve the prognosis of pulmonary nocardiosis in this case. Nocardia pneumonia is rare in clinical practice; it is of great medical significance to improve the understanding of pulmonary nocardiosis.

KEYWORDS
etiological examination, next-generation sequencing, Nocardia terpenica, pneumonia, Sjogren's syndrome

1 INTRODUCTION
Nocardia is Gram-positive, weakly acid-fast, catalase-positive, non-motile, branching rod-shaped aerobic bacteria, belonging to actinomycetales.1,2 Nocardia widely exists in soil, water, air, and rotten plants. It is common in patients with T-cell deficiency (leukemia or AIDS), long-term usage of immunosuppressants (such as organ transplantation and malignant tumor), or patients with underlying diseases (such as diabetes and chronic kidney disease).3–6 Pulmonary nocardiosis is a purulent and granulomatous disease caused by Nocardia invading the lung through respiratory tract inhalation or skin lesions. It can spread into the brain, kidney, and other organs by blood dissemination and even form life-threatening sepsis.

The clinical manifestations of pulmonary nocardiosis are fever, cough, expectoration, dyspnea, chest pain, hemoptysis, weight loss, fatigue, and other symptoms. Pulmonary nocardiosis is commonly characterized by infiltrative lesions, cavities, nodules, or masses in lung segments or lobes in computed tomography. Because its clinical manifestations and imaging are not specific to common bacterial infection, pulmonary aspergillosis, lung cancer, pulmonary abscess,
and tuberculosis, it often leads to misdiagnosis and missed diagnosis. What is worse, than other bacteria, *Nocardia* grows slowly. After 7 days of aerobic culture at 37 °C, the wrinkled milky white colonies embedded in the culture medium can be observed. Therefore, it is easy to be missed in the laboratory diagnosis process. Diagnosis and treatment may be delayed due to the late results of pathogen identification. We describe a patient with pulmonary nocardiosis co-morbid with SS with hemoptysis for more than 20 years.

## 2 | CASE PRESENTATION

### 2.1 | Clinical features

A 70-year-old male patient was admitted because of hemoptysis for more than 20 years without obvious inducement. The patient had a history of drinking and smoking for 50 years, about 500 ml of wine, and 20 cigarettes a day. He presented with bright red blood, cough and expectoration, no chest tightness, chest pain, shortness of breath, chills, or fever. Chest CT from the local hospital showed multiple nodules and bronchiectasis in both lungs. He did not have any treatment in the local hospital and came to Zhejiang Provincial People's Hospital (Zhejiang province, China) for further diagnosis. Later, he was treated with pituitrin and tranexamic acid injection for hemostasis, ceftriaxone sodium for anti-infection, and ambroxol for resolving phlegm. His condition improved while he still had repeated intermittent hemoptysis for last 2 years, with small amount, bright red blood, cough and expectoration, dark brown sputum, and occasional active chest tightness.

### 2.2 | Imaging examination

High-resolution computed tomography (HRCT) showed that the nodules in the upper lobe of the left lung were newly found and could not currently completely exclude tumor lesions. There were multiple bronchiectasis and some bronchial mucus embolism in both lungs. Inflammatory foci were scattered in both lungs (Figure 1). Therefore, doctors suggested improving laboratory examination to differentially diagnose between pulmonary tuberculosis and lung cancer. The patient was recommended to review and further examination such as acid-fast staining of sputum and tuberculin purified protein derivative (PPD) test after anti-inflammatory treatment.

![Image of HRCT showing bronchiectasis and inflammation](image)

**Figure 1** High-resolution computed tomography (HRCT) of the thorax showed bronchiectasis and inflammation involving in both lungs. Patchy and nodular high-density shadows were scattered in both lungs, with unclear margin. Bilateral bronchiectasis and wall thickening were observed. Nodular high-density shadows were found in local lumen, especially in right lung. The right upper lobe (Se4, im69) showed nodular high-density shadow with unclear edge, about 9 mm in diameter. Small nodules and dense foci were seen in the right lung. In addition, small cystic areas without lung markings were found in both lungs, with clear edges.

### 2.3 | Immunologic examination

The main serological abnormalities were antinuclear antibody (ANA)-positive (+++, 1:320); the immunofluorescent pattern of ANA was granule type and cytoplasmic granule type; antinuclear extract antibody (ENA)-positive (+); anti-SSA (60 KD) antibody-positive (+++); anti-Ro antibody (52 KD)-positive (+++); anti-histone antibody weakly positive (+); Ig G (20.30 g/L, the normal reference interval was 7.51–15.6 g/L) and Ig E (123.0 IU/ml, the normal reference interval was 0–87 IU/ml) increased significantly, ANCA was negative. The abnormal results were consulted by the rheumatology department and ophthalmology department, combined with tear secretion test. The tear film rupture time was 55/75. The final diagnosis was SS, involving both eyes.

### 2.4 | Hematologic examination

The increase in inflammatory indexes in peripheral blood suggested that there might be infection in the patient. The main abnormal results were increases in white blood cell count (13.01 × 10^9/L), neutrophil proportion (86.6%), high sensitivity C-reactive protein (87.2 mg/L), and erythrocyte sedimentation rate (62 mm/h) and decreases in albumin (36.2 g/L). Therefore, the doctor gave the patient 100 ml levofloxacin injection containing 0.5 g levofloxacin and 0.9 g...
sodium chloride every day for anti-infection treatment and suggested etiological examination for further diagnosis.

2.5 | Histopathology and cytology examination

Cytopathological examination showed that no cancer cells were found in brush biopsy of the middle lobe of the right lung. But the high proportion of neutrophils in BALF indicated that there might be acute inflammatory infection, and it was necessary to pay attention to the pile of radial rod-shaped bacteria (Figure 2).

2.6 | Etiological examination

No acid-fast bacilli were found in the smear of acid-fast staining of the smears of transcatheter bronchial brushing. No fungi were observed under an ultraviolet microscope after the fungal fluorescence staining of BALF. The tuberculosis DNA of sputum detected by fluorescence PCR was negative (-). In the process of smear for acid-fast bacilli in clinical laboratory, Gram-positive, weakly acid-fast, and filamentous bacilli were found and were highly suspected to be *Nocardia* (Figure 3A,B).

2.7 | NGS analysis

Sample processing and nucleic acid extraction were according to the steps of the TIANamp Micro DNA Kit (DP316, TIANGEN BIOTECH). 600 μL sputum or BALF of the patient was mixed and shaken with glass beads, and the extracted DNA was sonicated to fragments with a size of 100–150 bp. NGSmaster fully automated library construction and MGIseq-2000 were used for sequencing and analyzing. DNA fragments were amplified by terminal repair, ligation, and nonbiased PCR. The size of inserted fragments (200–300 bp) was determined by Agilent 2100 Bioanalyzer quality control library, and the concentration of DNA library (>2 ng/μl) was determined by using a qubit dsDNA HS assay kit (Thermo Fisher Scientific Inc.). The qualified library sequences were cyclized to form a chain ring structure. After cyclization, DNB nanospheres were generated by rolling ring replication (RCA). The prepared DNB nanospheres were loaded into the sequencing chip and sequenced by MGIseq-2000. Sample results were compared with a microbiological database including pathogenic bacteria (6350 species), fungi (1064 species), viruses (4945 species), and parasites (234 species) to obtain the number of sequences that could be matched to a certain pathogen. The results showed that it was *N. terpenica* with a sequence number of 306 and a 90.53% relative abundance. The patient’s laboratory test results are shown in Tables 1 and 2.

2.8 | Treatment and prognosis

The doctor decided to stop levofloxacin intravenous drip QD (once a day), instead of isepamicin 0.4 g with sodium chloride 250 ml intravenous drip QD, continue to give cefmetazole sodium 2 g intravenous drip BID (twice a day) for anti-infection, plus sulfamethoxazole tablets (SMZ) for treatment of *Nocardia* infection. Vitamin B6 10 mg oral QD, vitamin-B1 10 mg oral TID (three times a day), sodium bicarbonate 1 g oral TID for alkalization of urine, and compound sulfamethoxazole 1.44 g oral TID for anti-inflammatory. After a week of medication, the patient’s cough and expectoration improved, no chest tightness, shortness of breath, no fever and chills, the breath sounds of both lungs were thick, no obvious rhonchus and moist rales were heard, the rhythm was regular, and no obvious pathological murmur was heard in the auscultation area of each valve. Experts agreed that the diagnosis of *Nocardia* infection was clear, and the treatment of the patient was effective.

3 | DISCUSSION

The clinical manifestations of nocardiosis are similar to fungal, mycobacterium and bacterial infection, and lung adenocarcinoma. Nocardia can cause granuloma, abscess, and pulmonary nodules. The main respiratory symptoms are cough, expectoration, hemoptysis, chest pain, fever, dyspnea, fatigue, and empyema. Chest CT and other imaging findings are more than medium density of patchy infiltration, nodules, lung abscess, cavity, and hilar lymph node enlargement. Therefore, pulmonary nocardiosis is often misdiagnosed before definite etiological examination results have been obtained.9,10

For infected patients, timely ascertaining of pathogenic bacteria is important for effective treatment. It can reduce the rate of mortality and readmission and shorten the length of hospitalization. In this case, the patient was elderly and immunocompromised with SS and chronic diseases of bronchiectasis and hemoptysis that might be often attacked by more than one pathogen. NGS helped clinicians quickly and accurately find the specific pathogens of infection and exclude other bacterial co infection, which played a decisive role in the selection of appropriate antimicrobial therapy. We used NGS to determine the exact species type of *Nocardia* within one day, and he was diagnosed with infection of *N. terpenica*, which was rarely documented elsewhere. Thus, SMZ was used for anti-infection treatment according to the NGS result of Nocardia, which showed notable curative effectiveness.

NGS has been applied in the pathogenic diagnosis of diseases because it is more sensitive than 16S rDNA sequencing analysis in the diagnosis of unspecified pathogens, especially rare pathogens. It can detect almost all kinds of pathogens in the samples, while 16S rDNA sequencing technique can only detect a specific target pathogen that matches the corresponding primers and rare pathogens may be missed, or primers containing mismatches with the tested pathogens may be used, resulting in detection failure and reduced sensitivity.11

Cases of *N. terpenica* infection are rare in clinic. *Nocardia* is an opportunistic pathogen and usually infected in immunocompromised patients.12–15 Patients with a history of solid organ transplantation, hematopoietic stem cell transplantation, malignant tumor,
HIV infection, and chronic glucocorticoid therapy are often at higher risk. This article reported a case of pulmonary nocardiosis co-morbid with SS that has been rarely reported before. SS is a chronic inflammatory disease mediated by autoimmunity, which is characterized by infiltration of T cells, B cells, macrophages, and other immune cells in exocrine glands such as salivary gland and lacrimal gland, accompanied by clinical manifestations such as keratoconjunctivitis sicca and xerostomia. There are antinuclear antibody, anti-SSA antibody, anti-SSB antibody, antiplatelet antibody, antoglobulin antibody, and other autoantibodies in the serum and usually accompanied by hyperimmunoglobulinemia. In our case, the patient with SS was confirmed to have abnormal immune function according to immunological test results and clinical manifestations, which might be one of the inducing factors of Nocardia infection.

The course and prognosis of infectious diseases are closely related to the pathogenicity of pathogens and are more important to the body's own immune function against infection. Patients with autoimmune diseases such as SS and abnormal immune function usually cannot induce and produce effective protective antibodies after Nocardia infection. Those patients often have a higher risk of reinfection and preventive antibacterial treatment may be necessary. What is worse, the use of immunosuppressive drugs for autoimmune diseases or tumors will often aggravate Nocardia infection. Therefore, we should pay more attention to Nocardia infection in patients with immunodeficiency or chronic underlying diseases.

4 | CONCLUSION

The clinical manifestations of Nocardia infection are not characteristic, and such cases are rarely reported. Thus, pathogenic detection has irreplaceable significance in the diagnosis of pulmonary nocardiosis. The possibility of Nocardia should be considered by the technical personnel of clinical laboratory when they observe weak acid-fast, fibrinous bacteria with branched vascular hyphae in sputum samples. NGS has unique advantages in determining the types of pathogens in samples and identifying rare pathogens such as Nocardia, which is worthy of promotion and application in clinical diagnosis. In addition, Nocardia infection with autoimmune diseases in patients with clinical medication and anti-infection therapy has particularity. We should eliminate Nocardia infection first and then use the treatment for their underlying diseases and prophylactic anti-infection also should be considered later.

5 | HIGHLIGHT

(1) Pulmonary nocardiosis comorbid with Sjogren's syndrome was rare in clinic, and its diagnosis is challenging. (2) NGS is more sensitive than 16S rDNA sequencing technique in the diagnosis of unspecified pathogens and can detect almost all kinds of pathogens
TABLE 1  Clinical parameter detection of peripheral blood of the patient

| Clinical laboratory test                                      | Reference value of normal subjects | Unit       | Patient  |
|---------------------------------------------------------------|------------------------------------|------------|----------|
| Perinuclear- ANCA                                             | Negative (<1:3.2)                  |            | Negative (-) |
| PR3- ANCA                                                    | Negative (<1:3.2)                  |            | Negative (-) |
| Untypical ANCA                                               | Negative (<1:3.2)                  |            | Negative (-) |
| Anti-endothelial cell antibodies                             | Negative (<1:32)                   |            | Negative (-) |
| Anti-proteinase 3 antibody                                    | 0.0–20.0 RU/ml                     | 2.5        |          |
| Anti-MPO antibody                                             | 0.0–20.0 RU/ml                     | 1.8        |          |
| Anti-globular basement membrane Antibody (anti-GBM)          | 0.0–20.0 RU/ml                     | 0          |          |
| SCC                                                          | 0–3 ng/ml                          | 1.6        |          |
| BNP                                                          | 0–160 pg/ml                        | 10.1       |          |
| cTnI                                                         | 0–0.05 µg/ml                       | 0.045      |          |
| Total triiodothyronine (TT3)                                 | 0.66–1.61 µg/L                     | 1.15       |          |
| Total thyroxine (TT4)                                        | 54.4–118.5 µg/L                    | 91.43      |          |
| Thyroid stimulating hormone (TSH)                            | 0.34–5.6 mIU/L                     | 5.51       |          |
| Free triiodothyronine (FT3)                                  | 2.14–4.21 ng/L                     | 3.28       |          |
| Free thyroxin (FT4)                                          | 5.9–12.5 ng/L                      | 7.43       |          |
| Thyroglobulin antibody (TGA)                                 | <4.00 IU/ml                        | <0.9       |          |
| Thyroid peroxidase antibody (TPO)                            | <9.00 IU/ml                        | 2.5        |          |
| Neuron special endolase (NSE)                                | 0.0–16.3 ng/ml                     | 11.1       |          |
| Procalcitonin PCT                                            | 0.00–0.25 ng/ml                    | 0.02       |          |
| AFP                                                          | 0.0–20.0 µg/L                      | 4          |          |
| Carcinoembryonic antigen (CEA)                               | 0.0–5.0 µg/L                       | 1.9        |          |
| Carbohydrate antigen 12-5 (CA12-5)                           | 0.0–35.0 U/ml                      | 34.1       |          |
| Carbohydrate antigen 19-9 (CA19-9)                           | 0.0–37.0 U/ml                      | 28.4       |          |
| Carbohydrate antigen 15-3 (CA15-3)                           | 0.0–28.5 U/ml                      | 16.2       |          |
| Total PSA                                                    | 0.00–4.00 µg/L                     | 0.72       |          |
| Cytokeratin19                                                | 0.0–3.8 ng/ml                      | 2.5        |          |
| Carbohydrate antigen 72-4 (CA72-4)                           | 0.0–19.3 U/ml                      | 3.3        |          |
| Progastrin releasing peptide, ProGRP                         | 25.0–78.0 pg/ml                    | 39.7       |          |
| Immunoglobulin G (IgG)                                       | 7.51–15.60 g/L                     | 20.3       |          |
| Immunoglobulin E (IgE)                                       | 0–87 IU/ml                         | 123        |          |
| Immunoglobulin A (IgA)                                       | 0.82–4.53 g/L                      | 2.01       |          |
| Immunoglobulin M (IgM)                                       | 0.46–3.04 g/L                      | 0.69       |          |
| Complement C3                                                | 0.79–1.52 g/L                      | 1.01       |          |
| Complement C4                                                | 0.16–0.38 g/L                      | 0.24       |          |
| Rheumatoid factor                                             | 0.0–20.0 IU/ml                     | <20        |          |
| Antinuclear antibody                                          | Negative (<1:32)                   |            | Positive (++ 1:320) |
| Types of antinuclear antibody                                |                                    |            |          |
| Anti-ds-DNA qualitative                                       | Negative (<1:3.2)                  |            | Negative (-) |
| Anti-ds-DNA quantitative                                      | 0.0–75.0 IU/ml                     | 8.2        |          |
| Antinuclear extract antibody                                  | Negative (-)                       |            | Positive (+) |
| Anti-nucleosome antibody (AnuA)                              | Negative (-), 0–15                 |            | Negative (-) 0 |
| Anti-Sm antibody                                              | Negative (-), 0–15                 |            | Negative (-) 0 |
| Anti-U1RNP antibody                                           | Negative (-), 0–15                 |            | Negative (-) 8 |
| Anti-SSA antibody                                             | Negative (-), 0–15                 |            | Positive (+++) 31 |
| Anti-RO antibody                                              | Negative (-), 0–15                 |            | Positive (+++) 52 |

(Continues)
| Clinical laboratory test                                                      | Reference value of normal subjects | Unit     | Patient       |
|------------------------------------------------------------------------------|------------------------------------|----------|---------------|
| Anti-SSB antibody                                                            | Negative (−), 0–15                 |          | Negative (−) 2 |
| Anti-scl-70 antibody                                                          | Negative (−), 0–15                 |          | Negative (−) 2 |
| Anti-PM-Scl antibody                                                          | Negative (−), 0–15                 |          | Negative (−) 1 |
| Anti-Jo-1 antibody                                                            | Negative (−), 0–15                 |          | Negative (−) 1 |
| Anti-histone antibody                                                         | Negative (−), 0–15                 |          | Positive (+) 20 |
| Antiproliferative extractable nuclear antigens                               | Negative (−), 0–15                 |          | Negative (−) 10 |
| ARPA/Rib-P                                                                   | Negative (−), 0–15                 |          | Negative (−) 1 |
| Anticentromere antibody                                                       | Negative (<1:32)                   |          | Negative (−)  |
| Centromere antibody (Cenp B)                                                 | Negative (−), 0–15                 |          | Negative (−) 1 |
| Anti-mitochondrial antibody                                                  | Negative (<1:32)                   |          | Negative (−)  |
| Mitochondria antibodyM2                                                       | Negative (−), 0–15                 |          | Negative (−) 2 |
| Antinuclear membrane antibody                                                | Negative (<1:32)                   |          | Negative (−)  |
| Anti-NOR antibody                                                            | Negative (<1:32)                   |          | Negative (−)  |
| Anti-actin antibody                                                          | Negative (<1:32)                   |          | Negative (−)  |
| Microtubule spindle antibodies                                               | Negative (<1:32)                   |          | Negative (−)  |
| Nucleolinus antibody                                                         | Negative (<1:32)                   |          | Negative (−)  |
| Anticentriole antibody                                                       | Negative (<1:32)                   |          | Negative (−)  |
| Anti-chromosome antibody                                                     | Negative (<1:32)                   |          | Negative (−)  |
| Antinuclear skeleton protein antibody                                         | Negative (<1:32)                   |          | Negative (−)  |
| Normal control value PT                                                      | 9.3–12.6                           | Seconds  | 11.8          |
| Prothrombin time                                                             | 0.85–1.20                          |          | 1.08          |
| Normal control value appt                                                    | 22.7–34.1                          | Seconds  | 26.2          |
| Partial thromboplastin time                                                  | 21.0–32.8                          | Seconds  | 25.4          |
| Partial thromboplastin time Ratio                                            | 0.80–1.20                          |          | 0.92          |
| Normal control value TT                                                      | 13.7–20.5                          | Seconds  | 18            |
| Thrombin time                                                                | 0.80–1.20                          |          | 0.92          |
| Fibrinogen                                                                   | 2.00–4.00                          | g/L      | 4.62          |
| D-dimer                                                                      | 0.0–550.0                          | µg/L     | 430           |
| Total protein                                                                | 65–85                               | g/L      | 74.3          |
| Albumin                                                                      | 40–55                               | g/L      | 38.3          |
| Globulin                                                                     | 20–40                               | g/L      | 36            |
| Albumin globulin ratio                                                       | 1.2–2.4                             |          | 1.06          |
| ALT                                                                          | 9–50                                | U/L      | 8             |
| Aspartate aminotransferase (AST)                                             | 15–40                               | U/L      | 24            |
| AST:ALT                                                                      | 0.45–1.80                           |          | 3             |
| γ glutamyltranspeptidase (γ GT)                                              | 10–60                               | U/L      | 30            |
| Alkaline phosphatase                                                         | 45–125                              | U/L      | 103           |
| Total bilirubin                                                             | 3.4–24                              | µmol/L   | 7.3           |
| Direct bilirubin                                                            | 0.0–6.8                             | µmol/L   | 1.4           |
| Indirect bilirubin                                                          | 1.7–17.2                            | µmol/L   | 5.9           |
| Total bile acid                                                             | 0.0–15.0                            | µmol/L   | 2             |
| Glucose                                                                      | 3.92–6.16                           | mmol/L   | 3.99          |
| Urea                                                                         | 3.10–8.00                           | mmol/L   | 8.5           |
| Creatinine                                                                  | 44.0–133.0                          | µmol/L   | 69.2          |
| Clinical laboratory test                      | Reference value of normal subjects | Unit       | Patient |
|----------------------------------------------|------------------------------------|------------|---------|
| Urea nitrogen:creatinine                     | 7.5–27.5                           |            | 30.71   |
| Uric acid                                    | 208–428                            | μmol/L     | 375     |
| Potassium                                    | 3.5–5.3                            | mmol/L     | 3.65    |
| Sodium                                       | 137–147                            | mmol/L     | 141.9   |
| Chlorine                                     | 99–110                             | mmol/L     | 107.9   |
| Calcium                                      | 2.11–2.52                          | mmol/L     | 2.19    |
| Magnesium                                    | 0.75–1.02                          | mmol/L     | 0.91    |
| Phosphorus                                   | 0.85–1.51                          | mmol/L     | 1.25    |
| Osmotic pressure                             | 275–300                            | mmol/L     | 285     |
| Total cholesterol                            | 3.11–5.96                          | mmol/L     | 5.04    |
| Triglyceride                                 | 0.34–1.70                          | mmol/L     | 0.97    |
| High-density lipoprotein cholesterol         | 1.04–2.05                          | mmol/L     | 1.24    |
| Low-density lipoprotein cholesterol          | 2.10–3.10                          | mmol/L     | 3.15    |
| Non-high-density lipoprotein cholesterol     | 0.86–4.1                           | mmol/L     | 3.8     |
| Apolipoprotein A                             | 1.2–1.8                            | g/L        | 1.38    |
| Apolipoprotein b                             | 0.6–1.14                           | g/L        | 1.01    |
| APOB/APOA                                    | 0.4–1.1                            |            | 0.73    |
| Serum-free fatty acid                        | 129–769                            | μmol/L     | 526     |
| Lactate dehydrogenase                        | 120–250                            | U/L        | 167     |
| Lipoprotein A                                | 0–300                              | mg/L       | 76      |
| Creatine kinase                              | 50–310                             | U/L        | 66      |
| Cholinesterase                               | 4500–13,000                        | U/L        | 8396    |
| Dipeptidyl peptidase IV                     | 44–116                             | U/L        | 53      |
| α-1-fucosidase                               | 0–40                               | U/L        | 29      |
| Homocysteine                                 | 0.0–20                             | μmol/L     | 17.1    |
| WBC count                                    | 3.5–9.5                            | ×10⁹/L     | 13.01   |
| Lymphocyte classification                    | 20–50                              | %          | 7.8     |
| Monocyte classification                      | 3–10                               | %          | 4.3     |
| Neutrophil classification                    | 40–75                              | %          | 86.6    |
| Eosinophil classification                    | 0.4–8.0                            | %          | 1.1     |
| Basophil classification                      | 0–1                                | %          | 0.2     |
| Lymphocyte count                             | 1.1–3.2                            | ×10⁹/L     | 1       |
| Monocyte count                               | 0.1–0.6                            | ×10⁹/L     | 0.6     |
| Neutrophil count                             | 1.8–6.3                            | ×10⁹/L     | 11.3    |
| Basophil count                               | 0–0.06                             | ×10⁹/L     | 0.03    |
| Eosinophil count                             | 0.02–0.52                          | ×10⁹/L     | 0.14    |
| Red blood cell count                         | 4.3–5.8                            | ×10¹²/L    | 4.4     |
| Hemoglobin                                   | 130–175                            | g/L        | 135     |
| Hematocrit                                   | 0.40–0.50                          |            | 0.411   |
| Mean corpuscular hemoglobin                  | 27–34                              | pg         | 30.7    |
| Mean corpuscular hemoglobin concentration    | 316–354                            | g/L        | 328     |
| Red blood cell distribution width            | 11.6–14.8                          | %          | 13.6    |
| Platelet count                               | 125–350                            | ×10⁹/L     | 197     |
| Platelet hematocrit                          | 0.1–0.25                           | %          | 0.2     |
| Platelet large cell ratio                    | 13.0–43.0                          | %          | 26.3    |
| Erythrocyte sedimentation rate               | 0–43                               | mm/h       | 62      |
in the samples. *Nocardia terpenica* was ascertained in BALF of this patient by NGS. (3) Patients with autoimmune diseases such as Sjogren's syndrome should be given more attention for anti-*Nocardia* infection.

**ACKNOWLEDGEMENTS**

Open access funding provided by National Natural Science Foundation of China, Zhejiang Medical and Health Science and Technology Project of China, Zhejiang Provincial Natural Science Fund, and Research Initiation Fund of Zhejiang People's Hospital in China.

**CONFLICT OF INTERESTS**

The authors declare that they have no competing interests.

**AUTHOR CONTRIBUTIONS**

YMP collect the patient clinical information. YMP, XYD, YZZ, and HYL analyzed the data. YMP and YMG drawn the manuscript. All authors read and approved the final manuscript.

**CONSENT FOR PUBLICATION**

Written and informed consent was obtained from the patient for publication of this case report and any accompanying images.

**DATA AVAILABILITY STATEMENT**

The datasets used and/or analyzed during the current study are available from the corresponding author Yumei Ge on reasonable request.

**ORCID**

Yumei Ge https://orcid.org/0000-0003-3321-2176

**REFERENCES**

1. Fatahi-Bafghi M. Nocardiosis from 1888 to 2017. *Microb Pathog*. 2018;114:369-384.
2. Karunakaran R, Halim HA, Ng KP, et al. *Tsukamurella tyrosi-nosolvens* intravascular catheter-related bacteremia in a haematology patient: a case report. *Eur Rev Med Pharmacol Sci*. 2011;15(11):1343-1346.
3. Kurosawa S, Sekiya N, Doki N, et al. The emergence of rare nocardiosis following allogeneic hematopoietic stem cell transplantation in the era of molecular taxonomy. *Int J Infect Dis*. 2019;89:154-162.
4. Zhang L, Yang Y, Huang S. Disseminated *Nocardia farcinica* infection in a patient with EGPA receiving immunotherapy. *Lancet Infect Dis*. 2021;21(1):148.
5. Senard O, Blanot S, Jouvion G, et al. Fulminant *Nocardia* due to a multidrug-resistant isolate in a 12-year-old immunocompetent child. *Pediatrics*. 2018;141(2):e20163131.
6. Muggia VA, Puius YA. *Nocardia ignorata* infection in heart transplant patient. *Emerg Infect Dis*. 2020;26(11):2788-2789.
7. Chen YC, Lee CH, Chien CC, Chao TL, Lin WC, Liu JW. Pulmonary nocardiosis in southern Taiwan. *J Microbiol Immunol Infect*. 2013;46(6):441-447.
8. Coussement J, Lebeaux D, El Biri N, et al. *Nocardia* polymerase chain reaction (PCR)-based assay performed on bronchoalveolar lavage fluid after lung transplantation: a prospective pilot study. *PLoS One*. 2019;14(2):e0211989.
9. Troumani Y, Touhami S, Beral L, David T. Corneal *Nocardia* mistaken for fungal infection. *J Fr Ophtalmol*. 2015;38(1):e7-e9.
10. Wang A, Xu Q, Wang Y, Liao H. Orbital and intracranial *Nocardia farcinica* infection caused by trauma to the orbit: a case report. *BMC Infect Dis*. 2019;19(1):953.
11. Gu W, Miller S, Chiu CY. Clinical metagenomic next-generation sequencing for pathogen detection. *Annu Rev Pathol*. 2019;14:319-338.
12. Jiao M, Deng X, Yang H, Dong J, Lv J, Li F. Case report: a severe and multi-site *Nocardia farcinica* infection rapidly and precisely identified by metagenomic next-generation sequencing. *Front Med*. 2021;8:669552.

| Clinical laboratory test | Reference value of normal subjects | Patient | Unit |
|-------------------------|------------------------------------|---------|------|
| HBsAg                  | Negative (−)                       | Negative (−) |
| Hepatitis B surface antibody | Negative (−)                     | Negative (−) |
| HBeAg                  | Negative (−)                       | Negative (−) |
| HBeAb                  | Negative (−)                       | Negative (−) |
| Anti-HBC               | Negative (−)                       | Negative (−) |
| HCV antibody           | Negative (−)                       | Negative (−) |
| HIV-1+2 antibody+P antigen | Negative (−)                     | Negative (−) |
| TRUST                  | Negative (−)                       | Negative (−) |
| TP-Ab                  | Negative (−)                       | Negative (−) |
| MP-IgM                 | Negative (−)                       | Negative (−) |
| DNA of *Mycobacterium tuberculosis* | Negative (−)               | Negative (−) |
| Galactomannan (GM)     | Negative (−)                       | Negative (−) |
| 1-3-β-D glucan         | 0–60                               | 58.13    | pg/ml |
| Antistreptolysin-O (ASO) | 0.0–116.0                        | 74.5     | IU/ml |
| High-sensitivity C-reactive protein | 0.0–8.0                         | 87.2     | mg/L  |

**TABLE 2** Serum-infected markers of the patient
13. Lin J, Wu XM, Peng MF. Nocardia cyriacigeorgica infection in a patient with pulmonary sequestration: a case report. World J Clin Cases. 2021;9(10):2367-2372.

14. Qin L, Zhang FZ, Yang TY, Tao XF, Tang LF. Pulmonary Nocardia infection in a child with idiopathic pulmonary hemosiderosis. BMC Pulm Med. 2021;21(1):182.

15. Abu-Gazala M, Engel A, Stern A, Guralnik L. An unusual case of nocardiosis presented as a mediastinal mass in an immunocompetent patient. Am J Respir Crit Care Med. 2014;189(4):492-493.

16. Molina A, Winston DJ, Pan D, Schiller GJ. Increased incidence of Nocardial infections in an era of Atovaquone prophylaxis in allo- geneic hematopoietic stem cell transplant recipients. Biol Blood Marrow Transplant. 2018;24(8):1715-1720.

17. Coussement J, Lebeaux D, van Delden C, et al. Nocardia infection in solid organ transplant recipients: a multicenter European case-control study. Clin Infect Dis. 2016;63(3):338-345.

18. Lafont E, Marciano BE, Mahlaoui N, et al. Nocardiosis associated with primary immunodeficiencies (Nocar-DIP): an International retrospective study and literature review. J Clin Immunol. 2020;40(8):1144-1155.

19. Wang T, Jia Y, Chu B, Liu H, Dong X, Zhang Y. Nocardiosis in kidney disease patients under immunosuppressive therapy: case report and literature review. Int J Med Sci. 2019;16(6):838-844.

20. Kurien BT, Mathews SA, Scofield RH. Can low dose diagnostic dental radiation trigger Sjögren’s syndrome? Med Hypotheses. 2007;69(5):995-1000.

21. Baer AN, Gottenberg J-E, St Clair EW, et al. Efficacy and safety of abatacept in active primary Sjögren’s syndrome: results of a phase III, randomised, placebo-controlled trial. Ann Rheum Dis. 2021;80(3):339-348.

22. Sharon Y, Cui D, Akpek EK, Chu DS. Cicatrizing conjunctivitis as an uncommon manifestation of primary Sjögren’s syndrome. Ocul Surf. 2020;19:38-42.

How to cite this article: Peng Y, Dong X, Zhu Y, Lv H, Ge Y. A rare case of pulmonary nocardiosis comorbid with Sjögren’s syndrome. J Clin Lab Anal. 2021;35:e23902. https://doi.org/10.1002/jcla.23902