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ABOUT COVER

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The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

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CASE REPORT

Interstitial pneumonia combined with nocardia cyriacigeorgica infection: A case report

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Abstract

BACKGROUND

Nocardia infection is a relatively uncommon disease, with no reports among patients with interstitial pneumonia. Due to its atypical clinical symptoms and chest computed tomography (CT) findings and the frequent yielding of negative results by conventional cultures, it poses challenges for timely diagnosis and treatment.

CASE SUMMARY

A 63-year-old female patient presented to our hospital in July 2022 with a 3-mo history of intermittent cough and poor appetite, accompanied by a 2-wk long duration of headaches. She had a previous medical history of interstitial pneumonia and was on oral prednisone and cyclosporine. Chest CT revealed the presence of newly developed round nodules. The diagnosis of *Nocardia cyriacigeorgica* infection was confirmed through metagenomic next-generation sequencing (mNGS) performed on bronchoalveolar lavage fluid. Targeted anti-infection therapy was initiated, resulting in symptom improvement and radiological resolution, further validating the mNGS results.

CONCLUSION

Nocardia cyriacigeorgica infection is a clinically rare condition that is primarily observed in immunocompromised patients. Its clinical and radiological manifestations lack specificity, but mNGS can aid in rapidly obtaining pathogenic information. Early initiation of targeted antimicrobial therapy based on mNGS results can improve patient prognosis.

Key Words: Interstitial pneumonia; Nocardia cyriacigeorgica infection; Literature review;

Case report

Core Tip: In patients with interstitial pneumonia receiving oral steroids and immunosuppressants, the presence of new nodules, masses, or cavitary lesions should raise suspicion of concurrent Nocardia infection. In addition to routine examinations and tests, metagenomic next-generation sequencing can provide rapid pathogen identification, facilitating early targeted antimicrobial therapy and ultimately improving patient outcomes.

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INTRODUCTION

Nocardia is an opportunistic pathogen commonly found in immunocompromised patients[1]. Currently, over fifty species of Nocardia have been identified[2], including *Nocardia asteroides*, *Nocardia brasiliensis*, *Nocardia farcinica*, and *Nocardia otitidiscaviarum*. These species constitute the main causative agents of human diseases. Given that inhalation is the primary route of exposure, clinical infections often manifest as pulmonary nocardiosis. *Nocardia cyriacigeorgica* is a relatively uncommon pathogen[3] and is observed in organ transplant recipients, individuals on prolonged corticosteroid therapy, and patients with various chronic lung diseases[4,5]. However, cases of *Nocardia cyriacigeorgica* infection combined with interstitial pneumonia have not yet been documented. In this study, we report a case of a patient diagnosed with interstitial pneumonia and concurrent pulmonary *Nocardia cyriacigeorgica* infection at the Second Hospital of Nanjing, China. By reviewing the relevant literature, we aim to enhance the understanding of interstitial pneumonia concomitant with pulmonary Nocardia infection.

CASE PRESENTATION

Chief complaints

A 63-year-old female patient was admitted in July 2022 with intermittent cough and poor appetite for three months, accompanied by two weeks of headache.

History of present illness

The patient had experienced paroxysmal cough without significant sputum production since April 2022, and the cough initially went unnoticed. Subsequently, the aforementioned symptoms recurred intermittently. In early June 2022, the patient sought outpatient care at a tertiary hospital in Nanjing, where chest computed tomography (CT) indicated interstitial pneumonia, and rheumatologic autoantibody testing yielded positive results for anti-Sjogren's syndrome A. A diagnosis of interstitial pneumonia associated with Sjögren's syndrome was made, and treatment with prednisone (30 mg qd) and cyclosporine (75 mg, bid) was initiated. The patient's cough improved gradually following treatment. A follow-up CT on July 8, 2022 showed marked absorption of interstitial pneumonia, with a newly developed circular nodule in the right upper lobe measuring approximately 22 mm × 21 mm. However, a week later, the patient developed a fever, with a peak temperature of 39.2 °C, prompting her visit to our hospital.

History of past illness

The patient had no significant past medical history.

Personal and family history

The patient had no significant personal history, reproductive history, or family history.

Physical examination

On admission, the patient's vital signs were as follows: temperature 36.5 °C, pulse rate 105 beats/min, respiratory rate 18 breaths/min, blood pressure 120/83 mmHg, and SpO_2 94% (without oxygen supplementation). The patient was alert, breathing normally, without cyanosis of the lips, and the patient had no superficial lymph node enlargement. Decreased breath sounds were auscultated in the right upper lung, while no crackles or wheezes were detected in either lung. No abnormalities were observed on cardiac auscultation or abdominal palpation, and there was an absence of lower extremity oedema and pathological reflexes.

Laboratory examinations

The highly C-reactive protein (CRP) level was > 10.00 mg/L. Routine blood tests were as follows: white blood cell count 6.00 × 10^9/L, neutrophil percentage (N%) 80.6%, absolute lymphocyte count 0.83 × 10^9/L, lymphocyte percentage (L%) 13.8%, haemoglobin 133 g/L, and platelet count 143 × 10^9/L. Biochemical parameters included total bilirubin 22.7 μmol/L, direct bilirubin 12.5 μmol/L, alanine aminotransferase 46.9 U/L, albumin 29.4 g/L, and globulin 29.9 g/L. The lymphocyte subset counts were as follows: $CD4^+$ T cells 83 cells/μL and $CD8^+$ T cells 601 cells/μL. Rheumatologic autoantibody tests yielded positive results for antinuclear antibodies. In addition, tumour marker tests, sputum fungal and bacterial cultures, acid-fast bacilli smears, galactomannan (GM) tests, beta-glucan (G) tests, cryptococcal antigen qualitative assays, tuberculosis infection T-cell assays, and respiratory pathogen IgM screening all yielded negative results.

Imaging examinations

Lesion changes occurred on chest CT at different periods (Figure 1).

FINAL DIAGNOSIS

The patient was diagnosed as an interstitial pneumonia combined with Nocardia cyriacigeorgica infection.

TREATMENT

The patient was initiated on treatment with prednisone 15 mg/d orally for Sjögren's syndrome and moxifloxacin 0.4 g/d intravenously for empirical broad-spectrum antibacterial therapy. Voriconazole was added (initial dose 360 mg bid, maintenance dose 240 mg bid) for empirical antifungal prophylaxis. Considering nutritional risk (NRS2002 score of 3, MNA-SF score of 5), oral nutritional supplementation was administered as oral nutrition supplements. The patient also received symptomatic treatments such as nebulization, hepatoprotection, and gastric protection.

Despite the initial treatment, the patient continued to experience fever. A follow-up CT on July 15, 2022 indicated a block-shaped high-density shadow with cavitation formation in the anterior segment of the right upper lobe. The lesion (48 mm × 47 mm) had significantly progressed compared to July 8th, with interstitial inflammation observed in both lungs. Given the patient's low $CD4^+$ T-cell count and the history of long-term oral corticosteroid and immunosuppressant use, as well as chest CT showing shadow, compound sulfamethoxazole (SMZ) tablets (2 tablets/1.6 g SMZ bid) and carpofungin (50 mg/d) were used for pneumocystis pneumonia prevention. Meanwhile, percutaneous lung puncture was recommended to identify the pathogen, but the patient declined. Consequently, fibreoptic bronchoscopy examination and BAL were performed. The regular bronchoalveolar lavage fluid (BALF) test results (fungal and bacterial cultures, acid-fast staining for tuberculosis, G/GM test, and tumour cell exfoliation) were all negative. Metagenomic next-generation sequencing (mNGS) of the BAL fluid indicated the presence of *Nocardia cyriacigeorgica*, with a sequence count of 286487 and a relative abundance of 28.20%. Consequently, targeted antimicrobial therapy was promptly initiated. Moxifloxacin and carbapenems were discontinued, and compound sulfamethoxazole tablets were escalated to 3 tablets/2.4 g SMZ tid, complemented by the addition of third-generation cephalosporins for enhanced antimicrobial coverage.

OUTCOME AND FOLLOW-UP

After 14 d of hospitalization, the patient's cough, headache, and fever had disappeared, and her diet had returned to normal. Follow-up blood tests showed highly sensitive CRP < 10.00 mg/L, white blood cell count 5.17 × 10^9/L, neutrophil percentage 45.5%, absolute lymphocyte count 2.5 × 10^9/L, and lymphocyte percentage 48.3%. The lymphocyte subset counts were as follows: $CD4^+$ T cells 158 cells/μL and $CD8^+$ T cells 2134 cells/μL. CT scans indicated a reduction in the size of the right upper lung lesion compared to previous images. Subsequently, the patient was discharged and continued oral administration of complex sulfamethoxazole tablets and prednisone. Regular outpatient follow-up was recommended.

DISCUSSION

Nocardia is a filamentous bacterium characterized by its aerobic, gram-positive, and weakly acid-fast staining properties, and it belongs to a genus within the Actinobacteria phylum. It is widely distributed in natural environments, particularly in soil and humus, frequently causing opportunistic infections in immunocompromised patients. However, approximately one-third of Nocardia infections can also occur in immunocompetent individuals[1].

Patients with pulmonary nocardiosis typically lack specific symptoms, leading to diagnostic challenges. Definitive diagnosis often relies on histopathological examinations and/or culturing. Identification through mass spectrometry following bacterial cultivation serves as the "gold standard" for distinguishing different subtypes of Nocardia[6]. Sputum is the most commonly used respiratory sample for Nocardia isolation, and BALF or percutaneous needle aspiration

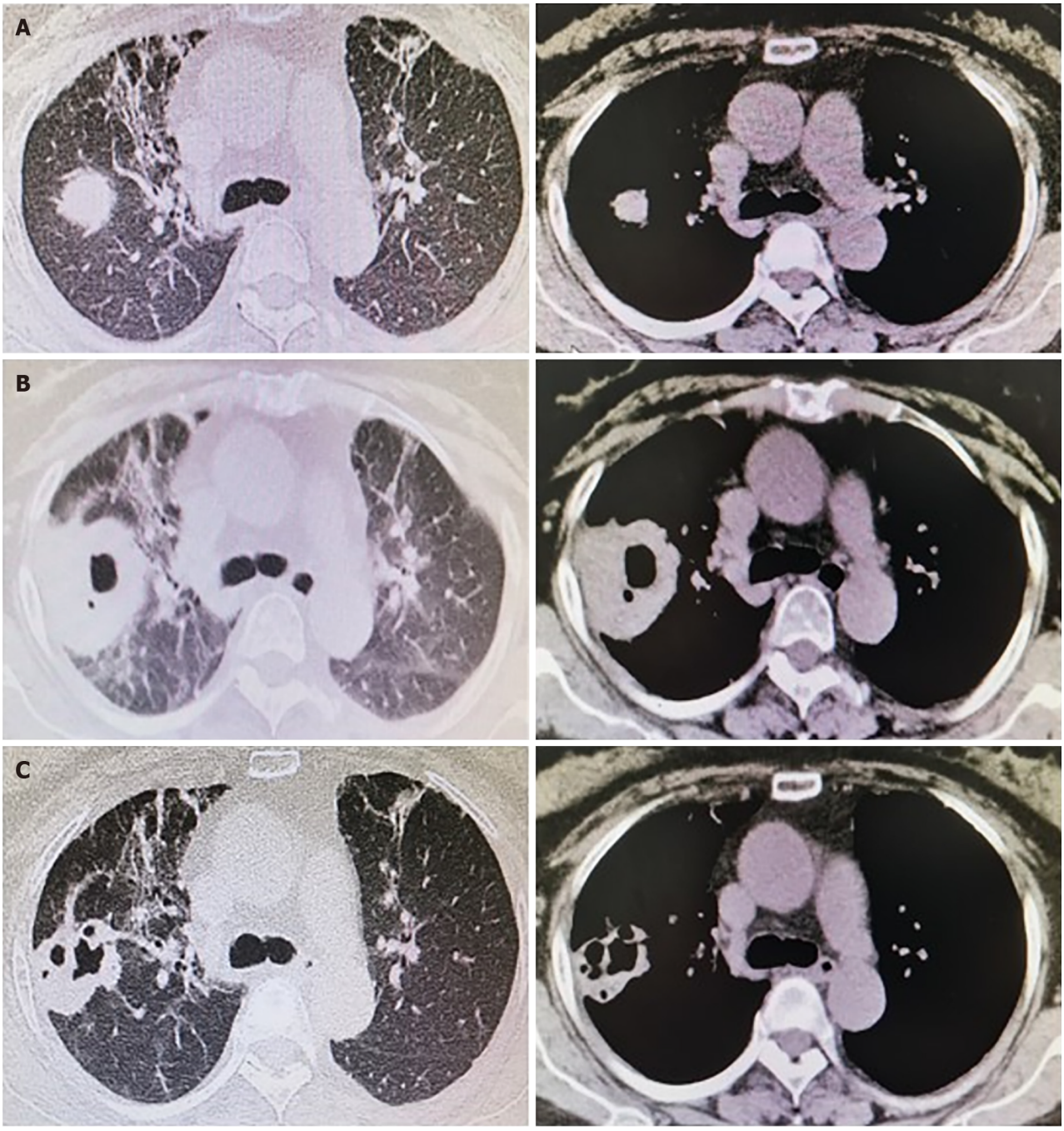

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Figure 1 Changes in chest computed tomography. A: Chest computed tomography (CT) on July 8, 2022. A right upper lobe pulmonary mass measuring 2.2 cm × 2.2 cm, with relatively smooth margins; B: Chest CT on July 15, 2022. A right upper lobe pulmonary mass measuring 4.8 cm × 4.7 cm, with internally regular cavities; C: Chest CT on July 28, 2022. A right upper lobe pulmonary mass measuring 2.7 cm × 3.3 cm, with multiple small cavities within.

biopsy is also used as an invasive method for obtaining samples[7]. BALF offers advantages such as simplicity of operation, minimal specimen contamination, and relatively reliable results. In contrast, percutaneous lung puncture biopsy carries the risk of pneumothorax or bleeding. In this case, the patient was more willing to undergo less invasive bronchoalveolar lavage through fibreoptic bronchoscopy.

However, Nocardia species are slow-growing and difficult to isolate, requiring extended incubation periods of up to 14 d. Conventional cultures often yield false-negative results, leading to a delayed diagnosis and a delay in the initiation of targeted treatment, and subsequently contribute to disease spread and increased morbidity and mortality rates[8,9]. mNGS is a highly sensitive, high-throughput detection method that identifies present microorganisms and their proportions by aligning all nucleic acids in the sample to a reference genome[10,11]. Compared to traditional culture methods, mNGS has a shorter detection period and higher sensitivity, especially for traditionally culture-negative samples[12,13]. By sequencing deoxyribonucleic acid or RNA fragments, theoretically all infectious pathogens present in clinical specimens can be identified, particularly for rare and atypical complex infectious diseases[14]. Moreover, the detection rate is not compromised by prior antibiotic treatment[15]. In this case, traditional pathogen testing failed to

identify a definitive pathogen. However, BALF mNGS quickly detected *Nocardia cyriacigeorgica*, leading to timely adjustments in the patient's antimicrobial regimen and significant clinical improvement, as evidenced by radiographic absorption.

Nocardia infection is a relatively rare cause of pneumonia, primarily occurring in immunodeficient patients, particularly those with cellular immune defects. In this case, the use of cyclosporine prior to infection is one of the risk factors, as cyclosporine specifically suppresses T-cell function and increases susceptibility to Nocardia infection. The use of glucocorticoids also contributed to the susceptibility in this patient, which was also observed in chronic obstructive pulmonary disease patients[1]. Beyond chronic obstructive pulmonary disease, patients with structural lung diseases such as bronchiectasis, allergic bronchopulmonary aspergillosis, and nontuberculous mycobacterial lung disease can also develop concurrent Nocardia infections[5,16,17]. However, Nocardia infections that occur in patients with interstitial pneumonia are relatively uncommon. Odashima *et al*[18] analysed pathogens in 46 patients with idiopathic pulmonary fibrosis complicated with chronic lung infection and detected Nocardia infection in only one patient. Farina *et al*[19] collected data from 30 Nocardia infection cases, and only one patient had lung fibrosis among them.

Pulmonary Nocardia infection mainly exhibits a subacute or chronic course, while cases with an acute presentation, similar to the one in this instance, are rare. Clinical symptoms are nonspecific and include fever, cough, chest pain, night sweats, and weight loss. Common CT findings of pulmonary Nocardia infection include consolidation, nodules, and masses, with a predilection for the upper lobes. Cavitary lesions may develop in approximately 33% of patients, and a minority may experience chest wall involvement. Enlargement of the mediastinal and hilar lymph nodes is not a typical feature of pulmonary nocardiosis[20]. The combination of these findings with nonspecific clinical symptoms often leads to misdiagnoses such as tuberculosis infection, fungal infection, vasculitis, or malignancy[21-23]. In this case, the patient's rapidly progressing nodular opacities and cavities posed a diagnostic challenge, as they were difficult to distinguish from pulmonary aspergillosis. The diagnosis was eventually achieved through BALF mNGS examination, leading to targeted antimicrobial therapy and significant clinical improvement, with radiographic evidence of absorption, further validating the mNGS results.

Sulphonamides are the first-line treatment choice for Nocardia infections. Amikacin, imipenem, and linezolid are also alternative options. Carbapenems and linezolid have been found to be effective against all pathogenic Nocardia species. Immunodeficient or critically ill patients often require combination therapy. The duration of Nocardia infection treatment is generally more than 6 mo, depending on disease severity, immunodeficiency, and clinical course. Patients with central nervous system involvement may require extended treatment[1]. Some cases involving lung abscesses and empyema may require surgical interventions such as drainage and debridement[23]. Compound SMZ, a combination of sulfamethoxazole and trimethoprim (TMP), is the most commonly employed oral sulphonamide. TMP acts as an enhancer of sulfamethoxazole, amplifying its therapeutic effects while concurrently mitigating potential adverse reactions. In fact, in this particular case, the patient experienced relief in body temperature and symptoms upon receiving prophylactic treatment with compound SMZ against *Pneumocystis pneumonia*, thus substantiating the accuracy and timeliness of both the diagnosis and treatment.

CONCLUSION

In summary, in patients with interstitial pneumonia receiving oral steroids and immunosuppressants, the presence of new nodules, masses, or cavitary lesions should raise suspicion of concurrent Nocardia infection. In addition to routine examinations and tests, mNGS can provide rapid pathogen identification, facilitating early targeted antimicrobial therapy and ultimately improving patient outcomes.

FOOTNOTES

Author contributions: All authors examined the patient; Zhuang Y and Gu Y participated in the discussion for the treatment and gave important suggestions; Qi DD and Chen Y drafted the manuscript; All authors critically revised the paper for important intellectual content, and all authors approved the final version of the manuscript.

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