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CASE REPORT

Disseminated *Nocardia* Infection in an Old Male Patient with Nephrotic Syndrome

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SUMMARY

Background: **Nocardia infection is a very rare bacterial infection caused by Gram-positive, aerobic nocardia species. However, in recent years, it has become a serious infection in immunocompromised patients. Earlier diagnosis plays a pivotal in the effective treatment of nocardia infection.**
Methods: **In this study, we reported a 65-year-old male patient with nephrotic syndrome who had disseminated abscesses in the lungs, right lower limb, and right cheek.**
Results: **Bacterial culture from these lesions confirmed the presence of nocardia. Timely administration of sensitive antibiotics resulted in a quick recovery for this patient.**
Conclusions: **Nocardia infection should be considered in the differential diagnosis of infectious lesions, especially when a patient has multiple abscesses and an underlying disorder in which the immune function of the patient may be compromised.**
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KEY WORDS

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INTRODUCTION

Nocardia infection, also called nocardiosis, is an uncommon opportunistic infectious disease caused by *Nocardia* which are aerobic, filamentous gram-positive, atypical acid-fast bacteria [1,2]. *Nocardia* is common in the environment and can be found in water, air, soil, and dust all over the world [3]. Nocardiosis can occur by direct skin inoculation with or inhalation of *Nocardia* [4]. *Nocardia* can cause lung, skin, or systemic infections [5]. Most nocardia infections occur in immunocompromised populations [6]. Nephrotic syndrome is a series of symptoms caused by kidney injury. It includes protein in the urine, low levels of albumin, high levels of lipids, and significant swelling [7]. Patients with nephrotic syndrome are at high risk of getting bacterial infections including *Nocardia* because of the compromised immunity due to the usage of steroids [8]. *Nocardia* might induce multisystem infections that can be life-threatening, so prompt diagnosis and appropriate treatment are critical. Here, we report a case of pulmonary and systemic nocardiosis caused by *Nocardia* in an old patient with nephrotic syndrome.

CASE REPORT

A 65-year-old male presented with repeated edema of both lower extremities for half a year and right chest pain accompanied by cough for more than two weeks. He has had hypertension for 10 years and had a cerebral hemorrhage 10 years ago. He was diagnosed with primary nephrotic syndrome (membranous nephropathy stage II) 3 months ago and is now taking prednisone and tacrolimus. The patient had no history of diabetes or coronary heart disease. No history of infection such as hepatitis B or tuberculosis; no history of surgery, drug or food allergy. He had a history of injury due to falling from a bicycle two weeks ago, followed by a gradually enlarged lump in his right lower extremity. No history of smoking or drinking. T 36°C, P 84 bpm, R 18 bpm, BP 115/67 mmHg. The patient's breathing was stable, the chest was normal, the percussion of both lungs was clear, the breath of both lungs was coarse, and no obvious dry or wet rales were detected. A 4 cm x 3 cm mass was found in the right lower extremity with tenderness (Figure 1A), however, there was no redness or swelling on the local skin. Other positive findings included ulceration on his lip and the right cheek with a scab on its surface. Examination of other systems was negative. WBC (white blood cell) 28.89 x 10^9/L with 97.83% neutrophils, HGB 106 g/L, PLT 358.8 10^9/L, BUN 19.2 mmol/L, Cr 188 μmol/L, albumin 25.5 g/L, 24 hours urinary protein 1773.5 mg. The patient's sputum culture showed no growth of pathogenic bacteria. The color Doppler ultrasonography revealed a 39 mm x 14 mm x 23 mm hypoechoic zone in the muscle tissue of the right lower extremity with clear and regular perimeter indicating a possible hematoma. Chest CT showed the occupying lesion of the right lung (Figure 1B), pericardium, and a small amount of pleural effusion on both sides. CT results of the skull suggested multiple lacunar infarcts in the basal ganglia region on both sides and degenerative changes. CT of liver, gallbladder, pancreas, and spleen showed no obvious abnormality. Thus, the patient was diagnosed as right lung space occupying lesion, mass on right lower extremity, chronic kidney disease stage 3, nephrotic syndrome (membranous nephropathy), hypertension stage 3, multiple lacunar cerebral infarction. The patient was initially treated with piperacillin sulbactam combined with levofloxacin.

Biopsy of the lung lesion revealed granulomatous inflammation (Figure 1C). *Nocardia* were identified from lung biopsy tissue. *Nocardia* were also identified from the puncture fluid from the mass in the right lower extremity and cheek secretions (Figure 1D). Thus, the final diagnoses were disseminated nocardiosis, chronic kidney disease stage 3, nephrotic syndrome (membranous nephropathy), hypertension stage 3, and multiple lacunar infarcts. SMZ was added for treatment. Based on GFR, the following drugs were used: cefotaxime 2 g q12h + levofloxacin 0.2 qd + SMZ 1 q8h. After treatment, overall, the patient's cough, expectoration, and chest pain were significantly relieved. WBC showed a continuous downward trend, with increased albumin, increased creatinine clearance, and decreased creatinine. Chest CT (Figure 1E) and superficial color Doppler ultrasound of the mass in the right lower extremity were significantly improved. The patient was discharged with medication including prednisone 20 mg Po qd, minocycline 100 mg Po Bid, and SMZ 1# Po q6h.

DISCUSSION

Nocardiosis is a rare local or systemic suppurative disease caused by *Nocardia* which can spread to all organs of the body through the blood [9]. Pulmonary infection is the main lesion. Tissue destruction and abscess formation are also characteristics of nocardiosis.

Nocardiosis can occur by direct skin inoculation or inhalation [4]. Most *Nocardia* infections occur in immunocompromised populations [6]. *Nocardia* induces multisystem infections that can be life-threatening, so prompt diagnosis and appropriate treatment are critical. Cellular immunity is the body's main defense mechanism against nocardiosis. The occurrence of nocardiosis can be caused by a variety of diseases that lead to low or defective cellular immunity [9]. Typical nocardial abscesses tend to fuse, are less prone to encapsulation and fibrosis, and are more likely to form intrapulmonary spread from primary lung foci, forming multiple abscesses of varying sizes [2]. Occasionally, granulomatous formation is seen.

Sixty percent to eighty percent of people infected with *nocardia* have underlying diseases that affect immune function [10]. Long-term use of glucocorticoids, the use of immunosuppressants and other basic diseases such as lung diseases, tumors, diabetes, or connective tissue diseases are three main reasons. The study of pulmonary nocardiosis found that about 85% of the patients had immunodeficiency and pulmonary basic diseases, and about 15% of the patients had normal immune function, indicating that occurrence with normal immune function is rare [11]. The course of treatment for patients with normal immune function and no central nervous system infection was 6 - 12 months [12]. Patients with disseminated infection and immune deficiency should be treated with sulfonamides as the center, combined with quinolones, carbapenems, and linezolid [13]. Single drug maintenance therapy can be used after the clinical symptoms are relieved, and the course of treatment should be more than 12 months to reduce the recurrence rate of the disease [14]. The prognosis of nocardiosis is

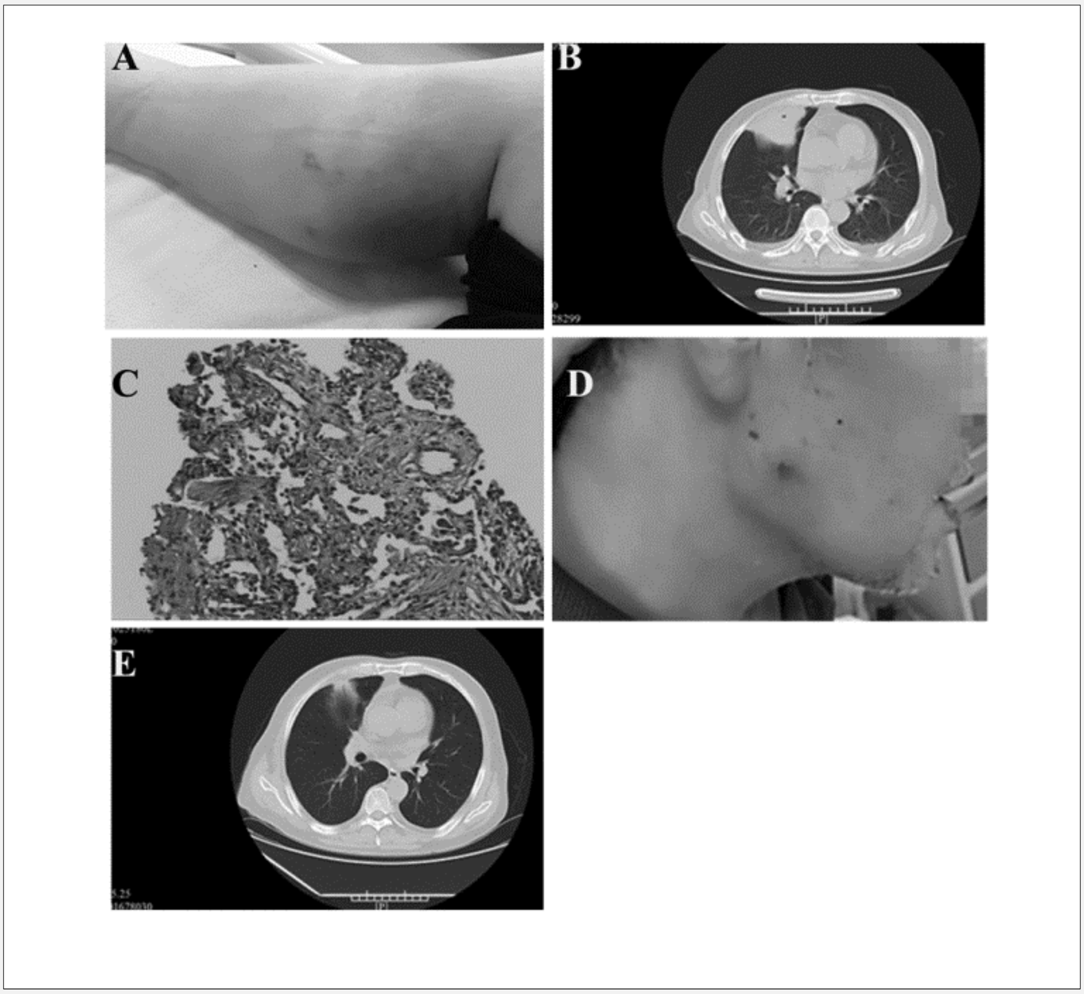

Figure 1. A - The mass in the right extremity. B - Chest CT before treatment. C - Microscopic image for biopsy of the mass in the right lung. D - The right cheek lesion. E - Chest CT after treatment.

related to the timely diagnosis rate and the immune status of patients [15]. If timely treatment is given, the cure rate of nocardiosis is about 90%. The death rate of patients with central nervous system involvement is 50% [16]. Clinicians should be aware that even patients with strong immunity, especially those with underlying lung disease, can be infected with PN, and resistance to PN in lung disease, aging, pulmonary aspergillosis, and TMP-SMZ is associated with an increased risk of death. Not using TMP-SMZ based on inaccurate drug susceptibility results may be a real risk factor for overall mortality, rather than TMP-SMZ resistance [17].

The clinical manifestations and imaging findings of pulmonary infection with *nocardia* are not specific, so misdiagnosis and missed diagnosis are common. Therefore, more attention should be paid to the acid-fast staining of the sputum smear. Nephrotic syndrome is the most common basic disease, and long-term use of hormones, immunosuppressive agents, and organ transplantation are the high-risk groups for nocardiosis [18]. The treatment of pulmonary nocardiosis is mainly a combination of sulfonamides. At present, due to the high drug resistance rate of sulfonamides, the combination of carbapenems and linezolid are two drugs with high sensitivity [2]. Currently, amikacin, carbapenems, ceftriaxone, linezolid, minocycline, moxifloxacin, and levofloxacin are available for combined treatment. For patients requiring hormone and immunosuppressive therapy for basic diseases complicated with nocardiosis infection, if the immunosuppressive therapy for basic diseases is not allowed to stop, the dose of such drugs should be reduced as far as possible, and the treatment time of

TMP-SMZ should be extended to prevent recurrence of the disease. On the other hand, we should not neglect the reasonable treatment and necessary supportive therapy for the basic diseases while resisting infection. Due to the high fatality rate of disseminated nocardiosis, patients with low immunity and multiple abscesses should be vigilant against nocardiosis infection when conventional drug treatment fails [6]. Early etiological diagnosis, early reasonably adequate dosage and sufficient course of treatment are the keys. For patients requiring immunosuppressive agents, the underlying disease should be treated appropriately. In this case, due to the high suspicion of nocardiosis, we conducted an empirical treatment. The patient received anti-infection and hormone anti-inflammatory treatment according to the creatinine clearance rate of the patient. SMZ was gradually increased and the hormone dose was gradually reduced. Early diagnosis and treatment are the key to curing these patients and avoiding long-term antimicrobial therapy.

CONCLUSION

In summary, for a patient taking immunosuppressive agents for a long time, if multiple abscesses all over the body are identified, disseminated nocardiosis should be considered.

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Declaration of Interest:
The authors have nothing to disclose.

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