Clinical Case Report

Medicine®

OPEN

Pulmonary and cutaneous infection caused by *Nocardia farcinica* in a patient with nephrotic syndrome

A case report

Ning Zhu, MD[a,*], Yuan Zhu, MD[b], Yi Wang, MD[a], Shaoshao Dong, MD[b]

Abstract

Rationale: Nocardia species is known as conditional pathogenic bacteria. Disseminated infection caused by Nocardia species is rare and occurs primarily in immunosuppressed patients. Signs and symptoms of this infection are frequently nonspecific making early diagnosis and treatment difficult.

Patient concerns: We report a case of subcutaneous and pulmonary nocardiosis due to *Nocardia farcinica* (*N farcinica*) in a patient with nephrotic syndrome who is undergoing long-term corticosteroid therapy. In this patient, systemic and pulmonary symptoms (usually found in nocaria infection) such as fever, cough, and expectoration were absent.

Diagnoses: Early diagnosis was made by pus culture from subcutaneous abscesses and 16S rRNA gene sequencing, which confirm the diagnosis of *N farcinica* infection.

Interventions: The patient was treated with combination therapy of cefatriaxone and trimethoprim-sulfamethoxazole (TMP-SMX) for 2 weeks, and the treatment with TMP-SMX continued to 6 months.

Outcomes: The abscesses were cured in 4 weeks and a lesion in the upper lobe of left lung resolved in 3 months.

Lessons: This case indicates that disseminated infection due to *N farcinica* could occur in patients with nephrotic syndrome, even during the period of maintenance therapy with a low-dose corticosteroid and common signs and symptoms of infections could be absent.

Abbreviations: *N farcinica* = *Nocardia farcinica*, TMP-SMX = trimethoprim-sulfamethoxazole.

Keywords: nephrotic syndrome, *Nocardia farcinica*, pulmonary and cutaneous infection

1. Introduction

Nocardia infections are uncommon and occur mostly in patients receiving immunosuppressive therapy, organ transplant recipients, or patients infected with human immunodeficiency virus (HIV).[1–3] Recognition of clinical isolates is vital because Nocardia species differ in the clinical spectrum of the disease they can cause and their susceptibility to antimicrobial agents.[4] Patients with nephrotic syndrome are at a high risk of infections, for example, Cryptococcus,[5] cytomegalovirus,[6] toxoplasmosis,[7] often augmented by the need for immunosuppressive therapy. Here, we present an unusual case of *Nocardia farcinica* in a patient with nephrotic syndrome on long-term corticosteroid therapy.

1.1. Case presentation

This case report has been approved by the ethics committee of Wenzhou People's Hospital. A 60-year-old man was admitted to Wenzhou People's Hospital with a 1-week history of a subcutaneous abscess on his left lower limb. He reported no constitutional symptoms or cough and had not incurred any trauma to his leg. On admission, the patient was tachycardic but not in septic shock and had a normal systems examination. The largest subcutaneous abscess on his left lower limb was 9 cm*10 cm and was warm and tender with intact overlying skin. He later developed further abscesses on his buttock, which were 3 cm*3 cm in diameter.

The patient had a background history of idiopathic membranous nephropathy diagnosed on renal 14 months before admission. He was initially treated with oral methylprednisolone and Tacrolimus and achieved a complete remission. However, he later relapsed and was treated with intravenous (IV) methylprednisolone and oral Tacrolimus. Due to a lack of clinical response cyclophosphamide, he was started on oral Cyclophosphamide with an accumulated dosage of approximately 8 g. Subsequently,

Editor: Ikechi Okpechi.

The authors confirm that there are no conflicts of interests.

[a] Department of Cardiology, [b] Department of Nephrology, The Third Clinical College of Wenzhou Medical University, Wenzhou People's Hospital, Wenzhou, Zhejiang Province, PR China.

[*] Correspondence: Ning Zhu, The Third Clinical College of Wenzhou Medical University, Wenzhou People's Hospital, No. 57 Canghou Street, Wenzhou 325000, Zhejiang Province, PR China (e-mail: zhuningccc@126.com).

Medicine (2017) 96:24(e7211)

Received: 12 January 2017 / Received in final form: 13 May 2017 / Accepted: 16 May 2017

http://dx.doi.org/10.1097/MD.0000000000007211

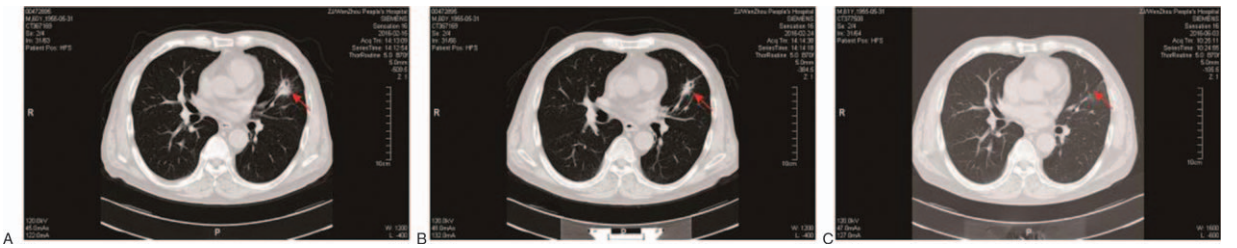

Figure 1. Changes of the lesion after treatments. (A) The lesion in the upper lobe of left lung. (B) The lesion after treatment with TMP-SMX for 4 weeks. (C) The lesion disappeared following treatment for 4 months.

TCCCACAAGGGGTTAGGCCACCGGCTTCGGGTGTTACCGACTTTCATGACGTGACGGGCGGTGTGTACAAGGCCCGGGAACGTATTCACCGCAGCGTTGC
TGATCTGCGATTACTAGCGACTCCAACTTCACGGGGTCGAGTTGCAGACCCCGATCCGAACTGAGACCGGCTTTAAGGGATTGGCTCCACCTCACGGTATC
GCAGCCCTCTGTACCGGCCATTGTAGCATGTGTGAAGCCCTGGACATAAGGGGCATGATGACTTGACGTCGTCCCCACCTTCCTCCGAGTTGACCCCGGCA
GTCTCCTGCGAGTCCCCGCCATAACGCGCTGGCAACACAGGACAAGGGTTGCGCTCGTTGCGGGACTTAACCCAACATCTCACGACACGAGCTGACGACA
GCCATGCACCACCTGTACACCGACCACAAGGGGGCCTACATCTCTGCAGGTTTCCGGTGCATGT

Figure 2. Gene sequence of *N farcinica* identified from the pus.

his renal disease was stable and the dose of oral methylprednisolone was slowly tapered down.

On blood tests, the total white cell count was 8.4 x 10^9/L with 85.5% neutrophils and 8.1% lymphocytes. The subset of lymphocytes was almost normal: CD3+ 72.5%, CD4+ 28.6%, CD8+ 41.9%, CD4+/CD8+ 0.68, CD19+ 4.7%. His erythrocyte sedimentation rate (ESR) was elevated at 113 mm/h and C-reactive protein (CRP) was mildly elevated at 12.2 mg/L. He was found to still be nephrotic: 24-hour urine protein was raised at 8.23 g low serum albumin 18.4 g/L and cholesterol with mild renal impairment (creatinine 131 μmol/L). A computed tomography (CT) brain scan was normal while patient's pulmonary CT scan showed an inflammatory nodule in the upper lobe of left lung (Figure 1A). Ultrasound of abscesses revealed subcutaneous anechoic lesions. Blood cultures were sterile.

The abscesses were drained and the patient was empirically treated with IV penicillin and oral trimethoprim-sulfamethoxazole (TMP-SMX). Culture subsequently yielded Nocardia, later identified as *N farcinica* on rRNA gene sequencing (Figure 2). Combination therapy of IV cefatriaxone (2 g/day) and oral TMP-SMX (1.92 g/d) was used according to drug sensitivity. The patient's inflammatory markers and clinical state improved and IV ceftriaxone was stopped after a 2 weeks oral. After 4 weeks, the subcutaneous abscesses disappeared and the lesion in the upper lobe of left lung had improved (Figure 1B). The patient was discharged on a 5-month course of oral TMP-SMX therapy. Oral methylprednisolone was stopped 2 months later and his nephrotic syndrome had improved. A follow-up CT after 3 months showed that the lesion in the upper lobe of left lung completely disappeared (Figure 1C) and his renal disease was stable.

2. Discussion

Nocardia farcinica is a gram-positive, partially acid-fast, methenamine silver-positive aerobic actinomycete.[8] The genus-Nocardia contains more than 100 species that have been identified by phenotypic and molecular methods and 16S RNA gene sequencing. Nocardiae are common in the environment and can be found worldwide in water, soil, dust, decaying vegetation, and organic matter. After inhalation or percutaneous inoculation, particularly in immunocompromised hosts, Nocardia can induce multisystem infection that can be life-threatening.[9]

N farcinica is characterized by higher pathogenicity [10] and also known to be resistant to multiple antibiotics.[11] Timely diagnosis of the infection is important, as appropriate treatment can be lifesaving.

On the whole, early diagnosis of *N farcinica* infections remain a challenge and treatment is often empiric. This patient's clinical presentation was atypical.[12] This may be explained by long-term corticosteroid therapy masking the symptoms and signs of infection. Because of the absence of history of percutaneous inoculation, it was assumed that the patient may had inhaled *N farcinica* initially with dissemination to the skin. The patient's blood cultures were negative, which is consistent with literature, as blood cultures for patients with Nocardia infection are rarely positive.[13] Therefore, other tests, in this case the pus culture and gene sequencing, are necessary for diagnosis.

Standard treatment for this infection includes Ceftriaxone, Cefotaxime and, more commonly, TMP-SMX. Sulfonamides have been extensively used, with good outcomes; however, some strains of Nocardia, including *N farcinica*, may be resistant.[13,14] Although the duration of therapy required remains controversial, reports in the literature recommend 6 months to 1 year in disseminated Nocardiosis.[15] In our case, the patient received the treatment of TMP-SMX for 6 months and was completely cured.

In conclusion, this is the first report of pulmonary and cutaneous infection caused by *N farcinica* in a patient with nephrotic syndrome. Our case highlights that even on maintenance immunosuppression, patients can develop opportunistic infections such as Nocardia and can present atypically. Early diagnosis and treatment is the key to curing such patients, which may also avoid prolonged antimicrobial therapy.

References

[1] Ambrosioni J, Lew D, Garbino J. Nocardiosis: updated clinical review and experience at a tertiary center. Infection 2010;38:89–97.
[2] Lebeaux D, Morelon E, Suarez F, et al. Nocardiosis in transplant recipients. Eur J Clin Microbiol Infect Dis 2013;33:689–702.
[3] Anderson M, Kuz 'niar TJ. Pulmonary nocardiosis in a patient with chronic obstructive pulmonary disease; case report and literature review. Pol Pneumonol Allergol 2012;80:565–9.

[4] Beaman BL, Beaman L. Nocardia farcinica bacteraemia presenting as a prostate abscess. Clin Microbiol Rev 1994;7:213–64.
[5] Liu Y, Qunpeng H, Shutian X, et al. Fatal primary cutaneous cryptococcosis: case report and review of published literature. Ir J Med Sci 2016;185:959–63.
[6] Lopez-Lluva MT, de la Nieta-Garcia MD, Piqueras-Flores J, et al. Chlorambucil-induced cytomegalovirus infection: a case report. J Med Case Rep 2014;8:280.
[7] Barrios JE, Duran Botello C, Gonzalez Velasquez T. Nephrotic syndrome with a nephritic component associated with toxoplasmosis in an immunocompetent young man. Colomb Med (Cali) 2012;43: 226–9.
[8] Boamah H, Puranam P, Sandre RM. Disseminated Nocardia farcinica in an immunocompetent patient. IDCases 2016;6:9–12.
[9] Schiff TA, McNeil MM, Brown JM. Cutaneous Nocardia farcinica infection in a nonimmunocompromised patient: case report and review. Clin Infect Dis 1993;16:756–60.
[10] Torres OH, Domingo P, Pericas R, et al. Infection caused by Nocardia farcinica: case report and review. Eur J Clin Microbiol Infect Dis 2000; 19:205–12.
[11] Anil KV, Deepthi A, Dilip P, et al. Nocardia farcinica brain abscess: epidemiology pathophysiology, and literature review. Surg Infect 2014; 15:640–6.
[12] 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;63:338–45.
[13] Peters BR, Saubolle MA, Costantino JM. Disseminated and cerebral infection due to Nocardia farcinica: diagnosis by blood culture and cure with antibiotics alone. Clin Infect Dis 1996;23:1165–7.
[14] Wilson JW. Nocardiosis: updates and clinical overview. Mayo Clin Proc 2012;87:403–7.
[15] Menéndez R1, Cordero PJ, Santos M, et al. Pulmonary infection with Nocardia species: a report of 10 cases and review. Eur Respir J 1997; 10:1542–6.