Research Article

Yiqing Li#, Ting Tang#, Jie Xiao, Jieyu Wang, Boqi Li, Liping Ma, Shuangfeng Xie, Danian Nie*

Clinical analysis of 11 cases of nocardiosis

https://doi.org/10.1515/med-2020-0196
received May 17, 2020; accepted February 24, 2021

Abstract: Nocardiosis is a rare, life-threatening, opportunistic, and suppurative infection. Its clinical manifestation lacks specificity, which makes early diagnosis difficult. A retrospective analysis of the clinical records of 11 patients with nocardiosis admitted to our hospital from January 2013 to November 2018 was conducted. All patients had at least one underlying disorder, such as an autoimmune disease (6/11), a blood malignancy (2/11), avascular necrosis of the femoral head (1/11), bronchiectasis (1/11), or pneumonia (1/11). The first-line treatment was trimethoprim–sulfamethoxazole (TMP–SMX); one or two additional antibiotics were given according to the drug-sensitive test. The median time from onset to treatment was 3 weeks (ranging from 1 to 9 weeks). The median duration of treatment after diagnosis was 20.5 weeks (ranging from 7 to 47 weeks). Eight patients were discharged and survived, and three patients died. This indicates that early use of TMP–SMX combined with sensitive antibiotics could improve the condition of patients and improve the cure rate (8/11). Clinically, it is necessary to consider the possibility of nocardiosis in patients with long-term use of immunosuppressants and poor response to treatment of common bacterial infections. Early diagnosis, timely treatment, and combination drug therapy are keys to improving the outcomes of patients with nocardiosis.

Keywords: Nocardia infections, immunosuppressive agents, diagnosis, therapeutics

1 Introduction

The pathogen of nocardiosis is Nocardia, which is a slow-growing gram-positive aerobic bacterium with acid-fast staining properties [1]. Nocardia is an opportunistic pathogen that can cause local or systemic suppurative infections in humans and animals, some of which are life-threatening [2]. The clinical features of nocardiosis always lack specificity, making early diagnosis difficult. The gold standard for diagnosis of Nocardia infection is based on the isolation and identification of Nocardia via 16S ribosomal ribonucleic acid (rRNA) sequencing from humoral secretions or tissues, such as blood, sputum, pus, pleural effusion, cerebrospinal fluid, and pulmonary puncture samples [3–5]. A full 2–3 weeks may lapse between specimen collection and detection of Nocardia [1,6]. Nocardia spp. can be classified into different species with the comprehensive application of biochemical techniques, including 16S rRNA PCR-based assays and multi-site sequencing analysis [3,7,8]. Because of the relatively long duration and strict requirements for Nocardia detection, gene sequencing is not always available. In our report, the strains of Nocardia in six patients could not be identified because of the limitations of the experimental conditions.

Positive results for nocardiosis are frequently followed by immediate appropriate treatment and prolonged maintenance therapy. In terms of treatment for Nocardia infection, the optimal therapeutic agent, route of administration, and duration of treatment have not been well established. Most treatments are based on the results of basic research, animal models, and recommendations from experts [7,9]. Trimethoprim–sulfamethoxazole (TMP–SMX) and linezolid have strong inhibitory effects on Nocardia in vitro [3]. TMP–SMX can be used as an initial empirical treatment [10,11]. Different strains of Nocardia have different levels of antimicrobial resistance, and some of them may be resistant to sulfonamides [12,13]. It is particularly important to identify Nocardia and perform drug-sensitive tests. In 2011, the Clinical and Laboratory Standards...
Institute M24-A2 guidelines published an approved broth-microdilution method for susceptibility testing of aerobic actinomycetes [14]. The first-line medications include TMP–SMX, oxazolidinones (linezolid), aminoglycosides (amikacin and tobramycin), carbapenems (imipenem), β-lactams (ceftriaxone and amoxicillin-clavulanic acid), macrolides (clarithromycin), quinolones (moxifloxacin, ciprofloxacin, and levofloxacin), and tetracyclines (minocycline). The second-line medications include cephalosporins (cefepime and cefotaxime) and tetracyclines (doxycycline). For patients with disseminated diseases, central nervous system (CNS) involvement, and/or severe Nocardia infection, a three-drug regimen including TMP–SMX, amikacin, and imipenem or ceftriaxone is recommended [8,15]. Although the duration of treatment for nocardial infections is unclear, 6 weeks of treatment for topical nocardiosis and 6 months to 1 year of treatment for systemic nocardiosis are recommended. The duration of treatment depends on the response to the therapy and the immune function of the patient [8,15].

In this study, we retrospectively analyzed the clinical records of patients with nocardiosis who were admitted to our hospital in the last 5 years (January 2013 to November 2018). We also reviewed the relevant literature to provide references for early diagnosis and treatment of nocardiosis.

2 Methods

In this retrospective study, 11 patients with nocardiosis from our hospital who were diagnosed with conventional phenotypic and biochemical species identification were included. Over the 5-year period from January 2013 to November 2018, demographic data (such as age, sex, underlying diseases, and risk factors), clinical manifestations, radiological investigation, pathology features, treatment, and patient outcomes were reviewed. Mixed infection was considered if evidence of infection of microorganisms other than Nocardia was found 7 days before or 7 days after the date of the nocardiosis diagnosis. The research related to human use has been approved by the Medical Ethics Committee of Sun Yat-sen Memorial Hospital.

2.1 Statistical analysis

Statistical analyses were performed using Statistical Product and Service Solutions (SPSS) Software, version 25, to calculate the median.

3 Results

3.1 Demographic data and underlying diseases

Eleven patients (seven males and four females) were diagnosed with nocardiosis (Table 1). The median age was 42 years (12–78 years). All patients had at least one underlying disease, such as an autoimmune disease (6/11), blood malignancy (2/11), avascular necrosis of the femoral head (1/11), bronchiectasis (1/11), and pneumonia (1/11). Immunosuppressive or cytotoxic agents were used in eight patients. The median hospitalization time was 23 days (6–58 days). Six patients received invasive procedures. Mixed infection was present in three patients: Acinetobacter baumannii, Candida albicans, and Proteusbacillus vulgaris infection.

3.2 Clinical features and auxiliary examination

The clinical manifestations of nocardiosis were variable, nonspecific, and heterogeneous (Table 2). The most common symptoms were fever (10/11), cough (7/11), expectoration (7/11), and pain (7/11) including joint pain (2/11), chest pain (2/11), headache (1/11), back pain (1/11), and abdominal pain (1/11). Chest tightness, shortness of breath, weight loss, and fatigue were also frequently noted. In patients with pulmonary nocardiosis, mass shadows (4/11), pleural effusion (3/11), multiple nodules (2/11), cavities (2/11), and bronchiectasis (1/11) were shown by chest radiography. Routine blood examinations revealed seven cases of leucocytosis. The pathological features were neutrophil infiltration, suppurrative or granulomatous inflammation, and a suspiciously positive reaction to acid-fast staining (Figure 1).

3.3 Diagnosis, treatment, and outcomes

The diagnoses of all patients were confirmed by microbiologic studies. Patient specimens were obtained from blood (4/11), sputum (2/11), pus (2/11), joint fluid (1/11), and biopsy (1/11). Using 16S rRNA gene polymerase chain reaction (PCR) for species identification, 5 of 11 cases were classified into specific genotypes: N. asteroides, N. otitidiscaviarum, N. brasiliensis, N. farcinica, and
Table 1: Demographic and underlying disease for the patients with nocardiosis

| No. | Age (years) | Gender | Diagnosis                          | Underlying diseases                                                                 | Immunosuppressant or chemotherapy                      | Hospitalization time (days) | Invasive procedures                                                                 |
|-----|-------------|--------|-----------------------------------|-------------------------------------------------------------------------------------|------------------------------------------------------|-----------------------------|----------------------------------------------------------------------------------|
| 1   | 26          | Male   | Disseminated nocardiosis (Nocardia farcinica) (lung, head, blood) | Undifferentiated connective tissue disease, cerebral vasculitis                      | Methylprednisolone, azathioprine                      | 28                          | None                                                                            |
| 2   | 53          | Female | Pulmonary nocardiosis (Nocardia otitidiscaviarum) | Bronchiectasis                                                                      | None                                                  | 7                           | None                                                                            |
| 3   | 42          | Male   | Pulmonary nocardiosis             | Nephrotic syndrome, diabetes mellitus                                               | Methylprednisolone, cyclosporine                      | 58                          | Trachea cannula, pleural drainage, CVC, bronchofiberscope Arthroscopy, articular cavity cleaning |
| 4   | 57          | Male   | Left hip joint nocardiosis (Nocardia brasiliensis) | Avascular necrosis of the femoral head                                              | None                                                  | 52                          | None                                                                            |
| 5   | 23          | Male   | Disseminated nocardiosis (skin, blood) | Systemic lupus erythematosus, lupus nephritis, generalized psoriasis                | Methylprednisolone, hydroxychloroquine                | 15                          | None                                                                            |
| 6   | 78          | Male   | Disseminated nocardiosis (Nocardia asteroidis) (lung, blood) | Adult onset Still's disease                                                         | Methylprednisolone, cyclosporine                      | 6                           | None                                                                            |
| 7   | 22          | Female | Skin nocardiosis                  | Systemic lupus erythematosus, lupus nephritis, lupus gastrointestinal damage         | Prednisone, hydroxychloroquine, methotrexate         | 36                          | Incision and drainage for abscesses                                              |
| 8   | 58          | Female | Disseminated nocardiosis (lung, skin, abdominal cavity) | Systemic lupus erythematosus, lupus nephritis, lupus blood system damage, lupus cardiac system damage; secondary Sjogren's syndrome | Methylprednisolone, cyclosporine, hydroxychloroquine | 15                          | None                                                                            |
| 9   | 56          | Male   | Pulmonary nocardiosis             | Pneumonia                                                                           | None                                                  | 22                          | Bronchoscope submucosal biopsy, lung puncture biopsy Skin biopsy, nodule biopsy, PICC |
| 10  | 12          | Female | Disseminated nocardiosis (skin, lung) | Acute myelogenous leukemia (M1)                                                      | IA, MA                                                | 34                          | Skin biopsy, nodule biopsy, PICC                                                |
| 11  | 34          | Male   | Disseminated nocardiosis (Nocardia reynolds) (skin, soft tissue, lung) | T lymphocytic lymphoma, post-allogeneic HSCT, chronic graft versus host disease     | Methylprednisolone, cyclosporine                      | 23                          | Abscess incision, abscess debridement exploration                               |

Abbreviations: IA: idarubicin, cytarabine. MA: mitoxantrone, cytarabine. HSCT: hematopoietic stem cell transplantation. CVC: central venous catheter. PICC: peripherally inserted central catheter.
Table 2: Clinical, laboratory, and radiological features of the patients

| No. | Diagnosis                                      | Clinical manifestations                                      | Blood routine                  | Radiographic findings                                                                 |
|-----|-----------------------------------------------|-------------------------------------------------------------|--------------------------------|--------------------------------------------------------------------------------------|
| 1   | Disseminated nocardiosis (*Nocardia farcinica*) (lung, head, blood) | Fever (39.6°C), cough, expectoration, headache              | WBC: 10.9, Neut: 10.46, PCT: 0.18 | Chest CT showed multiple patchy, mass dense shadows and cavities                     |
| 2   | Pulmonary nocardiosis (*Nocardia otitidiscaviarum*) | Fever (39.0°C), cough, expectoration, blood-stained sputum, chest tightness | WBC: 4.36, Neut: 2.66, PCT: None | Chest CT showed multiple bronchiectasis with infection                                |
| 3   | Pulmonary nocardiosis                          | Fever (39.5°C), cough, expectoration, chest tightness, chest pain, shortness of breath | WBC: 10.25, Neut: 8.8, PCT: 5.8 | Chest CT showed multiple nodules, cavities, and pleural effusion                      |
| 4   | Left hip joint nocardiosis (*Nocardia brasiliensis*) | Left hip pain, weight loss                                  | WBC: 7.37, Neut: 5.51, PCT: 0.42 | X-ray of hip joint showed ischemic necrosis combined with osteoarthritis on bilateral femoral head |
| 5   | Disseminated nocardiosis (skin, blood)         | Fever (39.6°C), skin erythema, desquamation and pruritus, back pain | WBC: 11.46, Neut: 9.9, PCT: 0.14 | Lumbar X-ray and chest X-ray showed no abnormalities                                 |
| 6   | Disseminated nocardiosis (*Nocardia asteroides*) (lung, blood) | Fever (39.4°C), chills, cough, expectoration, limbs weakness | WBC: 10.38, Neut: 10.06, PCT: None | Chest X-ray showed multiple cloud-like mass shadows                                     |
| 7   | Skin nocardiosis                               | Fever (38.2°C), abdominal pain, vomiting, fatigue, purulent, and ulcerated on right foot | WBC: 10.69, Neut: 10.18, PCT: None | Chest X-ray and abdominal ultrasound showed no abnormalities                           |
| 8   | Disseminated nocardiosis (lung, skin, abdominal cavity) | Fever (40.0°C), cough, expectoration, skin abscess, abdominal distension | WBC: 7.1, Neut: 6.63, PCT: 0.25 | Chest CT showed double pneumonia and pleural effusion                                  |
| 9   | Pulmonary nocardiosis                          | Fever (39.0°C), cough, expectoration, chest tightness, chest pain, shortness of breath, weight loss | WBC: 27.75, Neut: 24.21, PCT: 1.07 | PET–CT showed massive hypermetabolic lesions, multiple strips, and mass shadows around the lesion, pleural effusion |
| 10  | Disseminated nocardiosis (skin, lung)          | Fever (40.0°C), skin abscess in both lower extremities       | WBC: 4.45, Neut: 3.08, PCT: 0.1 | Chest CT showed high-density shadow and exudation                                       |
| 11  | Disseminated nocardiosis (*Nocardia reynolds*) (skin, soft tissue, lung) | Fever (38.6°C), cough, expectoration, pain on left elbow    | WBC: 13.4, Neut: 8.13, PCT: 0.17 | Chest CT showed multiple nodules                                                       |

Abbreviations: WBC: white blood cell, N: neutrophilia cell, PCT: procalcitonin, CT: computed tomography, PET–CT: positron emission tomography-computed tomography.
Two cases were initially misdiagnosed as pulmonary tuberculosis (Table 3). In all cases, treatment was initiated after diagnosis based on TMP–SMX combined with one or two antibiotics according to the results of drug-sensitive tests. These additional antibiotics were carbapenems (4/11), quinolones (4/11), oxazolidinones (3/11), streptomycin (2/11), tetracycline (1/11), piperacillin β-lactams (1/11), and rifampicin (1/11). Six patients (6/11) were treated with two antibiotics, and five patients (5/11) were treated with three antibiotics. Most of the patients received antibiotic therapy for a prolonged period. The median time from onset to treatment was 3 weeks (1–9 weeks), and the median duration of treatment after diagnosis was 20.5 weeks (7–47 weeks). The defined response time to Nocardia treatment mainly referred to the time when the clinical symptoms began to abate, including improvement confirmed by chest imaging, a return to normal body temperature, and a reduction in other clinical symptoms. In patients who responded to anti-Nocardia treatment, the median response time was 2.5 weeks (1–8 weeks). Regarding outcomes, eight patients were discharged after improvement and survived, and three patients died (Table 3).

### Discussion

Nocardia is a genus of prokaryotes, firmicutes, actinomycetes, and gram-positive aerobic bacteria. This genus is widely distributed in the environment (e.g., soil, water, air, grass, and rotting plants), and most of the species are saprophytic non-pathogenic bacteria [4]. Since the French veterinarian Edmund Nocard first discovered them in 1888 [15], more than 100 species of Nocardia have been reported [1]. The important pathogens involved in human nocardiosis are Nocardia asteroides, Nocardia brasiliensis, Nocardia farcinica, Nocardia cyriacigeorgica, and Nocardia otitidiscaviarum. N. asteroides is the most common isolated species [7,16].

Nocardia is a genus of opportunistic pathogens that mainly affects patients with deficient cellular immunity, such as those with a history of long-term steroid or...
Table 3: Antibiotic regimens and outcomes of the patients

| No. | Diagnosis                                | Diagnostic approach | Misdiagnosis | Time from onset to treatment (weeks) | Treatment time after diagnosis (weeks) | Therapeutic response time (weeks) | Antimicrobials before diagnosis | Antimicrobials after diagnosis | Outcomes                      |
|-----|-----------------------------------------|---------------------|--------------|--------------------------------------|---------------------------------------|----------------------------------|---------------------------------|---------------------------------|-------------------------------|
| 1   | Disseminated nocardiosis (Nocardia farcinica) (lung, head, blood) | Blood culture       | None         | 2                                    | 47                                    | 8                                | Meropenem, Linezolid            | TMP–SMX, Meropenem            | Improved and survival         |
| 2   | Pulmonary nocardiosis (Nocardia otitidiscaviarum) | Sputum culture      | None         | 1                                    | 17                                    | 3                                | Piperacillin Sodium and Sulbactam sodium | TMP–SMX, Piperacillin tazobactam | Improved and survival         |
| 3   | Pulmonary nocardiosis                   | Sputum culture      | None         | 3                                    | 7                                     | 2                                | Linezolid                        | TMP–SMX, Meropenem            | Improved and survival         |
| 4   | Left hip joint nocardiosis (Nocardia brasiliensis) | Joint fluid culture | None         | 9                                    | 20                                    | 1                                | Cefuroxime sodium, Doxycycline, Vancomycin, Cefoperazone Sodium and Sulbactam sodium | TMP–SMX, Levofl oxacin, Streptomycin | Improved and survival         |
| 5   | Disseminated nocardiosis (skin, blood)  | Blood culture       | None         | 2                                    | 23                                    | 1                                | Cefoperazone Sodium and Sulbactam Sodium | Meropenem, Linezolid            | Improved and survival         |
| 6   | Disseminated nocardiosis (Nocardia asteroidis) (lung, blood) | Blood culture       | Pulmonary tuberculosis             | 3                                    | Unknown                               | Unknown                          | Cefoperazone Sodium and Sulbactam Sodium | Meropenem, Linezolid            | Discharged to another hospital and died |
| 7   | Skin nocardiosis                        | Pus culture         | None         | 8                                    | 40                                    | 4                                | Cefoperazone Sodium and Sulbactam Sodium, Omidazole | Meropenem                     | Improved and survival         |
| 8   | Disseminated nocardiosis (lung, skin, abdominal cavity) | Blood culture       | None         | 2                                    | Unknown                               | Unknown                          | Cefoperazone Sodium and Sulbactam Sodium | Meropenem                     | Discharged to home and died   |
| 9   | Pulmonary nocardiosis                   | Tissue biopsy       | Pulmonary tuberculosis             | 9                                    | Unknown                               | Unknown                          | Amikacin, Levofloxacin          | TMP–SMX Levofloxacin           | Discharged to home and died   |
| 10  | Disseminated nocardiosis (skin, lung)   | Diagnostic therapy  | None         | 2                                    | 21                                    | 4                                | Cefoperazone Sodium and Sulbactam Sodium, Vancomycin, Piperacillin Sodium and Sulbactam sodium | TMP–SMX, Linezolid, Levofloxacin | Improved and survival         |
| 11  | Disseminated nocardiosis (Nocardia reynolds) (skin, soft tissue, lung) | Pus culture         | None         | 3                                    | 12                                    | 1                                | Cefoperazone Sodium and Sulbactam Sodium, Vancomycin, Piperacillin Sodium and Sulbactam sodium | TMP–SMX, Linezolid, Levofloxacin | Improved and survival         |
immunosuppressant use, organ or stem cell transplantation, diabetes, acquired immune deficiency syndrome (AIDS), or chronic lung disease [6,9]. As widely described in the literature, the administration of corticosteroids and/or immunosuppressants is the most common predisposing factor [17,18]. Eight patients in our report received immunosuppressive or cytotoxic agents, which was consistent with previous reports and indicated that nocardiosis is an opportunistic infection usually occurring in patients with immune deficiencies.

*Nocardia* can spread to almost all parts of the body through the blood from the lungs (especially the upper lobes of the lungs) or infected areas of the skin. As inhalation is the main route of transmission for *Nocardia*, the respiratory tract is the most affected organ, followed by the CNS, skin and soft tissue, kidneys, and peritoneum [19–21]. The symptoms of CNS infection include headache, meningeal irritations, seizures, and focal neurological dysfunction. The main manifestations of skin and soft tissue infection are local abscesses [3,5,8]. In this study, 8 of 11 patients (72.73%) had pulmonary infections and presented with cough, expectoration, chest pain, and hemoptysis. Six patients showed disseminated nocardiosis involving lung, blood, joint, head, skin, and soft tissue. All six patients had received corticosteroid or immunosuppressant treatment. The radiological abnormalities in pulmonary nocardiosis are diverse, not pathognomonic, and may mimic a multitude of pulmonary diseases. As the clinical symptoms are similar to tuberculosis, pulmonary nocardiosis is easy to misdiagnose as pulmonary tuberculosis when cultures are not available or confirmative. Two patients in our study (No. 6 and 9) were initially misdiagnosed with pulmonary tuberculosis and received anti-tuberculosis treatment before nocardiosis was confirmed. Both patients died as a result of the progression of nocardiosis, suggesting that misdiagnosis and delayed treatment could cause patient deaths.

In our study, all patients received combination therapy with antibiotics. Eight patients were discharged from the hospital after timely diagnosis and treatment. Patient No. 11 was a recipient of allogeneic hematopoietic stem cell transplant (HSCT) with chronic graft-versus-host-disease (cGVHD) and was receiving corticosteroids and cyclosporins. He was admitted to the hospital with fever, swelling, and pain in the left upper limb and trunk. An incision to drain an abscess on the left upper limb was performed (Figure 2). A bacterial culture of pus suggested nocardiosis (identified and classified as *Nocardia reynolds* several days later). Then, TMP–SMX and levofloxacin were given. After 3 days, linezolid was added according to the results of a drug-sensitive test. The symptoms of the patient significantly regressed with no new lesions occurring 1 week after treatment. The duration of therapy was 12 weeks. No relapse was noted after 12 months. Patient No. 10 was a 12-year-old female with acute myeloid leukemia. She complained of fever and painful swelling erythematous lesions on both lower extremities. Bacterial cultures of pus were repeatedly performed, but the results were negative. A biopsy of the left gastrocnemius muscle was performed, displaying neutrophil infiltration, which was consistent with suppurative inflammation. Acid-fast staining was also suspiciously positive. TMP–SMX plus linezolid was used as a diagnostic treatment. The lesions on the lower extremities healed significantly. The duration of therapy was 21 weeks. She had no evidence of recurrence after an 18-month follow-up. Three patients died. One patient (No. 8), who had systemic lupus erythematosus (SLE), was admitted to the hospital with fever, cough, and expectoration. A blood culture was performed immediately, and a positive result of *Nocardia* was reported 6 days later. She was diagnosed with disseminated *Nocardia*.

![Figure 2](image_url)

**Figure 2:** Abscess on the left upper limb of patient No. 11. (a and b) Surgical debridement of the abscess on the left upper limb was performed. (c) The photograph of the left upper limb 12 months after surgery showed that the wound was entirely healed.
TMP–SMX and levofloxacin were given initially, but her condition worsened. After 3 days, the drug-sensitive test indicated that the bacterium was sensitive to linezolid and aminoglycoside, but the patient gave up and was discharged from the hospital for economic reasons. Active stage SLE, bloodstream infection, and no use of sensitive antibiotics contributed to the death of the patient. The other two patients did not receive anti-Nocardia treatment because they were initially misdiagnosed with pulmonary tuberculosis. Both of these patients died because of delayed treatment of Nocardia. Therefore, our study suggests that nocardiosis should be considered in patients with impairment of immunity, particularly in those who do not respond to routine antibiotic therapy. Misdiagnosis and inappropriate management may cause poor outcomes.

In summary, nocardiosis is a relatively rare, opportunistic infection with variable clinical manifestations. Nocardiosis should be considered in patients with infections that rapidly progress or who respond poorly to treatment for common bacterial infections, especially those with a history of long-term steroid and/or immunosuppressant use. In this study, symptoms improved quickly after initiation of therapy based on TMP–SMX combined with carbapenems or other antibiotics according to drug sensitivity in 8 of 11 Nocardia infections. Our work suggests that early diagnosis, timely treatment, and combination drug therapy are keys to improving patient outcomes.

Funding information: This study was supported by the Guangdong Science and Technology Department (grant no. 2016A020215062 and A2019207), and the Natural Science Foundation of Guangdong Province (grant no. 2017A030313612, 2016A030313270, and 2016A030313360).

Conflict of interest: The authors have no conflicts of interest.

Data availability statement: All data generated or analyzed during this study are available from the corresponding author on reasonable request.

References

[1] Coussement J, Lebeaux D, Rouzaud C, Lortholary O. Nocardia infections in solid organ and hematopoietic stem cell transplant recipients. Curr Opin Infect Dis. 2017;30(6):545–51.
[2] Abreu C, Rocha-Pereira N, Sarmento A, Magro F. Nocardia infections among immunomodulated inflammatory bowel disease patients: a review. World J Gastroenterol. 2015;21(21):6491–8.
[3] Mazzaferrri F, Cordioli M, Segato E, Adami I, Maccacaro L, Sette P, et al. Nocardia infection over 5 years (2011–2015) in an Italian tertiary care hospital. New Microbiol. 2018;41(2):136–40.
[4] Paige EK, Spelman D. Nocardiosis: 7-year experience at an Australian tertiary hospital. Intern Med J. 2019;49(3):373–9.
[5] Takiguchi Y, Ishizaki S, Kobayashi T, Sato S, Hashimoto Y, Suruga Y, et al. Pulmonary nocardiosis: a clinical analysis of 30 cases. Intern Med. 2017;56(12):1485–90.
[6] Rouzaud Y, Rodriguez-Nava V, Catherinet E, Mèchafi F, Bergeron E, Farfou E, et al. Clinical assessment of a Nocardia PCR-based assay for diagnosis of nocardiosis. J Clin Microbiol. 2018;56:6.
[7] You Y, Chen W, Zhong B, Song Z, Yang X. Disseminated nocardiosis caused by Nocardia elegans: a case report and review of the literature. Infection. 2018;46(5):705–10.
[8] Datta R, Kramer E, Reinhart H, Campbell S, Wong E, Gupta S. Menace elbow: disseminated nocardiosis. Am J Med. 2018;131(11):1307–9.
[9] Ambrosioni J, Lew D, Garbino J. Nocardiosis: updated clinical review and experience at a tertiary center. Infection. 2010;38(2):89–97.
[10] Welsh O, Vera-Cabrera L, Salinas-Carmona MC. Current treatment for Nocardia infections. Expert Opin Pharmacother. 2013;14(17):2387–98.
[11] Larruskain J, Idigoras P, Marimón JM, Pérez-Trallero E. Susceptibility of 186 Nocardia sp. isolates to 20 antimicrobial agents. Antimicrob Agents Chemother. 2011;55(6):2995–8.
[12] Hinson KR, Herres JA, Chow SK. Answer to July 2018 photo quiz. J Clin Microbiol. 2018;56:7.
[13] Ott SR, Meier N, Kolditz M, Bauer TT, Rohde G, Presterl E, et al. Pulmonary nocardiosis in Western Europe clinical evaluation of 43 patients and population-based estimates of hospitalization rates. Int J Infect Dis. 2019;81:140–8.
[14] Wayne PA. Susceptibility testing of mycobacteria, Nocardiae, and other aerobic actinomycetes; approved standard-second edition. CLSI document M24-A2. Pennsylvania: Clinical and Laboratory Standards Institute; 2011. p. 43.
[15] Brown-Elliott BA, Brown JM, Conville PS, Wallace RJ Jr. Clinical and laboratory features of the Nocardia spp. based on current molecular taxonomy. Clin Microbiol Rev. 2006;19(2):259–82.
[16] Clark NM, Reid GE. Nocardia infections in solid organ transplantation. Am J Transplant. 2013;13(Suppl 4):83–92.
[17] Cattaneo C, Antoniazzi F, Caira M, Castagnola C, Delia M, Tumbarello M, et al. Nocardia spp infections among hematological patients: results of a retrospective multicenter study. Int J Infect Dis. 2013;17(8):e610–4.
[18] de Montmollin E, Corcos O, Nossair L, Leflon-Guibout V, Belmatoug N, Joly F, et al. Retropertioneal abscesses due to Nocardia farcinica: report of two cases in patients with malnutrition. Infection. 2012;40(1):93–6.
[19] Flateau C, Jurado V, Lemâbre N, Loiez C, Wallet F, Saiz-Jimenez C, et al. First case of cerebral abscess due to a novel Nocardia species in an immunocompromised patient. J Clin Microbiol. 2013;51(2):696–700.
[20] Plau C, Kerjouan M, Le Mouel M, Patrat-Delon S, Henaux PL, Brun V, et al. First case of disseminated infection with Nocardia cerradoensis in a human. J Clin Microbiol. 2015;53(3):1034–7.
[21] Chen N, Qin Q, Sun KD, Luo D, Cheng QH. An unusual successful treatment with non-sulfonamides: primary cutaneous nocardiosis caused by Nocardia brasiliensis. Ther Clin Risk Manag. 2018;14:1661–4.