

Nocardia Infection in Patients with Rheumatic Diseases: Clinical Presentation and Management

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Abstract

Nocardia is a pathogen responsible for a variety of clinical infections. Here, we aimed to investigate the species distribution, clinical manifestations, and antimicrobial susceptibility of Nocardia species over 3 years in two tertiary general hospitals in China. Nocardia isolates were identified to species level by mass spectrometry and 16S rRNA PCR sequencing. Clinical data were collected from medical records. Antimicrobial susceptibility was determined by the standard Broth microdilution method. Possible predisposing factors for Nocardia infection were high-dose glucocorticoid treatment, concomitant use of immunosuppressants, preexisting pulmonary diseases, and diabetes mellitus. All patients had pulmonary Nocardiosis, and six of them had disseminated Nocardiosis when their pulmonary lesions were identified.

Introduction

Rheumatic diseases encompass a wide range of chronic conditions that affect the joints, muscles, and connective tissues. Patients with these diseases often receive immunosuppressive therapy, which increases their susceptibility to various infections. One such infection is caused by Nocardia, a group of bacteria that can lead to serious complications if not promptly diagnosed and treated [1]. Understanding the clinical characteristics of Nocardia infection in patients with rheumatic diseases is crucial for early detection and appropriate management.

Nocardia infection and rheumatic diseases

Nocardia is an aerobic, filamentous, gram-positive bacterium found in soil, decaying vegetation, and water. Inhalation of Nocardia species can lead to pulmonary infections, while direct inoculation can cause localized cutaneous infections. In patients with rheumatic diseases, such as rheumatoid arthritis, systemic lupus erythematosus, and vasculitis, the risk of Nocardia infection is increased due to the use of immunosuppressive medications.

Nocardia species, an aerobic actinomycete, exist in a wide range of environments around the world. Currently, only a small proportion of described Nocardia species are known to be human pathogens that affect patients. Nocardia species are facultative intracellular pathogens, which are capable of causing either a localized or disseminated infection both in immunocompetent and immunocompromised hosts. In recent decades, an increased number of Nocardia infection cases have been reported worldwide [2]. Nocardia infection is characterized by a variety of clinical manifestations with the involvement of the lungs, central nervous system, skin, and other organs. More seriously, Nocardia can cause severe, life-threatening disseminated infections, such as osteomyelitis and nocardial sepsis. Early recognition and effective therapy are imperative to achieve successful outcomes. Thus, elaboration of the molecular characteristics, infection, and clinical manifestations of Nocardia species is necessary for timely detection and diagnosis.

Despite numerous Nocardia species have been characterized both phenotypically and genotypically within the genus, the genotype remains heterogeneous and continues to evolve. In addition, the genus of Nocardia is rapidly expanding and the species distribution varies with different geographical locations. Reports about Nocardia species in China are limited to a few case reports, case series, and research studies. Particularly, there is only limited information about the species

distribution and drug susceptibility of Nocardia [3]. Thus, the present study was designed to identify Nocardia species using 16SrRNA and mass spectrometry (MS) in two tertiary hospitals in China and to investigate the species distribution, clinical manifestations, microbiological characteristics, and antimicrobial susceptibility of the Nocardia species. In addition, we retrospectively analyzed the therapeutic effects and prognosis of patients with Nocardia infection.

Clinical presentation

Pulmonary nocardiosis is the most common form of Nocardia infection in patients with rheumatic diseases. It typically presents with symptoms such as cough, chest pain, and shortness of breath, fever, and sputum production. Radiological findings may include lung nodules, cavitory lesions, and consolidations.

Cutaneous nocardiosis can occur through direct inoculation of Nocardia into skin wounds or compromised areas. It presents as painful, erythematous nodules, abscesses, or cellulitis. The lesions may be accompanied by purulent discharge and tenderness [4].

Nocardial CNS infections are rare but can occur in immunocompromised individuals, including those with rheumatic diseases. Symptoms may include headache, altered mental status, focal neurological deficits, seizures, and signs of meningeal irritation. Imaging studies, such as brain MRI, may reveal abscesses or meningitis.

Diagnosis

The diagnosis of Nocardia infection involves a combination of clinical suspicion, microbiological cultures, and histopathological examination. Sputum, tissue, or fluid samples are collected and cultured

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under appropriate conditions for Nocardia growth. Microscopic examination of stained specimens can reveal the characteristic filamentous branching bacteria [5]. Molecular techniques, such as polymerase chain reaction (PCR), can aid in species identification.

Management

Treatment of Nocardia infection in patients with rheumatic diseases requires a multidisciplinary approach involving rheumatologists, infectious disease specialists, and pulmonologists [6]. The choice of antibiotics depends on the site and severity of infection, as well as the susceptibility profile of the isolated Nocardia species. Trimethoprim-sulfamethoxazole is considered the first-line therapy, often combined with other agents like imipenem-cilastatin, amikacin, or linezolid. The duration of treatment is typically prolonged and may last several months to a year, depending on the clinical response.

Prevention

Preventive measures should be considered for patients with rheumatic diseases who are at risk of Nocardia infection. This includes educating patients about the potential risks of exposure to soil and contaminated water sources. It is essential to adhere to appropriate protective measures, such as wearing gloves and masks when gardening or engaging in activities that involve contact with soil [7]. Regular follow-up visits with healthcare providers are necessary to monitor for any signs of infection and adjust immunosuppressive medications as needed.

Discussion

Previous reports indicated an increasing trend of Nocardia infection over the past decade. In addition, Nocardia species are distributed differently across various geographic regions. Thus, it is necessary to investigate the epidemiology, clinical characteristics, and antimicrobial susceptibility of Nocardia species in different geographic regions, especially in China, a region with various geographical and climatic characteristics [8]. Based on this evidence, we speculated that Nocardia infection occurred more frequently in our two centers over the past 3 years, in accordance with the overall epidemiological trends of Nocardia infection.

Nevertheless, only a few species can be reliably identified by the traditional biochemical methods, including *N. farcinica*, *N. brasiliensis*, *N. asteroides* and *N. pseudobrasiliensis*. In general, the traditional biochemical methods are very time-consuming, resulting in a delayed diagnosis of infection. In recent years, 16S rRNA gene sequencing technique has become a reliable method for Nocardia identification. However, the high cost and lack of standardization has been the major obstacle for the application of 16S rRNA gene sequencing in China. Notably, matrix-assisted laser desorption/ionization time-of-flight MS has emerged as an alternative method in the routine laboratory identification of Nocardia and also has been widely applied in a large number of tertiary general hospitals in China [9]. In our study, we performed both the sequencing of 16S rRNA gene and MALDI-TOF MS to identify Nocardia species and obtained consistent identification results. Only one strain of *N. wallacei* was not identified to the specific species level by MS and whether this was due to technical operation or the limitations of MS remains to be further confirmed. Overall, MS has the potential to be a reliable technique for the identification of Nocardia species, according to the experience at our centers [10].

Treatment for Nocardia infection according to the susceptibility of the isolated species is essential whenever possible, thereby, understanding the species-specific antimicrobial susceptibility patterns

is very important. We reported the antimicrobial susceptibility patterns of the first-line and second-line drugs used for Nocardia infection. Here, the antimicrobial susceptibility profile was largely consistent with the results of the antibiograms available in the literature [11]. We found that the Nocardia species had good susceptibility to LNZ, TMP-SMX, and AMK in the present study. Furthermore, our isolates showed varying susceptibilities to different antibiotics. However, each species had a limited number of strains, which may not be enough to accurately represent the antimicrobial susceptibility. Thus, further studies with a larger sample size are still needed to confirm the antibiograms from our region.

In general, the majority of patients with Nocardia infection have a certain degree of immune deficiency, particularly patients with underlying diseases or immunosuppressive treatment [12]. In the present study, approximately 93% of patients had at least one known underlying disease responsible for immune deficiency, which was consistent with the previous data. The most common underlying diseases were type 2 diabetes mellitus, hypertension, and COPD. It is reported that impaired local pulmonary deficiency caused by COPD predispose to pulmonary nocardiosis, particularly in patients requiring long-term corticosteroid treatment. Among the 27 included cases, 2 cases showed no evidence of underlying diseases. This data ranges from 10% to 25% in other reports. Thus, Nocardia infection can occur both in immunocompetent and immunocompromised hosts [13].

Conclusion

Nocardia infection is an important consideration in patients with rheumatic diseases, particularly those receiving immunosuppressive therapy. Recognizing the clinical characteristics and promptly diagnosing Nocardia infection is crucial for initiating appropriate treatment and minimizing the risk of complications. Close collaboration between rheumatologists, infectious disease specialists, and other healthcare professionals is vital to optimize patient care and outcomes in this vulnerable population. Additionally, preventive measures and patient education are essential for reducing the risk of Nocardia infection in patients with rheumatic diseases. The present study retrospectively analyzed 27 non-repetitive clinical Nocardia isolates from two centers in Shandong, China. We found that the clinical manifestations of Nocardia infection and antimicrobial susceptibility profiles varied with different Nocardia species. Besides, MALDI-TOF MS was proved as a rapid and accurate identification for the Nocardia species. Our findings suggest the necessity of accurate species identification and confirmation of antimicrobial susceptibility patterns in the diagnosis and the choice of antibiotic treatment.

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