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Case Report

Suspected nocardiosis in an immunosuppressed patient: a case report highlighting diagnostic challenges and management strategies

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ABSTRACT

Nocardiosis is a rare but potentially fatal opportunistic infection caused by Nocardia species, predominantly affecting immunocompromised individuals. This case report details the clinical course, diagnostic workup, and management of a 63-year-old female with a history of renal transplantation. Initial investigations, including imaging studies, revealed multiple cavitary pulmonary nodules and a solitary brain lesion, raising concerns for disseminated infection. The diagnostic challenge was compounded by the broad differential diagnosis in this patient population, including fungal, mycobacterial, and other opportunistic infections. Empirical antimicrobial therapy was initiated, and subsequent microbiological confirmation of Nocardia asteroides from bronchoalveolar lavage specimens established the diagnosis. Despite initial therapeutic response, the patient developed worsening neurological symptoms indicative of CNS involvement, necessitating prolonged treatment with a combination of trimethoprim-sulfamethoxazole and imipenem. This report underscores the importance of early recognition, comprehensive diagnostic evaluation, and individualized therapeutic approaches in managing suspected nocardiosis in immunocompromised patients. Furthermore, it discusses the diagnostic pitfalls, highlights the need for a high index of suspicion, and reviews current therapeutic recommendations for both pulmonary and disseminated nocardiosis, providing a valuable reference for clinicians managing similar cases.

Keywords: Nocardiosis, Nocardia asteroides, Opportunistic infection, Immunosuppressed patient, Renal transplantation, Pulmonary nodules

INTRODUCTION

Nocardiosis is an uncommon, yet severe, opportunistic infection primarily caused by members of the Nocardia genus, a group of filamentous, gram-positive, weakly acid-fast bacteria that reside ubiquitously in the environment. It predominantly affects immunocompromised hosts, particularly those receiving long-term immunosuppressive therapies, such as patients with organ transplants, HIV/AIDS, or hematological malignancies.[1-3] Although the true incidence of nocardiosis is challenging to ascertain due to underdiagnosis and reporting discrepancies, it is estimated that the risk is markedly elevated in patients with compromised cell-mediated immunity. Nocardia species exhibit a predilection for pulmonary involvement but possess a propensity for hematogenous dissemination to the central nervous system (CNS) and other organs, resulting in a diverse clinical spectrum ranging from

localized pulmonary disease to life-threatening disseminated infections.[4-6] The clinical presentation of nocardiosis is highly variable and often nonspecific, manifesting with symptoms such as fever, cough, dyspnea, and weight loss. Pulmonary nocardiosis, the most common form, may mimic other opportunistic infections like tuberculosis, invasive fungal infections, or malignancies, thereby complicating the diagnostic process. Radiographic findings are heterogeneous and may include nodules, cavitary lesions, or infiltrates, further adding to the diagnostic ambiguity. Disseminated nocardiosis, defined as involvement of two or more non-contiguous organs, occurs in up to 44% of cases and is associated with a significantly worse prognosis. Central nervous system involvement, manifesting as single or multiple brain abscesses, can occur in up to one-third of patients and is a leading cause of morbidity and mortality.[7,8]

The diagnosis of nocardiosis requires a high index of suspicion, especially in at-risk populations, and hinges on the isolation of Nocardia spp. from clinical specimens through microbiological culture. However, due to its slow-growing nature and morphologic similarities to other organisms, Nocardia is frequently overlooked or misidentified, leading to diagnostic delays. Molecular techniques, such as 16S rRNA sequencing, have improved the sensitivity and specificity of pathogen identification but are not widely available in many clinical settings.[9,10]

Management of nocardiosis is challenging and necessitates prolonged antimicrobial therapy, often for 6 to 12 months, depending on the site of infection and immune status of the patient. The mainstay of treatment is trimethoprim-sulfamethoxazole, with additional agents such as imipenem, amikacin, or linezolid employed in severe or refractory cases. In patients with CNS involvement, achieving adequate drug penetration is crucial, and combination therapy is frequently recommended. Immunosuppressive regimens may need to be adjusted to optimize host defenses while balancing the risk of transplant rejection or flare of underlying disease.[11]

This article presents a complex case of suspected nocardiosis in a renal transplant recipient, outlining the diagnostic hurdles encountered and therapeutic strategies implemented. It emphasizes the need for heightened clinical vigilance in recognizing this elusive pathogen, the role of comprehensive diagnostic workup including advanced imaging and microbiological assays, and the critical importance of tailored antimicrobial regimens to improve patient outcomes. Through this report, we aim to contribute to the existing body of literature on nocardiosis in immunosuppressed patients and provide a framework for the approach to similar cases in clinical practice.[12]

CASE REPORT

Female patient aged 63 years, with no relevant here do familial history. Personal history of type 2 diabetes for 3 years in treatment, hypothyroidism of 15 years of evolution, systemic arterial hypertension diagnosed 3 years ago and chronic kidney disease diagnosed in 2013, in treatment with peritoneal dialysis for 5 years, later renal transplantation was performed (cadaveric donor), at her admission in management with immunosuppressant based on Cyclosporine and mycophenolic acid. His current condition began in December 2022 when he reported that while walking in the street he suffered a fall from his own support plane, with abrasion on his left calf. Subsequently, he presented a soft tissue infection, which required surgical cleaning and treatment with an unspecified antibiotic for 6 days in March 2023.

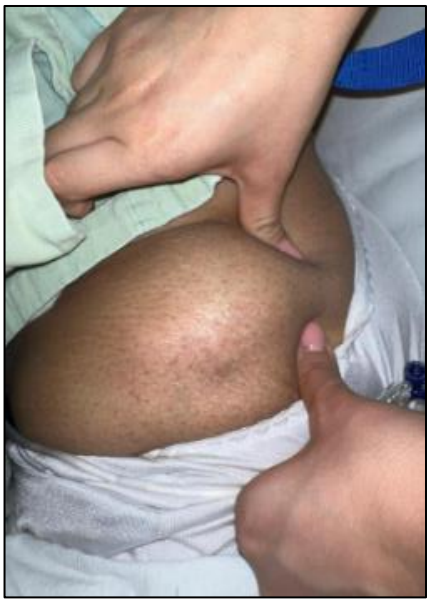

Figure 1: Nodule in the lumbar region.

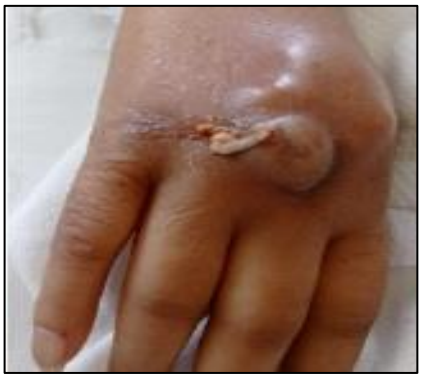

Figure 2: Nodule on the dorsum of the right hand.

At the end of March, she began with the appearance of nodules in the left infra clavicular region of approximately 2 cm in its largest diameter, of soft consistency, well delimited borders, hyperthermic,

erythematous, mobile, non-suppurative, with similar lesions in the dorsal region of the right hand, which presented purulent suppuration, in thighs it appeared bilaterally of 1 cm in diameter and another in the lumbar region of approximately 10 cm in size. She went to a control appointment with nephrology, which indicated hospitalization to rule out an infectious process.

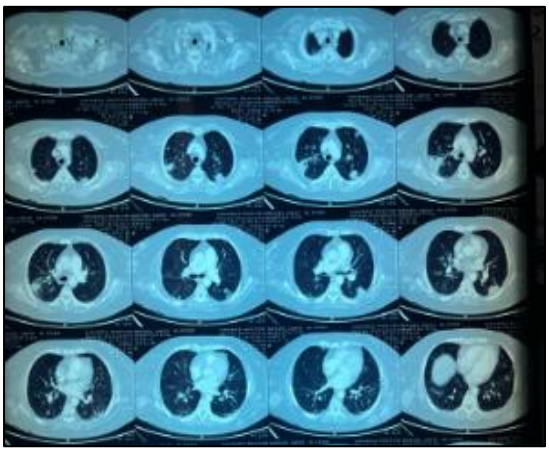

Figure 3: Well-defined lung cavitated lesion.

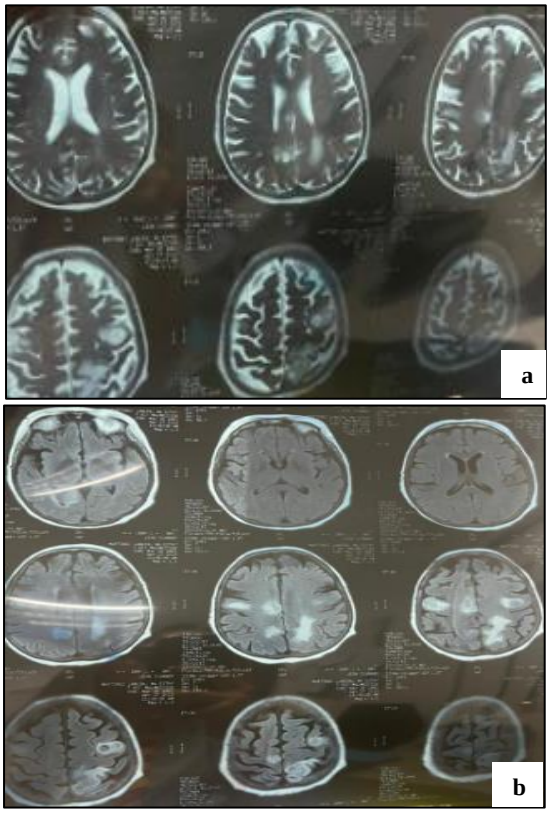

Figure 4 (a and b): Multiple intraparenchymal lesions were observed in the left frontal lobe, right occipital and left parietal lobe, with annular enhancement.

On admission she was neurologically oriented in time, place and space, cranial nerves without alteration, with the presence of bradilalia, Daniels strength 4/5 in lower extremities, upper extremities with preserved strength, sensibility without alterations. Gait not assessable. Normocephalic skull, with dehydration of mucous membranes and integuments ++, oral cavity with dehydration of mucous membranes +, cylindrical neck with central and mobile trachea, no palpable lymph nodes, left infra clavicular region with 2 cm nodule, soft, mobile, well-defined edges hyperemic and hyperthermic, not suppurative, painful on palpation. Cardiopulmonary without alterations, left lumbar region with lesion of the same characteristics described, this one 10 cm in size (Figure 1). Abdomen without alterations, integral extremities, presence of a nodule on the dorsum of the right hand, 2 cm approximately, well delimited borders, soft, with purulent suppuration (Figure 2).

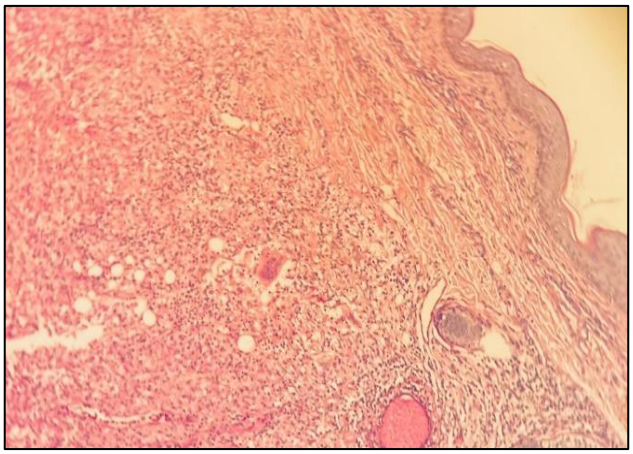

Figure 5: Presence of polymorphonuclear infiltrates.

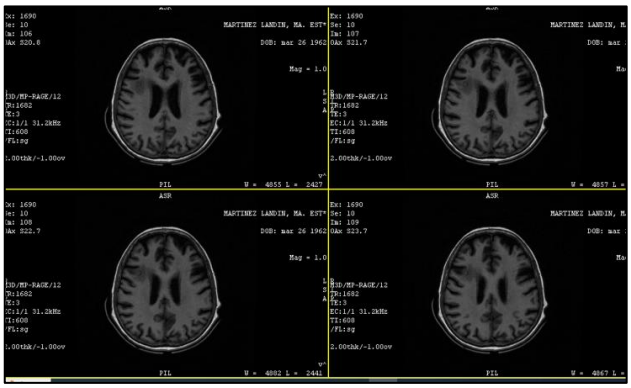

Figure 6: MRI of the skull after the start of empirical treatment.

Laboratory tests on admission showed severe normocitic normochromic anemia of WHO, with leukocytosis at the expense of neutrophils. A diagnosis of soft tissue infection, non-purulent, moderate SAIDI was made and treatment was started with Vancomycin adjusted to renal function. Transthoracic echocardiogram was performed and showed no alteration.

During her hospitalization, she was referred to the infectious disease department, which suggested

ultrasound of skin lesions, and if they were liquid, they should be cultured, as well as a blood culture, and adjustment of the medical treatment based on Meropenem and Linezolid. On April 14.04.23 a thorax tomography was performed, which showed: lesion in the left hemithorax measuring 10×0 cm, probable multiple focus pneumonia, as well as the presence of a well-defined cavitated lesion (Figure 3), as for the cranial MRI, multiple intraparenchymal lesions were observed in the left frontal lobe, right occipital and left parietal lobe, with annular enhancement (Figure 4).

After the tomographic findings, the dose of Meropenem was increased to meningeal dose. On April 17, 23, a lumbar puncture was performed, and the cerebrospinal fluid showed characteristics of rock water: the results were negative for BAAR, Gram, cytochemistry, cytopathology, Toxoplasma, Coccidiomycosis, Candida, Cryptococcus, Aspergillus, Chinese ink, and Mycobacteria. Blood culture report negative for bacterial growth at 48 hours. In new control laboratories, there was a decrease in leukocytes and neutrophils, only CRP of 74 mg was present.

Subsequently, a puncture of the lesion in the subscapular region was performed, 45 ml of purulent appearance were extracted, samples were sent for culture and a skin biopsy was taken from the left forearm. The culture was reported with *Staphylococcus hominis*. The biopsy was reported with polymorphonuclear infiltration and granulomatous reaction (Figure 5).

As there was no improvement of the lesions and the clinical picture based on bradilalia, as well as the progressive decrease of strength in the lower extremities, biopsies of brain lesions were suggested, which were denied by the patient. A diagnostic suspicion of Nocardia was made, due to the relationship of dermatological and cerebral lesions and clinical picture, once the rest of the differential diagnoses were ruled out. As no biopsy of brain lesions was accepted, empirical treatment with Linezolid and trimethoprim/sulfamethoxazole was started. A new MRI was requested 2 weeks after empirical treatment. No lesions previously described in the first MRI were observed (Figure 6). Therefore, it was decided to continue with trimethoprim/sulfamethoxazole until completing 12 weeks orally.

DISCUSSION

This case presents a diagnostic and therapeutic challenge in an immunosuppressed patient with a renal transplant, who developed cavitary pulmonary lesions and neurological involvement, suggesting a disseminated infection. The presence of Nocardia asteroides, confirmed from bronchoalveolar lavage samples, established the diagnosis, although its initial presentation was nonspecific and compatible with other opportunistic infections or malignancies.[6,7]

Regarding the interpretation of the results, the pulmonary and cerebral lesions, along with the patient's clinical picture, indicate hematogenous dissemination, a common complication in patients with disseminated nocardiosis. Disseminated infection occurs in up to 44% of cases and carries a poor prognosis, especially with central nervous system (CNS) involvement, which occurs in one-third of cases and is a major cause of morbidity and mortality.[8,9]

The management of the case included empirical treatment with trimethoprim-sulfamethoxazole, which is the cornerstone in the treatment of nocardiosis, and was intensified with imipenem due to suspected CNS involvement. This approach follows current guidelines that recommend prolonged and combined treatment in severe infections or with neurological involvement. The clinical response observed, with the disappearance of brain lesions on subsequent MRI, underscores the efficacy of this therapeutic combination.[10,11]

In comparison with previous studies, this case reinforces the diagnostic complexity in transplant patients. The studies by Saullo et al on Nocardia infections in solid organ transplants highlight that diagnostic delays are common due to nonspecific clinical manifestations and the need for advanced techniques, such as 16S rRNA sequencing, to improve diagnostic accuracy.[4] Additionally, the review by Peleg et al. in transplant patients shows that nocardiosis is associated with higher mortality, especially when there is CNS involvement, as in this case.[11]

This report contributes to the growing body of literature that emphasizes the importance of thorough and timely diagnostic evaluation in immunosuppressed patients, in order to initiate targeted treatment that improves the prognosis in such complex infections as nocardiosis.[11]

CONCLUSION

This case report not only elucidates the clinical nuances of diagnosing and managing nocardiosis in immunosuppressed patients but also reinforces the importance of an individualized, patient-centered approach that integrates prompt diagnostic investigations, tailored antimicrobial therapy, and judicious management of immunosuppressive regimens. As the landscape of immunosuppressive therapy continues to evolve, with an increasing number of patients at risk for opportunistic infections, future research should focus on optimizing diagnostic modalities, refining therapeutic protocols, and investigating novel antimicrobial agents to reduce the burden of this elusive pathogen. Clinicians must remain vigilant and proactive in recognizing and managing nocardiosis, particularly in high-risk groups, to improve outcomes and prevent the devastating consequences associated with delayed or inadequate treatment.

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