A Rare Case of Drug-Resistant Nocardia transvalensis Infection in a Renal Transplant Patient

Rajan Kapoor, MD1, Sreedhar Adapa, MD2, Anusha Vakiti, MD, Imran Yaseen Gani, MD, Laura Mulloy, DO, and Sandeep Anand Padala, MD

Abstract

Nocardia transvalensis is a rare species of Nocardia and is known to be a drug-resistant organism. Multiple cases have been reported of Nocardia species causing opportunistic infections in immunocompromised hosts. To our knowledge, we report the first case of successfully treated drug-resistant Nocardia transvalensis causing pulmonary nocardiosis in a renal transplant patient. Our case validates the importance of prompt identification of Nocardia species and their drug sensitivities to improve clinical outcomes and reduce mortality.

Keywords

kidney transplant, Nocardia, Nocardia transvalensis, disseminated nocardiosis, multidrug-resistant Nocardia transvalensis, pulmonary nocardiosis, immunocompromised, linezolid

Case Presentation

A 69-year-old male with past medical history of hypertension, asthma, coronary artery disease, end-stage renal disease secondary to hypertensive glomerulosclerosis s/p deceased donor kidney transplant 4 months back presented to the hospital with productive cough, fever, and anorexia of 2 weeks duration. Vitals on presentation were temperature of 38.5°C, heart rate of 72/min, blood pressure of 167/62 mm Hg, and respiratory rate of 22/min with oxygen saturation between 90% and 92% on room air. On physical examination, he had bibasilar crackles, more prominent on the left. Laboratory findings revealed an elevated white blood cell count of 15 100/µL, blood urea nitrogen of 21, and creatinine of 1.9 (baseline creatinine of 1.9-2.0). Urinalysis was unremarkable. Chest X-ray (CXR) showed a left lower lobe consolidation. Pan cultures were obtained, and treatment was started with intravenous vancomycin and piperacillin/tazobactam for empiric coverage. His posttransplant immunosuppressive regimen of mycophenolate mofetil, tacrolimus, and prednisone was continued with other supportive measures. His prophylactic medications of nystatin, valganciclovir, and trimethoprim-sulfamethoxazole (TMP-SMX) were discontinued 4 weeks prior to admission after completion of 3-month posttransplant prophylaxis course. On day 3, 1 out of the 4 blood cultures grew gram-positive bacilli for which ampicillin was added for better central nervous system (CNS) penetration to cover Listeria infection as well. The computed tomography (CT) scan of head and lumbar puncture ruled out any CNS involvement. On day 7, final report of the blood culture revealed weakly acid-fast filamentous gram-positive bacteria. On further review of the gram stain and colony morphology of the organisms, it was identified as Nocardia. The diagnosis of disseminated nocardiosis secondary to pulmonary source (left lower lobe pneumonia) was made. Treatment for Nocardia was initiated with imipenem/cilastatin, and initial antibiotics (vancomycin, piperacillin/tazobactam, and ampicillin) were discontinued. Despite changing the antibiotics, there was no significant improvement in his overall clinical condition, and the patient remained with supplemental oxygen–dependent, persistent cough and with productive phlegm. Speciation of the organism was consistent with Nocardia transvalensis, which was resistant to imipenem, bactrim, ceftriaxone, augmentin, and minocycline. It was
reported to be sensitive to linezolid, amikacin, moxifloxacin, clarithromycin, and tobramycin. Imipenem/cilastatin was discontinued, and linezolid along with moxifloxacin was initiated on day 14. Within the next 3 days, the patient started showing signs of improvement and was discharged home in a stable condition. He took linezolid 300 mg daily and moxifloxacin 400 mg daily for 12 months and remained asymptomatic. His follow-up visits were uneventful, and the patient was asymptomatic. Repeat CXR at the follow-up visit showed resolution of the pneumonia.

Discussion

Renal transplant patients are at a higher risk of infections as compared with the general population due to higher degree of immunosuppression posttransplant. Bacterial, viral, and fungal infections are all frequently seen in patients in the posttransplantation period. Bacterial infections causing urinary tract infections, diarrhea, pneumonia, and wound infections are the most common scenarios in the early posttransplant period. Highly invasive fungal infections have also been reported within first 4 weeks of transplantation, and concurrent infections with fungal and viral etiology have also been reported within first 12 months of transplant. Nocardia is a ubiquitous, slow-growing, variably acid-fast, gram-positive Bacillus. It appears as a filamentous bacterium with branching hyphae and is commonly found in fresh water as well as saltwater, and decomposing vegetation. Nocardia usually manifests as an opportunistic infection in immunocompromised hosts. Risk factors for Nocardia infection include impaired cell-mediated immunity states such as solid organ transplant or hematopoietic stem cell transplant recipients, lymphoma and other malignancies, human immunodeficiency virus (HIV) infection, cytomegalovirus infections, and patients with chronic obstructive pulmonary disease and diabetes. As per a review of 303 cases of nocardioses from Japan, the most common predisposing factors were immunosuppressive agents (22.4%), cancer (6.6%), diabetes (3.6%), and AIDS (2.0%).

Pulmonary nocardiosis is the most common presentation as the usual portal of entry for the bacteria is via inhalation. Usually, the onset of symptoms is subacute to chronic as was seen in our case. Common symptoms include productive cough, fever, shortness of breath, chest pain, hemoptysis, night sweats, anorexia, and weight loss. CXR findings can be variable and can present either as a consolidation, cavitary lesion or pleural effusion. The infection can disseminate via hematogenous spread, and bacteremia can be commonly seen in patients with pulmonary nocardiosis as presented in our case. Extrapulmonary presentation is usually an abscess formation, and the most common site is the CNS. Affected individuals can have one or more brain abscesses and associated pressure like symptoms such as headaches, visual disturbances, and changes in mentation or seizures. As Nocardia is neurotropic, CNS imaging should be considered in immunosuppressed patients with severe disease that was obtained in our case along with a lumbar puncture and showed no CNS involvement. Skin and soft tissue involvement with Nocardia-mimicking cellulitis is common in immunocompetent hosts as well. It can result from skin and soft tissue injuries with the contaminated soil. Bacteremia followed by cutaneous infection is less commonly seen. A review of literature from 1980 to 2010 on Nocardia infections in renal transplant patients by Yu et al also reported lung, brain, skin, and subcutaneous tissues as the most frequent organs involved. Kidney allograft, eye, pleura, pericardium, and joints were less commonly involved. Nocardia infection occurred more commonly in males after cadaver kidney transplants and developed after a mean duration of 34 months posttransplant. This is in contrast to our case where the Nocardia infection developed early on at 4 months posttransplant.

More than 80 species of Nocardia have been identified, of which more than half were described in past 15 years. As per a recent antibiotic susceptibility review of 1299 isolates by Schlaberg et al, the incidence of N transvalensis was only 6%. Yu et al reported 8 major Nocardia species in their review of transplant patients, of which 56% cases were of Nocardia asteroides, 18% Nocardia farcinica, 9% Nocardia brasiliensis, and the rest were under other Nocardia species or not classified. Queipo-Zaragoza et al reported 5 cases of Nocardia in a retrospective review of 1239 kidney transplant cases and none were Nocardia transvalensis. Nocardia transvalensis infection has been reported in heart transplant recipients, patients with lung cancer, patients with cystic fibrosis, and patients with bronchiectasis and tuberculosis. McNeil et al reported a renal transplant patient with pulmonary nocardiosis from N transvalensis but with an unfortunate outcome. TMP-SMX has traditionally been considered the gold standard for Nocardia therapy, either as monotherapy or as a part of combination therapy particularly for severe infections. The high dose of TMP-SMX, its adverse effects, and now with emerging resistance pattern for some species may limit its use. In the review by Schlaberg et al, antibiotic resistance was most noticeable with Nocardia pseudobrasiliensis (31%) and N transvalensis (19%). Imipenem/cilastatin is effective against most Nocardia species and is often used as the drug of choice in severe cases of disseminated nocardiosis but showed resistance pattern in 94% of isolates of N transvalensis as was clinically evident in our case as well. N transvalensis isolates were also found to be highly resistant to ceftriaxone (37%), augmentin (53%), amikacin (72%), ciprofloxacin (16%), minocycline (85%), clarithromycin (96%), and tobramycin (96%). Drug resistance was very commonly seen in N transvalensis isolates (83%), but all the isolates were susceptible to linezolid as shown in our case as well.

Early identification and susceptibility testing of N transvalensis could be challenging due to many reasons that include low level of clinical suspicion for Nocardia, drug-resistant species, slow rate of growth on cultures, and lack of resources in community hospitals to test for specific Nocardia species. However, if clinical suspicion for drug-resistant Nocardia species is high, susceptibility testing should be obtained early to reduce morbidity and mortality and to improve clinical
outcomes. Overall mortality has been reported to be about 16% to 25%. The mortality from pulmonary nocardiosis is around 39%, which increased to 64% in disseminated nocardiosis and 100% in the presence of CNS involvement.

**Conclusion**

We report a unique case of drug-resistant *N transvalensis* infection with pulmonary involvement within 4 months after cadaveric kidney transplant successfully treated with linezolid and moxifloxacin. Our case illustrates the diagnostic and therapeutic challenges faced in this rare species of *Nocardia* infection. Isolation of *Nocardia* in cultures should not be considered as a contaminant. It could be a life-threatening infection that is difficult to treat requiring protracted course of antibiotics. Guidelines typically recommend 3 to 6 weeks of intravenous antibiotics, followed by 6 to 12 months of oral antibiotics, with even a longer course being used in severe disease and immunocompromised hosts.

**Declaration of Conflicting Interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding**

The author(s) received no financial support for the research, authorship, and/or publication of this article.

**Ethics Approval**

Our institution does not require ethical approval for reporting individual cases or case series.

**Informed Consent**

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

**ORCID iDs**

Rajan Kapoor https://orcid.org/0000-0002-8633-7717
Sreedhar Adapa https://orcid.org/0000-0001-5608-5654
Sandee Anand Padala https://orcid.org/0000-0002-8773-073X

**References**

1. Karuthu S, Blumberg EA. Common infections in kidney transplant recipients. *Clin J Am Soc Nephrol*. 2012;7:2058-2070.
2. Gani I, Daroodchi A, Falkenstrom K, et al. Gastric mucormycosis in a renal transplant patient treated with isavuconazole monotherapy. *Case Rep Transplant*. 2019; 2019:9839780.
3. Gani I, Kosuru V, Saleem M, Kapoor R. Simultaneous *Candida albicans* and herpes simplex virus type 2 esophagitis in a renal transplant recipient. *BMJ Case Rep*. 2019;12:e230410.
4. Beaman BL, Burnside J, Edwards B, Causey W. Nocardial infections in the United States, 1972-1974. *J Infect Dis*. 1976;134:286-289.
5. Long PF. A retrospective study of *Nocardia* infections associated with the acquired immune deficiency syndrome (AIDS). *Infection*. 1994;22:362-364.
6. Peleg AY, Husain S, Qureshi ZA, et al. Risk factors, clinical characteristics, and outcome of *Nocardia* infection in organ transplant recipients: a matched case-control study. *Clin Infect Dis*. 2007;44:1307-1314.
7. Kageyama A, Yazawa K, Ishikawa J, Hotta K, Nishimura K, Mikami Y. *Nocardia* infections in Japan from 1992 to 2001, including the first report of infection by *Nocardia transvalensis*. *Eur J Epidemiol*. 2004;19:383-389.
8. Beaman BL, Beaman L. *Nocardia* species: host-parasite relationships. *Clin Microbiol Rev*. 1994;7:213-264.
9. Martínez R, Reyes S, Menéndez R. Pulmonary nocardiosis: risk factors, clinical features, diagnosis and prognosis. *Curr Opin Pulm Med*. 2008;14:219-227.
10. 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;19:259-282.
11. Yu X, Han F, Wu J, et al. *Nocardia* infection in kidney transplant recipients: case report and analysis of 66 published cases. *Transpl Infect Dis*. 2011;13:385-391.
12. Schlaber R, Fisher MA, Hanson KE. Susceptibility profiles of *Nocardia* isolates based on current taxonomy. *Antimicrob Agents Chemother*. 2014;58:795-800.
13. Queipo-Zaragozá JA, Broseta-Rico E, Alapont-Alacreu JM, Santos-Durantez M, Sánchez-Plumed J, Jiménez-Cruz JF. *Nocardia* infection in immunosuppressed kidney transplant recipients. *Scand J Urol Nephrol*. 2004;38:168-173.
14. Lopez FA, Johnson F, Novosad DM, Beaman BL, Holodniy M. Successful management of disseminated *Nocardia transvalensis* infection in a heart transplant recipient after development of sulfonamide resistance: case report and review. *J Heart Lung Transplant*. 2003;22:492-497.
15. Yorke RF, Rouah E. Nocardiosis with brain abscess due to an unusual species, *Nocardia transvalensis*. *Arch Pathol Lab Med*. 2003;127:224-226.
16. Aravantagi A, Patra KP, Broussard M, Jones K. A case of *Nocardia transvalensis* pneumonia in a 19-year-old cystic fibrosis patient. *Lung India*. 2012;29:283-285.
17. McNeil MM, Brown JM, Magruder CH, et al. Disseminated *Nocardia transvalensis* infection: an unusual opportunistic pathogen in severely immunocompromised patients. *J Infect Dis*. 1992;165:175-178.
18. Tomás RM, Villanueva RM, Calzada SR, et al. Pulmonary nocardiosis: risk factors and outcomes. *Respirology*. 2007;12:394-400.