CASE REPORT

Disseminated nocardiosis with infective endocarditis of a transplanted heart

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SUMMARY
Nocardiosis is caused by various species of Nocardia and typically occurs as an opportunistic infection. It frequently disseminates, most often involving the lungs, subcutaneous tissues and central nervous system. It has rarely been reported to affect native heart valves. We report the case of a 64-year-old man with disseminated nocardiosis involving the brain, lungs, muscle and tricuspid valve of a transplanted heart. Following antimicrobial therapy, the patient improved clinically and there was no evidence of residual infection on follow-up imaging. This case highlights the presentation of nocardiosis, current therapeutic guidelines and the question of prophylaxis against Nocardia in immunocompromised patients.

BACKGROUND
Infective endocarditis is a relatively common condition. The typical organisms of native valve endocarditis include Staphylococcus aureus, coagulase-negative staphylococci, streptococci and enterococci. Acid-fast bacilli are a rare cause of endocarditis.1 Nocardia has the ability to affect virtually any organ; however, literature describing cardiac disease is limited. This case demonstrates the disseminating potential of Nocardia and emphasises the importance of cardiac evaluation in affected patients. Questions remain about the optimal therapy for disseminated nocardiosis and the issue of prophylactic therapy in immunocompromised patients.

CASE PRESENTATION
A 64-year-old man with a history of chronic kidney disease and heart transplantation 3 months prior, for which he has since been treated with a stable immunosuppressive regimen (tacrolimus, prednisone and mycophenolate mofetil), was admitted to the hospital with fever and chills. Relevant history began 3 weeks prior to presentation when the patient experienced the onset of ‘dull aching’ pain in the right thigh. On the morning of admission, he developed fever and chills, prompting him to seek evaluation. There has been no recent escalation in the patient’s immunosuppressive therapy and tacrolimus blood levels have predominantly been in the therapeutic range since transplantation. On examination, temperature was 38°C and heart rate 130 beats/min. There was a new grade 2/6 holosystolic murmur best heard over the left lower sternal border that augmented with inspiration. There was dullness to percussion and decreased breath sounds over the base of the right lung. The right thigh was tender to palpation.

INVESTIGATIONS
Laboratory evaluation was notable for a peripheral white blood cell count of $3 \times 10^9/L$, which was stable from prior. CT imaging of the chest showed multiple peripheral lung nodules with a rightsided pleural effusion (figure 1). MRI of the right proximal leg demonstrated a $2 \times 1.5 \times 3$ cm fluid collection consistent with abscess within the right vastus lateralis muscle (figure 2). Gram stain of the blood demonstrated the presence of Gram-positive bacilli. A transthoracic echocardiogram showed new moderate tricuspid regurgitation, but no clear vegetation. A transoesophageal echocardiogram revealed a small mobile mass on the tricuspid valve (figure 3). Blood cultures eventually returned positive for Nocardia asteroides. Given the evidence of endocarditis and the disseminating nature of Nocardia, a brain MRI was obtained and revealed a 9 mm ring-enhancing lesion in the right temporal lobe (figure 4).

TREATMENT
Given the immunocompromised status of the host, the Gram stain results triggered initiation of oral trimethoprim–sulfamethoxazole (TMP/SMX) to cover the possibility of infection with Nocardia species. When central nervous system (CNS) involvement was confirmed by neuroimaging, imipenem–cilastatin was added to the antibiotic regimen. At hospital discharge, imipenem–cilastatin was replaced with ceftriaxone based on microbial sensitivity, and oral TMP/SMX was continued.

Figure 1 Chest CT demonstrating a 1.7 cm nodule in the periphery of the right lung with associated pleural effusion.
Unusual presentation of more common disease/injury

On development of nephrotoxicity 4 weeks after discharge, TMP/SMX was switched to linezolid. Intravenous ceftriaxone was continued for 12 weeks and then switched to oral minocycline for a planned 12-month course. However, minocycline was discontinued shortly thereafter due to gastrointestinal side effects. The patient was continued on linezolid monotherapy for 4 more months, bringing the total duration of antibiotic therapy to approximately 7 months.

OUTCOME AND FOLLOW-UP
The patient improved with treatment and there was no evidence of residual infection on follow-up imaging. On completion of therapy, a brain MRI revealed resolution of the abscess and an echocardiogram demonstrated stable tricuspid regurgitation.

DISCUSSION
*Nocardia* sp are aerobic Gram-positive bacteria that can cause localised or systemic disease in humans. The bacteria appear as filamentous branching rods that are weakly acid-fast staining. *Nocardia* is not part of normal human flora and can be found worldwide in soil, decaying vegetable matter and aquatic environments. Inhalation is the most common mode of entry.

*Nocardiosis* is most often a disease of the immunocompromised; however, roughly one-third of those infected are immunocompetent. *Nocardia* has the ability to disseminate, most commonly involving the lungs, subcutaneous tissues and CNS. It has rarely been reported to affect native heart valves. In this case, cardiac examination revealed a new regurgitant murmur, leading to the discovery of a vegetation on the tricuspid valve and associated tricuspid regurgitation by echocardiography, confirming infective endocarditis in the setting of disseminated nocardiosis. In a large case-control study evaluating solid organ transplant recipients over a 10-year period, 35 patients out of 5126 (0.7%) were identified as having *Nocardia* infection. Within this subpopulation, 10 patients (29%) were heart transplant recipients. These 10 cases occurred out of a total of 392 heart transplant recipients. Of all the patients with nocardiosis in this study, the lungs were the most frequent sites of infection. No cases of cardiac involvement were reported. A recent large-scale study of 54 cases of nocardiosis in solid organ transplant patients...
Learning points

- Nocardiosis is most often a disease of the immunocompromised; Nocardia has the ability to disseminate, most commonly involving the lungs, subcutaneous tissues and central nervous system.
- Heart transplant recipients represent a large proportion of immunocompromised patients who become infected with Nocardia.
- Infective endocarditis should be considered in patients with disseminated nocardiosis. Physical examination is essential for the identification of regurgitant murmurs and other suggestive findings.
- Trimethoprim–sulfamethoxazole (TMP/SMX) at doses used for Pneumocystis jirovecii prophylaxis in immunocompromised patients may not provide coverage for Nocardia. Higher doses of TMP/SMX should be considered for secondary prophylaxis.
- The treatment strategy for nocardiosis depends on severity, but generally requires a long duration of intravenous and oral antibiotics.

References

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