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CASE REPORT

Nocardia niigatensis infection in a kidney transplant recipient

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Summary

This is the first reported case of *Nocardia niigatensis* infection in an adult kidney transplant recipient. A 57-year-old Asian woman presented with multiple cutaneous abscesses and rapidly growing fungating mass on the left pretibial area for 2 months. She received a cadaveric kidney transplant 4 years previously and was undergoing immunosuppression with prednisolone, cyclosporine and mycophenolate sodium. The microbiological diagnosis was established by isolation of *Nocardia* from the purulent material expressed from a granule. The strain was identified to the species level by 16S rRNA gene-targeted PCR. The closest match was with *N. niigatensis*. Antibiotic treatment (trimethotrim–sulfamethoxazole) was continued for 6 months and the skin lesions improved.

Immunosuppressed patients are susceptible to infections by microorganisms of low virulence, such as *Nocardia* spp. There are many species within the genus of *Nocardia*, with the following strains being the most common causes of infection in transplant recipients: *Nocardia* asteroids complex (*N. asteroides sensu strictu*, *N. facinica*, and *N. nova*), *N. brasiliensis*, *N. otitidiscaviarum*, and *N. transvalensis* [1–3]. To our knowledge, this is the first reported case of *N. niigatensis* infection in an adult kidney transplant recipient.

Case report

A 57-year-old woman with kidney failure secondary to hypertension underwent a deceased kidney transplant 4 years previously presented for evaluation of multiple cutaneous abscesses and rapidly growing fungating mass on the left pretibial area of 2 months duration (Fig. 1). Immunosuppression regime consisted of basiliximab and methylprednisolone on induction and maintenance immunosupression was with prednisolone, cyclosporine, and mycophenolate sodium. Four months after transplantation, she was given a 750-mg pulse of methylprednisolone treatment for acute allograft rejection. Her serum creatinine level, which had been around 1.6–1.8 mg/dl, rose to 1.8 and 2.0 mg/dl after the pulse therapy. She sustained a lacerated wound in the left knee during outdoor activities 5 months before and the wound was sutured the day after the injury. She took amoxicillin for 10 days and the wound improved. Two months after the injury, she presented with a small erythematous cutaneous nodule on the left knee and an excisional biopsy was performed. Histopathology of the cutaneous nodule showed inflammation; no organisms were isolated. Four months after the injury, she presented with a 5×5 cm^2 fungating mass on the left knee and a 3×3 cm^2 fungating mass on the pretibial area (Fig. 1a and b). A biopsy and wound cultures were performed, which revealed a fungus. She was started on intraconazole for 20 days; however, no improvement was observed and another cutaneous lesion appeared on the left lower pretibial area. She denied fever, cough or headache. On physical examination, she was afebrile and her lung sounds were clear. The left leg was swollen and dermatological examination of the left

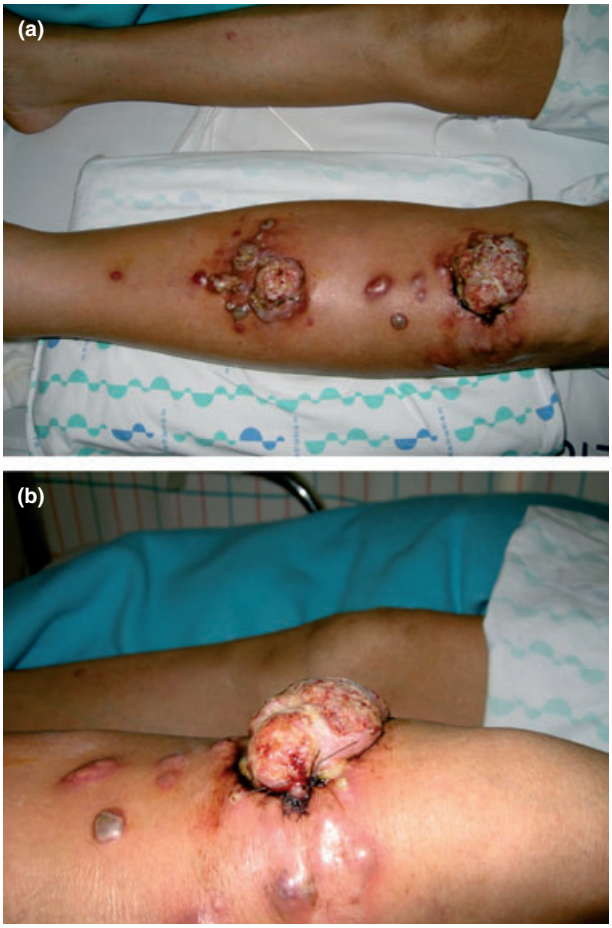

Figure 1 (a) Anterior view of mycetoma with multiple draining sinus tracts on the left lower leg. (b) Lateral view of mycetoma with multiple draining sinus tracts on the left lower leg.

pretibial cutaneous lesion showed swelling, suppuration, formation of multiple sinus tracts and granules in the draining purulent material. The microbiological diagnosis was made by isolation of *Nocardia* spp. from the purulent material expressed from a granule. The specimen was cultured on blood agar plates and Sabouraud's dextrose agar that were incubated in a CO_2 atmosphere at 37 °C. After incubation for only 2 days, wrinkled, dull, rough, white–orange colonies appeared on all media. The Gram stain showed Gram-positive branching filamentous bacilli, along with a positive modified AFB stain. We identified *Nocardia* spp. to the genus level in our laboratory using standard manual methods based on biochemical tests and enzymatic activities. The strain was identified to the species level by 16S rRNA gene-targeted PCR. Extraction of bacterial DNA was performed using a DNeasy kit (Qiagen GmbH, Hilden, Germany) according to the manufacturer's instructions. The sequences of the 16S ribosomal DNA primers were based upon previously reported

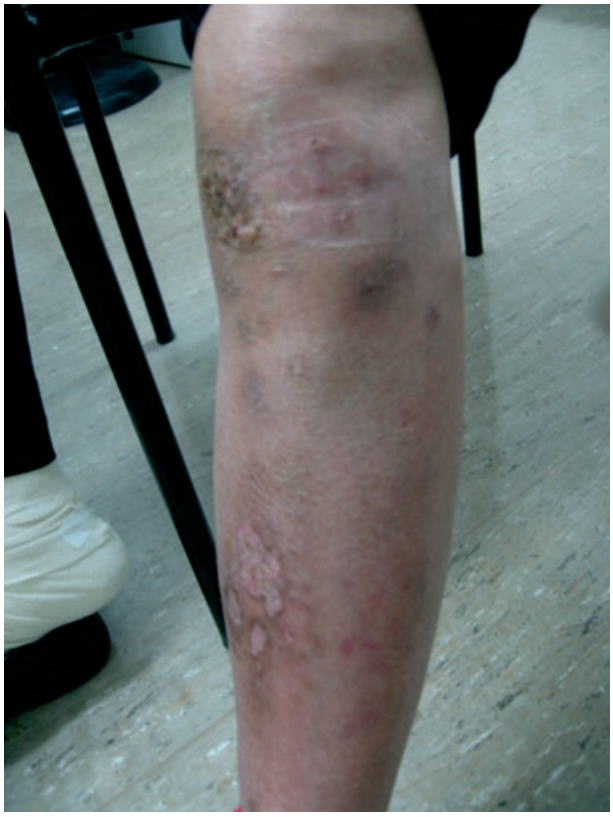

Figure 2 Antibiotic treatment (trimethotrim–sulfamethoxazole) was continued for 6 months and the skin lesions improved.

sequences [4]: forward primer, 16S-S, 5′-AGA GTT TGA TCC TGG CTC AG-3′; reverse primer, 16S-AS, 5′-AGG AGG TGA TCC AGC CGC A-3′. The purified PCR products were directly sequenced with an ABI Prism 3100 DNA sequencer (Applied Biosystems, Foster City, CA, USA). The resulting sequences were aligned with corresponding sequences of representative *Nocardia* species in the GenBank database using the BLASTN algorithm. The closest matches were obtained with *N. niigatensis* [GenBank accession no. DQ659910, 99% (553/556)]. Based on these findings, the patient was diagnosed with a *N. niigatensis* infection. We began treatment with trimethotrim–sulfamethoxazole and ampicillin–sulbactam and discontinued itraconazole and mycophenolate sodium. After 10 days, her general condition improved. We discontinued ampicillin–sulbactam and maintained trimethotrim–sulfamethoxazole for 6 months. Her serum creatinine level was around 1.8–2.0 mg/dl during the antibiotic therapy and the skin lesions improved (Fig. 2).

Discussion

Nocardia spp. are ubiquitous environmental saprophytes, living in soil, organic matter and water [5]. The frequency

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of nocardial infections in solid organ transplant recipients varies between 0.7% and 3% and has mostly been reported in heart, kidney and liver transplant recipients [6]. These are commonly misunderstood as fungal infections, as in this case. Immunosuppression is the major risk factor for nocardial infections and the organism is most commonly seen in solid organ transplant recipients, HIV-infected patients, patients with lymphoreticular malignancies or patients treated with chronic corticosteroid therapy. Inhalation of the organism appears to be the main route of transmission, but penetrating cutaneous injury, as in the patient described herein, is another route of inoculation [5]. Although there have been descriptions of clusters of outbreaks around construction sites, most patients develop sporadic infections and it remains unknown whether they were colonized prior to transplantation [7,8]. There are many species within the genus of *Nocardia*, with the following strains being the most common causes of infection in transplant recipients: *Nocardia* asteroids complex (*N. asteroides sensu strictu*, *N. facinica*, and *N. nova*), *N. brasiliensis*, *N. otitidiscaviarum*, and *N. transvalensis* [1–3]. This is the first reported case of *N. niigatensis* infection in an adult kidney transplant recipient. There are no recommended therapeutic regimens for the treatment of *N. niigatensis*, but trimethotrim–sulfamethoxazole is the preferred agent in treating nocardial infections [9]. Trimethotrim–sulfamethoxazole achieves high tissue concentrations in the lung, brain, skin and bone [10]. The recommended treatment dosing with trimethotrim–sulfamethoxazole is 15 mg/kg/day in 2–4 divided doses for organ transplant recipients and can be given intravenously or orally [11]. This is the first reported case of the successful treatment of *N. niigatensis* abscesses with trimethotrim–sulfamethoxazole.

Authorship

IP: wrote the paper as the first author. WL: identified *Nocardia niigatensis*. JC and SY: collected data. G-TS and HK: designed the paper.

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