CASE REPORT

Disseminated *Nocardia* infection in a renal transplant patient: the pitfalls of diagnosis and managementThomas Jorna,¹ Joanne Taylor²

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SUMMARY

This case report describes the progress of an immunosuppressed renal transplant patient who presented with signs and symptoms of community acquired pneumonia. He did not respond to conventional therapy and underwent further investigation. Definitive diagnosis proved challenging. On the basis of multiple investigation results he was treated variously for bacterial, viral and tuberculous infections. At one point it was thought pulmonary malignancy was likely. After excision of a subcutaneous nodule, microscopy and culture confirmed diagnosis of disseminated *Nocardia farcinica*. This case demonstrates the difficulty in diagnosing this rare infection in immunocompromised patients, the problems posed by concomitant infection and the potential hazards of multiple drug interactions. On initiation of optimum antimicrobial therapy and with safe levels of immunosuppression our patient made full recovery without any loss in graft function.

BACKGROUND

The prevalent population of transplant patients is growing and they can present with infections in numerous ways to all medical specialities. This case gives a flavour of the potential rare pathology encountered in immunosuppressed patients. The identity of infectious diseases in this population can often be difficult to identify, especially if the patient has already been treated with various antimicrobials or the infectious organism is fastidious by its nature. Treatment is complicated by the potential for over or under immunosuppression by drug interactions. This case highlights the dangers of drug interactions during prescription and the need to regularly monitor immunosuppressant drug levels.

CASE PRESENTATION

A 58-year-old man was admitted with a 6-week history of shortness of breath, fever and cough productive of purulent sputum. He had lost several kilograms in weight and had been suffering from night sweats. His general practitioner had treated him for lower respiratory tract infection with amoxicillin without any improvement in symptoms. He had a history of polycystic kidney disease causing end-stage renal failure and had received a cadaveric renal transplant 2 years prior to this presentation. He was immunosuppressed with mycophenolate mofetil (MMF) 1 g/day and tacrolimus 4.5 mg/day. Initial observations were as follows: temperature 38.3°C, pulse 80 beats/min and

regular, blood pressure 123/79 mm Hg, respiratory rate 20/min and oxygen saturations 98% on air. On examination, there was bronchial breathing at the apex of the right lung and a 1 cm subcutaneous lesion (initially thought to be a lipoma) in the left upper quadrant of the abdomen. The transplant kidney was non-tender and there was no palpable lymphadenopathy.

INVESTIGATIONS

Blood tests revealed a normocytic anaemia, haemoglobin 9.6 g/dl, white cell count $12.5 \times 10^9/l$, C reactive protein 115 mg/l, normal liver function tests and a stable creatine of 254 $\mu\text{mol/l}$. A chest x-ray showed consolidation in the right upper lobe (figure 1). An ultrasound scan of the abdomen showed no pathology related to the transplant kidney; both native kidneys and the liver contained multiple cysts.

Further tests were requested including blood and sputum cultures, tacrolimus level, *cytomegalovirus* (CMV), Epstein-Barr virus, herpes simplex virus PCR, urine for *Legionella* and pneumococcal antigens, serology for atypical respiratory pathogens and a CT of the chest. A bronchoscopy was performed after consultation with respiratory physicians and the samples were sent for alcohol and acid-fast bacilli, microscopy and culture, fungi, *Pneumocystis jirovecii*, histology and cytology.

Blood and sputum cultures were negative. CMV PCR was positive at $>30\,000$ copies/ml. The trough

Figure 1 Plain chest radiographs showing right upper lobe consolidation 5 weeks after the onset of symptoms.

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Figure 2 (A–C) CT scan of the thorax showing a large right upper lobe soft tissue mass. This abuts the mediastinum and is compressing the right upper lobe bronchus. (D) CT scan of the abdomen showing a subcutaneous soft tissue nodule on the anterior abdominal wall (top arrow) and polycystic kidneys (bottom arrows).

tacrolimus level was very high at 43 (target 4–8) because of an interaction with clarithromycin.

CT of the chest showed a large right upper lobe soft tissue mass, enlarged mediastinal lymph nodes and lesions in the right lower lobe and left lower lobe. The subcutaneous soft tissue nodule on the anterior abdominal wall measuring 2.5×0.7 cm was said to be 'indeterminate' (figure 2).

Since there had been no clinical improvement after 3 weeks, the history and examination were reviewed and the decision taken for biopsy of the subcutaneous lesion in the left upper quadrant of the abdominal wall. This was found to contain pus, the cavity was excised and samples were sent for microscopy and culture.

DIFFERENTIAL DIAGNOSIS

The patient had signs and symptoms of community acquired pneumonia but because he was immunosuppressed there was a wide differential diagnosis of potential bacterial, fungal and viral pathogens including mycobacteria. Consideration was also given to the possibility of malignancy including post-transplant lymphoproliferative disorder.

CMV PCR was positive indicating active disease.

The appearances of bronchoscopy and CT of the chest were suggestive of either a malignant tumour in the right upper lobe or *Mycobacterium tuberculosis*.

Microscopy of the pus taken from the abdominal wall lesion revealed Gram-positive rods with a differential of *Nocardia*, *Rhodococcus* or atypical mycobacteria.

TREATMENT

The initial presentation was of pneumonia and the admitting physicians started the patient on intravenous coamoxiclav, oral clarithromycin and intravenous fluids.

Ganciclovir was given to treat CMV and because of the very high levels tacrolimus was withheld and then reintroduced at a reduced dose after repeat testing of the level.

After CT of the chest and bronchoscopy the patient was started on antituberculous medication including rifampicin pending culture and histology results.

The CMV PCR fell significantly after treatment with ganciclovir. All other samples taken at bronchoscopy for microscopy and culture including acid and alcohol fast bacilli were negative. Samples for cytology and histology had shown inflammation however no evidence of malignancy was reported. The patient became neutropaenic probably as a result of MMF and sepsis, his MMF was therefore stopped.

While the identification and sensitivities of the Gram-negative rods identified from the abdominal wall lesion were pending, antimicrobial treatment was changed to cover the possibility of *Nocardia* with oral linezolid and intravenous cotrimoxazole. The patient continued to have fever and cotrimoxazole was changed to meropenem. After molecular characterisation the organism obtained from the abdominal wall abscess was identified as *Nocardia farcinica*. The patient was treated with 6 weeks of intravenous meropenem and then shifted to oral coamoxiclav for 6 months. This ran concurrently with moxifloxacin for 1 year.

While the nature of the Gram-negative rods seen in the pus from the abdominal wall was uncertain but possibly *N farcinica*, an MRI of the brain was requested to look for cerebral involvement, which was clear.

OUTCOME AND FOLLOW-UP

The patient was discharged on intravenous therapy and made swift recovery both clinically and biochemically. Ganciclovir was continued during this time with a plan to stop when the CMV

PCR was negative on two consecutive occasions. He remained on tacrolimus and prednisolone immunosuppression to prevent transplant rejection. At the time of discharge there had been no loss of graft function as compared with the preadmission estimated glomerular filtration rate. The patient was followed up closely in the clinic and made full recovery without any further complication.

DISCUSSION

Nocardiosis is a rare infectious disease and the possibility of this as the cause of our patient's illness was not considered until Gram-negative rods were identified on microscopy. There are a number of other case reports of renal transplant recipients developing *Nocardia* infections.^{1–3} These cases had similar features of disseminated disease commonly involving the skin, lungs and brain. There is often coinfection with CMV disease. In patients who are organ transplant recipients, independent risk factors for nocardiosis include high-dose glucocorticoids, therapy with calcineurin inhibitors (particularly with high drug levels) and CMV infection. Our patient had both high tacrolimus levels and concurrent CMV infection.

Immunosuppression for a variety of reasons such as transplantation, steroid therapy, malignancy, diabetes and HIV are all risk factors for nocardiosis, although up to one-third of the cases occur in immunocompetent individuals. Nocardiosis by its nature is an infectious disease that can affect multiple organs. For these reasons it is important that physicians of all specialities consider it in microbiological differential diagnosis when patients present with signs and symptoms of an atypical infection.

The appearances at CT have a wide differential diagnosis, as shown in this case, including tuberculosis (TB), fungal disease and malignancy.^{4–5} It is common to misdiagnose patients with malignancy or TB as occurred in our patient. Isolation from blood cultures is difficult due to the fastidious nature of the bacteria.

Patients with cutaneous lesions usually have disseminated disease, as was the case with our patient. All patients with pulmonary involvement should undergo imaging to look for cerebral involvement.

Definitive diagnosis requires isolation from a clinical specimen. Most routine culture media can support *N. farcinica* but more specialist culture media may be needed to reduce overgrowth by other organisms. Obtaining speciation is important as this has a range of sensitivities. There are no prospective randomised trials regarding optimal antimicrobial therapy. Severe infection should be treated empirically with two or three intravenous agents while identification and susceptibility testing is awaited.

Treatment should continue for up to 12 months given the relapsing nature of the disease. Long-term maintenance therapy, for example, cotrimoxazole or doxycycline may be necessary for immunocompromised patients.

Learning points

Learning points to be taken from this case when treating an immunosuppressed patient presenting with an atypical infection:

- ▶ Nocardiosis can present to a wide range of medical specialities with multiple differing signs and symptoms in both immunocompetent and immunosuppressed patients. It is important for physicians of all specialities to be aware of *Nocardia* as a possible differential diagnosis in patients with atypical infections.
- ▶ An immunosuppressed patient can pose diagnostic difficulty differentiating atypical infection from malignancy. In our case clinical, radiological and histological findings were inconclusive. Exhaustive efforts were needed to make a positive microbiological diagnosis.
- ▶ It is important to be aware of the potential for drug interactions, especially those between immunosuppressant medications and antimicrobials. Tacrolimus is a calcineurin inhibitor immunosuppressant commonly used for transplant recipients. Drug dosing is based on serum trough levels. Tacrolimus levels are increased by macrolides, antifungals (except caspofungin) and some antivirals, whereas levels are reduced by rifampicin. When treating septic patients immunosuppressed with tacrolimus awareness of these interactions is necessary in order to avoid coadministration of these drugs and to allow for dose adjustment to preclude dangerously high or low levels of immunosuppression. In our case, the patient developed a high level of tacrolimus owing to an interaction with clarithromycin which would have increased his susceptibility to serious infections. Difficulties were also encountered in maintaining adequate tacrolimus levels when the patient was put on antituberculous therapy with rifampicin. During this time the prescribed steroid dose was doubled to avoid rejection.
- ▶ Patients can present with multiple pathology, an example from this case was concomitant infection with *cytomegalovirus* and *Nocardia*.

Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Patel MP, Kute VB, Gumber MR, *et al.* Successful treatment of *Nocardia* pneumonia with cytomegalovirus retinitis coinfection in a renal transplant recipient. *Int Urol Nephrol*. Published Online First: 4 Jan 2012. doi:10.1007/s11255-011-0113-9
- 2 Kaswan KK, Vanikar AV, Feroz A, *et al.* *Nocardia* infection in a renal transplant recipient. *Saudi J Kidney Dis Transpl* 2011;22:1203–4.
- 3 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;13:385–91.
- 4 Beaman BL, Beaman L. *Nocardia* species: host-parasite relationships. *Clin Microbiol Rev* 1994;7:213.
- 5 Hwang JH, Koh WJ, Suh GY, *et al.* Pulmonary nocardiosis with multiple cavitary nodules in a HIV-negative immunocompromised patient. *Intern Med* 2004;43:852.

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