Disseminated *Nocardi a farcinica* infection in a uraemia patient with idiopathic thrombocytopenia purpura receiving steroid therapy

Chih-Cheng Lai, Li-Na Lee, Lee-Jene Teng, Ming Shiou Wu, Jui-Chang Tsai and Po-Ren Hsueh

Department of Internal Medicine and Department of Laboratory Medicine, National University Hospital, Taipei, Taiwan

School of Medical Technology and Center for Optoelectronic Biomedicine, National Taiwan University College of Medicine, Taipei, Taiwan

*Nocardia farcinica* has been reported as an increasingly frequent cause of localized and disseminated infections in immunocompromised patients in recent years, but *N. farcinica* bacteraemia remains a rare finding. Here, the case is described of a 68-year-old man with end-stage renal disease and idiopathic thrombocytopenia purpura treated with steroid therapy who developed disseminated infection (bacteraemia, multilobar pneumonia and brain abscesses) due to *N. farcinica*. The isolate was confirmed by partial sequencing analysis of the 16S rRNA gene. The patient recovered after prolonged trimethoprim-sulfamethoxazole therapy with no recurrence in over 1 year.

Introduction

*Nocardia farcinica* infection has been increasingly diagnosed because of the growing population of immunocompromised hosts and the use of improved methods for detection and identification of *Nocardia* species in the clinical laboratory. *N. farcinica* can cause a variety of clinical presentations including localized diseases and disseminated infections, especially in immunocompromised patients (Brown & McNeil, 2003; Boiron *et al.*, 1992; Torres *et al.*, 2000). In this report, we describe a disseminated infection (bacteraemia, multilobar pneumonia and brain abscesses) caused by *N. farcinica* that occurred in a patient with end-stage renal disease, and review the reported cases of *N. farcinica* bacteraemia in the English literature.

Case report

This 68-year-old man had chronic glomerulonephritis-related end-stage renal disease and had received regular haemodialysis for 3 years. His past medical history included splenectomy due to idiopathic thrombocytopenia purpura (ITP) 6 years before this admission, an episode of non-typhoidal salmonellosis with a mycotic abdominal aneurysm 3 years before and excision of colon cancer 7 months before. He had taken prednisolone (10 mg twice daily) orally for ITP for 2 months prior to this admission. He presented at our hospital complaining of fever, chills, headache and productive cough for 7 days. He reported having visited a farm about 2 weeks prior to admission. He did not recall any recent insect bites, injuries or wounds of the trunk or extremities. On physical examination, he was lethargic with clear consciousness. Vital signs included a temperature of 39.8°C, blood pressure of 160/80 mmHg, a pulse rate of 90 min⁻¹ and regular respiration of 20 min⁻¹. There was no meningeal or focal neurological sign. The breathing sounds were clear and no neck lymphadenopathy was found. The skin of the four limbs was intact, except for the clean puncture wound of the arterio-venous shunt over the left forearm.

Laboratory evaluations demonstrated the following values: white blood cell count, 15 890 cells μl⁻¹ (neutrophils 93.8% and lymphocytes 2.1%); C-reactive protein, 17.48 mg dl⁻¹ (reference value, 0.8 mg dl⁻¹); platelet count, 77 000 cells μl⁻¹; blood urea nitrogen, 21.9 mg dl⁻¹; and creatinine 3.4 mg dl⁻¹. Chest x-ray and computed tomography showed multilobar nodular lesions with central necrosis (Fig. 1A).

Treatment with intravenous ampicillin/sulbactam (1.5 g 24 h⁻¹) was initiated. One day after admission, a sputum smear was positive for Gram-positive, branching, filamentous rods, which were acid-fast by the modified Kinyoun method (Fig. 1B). Magnetic resonance imaging of the brain revealed two hypodense lesions with ring enhancement (one 4.2 mm × 4.6 mm nodule at the left parietal lobe and another 3.6 mm × 3.2 mm nodule at the right temporal lobe), indicating the presence of brain abscesses. Intravenous trimethoprim/sulfamethoxazole (160 mg/800 mg
day⁻¹) was administered for the treatment of suspected disseminated *Nocardi*a infection. Rapid resolution of the respiratory signs and symptoms was noted, with subsidence of fever. On the fourth day in hospital, cultures of the sputum sample and two sets of blood cultures collected on the first day all yielded a *Rhodococcus* or *Nocardia* species based on identification by the API CORYNE system (identification profile 3151004) (bioMérieux). Meropenem (500 mg every 2 days) was added to the antimicrobial regimen to cover the possibility of rhodococcal infection. The general condition of the patient continued to improve with this combination therapy.

The isolates were Gram-positive, branching, partially acid-fast bacilli. They were aesculin-positive, tyrosine-negative, arylsulfatase-negative and grew well at 45 °C in ambient air. Partial sequencing analysis of the 16S rRNA gene of the isolates was performed using primer pair 8FPL (5’-AGAGTTTGTGATCCTGGCTCAG-3’) and 1492 (5’-GTTACCTTGTATACGAC TT-3’) (Turenne et al., 2001). The sequences were compared with published sequences in the GenBank database using the BLASTN algorithm. The closest matches were obtained with *N.farcinica* [GenBank accession no. AB162795, 99-9 % (1388/1390) identity] and *N. otitidiscaviarum* [GenBank accession no. X80611, 99-9 % (1388/1390) identity]. Negative xanthine and hypoxanthine hydrolysis reactions and the 16S rRNA sequencing findings confirmed the identification of the isolate as *N. farcinica* (Brown & McNeil, 2003). MICs of the isolate were determined by the broth microdilution method and interpreted according to the guidelines provided by the National Committee for Clinical Laboratory Standards (2000). The isolate was resistant to ampicillin (MIC, >256 µg ml⁻¹), cephalotaxine (>256 µg ml⁻¹) and gentamicin (64 µg ml⁻¹), and susceptible to amoxycillin/clavulanic acid (8 µg ml⁻¹), ciprofloxacin (0.25 µg ml⁻¹), amikacin (8 µg ml⁻¹) and trimethoprim/sulfamethoxazole (1 µg ml⁻¹/19 µg ml⁻¹).

The patient was treated with intravenous trimethoprim/sulfamethoxazole alone. A follow-up chest radiograph 3 weeks after the start of treatment showed a gradual resolution of the nodular lesions. The patient was discharged on day 40 of hospitalization in good health with no detectable sequelae and a prescription of oral trimethoprim/sulfamethoxazole (160 mg/800 mg daily). A follow-up chest x-ray 2 months later showed complete resolution of the nodular lesions. During follow-up for 1 year, there was no evidence of recurrence.

**Discussion**

*Nocardia* species are ubiquitous soil-borne aerobic actinomyetes. Most reported human infections have been caused by *Nocardia asteroides* complex, *Nocardia brasiliensis* and, rarely, *N. farcinica* (Brown & McNeil, 2003). *N. farcinica*, which was originally isolated by Nocard in 1888 from a case of bovine farcy, is the classical pathogen in bovine nocardiosis (Brown & McNeil, 2003). Cases of human infection with *N. farcinica* are increasingly being diagnosed, because of the growing population of immunocompromised hosts and improved methods for detection and identification of *Nocardia* species in the clinical laboratory. *N. farcinica* was reported to constitute 19 % of 200 *Nocardia* isolates in a study from the USA (Wallace et al., 1990), and 60-3 % of 131 isolates in a study from Germany (Peters et al., 1996).

*N. farcinica* can cause a variety of clinical presentations including localized diseases and disseminated infections, especially in immunocompromised patients (Brown & McNeil, 2003; Boiron et al., 1992; Torres et al., 2000). This organism is usually resistant to multiple antimicrobial agents, especially broad-spectrum cephalosporins, which might make treatment of the infection difficult (Brown & McNeil, 2003; Wallace et al., 1990). Our patient presented with a disseminated infection (bacteraemia, multilobar pneumonia and brain abscesses) caused by *N. farcinica*, which was confirmed by the conventional identification method as well as 16S rRNA sequencing analysis (Wallace et al., 1990). The lack of accurate identification of the isolate by the API CORYNE system made the use of an alternative method necessary, although this test may be the most widely
Table 1. Summary of clinical characteristics, antimicrobial therapy and outcome of 14 reported cases of *Nocardia farcinica* bacteraemia

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patient age (years)/sex</th>
<th>Underlying disease(s) or condition(s)</th>
<th>Site(s) of infection</th>
<th>Antimicrobial therapy*</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ertl et al. (1987)</td>
<td>61/M</td>
<td>Aortic valve replacement</td>
<td>Aortic valve</td>
<td>SUL/AMC(S)+AM(S); IMP(S)+AM(S)/TMP-SMX(S)</td>
<td>Survived</td>
</tr>
<tr>
<td>Farina et al. (1995)</td>
<td>40/F</td>
<td>AIDS, IVDU</td>
<td>Lung</td>
<td>NA</td>
<td>Died</td>
</tr>
<tr>
<td>Kontoyiannis et al. (1998)</td>
<td>42/M</td>
<td>Liver transplant, immunosuppression treatment</td>
<td>Lung, brain</td>
<td>SAM; IMP(S)+AM+VAN</td>
<td>Died</td>
</tr>
<tr>
<td>Minamoto &amp; Sordillo (1998)</td>
<td>50/M</td>
<td>AIDS, IVDU</td>
<td>Lung, brain</td>
<td>AMP+CRO+AMN+TMP-SMX; VAN+IMP+AM+CPM(S)</td>
<td>Died</td>
</tr>
<tr>
<td>Peters et al. (1996)</td>
<td>64/M</td>
<td>DM, Wegener’s disease, renal insufficiency, steroid and cyclophosphamide therapy</td>
<td>Brain, subcutaneous tissue, pectoral region and forearm</td>
<td>TMP-SMX(S); MIN(S)+SUF</td>
<td>Survived</td>
</tr>
<tr>
<td>Torres et al. (2000)</td>
<td>85/M</td>
<td>Lymphoma, steroid therapy</td>
<td>Lung, kidney</td>
<td>CTX(R)</td>
<td>Died</td>
</tr>
<tr>
<td>Farina et al. (1995)</td>
<td>11/M</td>
<td>Astrocytoma</td>
<td>Brain, CSF</td>
<td>NA</td>
<td>Survived</td>
</tr>
<tr>
<td>Bhave et al. (1999)</td>
<td>53/M</td>
<td>Bone marrow transplant, chronic GVHD, steroid therapy</td>
<td>Lung</td>
<td>TMP-SMX(S)</td>
<td>Survived</td>
</tr>
<tr>
<td>Farina et al. (2001)</td>
<td>62/M</td>
<td>Kidney transplant</td>
<td>Soft tissue</td>
<td>TMP-SMX+CIP(R)</td>
<td>Survived</td>
</tr>
<tr>
<td>Farina et al. (2001)</td>
<td>60/F</td>
<td>Kidney transplant</td>
<td>Soft tissue</td>
<td>TMP-SMX</td>
<td>Survived</td>
</tr>
<tr>
<td>Farina et al. (2001)</td>
<td>50/F</td>
<td>Lymphoma</td>
<td>Blood</td>
<td>IMP(S)</td>
<td>Survived</td>
</tr>
<tr>
<td>Christidou et al. (2004)</td>
<td>52/M</td>
<td>Lung cancer</td>
<td>Lung</td>
<td>CAZ(R)+AM(S)</td>
<td>Died</td>
</tr>
<tr>
<td>Hitti &amp; Wolff (2005)</td>
<td>91/M</td>
<td>Idiopathic pulmonary fibrosis, steroid therapy</td>
<td>Lung, blood</td>
<td>TMP-SMX (R)</td>
<td>Died</td>
</tr>
<tr>
<td>Present report</td>
<td>68/M</td>
<td>ESRD, ITP with splenectomy, colon cancer, steroid therapy</td>
<td>Lung, brain</td>
<td>SAM; MEM+TMP-SMX; TMP-SMX</td>
<td>Survived</td>
</tr>
</tbody>
</table>

*In vitro* susceptibility results are given in parentheses where available. R, resistant; S, susceptible.
used and generally accepted method for identification of Gram-positive bacilli in the routine hospital laboratory.

Bacteraemia due to \textit{N. farcinica} is rarely encountered. A computer-based search (MEDLINE; years, 1966–2005) of the English-language literature identified 13 additional previously reported cases of \textit{N. farcinica} bacteraemia (Farina et al., 1995; Farina et al., 2001; Torres et al., 2000; Ertl et al., 1987; Peters et al., 1996; Minamoto & Sordillo, 1998; Kontoyiannis et al., 1998; Bhave et al., 1999; Christidou et al., 2004; Hitti & Wolff, 2005). Among the 14 cases (including the present case), there were 11 men and three women, with a mean age of 57.1 years. All patients had various underlying diseases (Table 1). Lung involvement was present in eight patients, central nervous system disease in five and soft tissue involvement in three. Six patients died, two of whom had human immunodeficiency virus (HIV) infection and another two of whom were patients with malignancies. The overall mortality rate was 42.0%, which is comparable to the 50% mortality rate reported by Kontoyiannis et al. (1998).

The portals of entry of \textit{N. farcinica} are the respiratory tract and surgical or traumatic skin wounds (Beaman & Beaman, 1994; Boiron et al., 1992). In our patient, we postulate that the organism might have gained access into the lung by aspiration or by haematogenous spread via a contaminated trivial cutaneous lesion at the farm visit. Because of the limited number of cases and often inadequate information on length of therapy, dose of antibiotics and drug sensitivity, the optimal treatment of \textit{N. farcinica} bacteraemia remains unclear.

In conclusion, we report a case of disseminated infection due to \textit{N. farcinica} in a uremic patient with ITP receiving steroid therapy, which was successfully treated with trimethoprim/sulfamethoxazole. Accurate identification of \textit{N. farcinica} remains a challenge in clinical microbiology laboratories.

References


