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Article

Infection Caused by *Nocardia farcinica*: Case Report and Review

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Abstract *Nocardia farcinica* is a rare *Nocardia* species causing localised and disseminated infections. A case of *Nocardia farcinica* infection is presented, and 52 cases previously reported in the literature are reviewed. The hosts usually had predisposing conditions (85%), and acquired the infection through the respiratory tract or skin; the infection then often spread to the brain, kidney, joints, bones and eyes. Pulmonary or pleural infections (43%), brain abscesses (30%) and wound infections (15%) which failed to respond to conventional antimicrobial therapy were the more frequent forms of infection. *Nocardia farcinica* was frequently isolated from pus (100% of samples), bronchial secretions (41%) and biopsy specimens (63%), but isolation from blood and urine, as in the case presented here, is rare. Antibiotic therapy was adequate in 61% of the patients in whom it was specified, the agents most frequently given being trimethoprim-sulfamethoxazole (54%), amikacin combined with imipenem (7%) and amoxicillin-clavulanate (7%). The high mortality (31%) can be attributed to the severe underlying diseases present, difficulties encountered in identifying the pathogen, inappropriate therapy and late initiation of therapy. Although an infrequent pathogen, *Nocardia farcinica* should be kept in mind as a cause of infection especially in immunosuppressed patients with indolent infections not responding to third-generation cephalosporins.

Introduction

Nocardiosis is a localised or disseminated infection caused by an aerobic actinomycete [1]. There are at least 12 taxonomically recognised species in the *Nocardia* genus, *Nocardia asteroides* being the predominant aetiological agent in human nocardiosis [2]. *Nocardia farcinica*, which was originally isolated by Nocard in 1888 from a case of bovine farcy, is the classical pathogen in bovine nocardiosis. It has recently been redefined as a separate species, as distinct from *Nocardia asteroides* [1, 3], and has been recognised as a human pathogen since 1975 [2, 4]. Cases of human infection with *Nocardia farcinica* are increasingly being diagnosed. This can be attributed to recent developments in taxonomy and in diagnostic methods, and possibly also to a change in the spectrum of human nocardiosis in countries such as Germany where *Nocardia farcinica* is the prevailing species [3, 5]. This change has implications for therapy since *Nocardia farcinica* is characteristically resistant to multiple antimicrobial agents, including third-generation cephalosporins [1, 3].

Nocardia farcinica causes localised or, especially in immunocompromised patients, disseminated infections. Prompt diagnosis of the infection with proper treatment may therefore be life-saving. However, delay in diagnosis is common and invasive diagnostic procedures must frequently be resorted to. To the best of our

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knowledge, isolation of *Nocardia farcinica* from blood and urine samples has rarely been reported. We present a case of disseminated infection caused by *Nocardia farcinica* isolated from multiple urine and blood cultures, and review all cases of *Nocardia farcinica* infection reported in the literature.

Case Report

An 85-year-old man with a non-Hodgkin lymphoma and a 5-day history of fever, a productive cough with greenish sputum, malaise and lower extremity weakness was admitted to our hospital. He had a history of tuberculosis treated with an iatrogenic pneumothorax in 1940, chronic bronchitis, diabetes mellitus and an acute myocardial infarct in January 1997. In June 1997 he presented with a mass in the left lateral cervical region, and a diffuse stage I-A large B-cell lymphoma was diagnosed. He was treated with cyclophosphamide and prednisone, but the response was poor and the lymphoma continued to expand.

On examination his temperature was 39 °C, and a soft mass with purplish-red overlying skin could be palpated in the left lateral cervical and supraclavicular regions. Basal crackles were audible over both lungs, predominantly on the right. The neurological examination showed lower extremity weakness which was more pronounced on the right (2/5), a pathological Babinski response on the right, and diminished reflexes in both lower limbs.

Laboratory findings included a haemoglobin level of 125 g/l, a leukocyte count of 12.6×10^9/l (with 87% polymorphonuclear cells, 8% monocytes, 3% lymphocytes), an ESR of 73 mm in the first hour, a total protein level of 45.8 g/l, an albumin level of 23.4 g/l, a gammaglobulin level of 4.2 g/l, and a lactate dehydrogenase level of 473 U/l. Analysis of arterial blood gases (FiO_2 21%) revealed a pH of 7.53, a PO_2 of 54 mm Hg and a PCO_2 of 34.9 mm Hg. A chest radiograph revealed post-tuberculosis pleural fibrosis, and infiltrates in the left upper lobe and base of the left lung. A computed tomography (CT) brain scan was normal. Urinalysis showed abundant leukocytes, some erythrocytes and a few epithelial cells; various microorganisms were seen on Gram stain but were thought to be contaminants. Two further urine specimens were sent to the microbiology laboratory. Ziehl-Neelsen staining and an analysis using the polymerase chain reaction to detect *Mycobacterium tuberculosis* complex (Gen-Probe, USA) were negative in two urine samples and two sputum samples. A skin biopsy of the cervical lesion revealed lymphomatous infiltration.

A tentative diagnosis of bacterial pneumonia, an ischaemic stroke in the region supplied by the anterior cerebral artery and a refractory, progressive lymphoma was established, and treatment with intravenous cefotaxime (1 g q.i.d.) and indomethacin was initiated. On day 4 of hospitalisation a culture of blood obtained for culture on day 1 was positive for a filamentous gram-positive bacillus. From day 5 onwards resolution of respiratory signs and symptoms and improvement of lower limb weakness was noted. An electromyogram was performed, showing a predominantly motor axonal neuropathy. The initial treatment was not modified because of the patient's improvement. On day 15 of hospitalisation, the patient became lethargic with progressive loss of consciousness. Low-grade fever (≤ 37.5 °C) and greenish sputum were again observed. The organisms isolated in cultures of the three urine samples and the first blood sample were identified as *Nocardia*. No additional antibiotic therapy was started in view of the progression of the patient's underlying disease and in accordance with and at the request of relatives. The patient died on day 20 of hospitalisation. Autopsy was refused.

Microbiological Findings

A gram-positive bacterium was isolated first from a blood culture and then from a urine sample 4 days later. Microscopic examination of the slide preparations showed gram-positive branching filaments which were partially acid-fast. Colonies appeared on Columbia blood agar within 2 days and became pink as they matured. The isolates were presumptively identified as a member of the *Nocardia asteroides* complex on the basis of their non-degradation of casein, tyrosine, xanthine, hypoxanthine and adenine, and production of urease [4, 6]. Both samples were sent to the Institut Pasteur (Paris) for definitive identification and susceptibility testing. Identification of *Nocardia farcinica* was confirmed by growth at both 45 °C and 35 °C after 3 days of incubation [1, 3], production of acid from rhamnose [1, 3], and opacification of supplemented Middlebrook 7H10 agar (Difco, USA) [5, 7]. Antibiotic resistance was determined by a disk diffusion test on Mueller Hinton agar (bioMérieux, France) after incubation for 24–36 h at 37 °C [6, 8]. The isolate was susceptible to amoxicillin-clavulanic acid, imipenem, amikacin and ciprofloxacin, and resistant to trimethoprim-sulfamethoxazole, cefamandole, cefotaxime, tobramycin, erythromicin and minocycline.

Review

We performed a search in Medline as far back as 1966 and in the literature references in the studies cited there for reports on cases of *Nocardia farcinica* infection. Published case reports of *Nocardia farcinica* infection were included in our review provided the diagnosis had been established by isolation and identification of *Nocardia farcinica* from a clinical specimen. Patients

reported on by the same institution in more than one article were recorded in our review as a single case. We also searched for reports on cases of *Nocardia farcinica* infection in the Spanish Medical Index (IME), and could thus confirm that no previous case had been described in Spain. Statistical analyses were performed with the SPSS-PC+ statistical package (SPSS, USA) [7, 9]. The Fisher's exact test was used to compare categorical qualitative variables.

A total of 118 reports on cases of *Nocardia farcinica* infection were found in the literature [2–5, 8–34], but we excluded 65 cases cited in reference 6 from our review because of incomplete clinical information. Including the case reported here, 53 cases were available for review; the clinical details on these 53 cases are shown in Table 1.

There were 35 (74%) men and 12 (26%) women with a mean age (±SD) of 57±17 years, ages ranging from 11 to 89 years. Sixteen (36%) patients were older than 65 years. Forty-five (85%) patients had other underlying diseases which are listed in Table 2. *Nocardia farcinica* infection occurred in only eight (15%) patients without underlying illness. The site of the *Nocardia farcinica* infection and the organs involved are shown in Table 3. Disseminated disease, defined as the presence of lesions in two or more organs [33–36], was present in 15 (28%) patients. Distant foci of infection were found in 14 (26%) patients. However, most clinicians considered cases of central nervous system (CNS) disease as disseminated infection since it was presumed that an underlying lung focus existed, whether identified or not [1, 14, 16, 31, 33, 35]. Hence, there were in fact 24 cases of disseminated infection altogether. The clinical specimens from which *Nocardia farcinica* was most frequently isolated were pus from the site of the infection (24/24 samples), sputum or bronchial secretions (13/32), and biopsy specimens (7/11). Blood cultures were positive in six patients, and urine cultures in two patients. The median time required for isolation of the pathogen in the various samples was 4 days. The antibiotic susceptibility of the *Nocardia farcinica* isolates is shown in Table 4. Antibiotic therapy was specified in 28 patients, 15 of whom received trimethoprim-sulfamethoxazole, either alone or in combination with other antimicrobial agents. Empirically based antibiotic treatment was appropriate in 18 patients: nine patients received trimethoprim-sulfamethoxazole, two amikacin combined with imipenem, two amoxicillin-clavulanate, and one received various antibiotic regimens that were later confirmed by susceptibility testing to be appropriate. Eight patients required surgery (this data was available for 30 patients). The outcome was specified in 32 patients, ten of whom died, giving an overall mortality rate of 31%. Three patients in whom the empirically based treatment was appropriate and four patients in whom it was not appropriate died (OR 6.67; 95% CI 0.66–69.72; $P=0.07$). One patient with a localised infection died, whereas nine of those with disseminated infection died (OR 0.1; 95% CI 0.0–1.01; $P=0.06$).

Nocardia species are ubiquitous soil-borne aerobic actinomycetes. Although originally classified as fungi, they are now considered to be bacteria [1, 18]. *Nocardia asteroides* is the predominant pathogen in humans; the other pathogenic species are *Nocardia nova, Nocardia farcinica, Nocardia brasiliensis, Nocardia otitidiscavarium, Nocardia transvalensis* and *Nocardia pseudobrasilensis* [1, 2, 35]. It has been estimated that between 500 and 1000 cases of nocardiosis occur annually in North America [33, 35]. However, the relative frequencies of the infections caused by the various *Nocardia* species are difficult to determine retrospectively and may vary geographically [26, 28]. *Nocardia farcinica* has been reported to constitute 13.8% of *Nocardia* isolates in Italy [25, 27], 19% in the USA [1, 3], 23.8% in France [36, 37] and 60.3% in Germany [53], whereas in other countries only isolated cases of infection with this organism have been reported. No case of *Nocardia farcinica* infection has been reported previously in Spain.

In our review, *Nocardia farcinica* infection was shown to occur in men three times more often than in women, the same figure being reported for other species of *Nocardia* [1, 35]. Infection occurred at any stage of adult life, but no case was reported in children under 11 years. Most of the patients (85%) had predisposing factors, the most frequent being immunosuppressive therapy, previous surgery, neoplasms (especially haematological neoplasms), transplantation and HIV infection. Chronic pulmonary diseases, diabetes mellitus, renal diseases, alcoholism, trauma and mycobacterial infections were also reported.

The portals of entry of *Nocardia farcinica* were the respiratory tract and surgical or traumatic skin wounds [33, 35]. The organisms sometimes subsequently invaded other sites by haematogenous dissemination. The clinical manifestations of *Nocardia farcinica* infections varied considerably. The lung was the most common site of infection (43%), which often manifested itself as subacute pneumonia, patients presenting with a productive cough, fever, malaise and dyspnoea [30, 32]. In other cases the infection presented as a lung abscess or empyema. Occasionally the infection spread directly to produce mediastinitis or pericarditis [3, 5, 28, 30]. Radiographic signs of infection included unilobar or multilobar consolidation, mild diffuse infiltrates, reticulonodular patterns, pleural effusion, cavitation and enlarged mediastinal nodes [37, 38]. Even in the case of subclinical or transient primary pulmonary infection, dissemination to the brain, skin, kidney, joints, bones or eyes could occur. CNS infection was present in one-third of the cases, often dominating the clinical picture [1, 4, 12, 14–17, 25, 27, 31, 33]. CNS

Table 1 Clinical characteristics of patients with *Nocardia farcinica* infections reported in the literature.

Case no. [ref.]	Age/ sex	Predisposing factors	Type or site of infection	Positive cultures	Therapy	Out- come	Comments
1 [8]	49/M	none	lung, brain & kidney abscesses	lung tissue (2d)	SUL/CHL/PEN/AMP/ STM/TET/ERY/INH	died	negative cultures of sputum (9), bronchial secretion (2), lung & node tissue, urine
2 [2]	NA	none	lumbar/psoas abscess	pus	NA	NA	positive culture in 3–4 d
3 [2]	NA	CML	lung	bronchial secretion	NA	NA	positive culture in 3–4 d
4 [2]	NA	CLL	lung infection & pyothorax	pleural fluid	NA	NA	positive culture in 3–4 d
5 [2]	NA	CLL	brain abscess	pus	NA	NA	positive culture in 3–4 d
6 [2]	NA	none	lung	bronchial secretion	NA	NA	positive culture in 3–4 d
7 [2]	NA	Hodgkin's disease	brain abscess	spinal fluid	NA	NA	positive culture in 3–4 d
8 [2]	79/M	none	subcutaneous abscess	pus	NA	NA	positive culture in 3–4 d
9 [9]	70/M	none	lung infection & pyothorax	sputum, pleural fluid	SMZ	survived	culture time not stated
10 [8]	76/M	*M. intracellulare* infection, DM	lung	sputum	INH + RIF + PAS	died	culture time not stated, diagnosed post mortem
11 [10]	61/M	aortic valve replacement	aortic valve (post-operative)	blood (14 d)	SUL/AMX-Clav + AMN/ IMI + AMN/TMP-SMZ	survived	negative sputum & urine cultures, surgical removal of prosthesis
12 [11]	69/M	steroid therapy, DM, nephrosis	lung	sputum	PEN/MIN + TMP-SMZ + CEF	survived	culture time not stated
13 [12]	43/M	alcoholism	brain abscess	pus (8d)	AMX-Clav + AMP + AMN/AMN + IMI	survived	NA
14 [13]	70/M	steroid therapy, nephrosis	lung	sputum	TMP-SMZ	survived	NA
15 [13]	73/M	previous pulmonary tuberculosis	lung	sputum	SMZ	survived	NA
16 [14]	72/F	none	brain abscess	pus	MEZ + FLX + AMN/ AMN + IMI/MIN	survived	culture time not stated, surgical excision
17 [15]	55/F	kidney transplant	brain abscess	pus	CTX/PYR + CLI + CTZ/ FLX + MET + CPX + PYR + AMB + FLU	died	culture time not stated, diagnosed post mortem
18 [16]	30/M	renal insufficiency, CAPD	peritonitis	dialysis fluid	adapted antibiotic therapy	survived	NA
19 [17]	36/M	von Willebrand's disease, HIV infection	lung, kidney abscess	sputum, kidney tissue	AMX + TMP-SMX/ IMI + RIF	survived	negative cultures of blood, pleural fluid, urine, bronchial secretion (2) & kidney tissue
20 [3]	45/F	Hodgkin's disease, extirpation of lymph nodes	wound	wound secretion	NA	NA	NA
21 [3]	NA/M	coronary bypass operation	wound	pus	NA	NA	NA
22 [3]	45/M	aortic valve replace-ment	wound abscess	pus	NA	NA	NA
23 [3]	60/F	alcoholism, cholecystectomy	peritonitis	ascites	NA	NA	NA
24 [3]	NA/M	kidney transplant	wound, lung abscess	wound secretion	NA	NA	NA
25 [3]	77/F	osteosynthesis	osteomyelitis	wound secretion	NA	NA	NA
26 [3]	55/M	coronary bypass operation	mediastinitis	pus	NA	NA	NA
27 [3]	65/M	surgery for perforated aortic aneurysm	infected haematoma	haematoma material	NA	NA	NA
28 [3]	54/F	kidney transplant	wound	pus	NA	NA	NA
29 [3]	59/M	surgery for multiple trauma	wound	pus	NA	NA	NA
30 [3]	70/F	plastic surgery of bladder	abdominal wall abscess	pus	NA	NA	NA

Table 1 Continued

Case no. [ref.]	Age/ sex	Predisposing factors	Type or site of infection	Positive cultures	Therapy	Out-come	Comments
31 [3]	74/M	coronary bypass operation	wound & mediastinum	pus	NA	NA	NA
32 [3]	78/F	resection of oesophageal carcinoma	wound	pus	NA	NA	NA
33 [18]	54/M	trauma	facial abscess, osteomyelitis	pus (5 d)	AMN/TMP-SMZ/ERY	survived	surgical debridement
34 [19]	44/M	none	lung, brain abscess	pleural fluid	IMI + CPX + AMN	died	pleural drainage
35 [20]	74/M	COPD	lung	bronchial secretion	CZL/CLX/CTR/ TMP-SMZ	NA	negative cultures of bronchial secretions (2)
36 [21]	89/F	bullous pemphigoid, pancytopenia, steroid therapy.	subcutaneous abscesses breast, buttock	pus (2 d)	TMP-SMZ	survived	negative blood cultures, surgical drainage
37 [22]	24/M	HIV infection, pulmonary tuberculosis	lung, brain & kidney abscesses	kidney tissue, sputum, CSF	TMP-SMZ/DOX + CPX	survived	negative urine & bronchial secretion cultures
38 [23]	57/M	heart transplant	soft-tissue abscess thigh	pus	AMP-Sulb + GEN/ IMI + AMN/DOX	survived	surgical drainage
39 [24]	72/M	Horton's disease, Guillain-Barré syndrome, COPD, steroid therapy	lung, skin, eye & brain	skin & lung tissue (<8d)	IMI + TMP-SMZ/ AMX-Clav + PEF	survived	NA
40 [24]	73/M	myeloma, COPD, steroid therapy.	lung	sputum (<8d)	CTX + CPX/TMP-SMZ + TOB	survived	NA
41 [24]	60/M	heart transplant	skin & brain abscess, arthritis	skin tissue (<8d)	AMX-Clav + IMI/TMP-SMZ + PEF	survived	NA
42 [25]	40/M	AIDS, IVDU	lung	blood	NA	died	diagnosed post mortem
43 [25]	29/M	AIDS, IVDU	brain	NA	NA	died	NA
44 [25]	35/F	AIDS, IVDU	lung	NA	medical therapy only	survived	NA
45 [25]	11/M	astrocytoma	brain	NA	NA	survived	NA
46 [26]	64/M	DM, Wegener disease, renal insufficiency, cyclophosphamide & steroid therapy	brain, subcutaneous tissue pectoral region & forearm	blood (3 d), skin lesion culture	TMP-SMZ/MIN + SUF	survived	1/2 blood cultures negative
47 [27]	46/M	kidney transplant	lung, meningitis, brain.	CSF	PIP + AMN	died	NA
48 [28]	41/M	alcoholic	lung, mediastinal & pericardial infection	mediastinal & pericardial pus	TMP-SMZ	survived	negative sputum, bronchial secretion & pericardium culture, surgical drainage
49 [29]	49/F	rigid contact lenses	keratitis	corneal scrapings	CZL/FUS/CHL/AMN/ SUL + AMN/TMP-SMZ/ DOX	survived	corneal transplant
50 [30]	56/F	sarcoidosis, breast carcinoma, *A. fumigatus* mastitis, chronic granulomatous disease	lung	bronchial secretion & tissue (4 d)	ERY/CTX + IMI	survived	NA
51 [31]	50/M	AIDS	lung, brain	blood (2d), CSF (10d)	AMP + CTR + AMN + TMP-SMZ/VAN + IMI + FLC + AMN + CP M	died	NA
52 [32]	42/M	liver transplant.	lung, brain	blood (3d), sputum (3d), urine (3d)	AMP-Sulb/ IMI + AMN + VAN	died	3/6 blood culture negative
53 [PR]	85/M	lymphoma, steroid therapy, COPD, DM	lung, kidney	blood (4d), urine (11d)	CTX	died	NA

NA, data not available; CML, chronic myeloid leukaemia; CLL, chronic lymphatic leukaemia; DM, diabetes mellitus; IVDU, intravenous drug use; CAPD, continuous ambulatory peritoneal dialysis; COPD, chronic obstructive pulmonary disease; AMB, amphotericin B; AMX, amoxicillin; AMN, aminoglycoside; AMP, ampicillin, CEF, cefmetazole; CHL, chloramphenicol; CLI, clindamycin; CLX, cloxacillin; Clav, clavulanate; CPM, cefipime; CPX, ciprofloxacin; CTX, cefotaxime; CTZ, ceftazidime, CTR, ceftriaxone; CZL, cefazoline; DOX, doxycyline; ERY, erythromycin; FLX, flucloxacillin; FLU flucytosine; FLC, fluconazole; FUS, fusidic acid; GEN, gentamicin; IMI, imipenem; INH, isoniazid; MET, metronidazole; MEZ, mezlocillin; MIN, minocycline; PAS, P-aminosalicylate; PEF, pefloxacin; PEN, penicillin; PIP, piperacillin; PYR, pyrimethamine; RIF, rifampicin; SMZ, sulfamethoxazole; SUF, sulfadiazine; SUL, sulphonamide; STM, streptomycin; Sulb, sulbactam; TET, tetracycline; TMP, trimethoprim; TOB, tobramycin; VAN, vancomycin

Table 2 Predisposing factors in the 53 patients with *Nocardia farcinica* infection. Most patients presented with more than one comorbid condition

Predisposing factors	No. (%) of patients
Immunosuppressive treatment[a]	15 (28)
Preceding operation	14 (26)
Haematological neoplasm	7 (13)
Transplant recipient	7 (13)
HIV infection	6 (11)
Chronic lung disease	5 (9)
Diabetes mellitus	4 (8)
Renal disease	4 (8)
Solid neoplasm	3 (6)
Alcoholism	3 (6)
Trauma	3 (6)
Mycobacterial infection	2 (4)
Miscellaneous[b]	6 (11)

[a] All patients were treated with steroids, and seven transplant recipients were also on treatment with azathioprine and cyclosporine

[b] One case each of continuous ambulatory peritoneal dialysis, Von Willebrand's disease, bullous pemphigoid and pancytopenia, Guillain Barré syndrome, contact lens-associated infection and chronic granulomatous disease

Table 3 Organ involvement in 53 patients with *Nocardia farcinica* infection. Some patients presented with infection at more than one site resulting from direct spread to adjacent organs ($n=4$) or distant spread ($n=11$)

Organ/Site	No. (%) of patients
Lung, pleura	23 (43)
Brain, meninges	16 (30)
Surgical wounds	8 (15)
Skin, subcutis	6 (10)
Deep-seated soft-tissue	4 (8)
Kidney, urinary tract	4 (8)
Mediastinum	3 (6)
Bones, joints	3 (6)
Peritoneum	2 (4)
Eye	2 (4)
Pericardium	1 (2)
Heart valves	1 (2)

infection presented in the form of brain abscesses at various sites, usually appearing as multiple enhancing lesions on computed tomography and occasionally accompanied by meningitis.

Infection of skin and subcutaneous tissue (10%), deep-seated soft-tissue (8%) and bone (6%) was in the form of either a metastatic focus in the case of disseminated infection or, more frequently, a primary lesion after traumatic injury [3, 5, 18, 20, 21, 23, 25–28]. Of particular interest were the 14 cases of nosocomial post-operative wound infection reported by Schaal et al. [3, 5, 10, 12], which were observed in two German hospitals between 1984 and 1991. The source of the pathogen was dust from construction work which contaminated the air of the operating theatre area. In most of the patients (9/14) no comorbid condition could be identified. The primary site of infection was the site of the previous operation, the clinical manifestations including wound infection ($n=6$ cases), mediastinitis ($n=2$), abdominal wall abscess ($n=1$), infected haematoma ($n=1$), peritonitis ($n=1$), osteomyelitis ($n=1$), lung abscess ($n=1$) and endocarditis ($n=1$). Other primary iatrogenic infections reported included isolated cases of peritonitis in patients on continuous ambulatory peritoneal dialysis [16, 18] and aggressive keratitis in a contact lens user [29, 31]. Thus, *Nocardia farcinica* can also be a nosocomial pathogen, infecting surgical or traumatic wounds even in immunocompetent patients, such infections possibly exhibiting an aggressive course.

In the cases reviewed here we observed that the initial clinical diagnosis was often wrong; cancer and infections with mycobacteria, other bacteria or *Pneumocystis carinii* were the most frequent initial diagnoses. This demonstrates the importance of considering *Nocardia* infection in the differential diagnosis. The laboratory should be informed of the suspected diagnosis since *Nocardia* spp. grow poorly in many culture media, and multiple specimens must be studied (pus,

Table 4 Antibiotic susceptibility of *Nocardia farcinica* isolates in cases in which data was available (cases no. 1, 11, 13, 16–19, 33, 34, 36–51). MICs are expressed in μg/ml

	Total no. of cases	Resistant (R)		Intermediate (I)		Sensitive (S)		Present case
		Cases	MIC	Cases	MIC	Cases	MIC	
Ampicillin	6	6	16	0	–	0	–	I
Amoxicillin-CA	11	1	NA	5	8/16	5	≤4/2	S
Imipenem	19	0	–	2	8	17	≤4	S
Ceftriaxone	8	6	>64	0	–	2	NA	R
Gentamicin	8	7	>16	0	–	1	NA	R
Amikacin	19	1	NA	0	NA	18	≤2	S
Vancomycin	2	1	NA	0	NA	1	NA	R
Erythromicin	6	5	>8	1	NA	0	–	R
Ciprofloxacin	6	2	NA	0	NA	4	≤2	I
Trimethoprim-sulfamethoxazole	19	9	NA	1	38/2	9	0.25/4.8	S

sputa, bronchial secretions, biopsies, blood, urine). *Nocardia farcinica* is isolated after 2 to 14 days, but misinterpretation of the findings as contaminating flora and difficulties in determining the precise species, best performed in reference laboratories, can delay the start of appropriate antibiotic therapy [5, 13]. Because of the aggressiveness and the tendency to disseminate of *Nocardia farcinica* infections, and the resistance of the organism to antibiotics [18–21, 31, 33, 38, 39], such a delay can have serious consequences. In such cases the empirically based antibiotic therapy was frequently inappropriate and mortality high (31%), while mortality rates as low as 10% were reported when nocardiosis was promptly diagnosed and treated [39, 40].

Nocardia farcinica isolates are usually susceptible to amikacin, imipenem, ciprofloxacin and trimethoprim-sulfamethoxazole. However, they are resistant to ampicillin, third-generation cephalosporins including cefotaxime and ceftriaxone, erythromycin, gentamicin and tobramycin [18–21, 31]. Trimethoprim-sulfamethoxazole has been considered the treatment of first choice, and even when in vitro studies show resistance it may be effective in vivo [12, 14, 15, 17, 24, 26]. In view of the possibility of trimethoprim-sulfamethoxazole resistance, some authors have proposed amikacin in combination with imipenem or amoxicillin plus clavulanic acid as the therapy of choice in patients with disseminated disease, especially of the CNS [15, 17, 25, 27, 34, 36]. Surgery may be required in some cases of soft-tissue infection, brain abscess, empyema or endocarditis. Information on the duration of therapy was inadequately documented in most reports, but therapy was often continued for many months after apparent cure because of high relapse rates. In immunocompetent patients pulmonary or systemic nocardiosis should be treated for 6 to 12 months; if the brain is involved or the patient is immunosuppressed treatment must be continued for 12 months [34, 36]. Primary cutaneous nocardiosis may be cured with a shorter therapy of 2 to 4 months after bone involvement has been excluded [34, 36]. In the immunocompromised host the infection is life-threatening [15, 17, 18, 20, 25, 28, 30]. Despite this, it does not appear mandatory to reduce or discontinue immunosuppressive therapy during treatment [29, 27].

In summary, *Nocardia farcinica* infection should be suspected in immunosuppressed hosts who present with soft-tissue and/or brain abscesses in conjunction with current or recent subacute pulmonary infection, as well as in patients with wound infections that fail to respond to conventional antimicrobial therapy. Multiple samples must be obtained and the laboratory should be alerted to the suspected diagnosis; if necessary, identification of nocardial isolates must be carried out in reference laboratories. The characteristic pattern of antibiotic resistance of this pathogen must be kept in mind when beginning empirically based treatment, so that a significant improvement in the chances of survival can be achieved by means of appropriate early therapy.

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