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Disseminated *Nocardia farcinica*: Literature Review and Fatal Outcome in an Immunocompetent Patient

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Abstract

Background: *Nocardia farcinica* is a gram-positive, partially acid-fast, methenamine silver-positive aerobic actinomycete. *Nocardia* spp. are opportunistic pathogens, and *N. farcinica* is the least common species of clinical importance.
Methods: Review of the recent literature and description of a immunocompetent patient with no known risk factors who contracted fatal *N. farcinica* sepsis.
Results: Positive pre-mortem and post-mortem cultures from the lung and synovium correlated with acute bronchopneumonia and synovitis at autopsy. Colonies of filamentous bacteria, which were not apparent in conventional hematoxylin and eosin-stained sections, were observed with gram and methenamine silver stains, but acid-fast stains were negative. A literature review revealed that disseminated *N. farcinica* often is associated with an underlying malignant tumor or autoimmune disease (88% of patients). Chemotherapy or corticosteroid treatments are additional risk factors.
Conclusions: Trimethoprim–sulfamethoxazole typically is the first-line therapy for *N. farcinica*; treatment with amikacin and imipenem-cilastatin is used less often (7% of patients). Despite aggressive therapy, we observed that the death rate (39%) associated with *N. farcinica* in recent publications was eight percentage points higher than reported in a review from 2000.

Nocardiosis is a localized or disseminated infection caused by the soil-dwelling, weakly gram-positive aerobic actinomycete *Nocardia* [1]. The organism, characterized by filamentous branches measuring less than 1 micron thick, is not easily observed on conventional hematoxylin and eosin-stained sections, possibly because of its failure to form the "granules" characteristic of other actinomycetes. *Nocardia* is partially acid-fast by conventional Ziehl–Nielsen staining and is reactive with Gomori methenamine silver. The typical portal of entry for *Nocardia* is the respiratory tract with subsequent dissemination to distant organs [2]. *Nocardia* is considered an opportunistic pathogen [3,4] and is associated with compromised immune function (for example, solid organ or bone marrow transplant [5], long-term steroid use, connective tissue disease, or human immunodeficiency virus [HIV] infection), chronic obstructive pulmonary disease (COPD), alcoholism, cirrhosis, systemic vasculitis, ulcerative colitis, or renal failure) [6]. *Nocardia asteroides* typically is reported as the most frequent cause of nocardiosis in the United States [4–6]. Other clinically significant species are *N. brasiliensis* [7], *N. farcinica, N. nova, N. pseudobrasiliens,* and *N. transvalensis*. *Nocardia brasiliensis* is commonly associated with primary cutaneous infection following trauma in immunocompetent patients. *N. farcinica* is one of the least frequent clinically important species, with a reported prevalence of 5% in Switzerland and 6.7% in Crete [6, 8] and a modestly increased prevalence in Turkey [9]. It is found in a 2:1 ratio over other strains of *Nocardia* in Germany [10]. A recent report identified *N. farcinica* as a nosocomial pathogen that infected three patients in the same ward over a six-month period [11]. In the United States, 500–1,000 cases of nocardiosis are diagnosed each year [4], with *N. farcinica* constituting 19% of isolates [12]. The present report of fatal systemic nocardiosis concerns *N. farcinica* in an immunocompetent patient for whom the portal of entry was not established definitively. The diagnostic elements of, and recent literature on, this unusual infection are reviewed.

Case Report

A 78-year old male presented with a one-day history of right knee pain and swelling. The patient had received a steroid injection in the same knee one week before admission. Three

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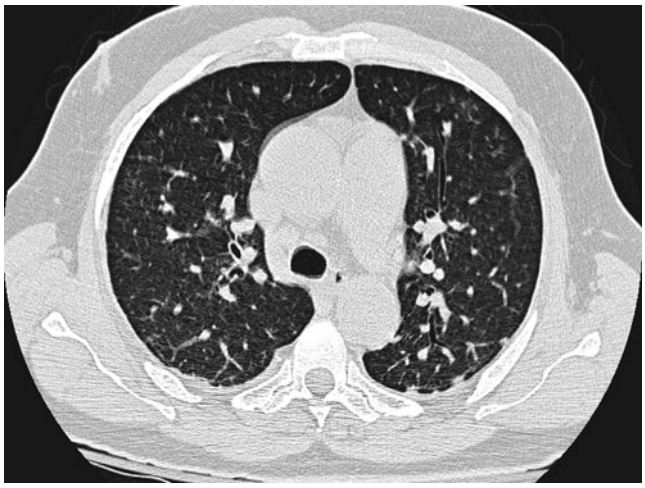

FIG. 1. Chest CT scan demonstrates multiple subcentimeter nodules in both lungs.

years prior to admission, the patient had an unexplained illness consisting of one month of fever (100.3°F), a 19-pound weight loss, and an elevated white blood cell count (15,300/mm^3). At that time, he also had an infected cyst in the posterior scalp, which was treated with cephalexin but was not cultured. The full extent of clinical evaluation at that time is unknown.

On admission, laboratory evaluation revealed hemoglobin 13.4 g/dL, hematocrit 40.1%, white blood cell count 23,300/mm^3, and platelets 435,000/mm^3. Pertinent chemistry findings were blood urea nitrogen 74 mg/dL, creatinine 2.6 mg/dL, and glucose 151 mg/dL. Cultures from six knee synovial fluid aspirations and peripheral blood grew *N. farcinica* susceptible to ciprofloxacin (minimum inhibitory concentration [MIC] 1 mcg/mL), linezolid (2 mcg/mL), amikacin (2 mcg/mL), and sulfamethoxazole (4 mcg/mL). A computed tomography (CT) scan revealed numerous subcentimeter non-calcific pulmonary nodules (Fig. 1). The patient was treated with intravenous trimethoprim–sulfamethoxazole (TMP-SMX). The patient's renal function improved with hydration. Eleven days after admission, the patient developed tachypnea and respiratory distress acutely and died.

Autopsy findings included bilateral serosanguinous pleural effusions (200–300 mL) and copious turbid, greenish fluid in the right knee. Histologically, there was acute suppurative and chronic synovitis (Fig. 2A). In both lungs, extensive organizing, nodular, intra-alveolar pneumonia (Fig. 2B, C) with abscesses and associated miliary granulomas (Fig. 2D) were observed. Cultures of both lungs and the synovial fluid were positive for *N. farcinica*. Gram-positive, methenamine silver-positive, beaded, branching, filamentous bacteria were identified in both locations. Although acid-fast stains were negative, *N. farcinica* was identified by polymerase chain reaction amplification and sequencing of the bacterial rRNA.

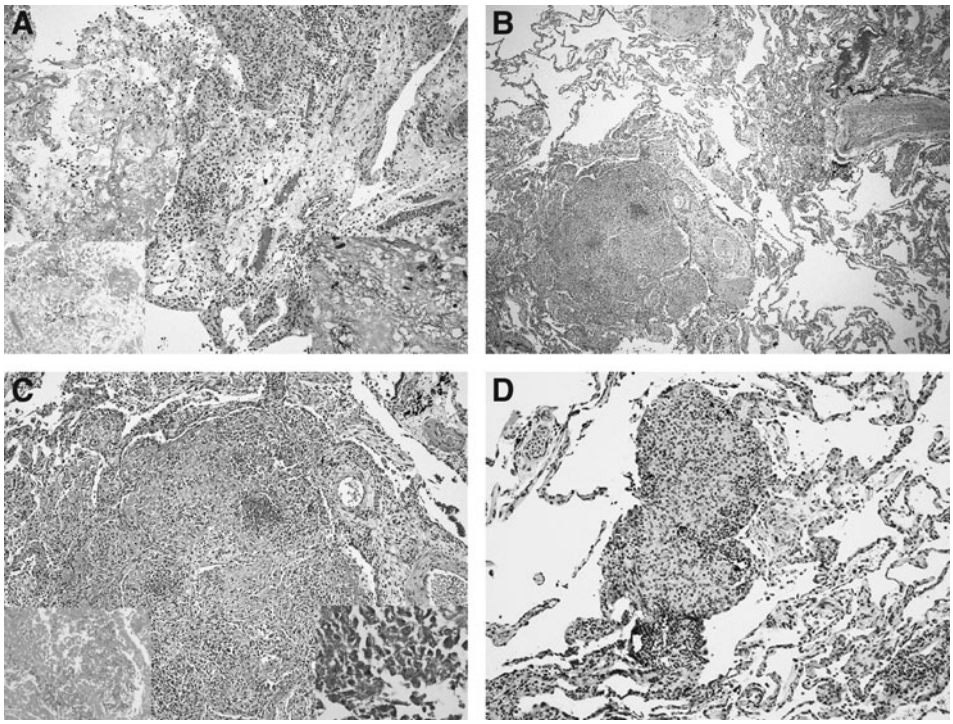

FIG. 2. Histologic views. (**A**) Acute fibrinous and chronic synovitis. No organisms are visible by hematoxylin and eosin stain. Insets show fibrinous exudates. **Lower right:** Gram stain demonstrating gram-positive thin, branching, filamentous forms. **Lower left:** Gomori methenamine silver (GMS) stain, similarly demonstrating organism morphology. (**B**) Lung nodule. Low-magnification view of lung with centrally necrotic nodule of organizing pneumonia, lower left. (**C**) Higher-magnification view of the nodule showing central necrotic focus and peripheral lymphoid infiltrate. **Lower right:** Gram stain of center of nodule demonstrating numerous gram-positive thin, branching, filamentous organisms. **Lower left:** GMS stain showing similar organisms. (**D**) Microscopic, non-necrotic granulomas were associated with nodular abscess.

Table 1. Clinical Characteristics of 67 Patients with *Nocardia farcinica* Infections since Last Review by Torres et al. [13]

Age/sex	*Underlying condition*	*Systemic steroids?*	*Prophylaxis with TMP-SMX*	*Disease*	*Therapy*	*Outcome*	*Ref.*
78/M	None	No	No	Lung, joint, blood	TMP-SMX (11 days)	Death	This study
85/M	NHL, DM, chronic bronchitis	Yes[a]	No	Lung, blood	IV CTX (1 g qid) + IND (20 days)	Death	14
67/M	Liver transplant	Yes	Yes	Lung	TMP-SMX (12 mos)	Survived	48
28/M	Sarcoidosis	Yes	No	CNS	TMP-SMX + MER (15 days); TMP-SMX (6 mos)	Survived	48
81/M	COPD	Yes	No	Lung[b]	AMK + AMX/CLAV (12 days)	Death: Related	48
65/F	CLL, hemolytic anemia	No	Yes	Disseminated	TMP-SMX + MER (1.5 mos); TMP-SMX + AMK (4 mos); TMP-SMX + AMX/CLAV (6 mos)	Survived	48
38/F	Transplantation of intestine (Gardner's syndrome)	Yes	No	Lung, liver[c]	TMP-SMX (800 mg/160 mg qd); CPX (200 mg q 12 h) + AMX/CLAV (2.2 g q 8 h) + CFZ + IMI	Death: Related	8
77/M	COPD, invasive *Aspergillus*	No	No	Lung	TMP-SMX (3 mos)	Survived	48
29/M	HIV	No	No	Cerebral	Surgery	Died	49
30/F	HIV, MAC	No	No	Cerebral, pulmonary	TMP-SMX; MIN (6 weeks)	Died	49
34/F	SLE, drug abuse	Yes	No	Brain abscess, subcutaneous leg abscess		Died	50
70/M	COPD, pneumoconiosis	Yes	No	Lung	TMP-SMX (10 mg/kg/d; 7 mos)	Death: Related	51
62/M	Kidney transplant	NR	NR	Soft tissue/blood	TMP-SMX + CPX	Survived	38
60/F	Kidney transplant	NR	NR	Soft tissue/blood	TMP-SMX	Survived	38
51/M	Kidney transplant	NR	NR	Soft tissue/lung/brain	TMP-SMX + CTR	Survived	38
50/F	Lymphoma	NR	NR	Blood	IMI	Survived	38
58/F	COPD	NR	NR	Lung	TMP-SMX + IMI + AMK	Survived	38
74/F	Glioma	Yes	No	Lung	MER (7 days); TMP-SMX (3 mos)	Survived	48
47/F	Lung transplant	Yes[d]	No	Lung	TMP-SMX + CTR + IMI	Death	20
46/M	Lung transplant	Yes[e]	Yes	Lung	TMP-SMX + CTR	Death	20
54/M	Alcoholism	No	No	Spine, CNS, psoas	Surgery, DXN + GEN	Survived	52
2 mo/M	None	No	No	Disseminated lymphatic abscesses	CTX + CXN + MET; AMK (3 weeks); TMP-SMX (3 mos)	Survived	24
37/M	HIV	No	No	Lung	TMP-SMX (7 mos)	Survived	48
	Leg fracture/trauma	No	No	Brain abscesses	VAN + GEN + CTZ; TEI + CTZ, TMP-SMX; VAN + AMK; LIN + MIN	Survived	53
62/M	Evans syndrome	Yes	No	CNS	TMP-SMX + IMI (90 days)	Death: Not related	48
68/M	COPD, DM2	Yes	No	Septic arthritis of knee[f]	TMP-SMX (6 mos)	Survived	54

(*continued*)

Table 1. (Continued)

Age/sex	Underlying condition	Systemic steroids?	Prophylaxis with TMP-SMX	Disease	Therapy	Outcome	Ref.
60/M	Insulin-dependent DM2, systemic vasculitis with ESRD	Yes	No	Brain abscess	MER (2 g/d) + AMP (2 g/d) (7 days)	Death	55
52/M	Non-small-cell lung cancer, radiation, chemotherapy	No	No	Bacteremia	IV CFZ 1 g tid; AMK 500 mg bid; MET (600 mg tid) (24 h)	Death	56
58/M	Immunosuppression	Yes	No	Brain abscesses	CFZ + MER; LIN + MER	Survived	57
75/M	Immunosuppression	Yes	No	Thyroid, psoas, spine, basal ganglia, lungs	TMP-SMX (320/1600 mg q 6 h; 2 days)	Death: Related	34
NR	Renal transplant, DM	Yes	No	Lung	CTR + AMK; IMI; TMP-SMX (6 mos)	Survived	11
NR	Bullous pemphigoid, DM	Yes	No	Pulmonary and cerebral	CTR + AMK; IMI; TMP-SMX, surgery (37 days)	Death	11
NR	None	No	No	Brain abscess	CTR + AMK; MER; TMP-SMX, surgery (6 mos)	Survived	11
NR	None	No	No	Brain abscess	CTR + AMK; TMP-SMX, surgery (6 mos)	Survived	11
NR	None	No	No	Brain abscess	CTR + AMK; MER; TMP-SMX, surgery (6 mos)	Survived	11
75/M	Interstitial pneumonia	Yes	No	Lung	CFP; TMP-SMX (12 mos)	Survived	7
28/M	Ulcerative colitis	Yes	No	Subcutaneous abscess in left popliteal space	Surgery, TMP-SMX	Survived	7
72/F	BOOP, cirrhosis	Yes	No	Lung	IMI + ITC; TMP-SMX	Death	7
68/M	ITP	Yes	No	Lung, brain abscesses, blood	AMP/SULB (1.5 g/day; TMP-SMX (160 mg/800 mg/day)	Survived	58
12/M	Renal transplant	Yes	Yes	Brain abscesses	TEI + CTR; LIN 600 mg bid, MER (20 days); AMX/CLAV (PO)	Survived	22
91/M	IPF	Yes[g]	No	Lung	IV TMP-SMX	Death	41
76/F	COPD, vasculitis	Yes[a]	Yes	Lung	LVX + CTX; MER	Survived	41
49/M	Renal transplant, alcoholism	Yes	No	Lung, brain	IMI (1 g tid) + TMP-SMX (320 mg/1600 mg qid); MOX	Survived	44
42/M	DM, alcoholism	No	No	Brain abscess	CTR + MET + TMP-SMX	Survived	36
26/F	SLE	Yes[a]	No	Subretinal abscess, lung abscess	Vitreous tap with injection of AMK; BAL; TMP-SMX IV (80 mg/400 mg/q 6 h); CPX PO (1 g qd)	Survived	42
57/M	None	No	No	Brain abscess	Surgery, TMP-SMX + IMI; MOX + IMI; MOX (1 yr)	Survived	59
62/F	SLE, COPD, DM	Yes	NR	Lung	Unknown	Death	60
35/M	HIV, COPD	No	NR	Lung, disseminated	SUF	Death	60

(*continued*)

Table 1. (Continued)

Age/sex	Underlying condition	Systemic steroids?	Prophylaxis with TMP-SMX	Disease	Therapy	Outcome	Ref.
78/M	COPD	Yes	NR	Lung	SUF	Survived	60
73/F	Hodgkin's disease	No	NR	Disseminated	TMP-SMX	Death	60
46/M	HIV	No	NR	Lung, disseminated	TMP-SMX	Death	60
65/F	COPD	No	NR	Lung	TMP-SMX	Death	60
79/M	Rheumatoid arthritis	Yes	NR	Lung, disseminated	IMI; AMK	Death	60
85/M	Lymphoma, COPD	Yes	NR	Lung, disseminated	CTR	Death	60
68/M	Renal transplant, HCV	Yes	NR	Lung	SUF	Survived	60
NR	NHL	No[h]	No	Lung, gluteal region, iliac fossa, kidney, cerebrum	TMP-SMX + IMI; AMK + TMP-SMX; TMP-SMX (630 days)	Survived	33
NR	Multiple myeloma	No[h]	No	Lung	TMP-SMX 2×1920 mg IV (60 days)	Survived	33
NR	Polymyalgia rheumatica	Yes	No	Upper leg abscess	TMP-SMX 2×1920 mg IV (90 days)	Survived	33
49/M	ITP	Yes	No	Lung	TMP-SMX (3 mos)	Death	61
8/M	CF, ABPA	Yes	No	Lung	TMP-SMX 80/400 mg (62 days)	Survived	23
73/M	Multiple myeloma	Yes	No	Disseminated subcutaneous nodules	TMP-SMX 800 mg (6 mos)	Survived	37
65/F	HIV, COPD, vasculitis	Yes	No	Lungs	IV TMP-SMX + IMI (5 days)	Death	62
43/M	None	No	No	Brain abscess	CTR; TMP-SMX + MOX	Survived	63
64/M	Lung transplant	No[i]	Yes	Lung	IMI + AMK; TMP-SMX IV	Survived	25
NR	Lung transplant	Yes[d,g]	Yes	Lung	TMP-SMX 160/800 mg PO bid)	Survived	31
53/M	None	No	No	Brain abscess, lung	TMP-SMX (7 days); IMI; LIN; TMP-SMX (1 yr)	Survived	19
71/M	Bladder cancer	Yes	No	Lung	IMI + AMK	Survived	10

[a]Plus cyclophosphamide.
[b]Co-infection with cytomegalovirus and *Pneumocystis jirovecii*.
[c]Co-infection with *Pseudomonas aeruginosa*.
[d]Plus tacrolimus.
[e]Plus cyclosporine.
[f]Co-infection of lungs with *P. aeruginosa*, and *Escherichia coli*.
[g]Plus azathioprine.
[h]Patients were treated with chemotherapy and immunotherapy for cancer.
[i]Microphenolate + tacrolimus immunosuppression.

ABPA = allergic bronchopulmonary aspergillosis; AMK = amikacin; AMP/SULB = ampicillin/sulbactam; AMX/CLAV = amoxicillin/clavulanic acid; BAL = bronchoalveolar lavage; BOOP = bronchiolitis obliterans organizing pneumonia; CF = cystic fibrosis; CFP = cefozopran; CFZ = ceftazidime; CLL = chronic lymphocytic leukemia; CPX = ciprofloxacin; COPD = chronic obstructive pulmonary disease; CTR = ceftriaxone; CTX = cefotaxime; CTZ = ceftazidine; CXN = cloxacillin; DXN = dicloxacillin; DM = diabetes mellitus; ESRD = end-stage renal disease; GEN = gentamicin; HCV = hepatitis C virus; HIV = human immunodeficiency virus; IMI = imipenem-cilastatin; IND = indomethacin; IPF = idiopathic pulmonary fibrosis; ITC = itraconazole; ITP = idiopathic thrombocytopenic purpura; IV = intravenous; LIN = linezolid; LVX = levofloxacin; MAC = *Mycobacterium avium* complex; MER = meropenem; MET = metronidazole; MIN = minocycline; MOX = moxifloxacin; NHL = non-Hodgkin lymphoma; NR = not reported; PO = orally; SLE = systemic lupus erythematosus; SUF = sulfadiazine; TEI = teicoplanin; TMP-SMX = trimethoprim–sulfamethoxazone; VAN = vancomycin.

Discussion

A relatively infrequent cause of nocardiosis, *N. farcinica* is a clinically aggressive infection, particularly in immunocompromised patients. For unknown reasons, small numbers of immunocompetent patients also are affected. In the last review of *N. farcinica* sepsis by Torres et al. in 2000, a retrospective analysis of 53 patients identified eight cases (15%) in which no predisposing factors for infection were discernible [13]. Of the eight patients, one presented with a brain abscess [14] and two had lung or kidney involvement or both [15,16]. Similarly, Beaman et al. reported that 15% of patients infected with *Nocardia* had no identifiable underlying condition [4]. In most cases, the pathogenesis of *Nocardia* infection is presumed to be via an airborne route from soil inhabited by latent forms. Following colonization of the respiratory tract, T lymphocyte-mediated cellular immunity is activated after phagocytosis of the organism [15,16]. The infection may remain localized or disseminate promptly. If the infection is localized, latency and subsequent reactivation may occur, resembling the pathogenesis of tuberculosis.

Our search of the literature for cases of *N. farcinica* published since the last review [14] demonstrates the continued rare occurrence of *N. farcinica* infection in immunocompetent patients [17]. Of the 67 cases reported since 2000, 59 (88%) patients suffered from a predisposing illness or had risk factors associated with diminished immunocompetence (Table 1). Of the eight immunocompetent patients in this cohort, six presented with brain abscesses and two with disseminated disease. Previous reports indicate that *Nocardia* spp. were responsible for 2%–20% of cerebral abscesses in immunocompromised patients [18,19], with a mortality rate of 30%–80% [14,20].

In agreement with previously published reports [13], the ratio of male:female infection was 3:1. Although typically responsible for infections in adults, *N. farcinica* also infected a 12-year-old adolescent following renal transplant [21], an 8-year-old boy with cystic fibrosis [22], and an otherwise-healthy 2-month-old boy [23]. Our review of the literature demonstrated that 10.4% of patients receiving TMP-SMX prophylaxis became infected. *Nocardia* infection also is reported in 60% of lung transplant recipients [19,24]. Furthermore, most of the patients (61.2%) infected with *N. farcinica* were receiving systemic steroids or chemotherapy. Corticosteroid treatment inhibits the cytokine response and phagocytic killing of microbes by macrophages [25].

Table 2 summarizes the co-morbidity factors most commonly associated with infection for the cases in Table 1. Hui et al. [26] reported that 63% of pulmonary nocardiosis patients had underlying respiratory disorders. In particular, COPD was identified as a risk factor in 23% of patients with pulmonary nocardiosis [27]. *Nocardia* infection is reported in as many as 3% of transplant recipients [7] with an associated mortality rate ranging from 0% to 75% in lung transplant recipients [19,28]. Alcoholism (3.0%), hematologic malignancy (4.5%), HIV infection (7.5%), idiopathic thrombocytopenic purpura (ITP) (3.0%), systemic lupus erythematosus (SLE)(4.5%), neoplastic disease (7.5%), diabetes mellitus (9.0%), and vasculitis (4.5%) were co-morbid conditions identified in at least two patients.

Disseminated nocardiosis is associated with a mortality rate ranging from 7% to 85% in immunocompromised hosts [29]. Disseminated disease and bacteremia occurred in 37% of the cases reported since 2000 (Table 3). Assuming that patients with central nervous system lesions also had a lung infection that was unrecognized [13], 39 patients (58%) had disseminated disease. Soft tissue infection involving muscles or connective tissue, including subcutaneous abscesses, was present in 17.9% of the cases. Torres et al. [13] reported a mortality rate of 31% in cases diagnosed before 2000; the mortality rate in the cases reported since then was 39%.

The diagnosis rests on the demonstration of organisms in tissue, cultures, or both. Histologically, organisms are difficult to recognize by hematoxylin and eosin stains. Also, as demonstrated here, acid-fast staining is variable and unreliable [1, 13]. Gram and methenamine silver (GMS) stains usually are positive, although gram staining may be weak. Cultures of *Nocardia* can take more than five days to grow [30]. Biochemical tests may be used for identification of a subset of *Nocardia* spp., but 16S rRNA gene sequencing or restriction analysis of amplified DNA (16S rRNA or *hsp65* genes) allows rapid identification [31, 32]. This is significant, as it is important to distinguish *N. farcinica* from *N. asteroides*—the former is more resistant to antimicrobial agents and has a

Table 2. Co-Morbid Conditions in 67 Cases of *Nocardia farcinica* Infection[a]

Predisposing factor	*No. (%) of patients*
Solid organ transplant recipient	12 (17.9)
Chronic obstructive pulmonary disease	9 (13.4)
Hematologic neoplasm	3 (4.5)
Human immunodeficiency virus infection	5 (7.5)
Idiopathic thrombocytopenic purpura	2 (3.0)
Systemic lupus erythematosus	3 (4.5)
Solid neoplasm	5 (7.5)
Alcoholism	2 (3.0)
Diabetes mellitus	6 (9.0)
Vasculitis	3 (4.5)
Immunosuppression (steroids or chemotherapy)	41 (61.2)
Miscellaneous[b]	17 (25.4)

[a]Some patients presented with more than one factor.
[b]One case each of invasive aspergillosis, *Mycobacterium avium* complex, drug abuse, pneumoconiosis, Evans syndrome, bullous pemphigoid, interstitial pneumonia, ulcerative colitis, bronchiolitis obliterans organizing pneumonia, idiopathic pulmonary fibrosis, polymyalgia rheumatica, cystic fibrosis, allergic bronchopulmonary aspergillosis, cirrhosis, sarcoidosis, trauma, and chronic bronchitis.

Table 3. Organ Involvement in 67 Patients with *Nocardia farcinica* Infection

Organ or site	*No. (%) of patients*
Lung	40 (59.7)
Brain	22 (32.8)
Soft tissue	12 (17.9)
Spine	2 (3.0)
Kidneys	1 (1.5)
Lymphatics	1 (1.5)
Disseminated[a]	25 (37.3)

[a]"Disseminated" includes bacteremia or more than one organ involved.

higher risk of dissemination [33]. The treatment for *N. farcinica* is complicated by its resistance to most β-lactam antimicrobials, tobramycin, and tetracyclines [12, 34]. The treatment of choice is TMP-SMX [35]. However, side effects such as skin reactions may necessitate alternative therapy [6,24,36]. In addition, as many as 50% of isolates demonstrate TMP-SMX resistance, emphasizing the need for antibiotic susceptibility testing of clinical isolates [13,37,38].

N. farcinica is susceptible to TMP-SMX, minocycline, linezolid, moxifloxacin, and amikacin and demonstrates variable susceptible to imipenem-cilastatin and ciprofloxacin [20, 39-43]. It is recommended that immunocompetent patients be treated for at least six months [44]. If the central nervous system is involved, 12 months of therapy is recommended [44]. Therapy for *N. farcinica* has become more aggressive, with increasing administration of multiple antimicrobials. In this review, 74.6% of patients (n = 50) received TMP-SMX as part of their treatment. Carbapenems (n = 25; 37.3%), amikacin (n = 16; 23.9%), and ceftriaxone (n = 12; 17.9%) also were used commonly (see Table 1). A previous review found TMP-SMX was administered in 54% of patients infected with *N. farcinica*, whereas amikacin with imipenem-cilastatin and amoxicillin/clavulanic acid were used in only 7% [13]. Nevertheless, the death rate was 31% with TMP-SMX and 38.8% with carbapenems and amikacin [13].

The patient described here was unusual in that he was immunocompetent. Although the primary origin of his infection is not documented, it is tempting to speculate that the prior febrile episode and infected cyst of three years earlier was his initial encounter with the organism. Subsequent reactivation with dissemination may have been prompted by unknown factors and perhaps facilitated by the local steroid injection. The distribution of his infection was pulmonary and musculoskeletal (limited to the right knee) with no radiologic or post-mortem evidence of central nervous system involvement. Despite therapy, the patient died from *Nocardia* sepsis, attesting to the virulence *N. farcinica*.

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Author Disclosure Statement

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References

1. Lerner PI. Nocardiosis. Clin Infect Dis 1996;22:891–903.
2. Beaman BL, Beaman L. *Nocardia* species: Host–parasite relationships. Clin Microbiol Rev 1994;7:213–264.
3. Mandell GL, Douglas RG, Bennett JE, Dolin R. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. New York. Elsevier/Churchill Livingstone. 2005:3661.
4. Beaman BL, Burnside J, Edwards B, Causey W. Nocardial infections in the United States, 1972–1974. J Infect Dis 1976;134:286–289.
5. Wiesmayr S, Stelzmueller I, Tabarelli W, et al. Nocardiosis following solid organ transplantation: A single-centre experience. Transplant Int 2005;18:1048–1053.
6. Matulionyte R, Rohner P, Uckay I, et al. Secular trends of *Nocardia* infection over 15 years in a tertiary care hospital. J Clin Pathol 2004;57:807–812.
7. Peleg AY, Husain S, Qureshi ZA, et al. Risk factors, clinical characteristics, and outcome of *Nocardia* infection in organ transplant recipients: A matched case-control study. Clin Infect Dis 2007;44:1307–1314.
8. Maraki S, Scoulica E, Nioti E, Tselentis Y. Nocardial infection in Crete, Greece: Review of fifteen cases from 2003 to 2007. Scand J Infect Dis 2009;41:122–127.
9. Yildiz O, Alp E, Tokgoz B, et al. Nocardiosis in a teaching hospital in the Central Anatolia region of Turkey: Treatment and outcome. Clin Microbiol Infect 2005;11:495–499.
10. Beaman BL, Boiron P, Beaman L, et al. *Nocardia* and nocardiosis. J Med Vet Mycol 1992;30(Suppl 1):317–331.
11. Kachi S, Okazaki M, Takeda H, et al. Outbreak of *Nocardia farcinica* infection with the same pattern in randomly amplified polymorphic DNA analysis. J Hosp Infect 2006;62: 502–506.
12. Wallace RJ Jr, Tsukamura M, Brown BA, et al. Cefotaxime-resistant *Nocardia asteroides* strains are isolates of the controversial species *Nocardia farcinica*. J Clin Microbiol 1990; 28:2726–2732.
13. Torres OH, Domingo P, Pericas R, et al. Infection caused by *Nocardia farcinica*: Case report and review. Eur J Clin Microbiol Infect Dis 2000;19:205–212.
14. Krone A, Schaal KP, Brawanski A, Schuknecht B. Nocardial cerebral abscess cured with imipenem/amikacin and enucleation. Neurosurg Rev 1989;12:333–340.
15. Bergstrom R, Edebo L, Fors B, Tegner KB. Systemic *Nocardia* infection. Scand J Respir Dis 1966;47:75–84.
16. Debieuvre D, Dalphin JC, Jacoulet P, et al. [Disseminated infection due to an unusual strain of *Nocardia farcinica*] (Fre). Rev Mal Respir 1993;10:356–358.
17. Schiff TA, McNeil MM, Brown JM. Cutaneous *Nocardia farcinica* infection in a nonimmunocompromised patient: Case report and review. Clin Infect Dis 1993;16:756–760.
18. Iannotti CA, Hall GS, Procop GW, et al. Solitary *Nocardia farcinica* brain abscess in an immunocompetent adult mimicking metastatic brain tumor: Rapid diagnosis by pyrosequencing and successful treatment. Surg Neurol 2009;72: 74–79.
19. Husain S, McCurry K, Dauber J, et al. *Nocardia* infection in lung transplant recipients. J Heart Lung Transplant 2002;21: 354–359.
20. Mamelak AN, Obana WG, Flaherty JF, Rosenblum ML. Nocardial brain abscess: Treatment strategies and factors influencing outcome. Neurosurgery 1994;35:622–631.
21. Vigano SM, Edefonti A, Ferraresso M, et al. Successful medical treatment of multiple brain abscesses due to *Nocardia farcinica* in a paediatric renal transplant recipient. Pediatr Nephrol 2005;20:1186–1188.
22. Petersen BE, Jenkins SG, Yuan S, et al. *Nocardia farcinica* isolated from bronchoalveolar lavage fluid of a child with cystic fibrosis. Pediatr Infect Dis J 2007;26:858–859.
23. Singh NP, Goyal R, Manchanda V, Gupta P. Disseminated nocardiosis in an immunocompetent child. Ann Trop Paediatr 2003;23:75–78.
24. Poonyagariyagorn HK, Gershman A, Avery R, et al. Challenges in the diagnosis and management of *Nocardia* infections in lung transplant recipients. Transpl Infect Dis 2008; 10:403–408.
25. Davenpeck KL, Zagorski J, Schleimer RP, Bochner BS. Lipopolysaccharide-induced leukocyte rolling and adhesion in the rat mesenteric microcirculation: Regulation by glucocorticoids and role of cytokines. J Immunol 1998;161:6861–6870.

26. Hui CH, Au VW, Rowland K, et al. Pulmonary nocardiosis re-visited: Experience of 35 patients at diagnosis. Respir Med 2003;97:709–717.
27. Martinez Tomas R, Menendez Villanueva R, Reyes Calzada S, et al. Pulmonary nocardiosis: Risk factors and outcomes. Respirology 2007;12:394–400.
28. Khan BA, Duncan M, Reynolds J, Wilkes DS. *Nocardia* infection in lung transplant recipients. Clin Transplant 2008; 22:562–566.
29. Agterof MJ, van der Bruggen T, Tersmette M, et al. Nocardiosis: A case series and a mini review of clinical and microbiological features. Neth J Med 2007;65:199–202.
30. Severo CB, Oliveira F de M, Cunha L, et al. Disseminated nocardiosis due to *Nocardia farcinica*: Diagnosis by thyroid abscess culture. Rev Inst Med Trop São Paulo 2005;47: 355–358.
31. Brown-Elliott BA, Brown JM, Conville PS, Wallace RJ Jr. Clinical and laboratory features of the *Nocardia* spp. based on current molecular taxonomy. Clin Microbiol Rev 2006;19:259–282.
32. Tatti KM, Shieh WJ, Phillips S, et al. Molecular diagnosis of *Nocardia farcinica* from a cerebral abscess. Hum Pathol 2006;37:1117–1121.
33. Angeles RM, Lasala RP, Fanning CV. Disseminated subcutaneous nocardiosis caused by *Nocardia farcinica* diagnosed by FNA biopsy and 16S ribosomal gene sequencing. Diagn Cytopathol 2008;36:266–269.
34. Farina C, Boiron P, Ferrari I, et al. Report of human nocardiosis in Italy between 1993 and 1997. Eur J Epidemiol 2001;17:1019–1022.
35. Lederman ER, Crum NF. A case series and focused review of nocardiosis: Clinical and microbiologic aspects. Medicine 2004;83:300–313.
36. Roberts SA, Franklin JC, Mijch A, Spelman D. *Nocardia* infection in heart–lung transplant recipients at Alfred Hospital, Melbourne, Australia, 1989–1998. Clin Infect Dis 2000; 31:968–972.
37. Hitti W, Wolff M. Two cases of multidrug-resistant *Nocardia farcinica* infection in immunosuppressed patients and implications for empiric therapy. Eur J Clin Microbiol Infect Dis 2005;24:142–144.
38. Dodds EM, Echandi LV, Puente SI, Kaufman S. Subretinal abscess due to *Nocardia farcinica* resistant to trimethoprim–sulfamethoxazole in a patient with systemic lupus erythematosus. Ocul Immunol Inflamm 2006;14:249–251.
39. Hansen G, Swanzy S, Gupta R, et al. In vitro activity of fluoroquinolones against clinical isolates of *Nocardia* identified by partial 16S rRNA sequencing. Eur J Clin Microbiol Infect Dis 2008;27:115–120.
40. Fihman V, Bercot B, Mateo J, et al. First successful treatment of *Nocardia farcinica* brain abscess with moxifloxacin. J Infect 2006;52:e99–e102.
41. Fleetwood IG, Embil JM, Ross IB. *Nocardia asteroides* cerebral abscess in immunocompetent hosts: Report of three cases and review of surgical recommendations. Surg Neurol 2000;53:605–610.
42. Peters BR, Saubolle MA, Costantino JM. Disseminated and cerebral infection due to *Nocardia farcinica*: Diagnosis by blood culture and cure with antibiotics alone. Clin Infect Dis 1996;23:1165–1167.
43. Jodlowski TZ, Melnychuk I, Conry J. Linezolid for the treatment of *Nocardia* spp. infections. Ann Pharmacother 2007;41:1694–1699.
44. Minero MV, Marin M, Cercenado E, et al. Nocardiosis at the turn of the century. Medicine 2009;88:250–261.

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