First Report of *Nocardia farcinica* Bursitis in a Patient with Diabetes Mellitus

Soon-Deok Park, Ph.D.1, Han Jun Kim, M.D.1, In Ho Jang, Ph.D.1, Young Uh, M.D.1, Juwon Kim, M.D.1, Kap Joon Yoon, M.D.1, and Jin-Rok Oh, M.D.2

Departments of Laboratory Medicine1 and Orthopedic Surgery2, Yonsei University Wonju College of Medicine, Wonju, Korea

Dear Editor

*Nocardia* species of the family Nocardiaceae form a homogeneous cluster within the order Corynebacteriales, formerly suborder Corynebacteriaceae [1]. *Nocardia*, a genus of aerobic actinomycetes, is characterized by filamentous, branching, gram positive, partially acid-fast bacteria found worldwide as soil saprophytes [2]. The most common site of *Nocardia* infection is the respiratory tract, with subsequent dissemination to distant organs. Disseminated nocardiosis to the brain, kidneys, joints, or eyes can occur by hematogenous spread of infection [3]. Microbiological diagnosis of nocardiosis and identification of *Nocardia* clinical isolates to the species level by conventional methods are difficult. However, identification to species level is important to characterize associated disease manifestations, to predict antimicrobial susceptibility, and for epidemiological and ecological purposes [2]. Various nucleic acid amplification methods targeting conserved *Nocardia* gene regions have been proposed for accurate species-level identification [4-6]. Sequence analysis of the 16S ribosomal RNA (rRNA) gene has become the gold standard for definitive species identification [2, 7].

*N. farcinica* is considered an opportunistic pathogen that usually affects patients with impaired cell-mediated immunity and predisposing factors like hematologic malignances, treatment with corticosteroids, chronic pulmonary conditions, renal diseases, and other conditions leading to immunosuppression. The organism is increasingly recognized as a human pathogen in infections of the lungs, brain, skin, wounds, and kidneys [5]. Here, we report a case of bursitis due to *N. farcinica* infection, confirmed by 16S rRNA sequencing, in a patient with long-standing diabetes mellitus.

A 67-yr-old man was admitted to the hospital complaining of right ankle pain that had persisted for 4 months. Swelling with an external wound was observed on the lateral malleolus of his right ankle (Fig. 1). The patient had been prescribed antihypertensive drugs for 5 yr and an oral hypoglycemic agent for 2 yr for hypertension and diabetes mellitus, respectively. On admission, his body temperature was 36.9°C, and his other vital signs were within normal limits. Hematological investigation revealed hemoglobin level of 13.6 g/dL, white blood cell count of 10.82×10^9/L, and platelet count of 341×10^9/L. Serum C-reactive protein level (0.38 mg/dL, reference range: <0.30 mg/dL) and erythrocyte sedimentation rate (31 mm/hr, reference range: 0-22 mm/hr) were slightly elevated. Prothrombin and activated partial thromboplastin times were within reference ranges. Renal and liver blood chemistry tests were also within reference ranges. The patient’s fasting blood glucose level and hemoglobin A1c concentration were 160 mg/dL and 6.0%, respectively. Simple chest radiograph and electrocardiograph findings were not remarkable.

On the basis of these clinical features, the patient was diag-
nosed as having lateral malleolar bursitis on the right ankle and underwent emergency bursotomy. The resected bursa revealed massive granulation tissue and fistula connecting the bursa to the subtalar joint (Fig. 2).

The surgical specimen taken during the operation was subjected to microscopy and culture analysis. The specimen was plated onto 5% sheep blood agar (BD Diagnostic Systems, Sparks, MD, USA) and MacConkey agar (BD Diagnostic Systems) for bacterial culture. After 24 hr of aerobic incubation at 35°C, chalky white colonies grew on 5% sheep blood agar (Fig. 3), but no colonies formed on MacConkey agar. The isolate was found to be a gram-positive rod with branched filaments (Fig. 4) and was catalase positive but oxidase negative. Ziehl-Neelsen staining of the bacteria revealed partially acid-fast organisms arranged in branching filaments. The VITEK 2 ANC identification system (bioMérieux, Marcy-l’Etoile, France) was used according to the manufacturer’s recommendations for initial identification of the isolate as Corynebacterium pseudobacterium and Corynebacterium urealyticum (bionumber: 2320020400105, confidence level: low discrimination). Identity was confirmed by sequencing analysis of isolated colony 16S rRNA.

After PCR amplification of a region of the 16S rRNA by using primers 518F (5’-CCA GCA GCC GCG GTA ATA CG-3’) and 800R (5’-TAC CAG GGT ATC TAA TCC-3’), sequencing was conducted using the Big Dye Terminator Cycle Sequencing kit (Applied Biosystems, Foster City, CA, USA) and ABI PRISM 3730 genetic

![Fig. 1. Lateral malleolus swelling with external wound.](image1)

![Fig. 2. Massive granulation tissue and fistula connecting bursa to subtalar joint.](image2)

![Fig. 3. Small chalky white non-hemolytic colonies on sheep blood agar.](image3)

![Fig. 4. Microscopic morphology of filamentous branching Gram-positive rods (×1,000).](image4)
Antimicrobial susceptibility of patient-isolated *N. farcinica*.

| Antimicrobial agents       | MIC (mg/L) | Susceptibility*
|--------------------------|-----------|----------------
| Ampicillin               | 0.25      | S              |
| Amikacin                 | ≤ 0.5     | S              |
| Amoxicillin-clavulanic acid | ≤ 0.5/0.25 | S            |
| Ceftriaxone              | ≤ 0.25    | S              |
| Ciprofloxacin            | ≤ 0.5     | S              |
| Imipenem                 | ≤ 1       | S              |
| Linezolid                | ≤ 2       | S              |
| Trimethoprim-sulfamethoxazole | ≤ 0.25/4.7 | S       |
| Tobramycin               | > 8       | R              |
| Ceftazidime              | ≤ 0.25    | S              |
| Cefotaxime               | ≤ 0.25    | S              |

*Broth microdilution interpretive criteria are used as indicated in CLSI M24-A2 [8].

Abbreviations: S, susceptible; R, resistant; MIC, minimal inhibitory concentration.

Table 1. Antimicrobial susceptibility of patient-isolated *N. farcinica*. 

To our knowledge, only seven cases (3 cases of brain abscess, 2 pulmonary infections, 1 intramuscular abscess, and 1 catheter-related bloodstream infection) of human infection with *N. farcinica* have been reported in Korea [9-15], although molecular confirmation of species identification was not performed in all cases. The frequency of organ involvement with *N. farcinica*, in decreasing order, was lung, brain, soft tissue, spine, kidneys, lymphatic, and disseminated [4]. We found only two cases of bursitis caused by *Nocardi*a species in English language literature. Chowdhary et al. [16] reported bursitis caused by *N. asteroides* in a healthy young man with no predisposing illness. Leitner et al. [17] reported *N. asiatica* olecranon bursitis in an immunocompetent patient. To the best of our knowledge, this is the first reported case of bursitis due to *N. farcinica* in a patient with diabetes mellitus.

It has been suggested that the increased diagnosis of *N. farcinica* infections is due to both the growing population of immunocompromised hosts and improved methods to detect and identify *Nocardi*a species [18]. However, information on the clinical significance of *N. farcinica* bursitis is very limited owing to the paucity of reported cases. The co-morbidity factors commonly associated with *N. farcinica* infections are, in decreasing order, immunosuppression (steroids or chemotherapy), solid organ transplant recipient, chronic obstructive pulmonary disease, diabetes mellitus, human immunodeficiency virus infection, and solid neoplasm [4]. Primary cutaneous nocardiosis is usually caused by trauma-related introduction of *Nocardi*a species. Although the exact infection route of *N. farcinica* is uncertain, it may be that an immunocompromised condition facilitates the invasion of *N. farcinica* via percutaneous trauma, which forms bursitis.

Trimethoprim-sulfamethoxazole (SXT) has been selected as the first-line therapy for patients with *Nocardi*a infections. Unlike other *Nocardi*a spp., resistance to commonly used antimicrobial agents occurs more frequently in *N. farcinica* [2, 4, 12]. Moreover, as many as 50% of *N. farcinica* isolates demonstrate SXT resistance, emphasizing the need for antibiotic susceptibility testing of clinical isolates [4, 5]. Hansen et al. [6] reported *N. farcinica* to be characteristically resistant to third-generation cephalosporins, Rivero et al. [19] reported successful treatment with linezolid of multidrug-resistant *N. farcinica* infection in an immunocompromised host. In the present case, the organism was susceptible to SXT, ampicillin, amikacin, amoxicillin-clavulanic acid, ceftriaxone, ciprofloxacin, imipenem, linezolid, ceftazidime, and cefotaxime, but was resistant to tobramycin. Our
patient was successfully treated with antibiotics such as cefoperazone and cefpodoxime in addition to surgical debridement.

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