



Septic arthritis due to *Nocardia*: Case report and literature review



Tasaduq Fazili, MD, FACP, FIDSA¹, Ekta Bansal, MD¹,
Dorothy Garner, MD¹, Vijender Bajwa, MD¹ and Shikha Vasudeva, MD²

¹ Carilion Clinic, Virginia Tech Carilion School of Medicine, Section of Infectious Diseases, Department of Medicine, Roanoke, VA, USA; ² Veterans Affairs Medical Center, Section of Infectious Diseases, Department of Medicine, Salem, VA, USA

ABSTRACT

Nocardia is an uncommon cause of septic arthritis. We found only 37 cases reported in the literature thus far. Amongst these, only five involved prosthetic joints. Three cases were caused by *N. nova* and one each by *N. farcinica* and *asteroides*. Septic arthritis due to *Nocardia* has a favorable outcome with a combination of surgical debridement and prolonged antimicrobial therapy of three to six months. For prosthetic joint infections, removal of hardware seems to carry a better prognosis. Trimethoprim-sulfamethoxazole continues to remain the drug of choice. [Am J Med Sci 2022;364(1):88-91.]

INTRODUCTION

Nocardia are Gram-positive filamentous bacteria that cause Nocardiosis, a rare opportunistic infection. The most common site of infection is the lungs, with metastatic spread usually to the central nervous system. Septic arthritis due to *Nocardia* is very rare. We report a case of septic arthritis of the knee due to *Nocardia veterana/elegans*, and review the literature.

CASE PRESENTATION

The patient was a 35-year-old male with history of nodular sclerosing Hodgkin's Lymphoma for which he received chemotherapy in 2017 (consisting of ABVD – Adriamycin, Bleomycin, Vinblastine and Dacarbazine) with subsequent remission, coronary artery disease, poorly controlled diabetes with a hemoglobin A1c of 13.8, and tobacco use with a 15-pack year history of smoking. He was involved in a motor vehicle accident in 2003, resulting in right open tibial plateau fracture, which required hardware placement (3 proximal tibial screws). The patient was admitted with a two week history of right knee pain and swelling. The right knee pain progressively worsened that led to difficulty with ambulation. He denied having any falls or trauma to his right knee. He also denied fevers, chills or sweats. There was no history of recent travel or tick exposure.

His physical exam revealed a severe antalgic limp favoring the right lower extremity. He had significant swelling to the right knee, consistent with a joint effusion, along with mild warmth to it. Range of motion to the knee was limited to 20-75 degrees with significant pain.

Magnetic resonance imaging (MRI) scan of the knee was performed which showed findings concerning for septic arthritis. The knee was aspirated revealing grossly purulent fluid. Synovial fluid analysis showed a white cell

count of 22,090/ μ L, with 78% neutrophils. He underwent right knee arthrotomy and upon opening the knee joint, extensive purulent fluid was identified. Thorough debridement of the knee joint was performed with removal of right tibial hardware, which was communicating with the joint.

Synovial fluid culture from the initial joint aspirate as well as the culture from the surgical debridement had significant growth of branching, partially acid fast, Gram positive rods, suggestive of *Nocardia* species.

The patient was empirically placed on oral linezolid, which he tolerated well. The *Nocardia* isolate was sent to a reference laboratory for identification and susceptibilities, and was identified by DNA technology (Pyrosequencing) as *Nocardia veterana/elegans*.

Antimicrobial sensitivities were performed by broth microdilution and the isolate was sensitive to trimethoprim/sulfamethoxazole, linezolid, clarithromycin, imipenem and amikacin. After antimicrobial susceptibilities became available (in several weeks), he was switched to oral trimethoprim/sulfamethoxazole. The patient subsequently completed a six-month course of therapy and did well clinically. He did not have any pulmonary or systemic symptoms/findings, and the infection was thought to have been locally introduced into the knee joint/hardware. Uncontrolled diabetes seemed to be the predisposing risk factor in our patient.

DISCUSSION

Nocardia are ubiquitous, saprophytic, filamentous Gram positive organisms that belong to the aerobic Actinomycetes group, which also includes *Corynebacterium*, *Mycobacterium*, *Rhodococcus*, *Streptomyces*, *Actinomadura*, *Gordonia* and *Tsukumurella*.¹ Anaerobic Actinomycetes include *Actinomyces*, *Arachnia*, *Rothia*, and

Bifidobacterium. *Nocardia* can appear similar to *Actinomyces* species on Gram's staining. However, *Nocardia* are usually acid fast compared to *Actinomyces*, which is due to the mycolic acid content of their cell wall.

Nocardia were first isolated in 1888 from cattle suffering from "bovine farcy" by the French veterinarian, Edward Nocard, and the organism was named *Nocardia farcinica*.¹ The first case in humans was reported by Eppinger in 1890, from a patient with brain abscess, and the isolate named *Nocardia asteroides*. Subsequently, for several decades, *N. asteroides* was considered the most important pathogenic species in humans. Additional species with somewhat similar biochemical properties were later discovered and added to the "*N. asteroides* complex". The advent of molecular diagnostic methodologies, in particular gene sequencing, has now been able to accurately identify *Nocardia* to the species level.¹ With the help of these molecular methods, along with antimicrobial susceptibility patterns, *Nocardia* species are now grouped into the following prominent complexes:

N. nova, *N. farcinica*, *N. cyriacigeorgica*, *N. transvalensis*, *N. brevicatena/paucivorans*, *N. abscessus* and *N. otitidiscavarium*.

N. veterana and *N. elegans*, identified in our patient, belong to the *N. nova* complex. The other species in this complex include *N. nova*, *N. africana*, *N. kruczai*, *N. aobensis*, *N. cerradoensis*, *N. mikamii* and *N. vermiculata*.

Nocardia infections are uncommon and the organisms are for the most part opportunistic pathogens. Infections occur mainly in persons with defects in cell mediated immunity – patients on immunosuppressive medications including steroids, organ transplant recipients, or those with malignancies or human immunodeficiency virus (HIV) infection. In addition, chronic obstructive lung disease, diabetes and alcoholism are also risk factors for infection. However, up to one-third of infected patients can be immunocompetent.

Nocardia species are present worldwide in soil, plants and water.² The predominant mode of entry of *Nocardia* in humans is considered to be via inhalation.³ The other less commonly encountered mode is cutaneous by direct inoculation.

The lungs are the main site of infection in humans, being involved in more than seventy-five percent of cases in some series.³ About half of these cases can have evidence of spread outside the lungs, especially to the brain. The clinical presentation can be non-specific with a subacute to chronic course. Presenting symptoms can be cough, shortness of breath, fever, sweats, hemoptysis and pleuritic chest pain. Imaging findings can include lung nodules, lung masses or lobar consolidation.

Cutaneous involvement from *Nocardia* usually presents as a primary infection of the skin.³ This can manifest as a skin/soft tissue infection resembling staphylococcal infection, a lymphocutaneous or sporotrichoid form, or as a more indolent mycetoma. Rarely, the skin can be secondarily involved from another source, mainly the lungs.

Bone and joint disease due to *Nocardia* is very uncommon.⁴ We performed a literature review using Pubmed and found only 37 cases of septic arthritis reported thus far, including our case.^{4–6}

Amongst the 37 patients with septic arthritis, all but 5 patients had involvement of a native joint. The majority of patients – 22 (60%), had infection due to hematogenous dissemination. All but 4 of these 22 patients had some underlying immunocompromising condition, which included in descending order of frequency, prolonged steroid use, solid organ transplantation, hematologic disease, diabetes, malignancy and HIV. 18 patients (50%) had evidence of pulmonary involvement.

Joint infection occurred in 11 patients as result of direct inoculation. All but 1 of these patients were immunocompetent. The mechanism of infection was unknown in 4 cases.

Majority of the patients were male, with a male-female ratio of 2.7:1. The median age at presentation was 50 years. The median time to diagnosis from the time of symptom onset was about 20 days. The knee joint was the most frequently affected, in more than 80% of the cases. One fourth of patients did not exhibit any fever, and only 4 patients (~10%) were bacteremic. *N. asteroides* was the most frequently isolated species in 19 cases. However, most of these were reported in the literature before the turn of the century, prior to availability of molecular techniques, and thus likely represented misclassification.

For native joint septic arthritis, less than half had any surgical procedure performed, while medical therapy alone was utilized in about half the cases. The median duration of total antibiotic therapy was 24 weeks. Two-thirds of the patients received intravenous antibiotics initially, the mean duration of which was 4 weeks. The most frequently used intravenous antibiotics were carbapenems (imipenem, meropenem), amikacin and ceftriaxone. Amongst the oral antibiotics, trimethoprim-sulfamethoxazole was the most frequently used, in more than 80% of the cases. A favorable outcome was achieved in about 80% of cases.

Prosthetic joint septic arthritis due to *Nocardia* is rare.⁴ Our literature search revealed only five cases.^{7–11} Clinical details of these patients are outlined in Table 1. Three cases were due to *N. nova*, and one each due to *N. asteroides* and *N. farcinica*. The joints involved were knee (3 cases) and hip (2 cases). The average age was 58 years, with the range being from 35 to 78 years. The time of presentation from the implantation of the prosthesis to diagnosis of infection varied widely, anywhere from a few days to 17 years. Half of the patients had an

Table 1. Prosthetic joint septic arthritis caused by *Nocardia*.

Reference no.	Age/Sex	Risk factor	Joint involved	Time after prosthesis implantation	Surgical treatment	Antibiotic therapy	Outcome
7	72/F	None	Hip	Few days	Two-stage removal of prosthesis	Minocycline and ofloxacin x 6 months	Favorable
8	43/F	Lupus	Hip	8 years	Two-stage removal of prosthesis	Imipenem and amikacin x 10 days, Imipenem and erythromycin x 35 days, Erythromycin x 2 months	Favorable
9	55/F	None	Knee	5 months	Debridement with joint retention	Clarithromycin and co-trimoxazole x 10 days, Clarithromycin, Co-trimoxazole and amoxicillin-clavulanate x 1 year, Clarithromycin and co-trimoxazole x 2 years	Favorable
10	64/M	Sarcoidosis with steroid use	Knee	13 months	One-stage exchange	Meropenem plus doxycycline x 50 days, Ceftriaxone plus doxycycline x 1 year	Favorable
11	78/M	None	Knee	15 years	Removal of prosthesis with spacer	Imipenem and amikacin x 20 months	Favorable

underlying immunocompromising condition – systemic lupus erythematosus, sarcoidosis with steroid use and Hodgkin's Lymphoma. All the patients had surgical intervention performed – three had the prosthetic joint removed, while one each had debridement with joint retention and a one-stage exchange. The duration of antibiotic therapy was variable, ranging from around three months to three years, with a median of 9 months. The outcome was favorable in all patients.

Our patient was the only one that had involvement of hardware other than a prosthetic joint. He did well clinically with a combination of a 6-month course of antibiotic therapy and removal of hardware.

In conclusion, our case highlights presentation of septic arthritis and infected hardware of a knee joint due to *Nocardia*, which was successfully treated with joint debridement, hardware removal and a prolonged course of antibiotic therapy. *Nocardia* species are an uncommon cause of septic arthritis. However, they should be kept in the differential, especially in immunocompromised patients with a negative Gram's stain and negative initial culture result. Overall prognosis is fair with joint debridement and prolonged antibiotic therapy. Trimethoprim-sulfamethoxazole continues to be the drug of choice. Device removal appears to be crucial in cases of prosthetic joint infection and infected hardware.

AUTHORS CONTRIBUTION

TF and EB conceived the manuscript. TF, EB and VB collected the data. All the authors contributed towards writing the manuscript.

SOURCE OF FUNDING

None.

CONFLICT OF INTEREST

None.

REFERENCES

1. **Fatahi-Bafghi Mehdi**. Nocardiosis from 1888 to 2017. *Microb Pathogenesis*. 2018;114:369–384.
2. **Brown-Elliott BA, Brown JM, Conville PS, et al**. Clinical and laboratory features of the *Nocardia* spp. based on current molecular taxonomy. *Clin Microbiol Rev*. 2006;19(2):259–282.
3. **Minero MV, Marin M, Cercenado E, et al**. Nocardiosis at the turn of the century. *Medicine (Baltimore)*. 2009;88(4):250–261.
4. **Chaussade H, Lebeaux D, Guillaume G, et al**. Nocardia arthritis: 3 cases and literature review. *Medicine*. 2015;94(42):1–7.
5. **Yong E, Cheong E, Boutlis C, et al**. *Nocardia* septic arthritis complicating an anterior cruciate ligament repair. *J Clin Microbiol*. 2015;53(8):2760–2762.
6. **Ishiguro T, Yoshioka H, Kawai S, et al**. A case of empyema and septic arthritis due to *Nocardia farcinica*. *Clin Case Rep*. 2017.
7. **Robinson D, Halperin N**. Nocardia asteroidis infection of an Austin-Moore hemiarthroplasty in a nonimmunocompromised host. A case report. *Bull Hosp Jt Dis Orthop Inst*. 1989;49:107–110.

8. **Amal C, Man H, Delisle F, et al.** Nocardia infection of a joint prosthesis complicating systemic lupus erythematosus. *Lupus*. 2009;9:304–306.
9. **Nizam I, Kohan L, Kerr D.** Nocardia nova septic arthritis following total knee replacement: a case report. *J Orthop Surg Hong Kong*. 2007;15:390–392.
10. **Laurent F, Rodríguez-Villalobos Cornu O, et al.** Nocardia prosthetic knee infection successfully treated by one-stage exchange: case report and review. *Acta Clin Belg*. 2015;70(4):287–290.
11. **Ozan F, Koyuncu S, Kizilay C, et al.** The *Nocardia farcinica* infection developing after total knee arthroplasty surgery. *Acta Orthop Traumatol Turc*. 2013;47(3):212–217.

Submitted March 11, 2021; accepted January 26, 2022.

Corresponding author. (E-mail: tasfazili@gmail.com).