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CLINICAL CASE REPORT

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Nocardia Arthritis: 3 Cases and Literature Review

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Abstract: Nocardia are Gram-positive filamentous bacteria responsible for infections ranging from opportunistic life-threatening disseminated diseases to chronic skin and soft-tissue infections.

Even if virtually all organs can be infected, articular involvement is rare. Therefore, we report 3 recent cases and performed a literature review of cases of *Nocardia* arthritis in order to describe clinical features, therapeutic challenges, and outcome of these patients.

Among 34 patients (31 in the literature plus our 3 cases), 21 (62%) were due to hematogenous dissemination, 9 (26%) were due to direct bacterial inoculation through the skin, and in 4 cases, the mechanism of infection was unknown. Four out of these 34 cases occurred on prosthetic joints.

Whereas hematogenous infections mostly occurred in immunocompromised hosts (17 of 21, 81%), direct inoculation was mostly seen in immunocompetent patients.

Eighty-two percent of patients (28 out of 34) received trimethoprim-sulfamethoxazole-containing regimens and median antibiotic treatment duration was 24 weeks (range, 12–120) for hematogenous infections and 12 weeks (range, 6–24) for direct inoculations. Outcome was favorable in 27 cases despite unsystematic surgical management (17 cases) without sequelae in 70% of the cases.

Nocardia arthritis is rare but its management is complex and should rely on a combined approach with rheumatologist, infectious diseases expert, and surgeon.

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Abbreviations: CNS = central nervous system, CMV = cytomegalovirus, GVHd = graft-versus-host disease, HIV = human immunodeficiency virus, HSCT = hematopoietic stem cell transplantation, IDSA = infectious disease society of America, IV = intravenous, MIC = minimal inhibitory concentration, MRI = magnetic resonance imaging, PJI = prosthetic joint infections, spp = species, TMP-SMX = trimethoprim-sulfamethoxazole.

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INTRODUCTION

Nocardia species (spp.) are ubiquitous environmental filamentous Gram-positive aerobic actinomycetes that are responsible for nocardiosis, a rare opportunistic infection.[1]

Nocardia infections are uncommon and occur mostly in individuals with chronic pulmonary diseases or cell-mediated immunity defects, including patients receiving immunosuppressive therapy, organ transplant recipients, or patients infected with human immunodeficiency virus (HIV).[2–5] Nocardiosis can occur after inhalation, causing lung infection, or because of direct bacterial inoculation through the skin, leading to skin and soft-tissue infections. Dissemination mostly occurs hematogenously from a lung infection. The most common sites for dissemination include the central nervous system (CNS), skin and subcutaneous tissues, and less frequently kidneys, bones, heart, eyes, and joints.[3,6] As Nocardia arthritis is rare, data are scarce. We report 3 cases of articular nocardiosis and performed a literature review in order to better describe the epidemiology, clinical manifestations, diagnosis, management, and outcome of articular nocardiosis.

CASE REPORT NO 1

A 55-year-old man presented with clinical signs of knee arthritis and fever that appeared progressively 3 weeks earlier. He had a history of Waldenström's macroglobulinemia treated with antineoplastic chemotherapy and allogeneic hematopoietic stem cell transplantation (HSCT) from matched related donor 1 year before. Hematopoietic stem cell transplantation was complicated by steroid-dependent chronic skin graft-versus-host disease (GVHd), type 2 diabetes, chronic renal failure, and supplemented hypogammaglobulinemia. Immunosuppressive treatment included 20 mg prednisone, tacrolimus (2 mg per day), and mycophenolate mofetil (2 g per day). Prophylaxis included atovaquone (1500 mg per day), oracillin (2 MUI per day), and posaconazole (600 mg per day).

The knee magnetic resonance imaging (MRI) revealed intra-articular fluid and synovial hypertrophy (Fig. 1A). The intra-articular fluid contained leucocytes and direct examination revealed filamentous Gram-positive bacillus. Blood and intra-articular fluid grew *Nocardia farcinica*. Nocardia pulmonary localization was suspected as thoracic computed tomography (CT) scan revealed a 20-mm pleural nodule, but biopsy was unconclusive. Brain MRI was normal. Treatment consisted in arthroscopic debridement and multiple-drug regimen (doses adapted to the renal function), including ceftriaxone (2 g per day) and levofloxacine (500 mg per day) for 7 days. As antibiotic susceptibility testings by broth microdilution revealed resistance toward ceftriaxone, antibiotic regimen was switched

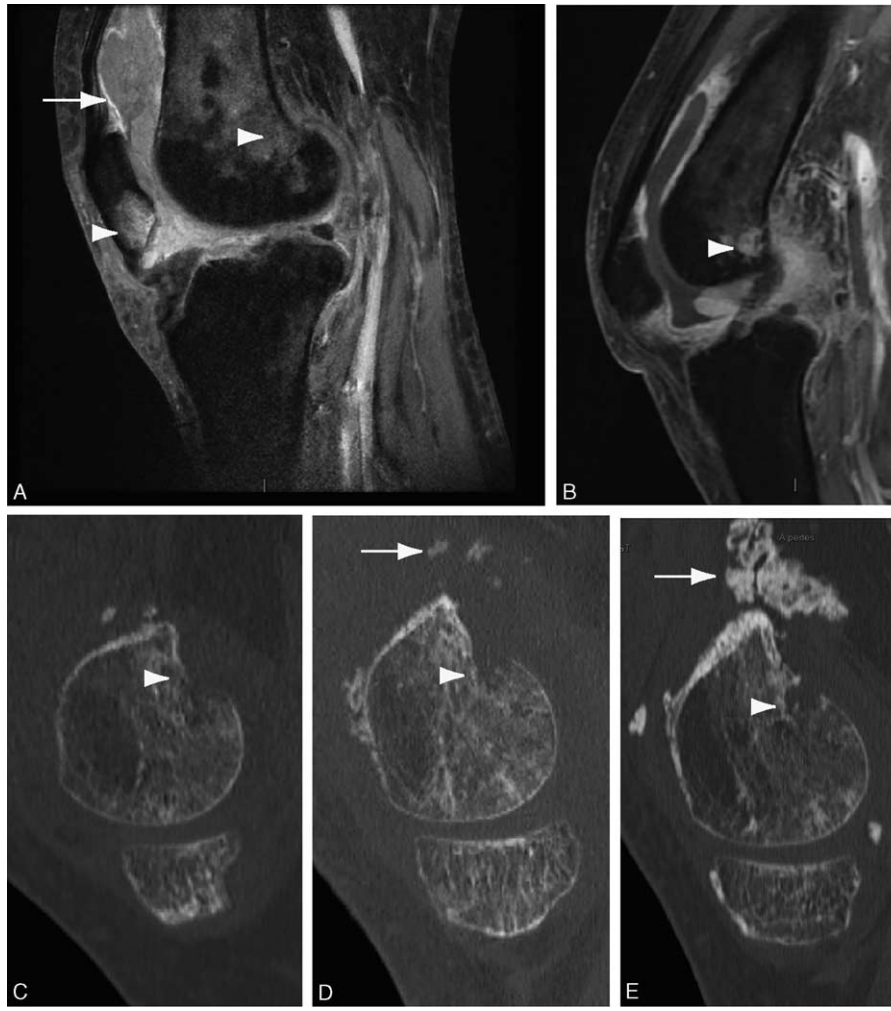

FIGURE 1. Magnetic resonance imaging (MRI) and computed tomography (CT) scans of the left knee of patient 1. (A) Postcontrast sagittal T1-weighted knee MRI at the diagnosis of nocardiosis (April 2012) showing joint effusion, enhancing synovitis (white arrow) and femoral and patelar osteomyelitis (white arrowheads: bone enhancement after gadolinium injection). (B) Second knee MRI performed 5 months (August 2012) after initial surgery with persisting joint effusion, enhancing synovitis and an increase in bone enhancement after gadolinium injection. (C) Concomitant (August 2012) sagital knee CT scan showing femoral osteolytic lesion on the location of the intense bone enhancement seen on the MRI. (D) and (E) Follow-up knee CT scans in October 2012 (D) and April 2013 (E) showing persisting osteolysis (white arrowheads) and extra articular calcifications (white arrows). CT = computed tomography; MRI = magnetic resonance imaging.

from day 10 to meropenem (4 g per day) and amikacin (750 mg every 48 h) for 15 days and then meropenem (4 g per day) and levofloxacin (500 mg per day) during 10 days. Multiple intra-articular fluid cultures were positive up to 17 days after surgical debridement. Therefore, linezolid (1200 mg per day) was added on day 35 to meropenem and levofloxacin but was stopped on day 52 because of thrombocytopenia and leg paresthesia. Antibiotic treatment was modified from day 57 in levofloxacin (500 mg) and minocyclin (200 mg). Because of chronic GVHd, a reduction of immunosuppressive drugs was not possible and rituximab treatment was necessary.

Despite this appropriate treatment and correct antibiotic blood dosages, clinic and radiologic failure were observed with fever and radiologic osteomyelitis persisting 5 months after debridement (Fig. 1B and C). Intravenous treatment with ticarcillin–clavulanate (9 g per day) and cotrimoxazole (2400 mg per day) was started on day 172 and surgical synovectomy performed on day 185. Synovial fluid and bone biopsies grew *N. farcinica*. New antibiotic susceptibility testing revealed the acquisition of resistance toward levofloxacin (Fig. 2). Seven days after the surgical synovectomy, antibiotic treatment was adapted to cefuroxime (2 g per day) and cotrimoxazole (2400 mg per day). Six months later, doxycycline was added because of clinical active infection. With this prolonged multiple-drug regimen, the osteolytic lesions seen on MRI were stable during 9 months (Fig. 1D and E). Patient died of septic shock due to *Klebsiella pneumoniae* bloodstream infection.

CASE REPORT NO 2

A 60-year-old man was hospitalized for fever (38.4°C) and multiple pulmonary nodules. He received allogeneic HSCT from matched related donor for relapsed follicular lymphoma 9 months before. He had type 2 diabetes treated with insulin.

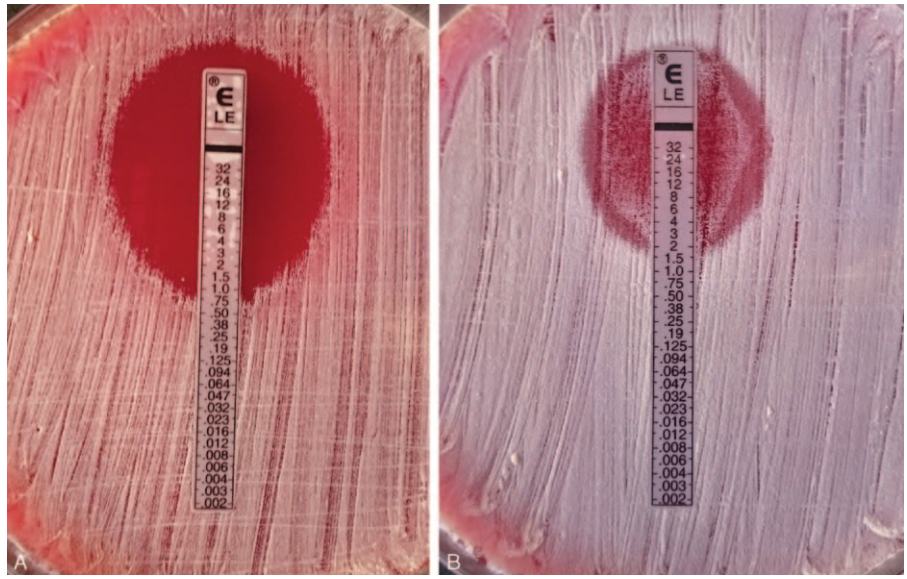

FIGURE 2. Acquisition of resistance toward levofloxacin during the antibiotic treatment of patient 1. Susceptibility was tested using an Etest® strip applied on blood agar plates inoculated by confluent swabbing of the surface with a 1 McFarland standard organism suspension. The plates were incubated at 35°C under a 5% CO_2 atmosphere and growth was monitored every 24 h for 3 days. A. Strain obtained in March 2012, with a levofloxacin MIC of 0.75 μg/mL (susceptible). B. Strain obtained in August 2012, with a levofloxacin MIC > 4 μg/mL (resistant).MIC = minimal inhibitory concentration.

Hematopoietic stem cell transplantation was complicated by Cytomegalovirus reactivation and acute GVHd. Immunosuppressive therapy consisted in corticosteroids (prednisone 60 mg per day) and ciclosporin (360 mg per day). He received atovaquone prophylaxis. Bronchoalveolar lavage (performed after starting antibiotics) was unconclusive. Staging revealed hepatic nodules and peritoneum thickening.

At admission, the patient had clinical knee arthritis present for 8 days. Gram staining of joint fluid was negative but culture grew *N. cyriacigeorgica* susceptible to cefuroxime, imipenem, amikacine, doxycycline, cotrimoxazole, and linezolid (minimal inhibitory concentration (MIC) determined with broth microdilution). Consequently, he received imipenem (2 g per day) and amikacin (1 g per day). There was no surgical management. After 1 month of intravenous antibiotics, cefuroxime (1 g per day) and doxycycline (200 mg per day) were started. Gammaglobulin therapy and decreasing immunosuppression (prednisone 40 mg) were also performed. After 4 months of treatment, pulmonary, hepatic, peritoneal, and articular outcome were favorable. No articular sequela was noted. Antibiotic treatment was maintained during 1 year and then stopped after a positron emission tomography showing no metabolic activity.

CASE REPORT NO 3

A 64-year-old man was found unconscious after a suicide attempt by benzodiazepines. On admission, he presented a left knee osteoarthritis. He had history of type 2 diabetes, myasthenia gravis treated with thymectomy, chemotherapy, and radiotherapy 16 years before, a MALT lymphoma in complete remission after treatment with chlorambucil and ischemic heart disease. Myasthenia was treated with pyridostigmine and 30 mg of prednisone. Patient claimed taking drugs because he suffered from unbearable knee pain for several weeks.

Surgical treatment of arthritis consisted in arthroscopic debridement. Intra-articular fluid revealed 120,000 leukocytes/mm^3 with 80% neutrophils. Gram staining was negative and culture yielded a growth of *N. nova* susceptible to amoxicillin, cefotaxime, imipenem, meropenem, and cotrimoxazole in broth microdilution.

Cerebral, pulmonary, and abdominal CT scan revealed no signs of dissemination. Blood cultures were steriles. The patient was first treated from day 0 to day 11 with imipenem (3 g per day) and cotrimoxazole (3200/640 mg per day). From day 12 to day 20, he received imipenem only and then linezolid (1200 mg per day) only at day 21. Antibiotic treatment was interrupted after an overall course of 2 months. Immunosuppression could not be reduced due to clinical signs of myasthenia. Three months after treatment discontinuation, arthritis relapsed. Treatment consisted in synovectomy and debridement. Positron emission tomography revealed no other sites of infection. Intra-articular fluid was purulent and culture grew *N. nova* with the same antibiotic susceptibility profile. Imipenem was introduced but the knee inflammation persisted and intra-articular fluid cultures still grew *N. nova* 15 days later. From day 18 to day 39 after synovectomy, ceftriaxone (2 g per day) was added to imipenem. This combination therapy resulted in clinical improvement. The patient was then treated from day 40 to day 80 with ceftriaxone and cotrimoxazole. He presented an acute renal failure, resolving after cotrimoxazole discontinuation. Consequently, a combination of amoxicillin (6 g per day) and clarithromycin (1 g per day) was started. Unfortunately, the patient suddenly died, probably because of heart failure.

Ethical Consideration

The patient or family's (if the patients died) provided informed consents for the publication of the cases details. No ethic committee approved the study because all investigations

have been performed retrospectively as part of normal health care and thus ethical approval was not obliged.

Discussion and Literature Review

We searched PubMed for papers published in English, reporting on articular nocardiosis. We used the search terms: « Nocardia infections » and « Arthritis, Infectious » or « Nocardia infections » and « Joint prosthesis ». We also searched the reference lists of retrieved papers.

Underlying conditions, microbiological features, clinical manifestations, antibiotic treatment, and outcome were analyzed. Two cases were identified among case series but could not be included due to the lack of precise clinical data.[7,8]

Physiopathology and Predisposing Conditions

Among the 34 patients described (31 cases in the literature and the 3 presented in this article), 21 (62%) were due to hematogenous dissemination. All patients except 4 were immunocompromised. No patient received trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis at diagnosis, probably because of the potential protective effect of the prophylaxis, but this information was only available for 7 cases.[3] Concerning the 4 cases involving immunocompetent patients, 2 occurred in elders (78 and 82 years old).[6,9] No data was available to describe local risk factors of joint infection except for the 2 patients with joint prosthesis.

Conversely, the 9 infections due to direct articular inoculation occurred in immunocompetent patients except in 1 case. Six cases (5 arthritis and 1 osteoarthritis) were the result of direct traumatism.[10–15] Besides, 1 was secondary to infiltration[16] and 2 occurred 2 and 5 months after arthroplasty.

In 4 cases, the mechanism of infection was unknown.[10,17–19]

Clinical Feature and Diagnosis

Among the 21 cases of hematogenous infections, the diagnosis was performed after a median of 15.5 (range, 2–90) days after the first symptoms. Knee localizations were the most common, in 83% of cases. Pulmonary localizations, described in 80% of cases, were asymptomatic in 4 cases (24%).[20–22] Others localizations of disseminated diseases are described in Table 1. Joint fluid Gram staining revealed the presence of Gram-positive filamentous bacteria in 57% of the cases (12 of 21).

In case of direct articular inoculation, there was no disseminated infection. Diagnosis was performed after a median of 24 (range, 8–90) days after the first symptoms. Intra-articular fluid direct examination revealed Gram-positive bacillus in 1 case.

Among the 34 cases, *Nocardia asteroides* was identified in 19 cases, mainly before 2000. These strains probably belong to others species, as molecular tools were not used in these cases.[1]

TREATMENT AND OUTCOME

Antibiotic Therapy

Different antibiotics used are listed in Table 2. Concerning hematogenous native arthritis, the median duration of antibiotic treatment was 24 weeks (range, 12–120) and 1 patient received suppressive antibiotic treatment.

For the 18 patients with no cerebral localizations, 9 (50%) received oral antibiotics (including TMP-SMX as a single-drug

TABLE 1. Characteristics and Clinical Features of 34 Patients With *Nocardia* Arthritis

Patients' Characteristics	Value n = 34 (31+3) (%)
Age at diagnosis, median year (range)	50 (4–82)
Sex (male/female)	24/10
Comorbidities	
Age ≥ 60 years	11 (32)
Kidney transplantation	4 (12)
Heart transplantation	1 (3)
Hematologic disease	4 (CML, CLL, 2 HSCT) (12)
Solid neoplasia (with cerebral localization)	2 (6)
HIV	1 (3)
Diabetes	3 (9)
Autoimmune disease (prolonged corticosteroids)	6 (18)
Absent	13 (38)
Temperature, median (range)	38 (37–39.5)
No fever	8 (24)
Nocardia spp.	
asteroides[*]	19 (56)
brasiliensis	3 (9)
nova	4 (12)
farcinica	3 (9)
beijingensis	1 (3)
elegans	1 (3)
cyriacigeorgica	2 (6)
caviae	1 (3)
Localization	
Native joint	21 knee, 4 hip, 1 ankle, 1 wrist, 1 shoulder, 3 elbow, 1 interphalangeal
Bone internal fixation	1 knee with screws
Prosthetic joint	2 hip, 2 knee prosthesis
Multiple articular localization	3
Mechanism	
Hematogenous	21 (70)
Direct inoculation (community/nosocomialy-acquired)	9 (6/3) (30)
Unknown	4
Coinfection	3 (2 *S. aureus*, 1 enterobacteria)
Other localizations	
Pulmonary	17 (50)
Cutaneous	4 (12)
Subcutaneous or muscle abscess	5 (15)
Cerebral	3 (9)
Renal abscess	1 (3)
Synovial fluid examination	
Leucocytes, median (range)	46,000 (5,700–415,000)
Positive direct examination (Gram staining), n	14 (42%)
Positive blood cultures	4 (12)
Time to diagnosis, median day (range)	20.5 (5–140)

CML = chronic myeloid leukemia; CLL = chronic lymphocytic leukemia; HIV = human immunodeficiency virus; HSCT = hematopoietic stem cell transplantation.

[*] Species assessment was probably inaccurate.

TABLE 2. Treatment and Outcome of 34 *Nocardia* Arthritis

Treatment and Outcome	Value n=34 (31+3) (%)
Treatment	
TMP-SMX	28 (82)
Amoxicillin	3 (9)
Amoxicillin-clavulanate	2 (6)
Ceftriaxone	5 (15)
Cefuroxime	1 (3)
Amikacin	6 (18)
Carbapenem (imipenem-meropenem)	6–3 (26)
Linezolid	3 (9)
Clarithromycin-azithromycin-erythromycin	2–1–1((12)
Ofloxacin-levofloxacin	1–1 (6)
Minocycline-doxycycline	6–3 (26)
Duration of treatment, median week (range)	20 (6–120)+2 maintenance antibiotics
Initial intravenous antibiotic treatment	
Yes	19 (66)
No	10 (34)
Unknown	5
Antibiotic combination $\geq$ 14 days	
Yes	20 (61)
No	13 (39)
Unknown	1
Exclusive 2-drug regimen	
Yes	11 (33)
No	22 (66)
Unknown	1
Treatment for native arthritis	n/29
Surgical treatment	12 (41)
Arthroscopy	3
Arthrotomy	6 (2 patients had 2 and 3 arthrotomy)
Arthroscopy before arthrotomy	2
Amputation	1
Medical treatment alone	15 (45)
Repeated needle aspiration	2 (7)
Treatment for bone internal fixation	n/1
Arthrotomy	1
Treatment for PJI, n (%)	n/4
Debridement	1
One-stage	1 (failure of previous debridement)
Two-stage	1
Resection arthroplasty	1
Evolution	
Favorable*	27 (84)
Favorable without sequelae	15
Favorable with sequelae	6
Amputation	1 (3)
Death due to nocardiosis (lung)	2 (6)
Death due to other cause	4 (2 acute and 2 late) (13)
Unknown	2

PJI = prosthetic joint infections.
* Lack of data on the presence of sequelae in 6 cases

in 7 cases) from day 1.[20,21,23–29] In case of intravenous (IV) treatment, the median duration of IV before oral treatment was 4 weeks (range, 1–24). Concerning patients treated exclusively with TMP-SMX, evolution was favorable in 5 cases, 1 patient died due to pulmonary nocardiosis[6] and evolution was not documented for another.[24]

For the 3 disseminated infections with cerebral localizations, 2 patients received IV antibiotic association for 7 and 96 weeks and 1 exclusive oral TMP-SMX during 12 weeks. Evolution was favorable in these 3 cases.[22,30,31]

The 2 prosthetic joint infections (PJI) were treated during 14 and 96 weeks with IV antibiotics association during 6 and 96 weeks, respectively.[31,32]

Concerning the 7 direct inoculation native arthritis, the median duration of antibiotic treatment was 12 weeks (range, 6–24). Oral single-drug regimen with TMP-SMX was introduced initially for 3 patients and for the other 4, the median maintenance of IV association treatment was 2 weeks (range, 1–3). Evolution was favorable in all cases except 1 acute death due to pneumonia without evidence of *Nocardia*.[16] Sequelae were reported in 1/7 case (not documented in 1 case). The 2 PJI were treated respectively with 30 weeks antibiotic association (IV during 6 weeks) and with suppressive oral association treatment.[33,34]

The oral antibiotics active against *Nocardia* spp. with good bone concentrations are TMP-SMX, linezolid, fluoroquinolones, tetracyclines, and macrolides. TMP-SMX is an agent of choice for 2 reasons: (i) recent susceptibility data from a large number of *Nocardia* strains suggest that overall resistance to TMP-SMX is rare (2–3%) (except among *N. pseudobrasiliensis* [31%] and *N. transvalensis* species [19%])[35–37] and (ii) it has proven to be effective for osteomyelitis.[38,39] Linezolid has been proposed recently because no resistant strain has been described so far[2,40] and this drug has excellent bone penetration.[41–43] Only 15 cases of nocardiosis treated with linezolid have been published, so far. Fourteen of 15 cases showed either an improvement or complete clearance of the infection.[41,44] In our study, only the first case received linezolid for 17 days. Neurological and hematological tolerance reduced its use for prolonged treatment. Fluoroquinolones, always in association, was used in only 2 cases probably because of a high frequency of resistance, with favorable outcome in 1 case.[33] Of the fluoroquinolones, intrinsic activity is slightly higher for moxifloxacin.[45,46] Tetracyclines were used in 9 cases (always in association except for 1 patient) with favorable outcome in 7 cases.[9,10,27,31,33,47] Macrolides were prescribed in association in 4 cases with favorable outcome in 3 cases.[13,32,34]

For hematogenous infections, experts recommend that antibiotic treatment should last at least 6 months for disseminated infections and 12 months in the case of CNS involvement.[2,3,46] The initial probabilistic association should combine 2 of these 3 drugs: TMP-SMX, β-lactam (cefotaxime/ceftriaxone or imipenem), and amikacin for at least 2 to 4 weeks and should probably be longer for CNS infections. Secondary, the choice of the antibiotic association depends on *in vitro* susceptibility, side effects, penetration in all infected sites and drugs interactions.

In the case of native arthritis due to direct inoculation, our review of the literature revealed a median treatment duration of 12 weeks (range, 6–24). These treatments are associated with high cure rate (86%) and were probably adequate. The 3 patients treated with exclusively TMP-SMX monotherapy cured.[11,19,21] Nevertheless, combination treatment for osteoarticular infections is frequently recommended to limit the development of

resistance. Initial 2-drug regimen can be proposed until clinical improvement.

For PJI, the duration of antibiotic association must probably be prolonged but we are unable to answer the question due to lack of data (only 4 patients).

Surgical Management

Concerning the 29 native arthritis, joint lavage was performed in 12 cases and amputation in 1 case.[22] Outcome was favorable in 81% of cases but functional outcome was mentioned only in 64% of cases. Favorable outcome was noticed in 75% and in 86% of the cases when surgery was performed or not, respectively. This difference could be explained by (i) the indication of surgery, proposed for the more severe arthritis or immunocompromised patients, (ii) publication bias, since authors mostly publish cases with favorable outcome, explaining the good results without surgery. Very likely, as *Nocardia* spp. is difficult to treat with a high risk of recurrence or chronic infection, arthritis must be managed with joint lavage.

All the 4 PJI were treated with surgery. Two were treated with debridement. One was performed 21 days after first symptoms but failed and 1-stage exchange was performed.[31] The second occurred 5 months after the insertion of a knee prosthesis and required suppressive antibiotic treatment.[32] The other treatment were 2-stage exchange and resection arthroplasty. Outcome was favorable in these 4 cases with functional sequelae in 2/4 cases. These few cases emphasize the importance of removing the prosthetic material. The infectious disease society of America (IDSA) recommends 2-stage exchange strategy for infections with difficult-to-treat organisms, such as *Nocardia*.[48] Consequently, this strategy is probably more indicated than 1-stage exchange, especially for immunocompromised patients, late infections, or in the case of TMP-SMX resistant *Nocardia* spp.

In conclusion, *Nocardia* spp. is a rare cause of septic arthritis. In disseminated nocardiosis, the infection usually stems from the lungs of an immunocompromised host, and arthritis is related to hematogenous seeding. In contrast, in immunocompetent patients, arthritis is localized and due to direct inoculation. For disseminated nocardiosis, antibiotic treatment must be prolonged (6–12 months) with bactericidal antibiotics reaching high concentrations in all infected sites. For infections due to direct inoculation, a shorter antibiotic course during 12 weeks is probably sufficient. Randomized trials are probably impossible to perform due to the rarity of the disease and further reports are warranted.

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REFERENCES

1. 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;19:259–282.
2. Ambrosioni J, Lew D, Garbino J. Nocardiosis: updated clinical review and experience at a tertiary center. *Infection.* 2010;38: 89–97.
3. Lebeaux D, Morelon E, Suarez F, et al. Nocardiosis in transplant recipients. *Eur J Clin Microbiol Infect Dis.* 2013;33:689–702.
4. Anderson M, Kuźniar TJ. Pulmonary nocardiosis in a patient with chronic obstructive pulmonary disease; case report and literature review. *Pol Pneumonol Allergol.* 2012;80:565–569.
5. Koll BS, Brown AE, Kiehn TE, et al. Disseminated Nocardia brasiliensis infection with septic arthritis. *Clin Infect Dis.* 1992;15:469–472.
6. Budzik JM, Hosseini M, Mackinnon AC, et al. Disseminated *Nocardia farcinica* literature review and fatal outcome in an immunocompetent patient. *Surg Infect.* 2012;13:163–170.
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. Mootsikapun P, Intarapoka B, Liawnoraset W. Nocardiosis in Srinagarind Hospital, Thailand: review of 70 cases from 1996–2001. *Int J Infect Dis.* 2005;9:154–158.
9. Shin S, Wilson MR. Nocardiosis in septic arthritis of the knee. *Orthopedics.* 2006;29:945–947.
10. Wilkerson RD, Taylor DC, Opal SM, et al. *Nocardia asteroides* sepsis of the knee. *Clin Orthop.* 1985;197:206–208.
11. Asmar BI, Bashour BN. Septic arthritis due to *Nocardia asteroides*. *South Med J.* 1991;84:933–934.
12. Freiberg AA, Herzenberg JE, Sangeorzan JA. Thorn synovitis of the knee joint with Nocardia pyarthrosis. *Clin Orthop.* 1993;287: 233–236.
13. Dinulos JG, Darmstadt GL, Wilson CB, Krengel WF 3rd, Burns JL. *Nocardia asteroides* septic arthritis in a healthy child. *Pediatr Infect Dis J.* 1999;18:308–310.
14. Uçkay I, Bouchuiguir-Wafa K, Ninet B, et al. Posttraumatic ankle arthritis due to a novel Nocardia species. *Infection.* 2010;38:407–412.
15. Kapur N, Adib N, Grimwood K. Nocardia brasiliensis infection mimicking juvenile idiopathic arthritis in a 4-year-old girl. *Pediatrics.* 2013;132:1424–1427.
16. Papanikolaou A, Kondyli L, Tserpe P, et al. *Nocardia asteroides* septic arthritis in a leukaemic patient: report of a case and review of the literature. *Eur J Orthop Surg Traumatol.* 2007;17:503–505.
17. Crouzet J, Juan LH, Poty F. *Nocardia asteroides*-induced septic arthritis. A case, review of the literature. *Rev Rhum Ed Fr.* 19931994;61:867–868.
18. Shah HR, Zamboni WA, Khiabani KT. Nocardial septic arthritis of the wrist diagnosed and treated by arthroscopy. *Scand J Plast Reconstr Surg Hand Surg.* 2005;39:252–254.
19. Masaki T, Ohkusu K, Ezaki T, et al. Nocardia elegans infection involving purulent arthritis in humans. *J Infect Chemother.* 2012;18:386–389.
20. Di Vittorio G, Carpenter JT, Bennett JC. Arthritis in systemic nocardiosis. *South Med J.* 1982;75:507–508.
21. Ostrum RF. Nocardia septic arthritis of the hip with associated avascular necrosis. A case report. *Clin Orthop.* 1993;288:282–286.
22. Baikie AG, Macdonald CB, Mundy GR. Systemic nocardiosis treated with trimethoprim and sulphamethoxazole. *Lancet.* 1970;2:261.
23. Rao KV, O'Brien TJ, Andersen RC. Septic arthritis due to *Nocardia asteroides* after successful kidney transplantation. *Arthritis Rheum.* 1981;24:99–101.
24. Boudoulas O, Camisa C. *Nocardia asteroides* infection with dissemination to skin and joints. *Arch Dermatol.* 1985;121:898–900.
25. Cons F, Trevino A, Lavalle C. Septic arthritis due to Nocardia brasiliensis. *J Rheumatol.* 1985;12:1019–1021.

26. Torre NP, Kim BK. Septic arthritis due to Nocardia caviae. *Ann Rheum Dis.* 1991;50:968–969.
27. Ray TD, Nimityongskul P, Ramsey KM. Disseminated *Nocardia asteroides* infection presenting as septic arthritis in a patient with AIDS. *Clin Infect Dis.* 1994;18:256–257.
28. Audenaert E, Almafragi A, Vuylsteke M, et al. *Nocardia farcinica* arthritis of the knee. A case report. *Acta Orthop Belg.* 2004;70:386–388.
29. Kahraman S, Genctoy G, Arici M, et al. Septic arthritis caused by *Nocardia asteroides* in a renal transplant recipient. *Transplant Proc.* 2004;36:1415–1418.
30. Velasco N, Farrington K, Greenwood R, et al. Atypical presentation of systemic nocardiosis and successful treatment with meropenem. *Nephrol Dial Transplant.* 1996;11:709–710.
31. Laurent F, Rodriguez-Villalobos H, Cornu O, et al. Nocardia prosthetic knee infection successfully treated by one-stage exchange: case report and review. *Acta Clin Belg.*
32. Arnal C, Man H, Delisle F, et al. Nocardia infection of a joint prosthesis complicating systemic lupus erythematosus. *Lupus.* 2000;9:304–306.
33. Robinson D, Halperin N. *Nocardia asteroides* infection of an Austin–Moore hemiarthroplasty in a nonimmunocompromised host. A case report. *Bull Hosp Jt Dis Orthop Inst.* 1989;49: 107–110.
34. 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.
35. Schlaberg R, Fisher MA, Hanson KE. Susceptibility profiles of Nocardia isolates based on current taxonomy. *Antimicrob Agents Chemother.* 2014;58:795–800.
36. Brown-Elliott BA, Biehle J, Conville PS, et al. Sulfonamide resistance in isolates of Nocardia spp. from a U.S. multicenter survey. *J Clin Microbiol.* 2012;50:670–672.
37. McTaggart LR, Doucet J, Witkowska M, et al. Antimicrobial susceptibility among clinical Nocardia species identified by multilocus sequence analysis. *Antimicrob Agents Chemother.* 2015;59:269–275.
38. Yeldandi V, Strodtman R, Lentino JR. In-vitro and in-vivo studies of trimethoprim-sulphamethoxazole against multiple resistant *Staphylococcus aureus*. *J Antimicrob Chemother.* 1988;22:873–880.
39. Stein A, Bataille JF, Drancourt M, et al. Ambulatory treatment of multidrug-resistant Staphylococcus-infected orthopedic implants with high-dose oral co-trimoxazole (trimethoprim-sulfamethoxazole). *Antimicrob Agents Chemother.* 1998;42:3086–3091.
40. Clark NM, Reid GE. Practice the AIDC of Nocardia infections in solid organ transplantation. *Am J Transplant.* 2013;13:83–92.
41. Moylett EH, Pacheco SE, Brown-Elliott BA, et al. Clinical experience with linezolid for the treatment of Nocardia infection. *Clin Infect Dis.* 2003;36:313–318.
42. Stein GE, Throckmorton JK, Scharmen AE, et al. Tissue penetration and antimicrobial activity of standard- and high-dose trimethoprim/sulfamethoxazole and linezolid in patients with diabetic foot infection. *J Antimicrob Chemother.* 2013;68:2852–2858.
43. Beer R, Engelhardt KW, Pfausler B, et al. Pharmacokinetics of intravenous linezolid in cerebrospinal fluid and plasma in neurointensive care patients with staphylococcal ventriculitis associated with external ventricular drains. *Antimicrob Agents Chemother.* 2007;51:379–382.
44. Tanioka K, Nagao M, Yamamoto M, et al. Disseminated *Nocardia farcinica* infection in a patient with myasthenia gravis successfully treated by linezolid: a case report and literature review. *J Infect Chemother.* 2012;18:390–394.
45. Larruskain J, Idigoras P, Marimón JM, et al. Susceptibility of 186 Nocardia sp. isolates to 20 antimicrobial agents. *Antimicrob Agents Chemother.* 2011;55:2995–2998.
46. Wilson JW. Nocardiosis: updates and clinical overview. *Mayo Clin Proc.* 2012;87:403–407.
47. Özgenç O, Avcı M, Arı A, Çelebi İY, Coşkuner SA. Long-term treatment of persistent disseminated Nocardia cyriacigeorgica infection. *Braz J Infect Dis.* 2014;18:556–560.
48. Osmon DR, Berbari EF, Berendt AR, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis.* 2013;56:1–25.