



Nocardia Farcinica infection of a reversed shoulder prosthesis : case report and review

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We present a case of *Nocardia farcinica* after placement of reverse shoulder prosthesis in a 73-year-old woman. One month after surgery, the patient was admitted to the hospital with a spontaneous drainage of the wound and complaints of aggravating pain in the operated shoulder. There was no history of an immunosuppressive disease or therapy. After cultivation and empiric therapy with flucloxacillin, *Nocardia farcinica* was found and treated with a combination of intravenous amikacin and ceftriaxone. Eight days after drainage, a rinse and replacement of the polyethylene cup and glenosphere was executed. The treatment was proven to be successful whereas X-ray scans showed no complications nor any other consequences up until five years after therapy. To our knowledge, this is the first shoulder prosthetic *Nocardia* infection published in English literature. The aim of this report is to review/gather the knowledge about this particular infection and inform health care providers about this uncommon case.

Keywords : shoulder prosthesis ; infection ; *Nocardia farcinica*.

rise in the use of the technique. The most common severe complications are instability and deep infection (4). A study by Zumstein et al. postulated that a postoperative infection is seen in 3,8% of all RTSAs (17) The most frequently implicated bacteria are *Propionibacterium acnes*, *Staphylococcus epidermidis* and *Staphylococcus aureus*.

An isolate of genus *Nocardia* was first obtained by veterinarian Edmond Nocard in 1888 from a case of bovine farcy (5). Two years later, Eppinger reported the first case of the aerobic pathogen in humans. Today, it forms a quite rare but alarming complication of total joint arthroplasty.

Literature shows only 6 other cases of joint prosthesis infections with *Nocardia* spp. which include only knee and hip prostheses (1,7-11). We report the first case in the literature of a patient who developed a periprosthetic joint infection (PJI) with *Nocardia Farcinica* after a reverse total shoulder arthroplasty.

INTRODUCTION

Reverse total shoulder arthroplasty (RTSA) is a technique that gained popularity after good initial results as treatment of osteoarthritis in elderly patients with a rotator cuff deficiency. Indications were broadly extended and there was an exponential

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CASE REPORT

An uncemented reverse shoulder prosthesis (delta-prosthesis, Dupuy) was implanted in a healthy immunocompetent 73-year-old female for painful osteoarthritis of the right shoulder. No complications were encountered during surgery and the initial postoperative follow-up was uneventful.

Medical history revealed nothing remarkable except bilateral knee replacement due to gonarthrosis dating back six years. The patient didn't suffer from any chronic disease, nor did she take immunosuppressants.

Twenty-five days after surgery, the wound turned red and, two days later, started to drain blurred yellow fluid. Samples were taken and blood tests performed. Laboratory parameters showed a C-reactive protein (CRP) of 63 mg/l, erythrocyte sedimentation rate (ESR) of 103 mm/h and leucocyte count (WBC) 10500/mm³. Body temperature was 37.5°C. The range of motion of the shoulder was limited and painful : active elevation reached 30° and passive elevation 80°. Radiologic examination of the right shoulder showed normal postoperative findings.

Since a bacterial prosthetic infection was suspected, the patient was admitted and intravenous antibiotics were started (flucloxacillin 500 mg, every 4 hours). The samples were evaluated for bacteriological and mycological infections. Gram staining showed filamentous and branching gram-positive bacilli, on cultures identified as *Nocardia* species. The sample was sent to AZ Groeninge (Kortrijk, Belgium) for 16S rRNA sequencing which revealed *Nocardia farcinica*. Biochemical tests confirmed this (urease +, α-mannidose -, α-glucosidase +, PYR +, γ-glutamyl-naphtylamide +). The antibiotic sensitivity test (Table I.) revealed sensitivity of the isolate to amikacin, meropenem, ceftriaxone and trimethoprim-sulfamethoxazole.

Following the sensitivity test, the antibiotic therapy was changed to amikacin 500 mg IV BID and ceftriaxone 1g BID.

A one-stage revision was performed after one week of antibiotic therapy. The original wound was opened, and an extensive debridement of hypertrophic tissue and irrigation with 10 liters

Table. I. — Antibiotic sensitivity test and MIC-testing (minimum inhibitory concentration)

ANTIBIOTIC SENSITIVITY TEST	
CEFTRIAZONE	S
MEROPENEM	S
AMIKACIN	S
BACTRIM (SULFAMETHOXAZOLE/ TRIMETHOPRIM)	S
MIC-TESTING	
CLARITHROMYCIN	8 MG/L
TOBRAMYCIN	16 MG/L
AMOXICILLIN	16 MG/L
PIPERACILLIN/TAZOBACTAM	>256 MG/L
AMOXICILLIN/CLAVULANIC ACID	1 MG/L
CIPROFLOXACIN	0,047 MG/L
CEFOTAXIM	>256 MG/L
AMIKACIN	1 MG/L
CEFTRIAZONE	4 MG/L

of saline water and rifocine was performed. The polyethylene cup as well as the glenosphere were replaced. A patch of Duracoll (bovine collagen with gentamycin) was put behind the new glenosphere.

Postoperatively, there was no problem of wound healing or excessive pain. Body temperature was normal immediately post-operative and the infectious parameters decreased progressively. After 6 weeks of intravenous antibiotics, CRP was 6 mg/l and the patient was discharged on oral antibiotics (trimethoprim-sulfamethoxazole 800/160 mg BID) for 3 months.

Lab results 4 ½ months after the revision surgery showed a normalization of inflammatory parameters (CRP 3 mg/l, ESR 26 mm/h and leucocyte count 4820/mm³). The shoulder was pain free with an active elevation of 110° and passive elevation of 150°.

Follow-up clinically and radiologically during the following 5 years showed no signs of relapse nor were there radiological signs of loosening (Fig. I). Six years postoperative, the patient died because of unrelated disease at the age of 79.

DISCUSSION

Nocardia species are a rare cause of disseminated and local infections. The various manifestations range

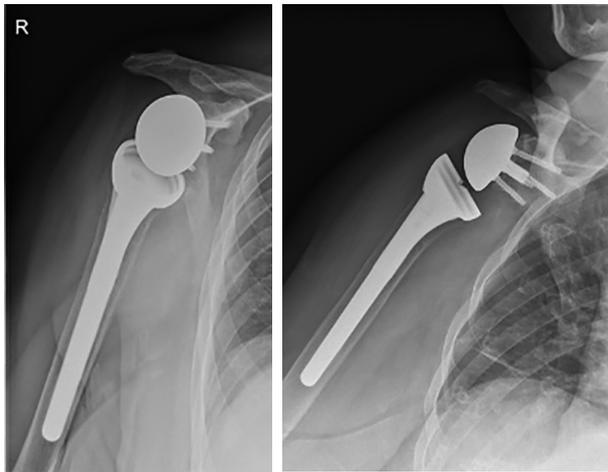


Fig. 1. — X-ray of the shoulder, 5 years after revision. No loosening of the prosthesis or osteolytic lesions visible.

from cutaneous infection to fulminant pneumonia or infection of the central nerve system. The soil-dwelling, aerobic gram-positive bacteria (order: *Actinomycetales*) is ubiquitous and causes infection in mostly immunocompromised patients (85%) (5). As the use of immunosuppressive agents in medicine is progressing, the incidence of infections caused by *Nocardia* spp. increases. However, 10-39% of the patients with nocardiosis are immunocompetent. The subtype *Nocardia farcinica* is infamous for its higher tendency to cause disseminated infections and have a higher mortality (overall : 31%) (13). In our patient, chest X-ray didn't show an infiltrate, nor were there any alarming clinical signs for a disseminated nocardiosis. However, in retrospect, we advise further screening after the cultivation of *Nocardia* species (especially when the patient is immunocompromised). Ozan et al. suggested CT thorax, ultrasonography of the abdomen, MRI of the brain in combination with hemocultures should be considered for detection of possible nocardiosis-related disseminated infection (10).

New molecular techniques have enabled researchers to identify more than 50 species that differ in phenotype, drug susceptibility patterns etc. (5). Of these species, more than 30 have been isolated in humans. Due to the fact that there are no pathognomonic features of a *Nocardia* infection, it is imperative that the laboratory keeps the possibility of the presence of this species in mind. Microscopic

and macroscopic inspection of the specimens are of paramount importance. Application of Gram stains and modified acid-fast (Kinyoun) stains are the first steps to providing a probable diagnosis. *Nocardiae* are microscopically characterized by their beaded, gram-positive, thin, branching, filamentous appearance and will be usually seen in the background of polymorphonuclear leukocytes. As cultures of *nocardiae* will take at least 48-70 hours before colonies are visible, these stainings can help steer the treatment of the patient pending the results of the cultures (3,6,12,14). Naturally, after the verification of the genus *Nocardia* microscopically, modern PCR techniques are able to rapidly differentiate *N. farcinica* from other *Nocardia* species by sequence determination of the 16S rRNA gene. This method allows a precise and easy identification of *Nocardia*. Since 16S rRNA sequencing isn't ubiquitous and the routine identification of *Nocardia* strains proves to be a challenge, Wauters et al. designed an algorithm for the biochemical identification of the six most relevant species of *Nocardia* (15). As such, *N. farcinica* dissociated itself from the other 5 species by a positive reaction with pyrrolidonyl aminopeptidase and gamma-glutamyl aminopeptidase which were added to the suspension respectively.

According to Wallace et al., isolates of *Nocardia farcinica* have a type V drug susceptibility pattern (14). The resistance and susceptibility pattern of 40 clinical isolates were elucidated and it was unraveled that the *N. farcinica* has a characteristic resistance to most beta-lactam antibiotics (cefotaxime (100%), ceftriaxone (80%), cefamandole (100%)) and aminoglycosides including genta-, kanamycin (both 100%) and tobramycin (90%), but is susceptible to amikacin. Furthermore, the isolates were susceptible to trimethoprim-sulfamethoxazole (100%), imipenem (82%) and ciprofloxacin (88%). Most clinicians recommend the administration of a three-drug regimen (TMP-SMX, amikacin and ceftriaxone/imipenem) for patients with CNS disease, serious disease or disseminated disease) as empirical therapy (5). Once susceptibility is known, an initial administration of a combination of drugs based on the susceptibility results is now preferred over TMP-SMX by the majority. In our case,

ceftriaxone and amikacin was dosed intravenously. Afterwards, we switched to TMP-SMX as simple oral maintenance antibiotic treatment with few side effects, considering the susceptibility pattern and universal recommendations.

There is no general consensus on the duration of the antibiotic treatment after surgery. The extent of antibiotic therapy in the other cases of periprosthetic joint infection (PJI) with *Nocardia* varied from 2 to 20 months (1,7-11). Overall, a treatment period of 1-3 months is thought to be sufficient for primary cutaneous infections. When the infection is pulmonary or systemic in immunosuppressed patients, this period should be extended up to 6-12 months (2). In case of CNS involvement, antibiotics can be administered for over 12 months (10,16).

An acute PJI presents itself within the first 3 months after the initial operation. In general, irrigation and debridement as well as replacement of all the parts that are easy to remove, is the attitude of choice. In this case, a one-stage exchange shoulder arthroplasty was performed. Even though no guidelines supporting any preference of technique in PJI with *Nocardia* spp. can be submitted due to the scarcity of the pathogen, our successful case and the report of Laurent et al. – who also published a successfully performed one-stage exchange in a N. Nova PJI of the knee – suggest this is a good approach on joint prosthesis infections with *Nocardia* spp. (9).

CONCLUSIONS

This first case of *Nocardia farcinica* PJI of the shoulder underlines the importance of the usage of Gram and fast-acid staining to rapidly detect the presence of nocardiae. Due to the variable resistance patterns to antibiotics, subtyping the pathogen is of pristine importance regarding the treatment of the patient. In future, we expect this kind of infection to be of increasing importance as both the use of shoulder prostheses and immunosuppressive agents is rising.

In this case, after an initial period of antibiotics, we successfully performed a one-stage exchange in an immunocompetent patient, followed by a three-month continuance of the antibiotics.

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REFERENCES

1. Arnal C, Man H, Delisle F, M'Bappe P, Cocheton J-J. *Nocardia* infection of a joint prosthesis complicating systemic lupus erythematosus. *Lupus*. 2000 ; 9 : 304-6.
2. Audenaert E, Almafragi A, Vuylsteke M, Verdonck C, Verdonk R. *Nocardia farcinica* arthritis of the knee. A case report. *Acta Orthop Belg*. 2004 ; 70 : 386-8.
3. Berd D. Laboratory Identification of Clinically Important Aerobic Actinomycetes. *Appl Microbiol*. 1973 4 ; 25 : 665-81.
4. Boileau P. Complications and revision of reverse total shoulder arthroplasty. *Orthop Traumatol Surg Res*. 2016 ; 1 : 102 : S33-43.
5. Brown-Elliott BA, Brown JM, Conville PS, Wallace RJ. Clinical and Laboratory Features of the *Nocardia* spp. Based on Current Molecular Taxonomy. *Clin Microbiol Rev*. 2006 4 ; 19 : 259-82.
6. Conville PS, Witebsky FG. *Nocardia*, *Rhodococcus*, *Gordonia*, *Actinomadura*, *Streptomyces*, and Other Aerobic Actinomycetes. 2011 ; 1 : 443-71.
7. Hadeed MM, Macdonell JR, Dempsey IJ, Moore CC, Browne JA. Chronic : A Case Report Periprosthetic Knee Infection Successfully Treated with a Two-stage Revision : A Case Report. *Jbjs Case Connect* [Internet]. 2017 [cited 2018 Jan 13] ; 7. Available from : <https://insights.ovid.com/pubmed?pmid=29286958>
8. I Nizam, L Kohan, D Kerr. *Nocardia* Nova Septic Arthritis following Total Knee Replacement : A Case Report. *J Orthop Surg*. 2007 ; 15 : 390-2.
9. Laurent F, Rodriguez-Villalobos H, Cornu O, Vandercam B, Yombi JC. *Nocardia* prosthetic knee infection successfully treated by one-stage exchange : case report and review. *Acta Clin Belg*. 2015 ; 70 : 287-90.
10. Ozan F. The *Nocardia farcinica* infection developing after total knee arthroplasty surgery. *Acta Orthop Traumatol Turc*. 2013 ; 47 : 212-7.
11. 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 : 107-10.
12. Saubolle MA, Sussland D. Nocardiosis Review of Clinical and Laboratory Experience. *J Clin Microbiol*. 2003 ; 41 : 4497-501.
13. Torres OH, Domingo P, Pericas R, Boiron P, Montiel JA, Vázquez G. Infection Caused by *Nocardia farcinica* : Case Report and Review. *Eur J Clin Microbiol Infect Dis*. 2000 ; 19 : 205-12.

14. **Wallace RJ, Brown BA, Tsukamura M, Brown JM, Onyi GO.** Clinical and laboratory features of *Nocardia nova*. *J Clin Microbiol.* 1991 ; 29 : 2407-11.
15. **Wauters G, Avesani V, Charlier J, Janssens M, Vanechoutte M, Delmée M.** Distribution of *Nocardia* Species in Clinical Samples and Their Routine Rapid Identification in the Laboratory. *J Clin Microbiol.* 2005 ; 43 : 2624-8.
16. **Yildiz O, Alp E, Tokgoz B, Tucer B, Aygen B, Sumerkan B, et al.** Nocardiosis in a teaching hospital in the Central Anatolia region of Turkey : treatment and outcome. *Clin Microbiol Infect.* 2005 ; 11 : 495-9.
17. **Zumstein MA, Pinedo M, Old J, Boileau P.** Problems, complications, reoperations, and revisions in reverse total shoulder arthroplasty : A systematic review. *J Shoulder Elbow Surg.* 2011 ; 20 : 146-57.