



Case report

Case of multi-drug resistant *Nocardia nova* as the causative agent of cervical spine osteomyelitis in an immunocompetent adult

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ABSTRACT

We report a case of a 54-year-old immunocompetent female with cervical spine discitis and osteomyelitis secondary to *Nocardia nova*. *Nocardia nova* is overall an exceedingly rare cause of infectious diseases. In this case, the patient was admitted for neck and right shoulder pain. One year prior, she had lumbar osteomyelitis (L4-L5) that required laminectomy. Cultures at that time grew *Staphylococcus schleiferi* and she was treated with cefazolin for six weeks. Six months later she presented with cervical spine (C4-C5) discitis/osteomyelitis. She underwent surgical laminectomy, biopsy and culture, which grew *Nocardia nova*. The patient was treated with intravenous amikacin and then transitioned to trimethoprim-sulfamethoxazole for a total of twelve months. Other case reports of spinal osteomyelitis secondary to nocardia describe treatment with antibiotics, surgical debridement plus or minus arthrodesis with favorable outcome in improving pain and functionality at 3 years.¹ In our case, the patient completed the course of antibiotics and 6 months later, imaging of the cervical spine showed mild height loss at C4 and C5, however no significant acute changes in the cervical spine, epidural or prevertebral soft tissue collections. She continues with chronic neck pain but repeated MRI of the cervical spine at 2 years shows no evidence of osteomyelitis or soft tissue edema.

Introduction

Nocardia is overall a rare cause of infectious diseases. It is a branching filamentous bacterium that is also uniquely acid-fast, urease-producing, and gram positive [1,2]. *Nocardia* is an obligate aerobe that has been implicated in pulmonary, skin, and soft tissue infections [2]. It is found naturally in soil and as such, inhalation of soil debris has been the primary means by which people acquire pulmonary nocardiosis [1]. Pulmonary nocardiosis can cause pneumonia typically in patients who are immunocompromised. Radiographic findings of pulmonary nocardiosis are not unique to the bacteria and include nodules, infiltrates, masses, pleural effusions, and lobar consolidation. Common skin and soft tissue infections caused by nocardia include cellulitis, ulcerations, nodules, and abscesses in immunocompetent hosts. Infrequently, nocardia has been implicated as the cause of brain abscesses and bacteremia [1,2]. In rare cases, nocardia can cause osteomyelitis [1,2].

Case report

We present a rare case of cervical spine osteomyelitis secondary to

multi-drug resistant *Nocardia nova* in an immunocompetent individual. The patient is a 54-year-old female with a past medical history of untreated rheumatoid arthritis, who had a remote history of *Serratia marcescens* osteomyelitis of the right wrist. She was admitted with the chief complaint of posterior neck pain. Six months prior, the patient was treated for *Staphylococcus schleiferi* lumbar (L) spine osteomyelitis. During that admission, a magnetic resonance imaging (MRI) of the lumbar spine showed collapsing L4-L5 disc space with concern for an epidural phlegmon or an abscess. Blood cultures at the time were negative and a laminectomy was done with intraoperative cultures proving to also be negative. Further workup revealed a normal erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Urine drug screen was negative. Infectious workup including a quantiferon gold analysis, human immunodeficiency virus (HIV) screen, aerobic/anaerobic culture, acid-fast bacilli (AFB) culture and fungal smear were negative. After a benign hospital course with normal white count, negative cultures, no fever, and normal CRP/ESR, it was thought that the cause of the collapsing lumbar disc was non-infectious and the patient was discharged without antibiotics.

The patient was then readmitted three weeks later for swelling at her

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wound site of the previous laminectomy. Intraoperative washout of the wound revealed superficial purulence but no obvious abscess. Complete blood count analysis showed a mildly elevated white blood cell (WBC) count at 10.9 (3.7–10.1 K/mm³) with 77.5% neutrophils. The patient was afebrile, however the wound cultures from the washout grew *Staphylococcus schleiferi*. The patient was discharged on cefazolin 2-grams intravenously every eight hours for six weeks.

The current admission started six months after prior treatment for *Staphylococcus schleiferi* osteomyelitis. At this time she presented with cervical spine pain and right arm weakness. During this admission, the patient endorsed compliance with previous antibiotic regimens and denied any illicit intravenous drug use or injections into the posterior neck space. Workup revealed normal white count, however ESR was elevated at 35 mm/hr (0–15 mm/Hour) and CRP on admission was 0.83 mg/L (0–0.99 mg/L). Infectious workup revealed a non-reactive rapid plasma reagin (RPR), negative *Bartonella henselae* IgG/IgM, *Bartonella quintana* IgG/IgM, interferon-gamma release assay, and (1–3)- β -D-glucan. Hepatitis B and C serologies were negative as well as repeat HIV. Blood cultures were negative. Urine histoplasma antigen was also negative. An MRI of the cervical spine showed C4/C5 discitis/osteomyelitis at the level of C4/C5 as shown in Fig. 1. A Computer Tomography (CT) and MRI of the Brain was also normal.

Once imaging showed evidence of disc collapse and suspicion for osteomyelitis, the patient was taken to the operating room for C4/C5 discectomy, washout and bone culture. Intraoperative cultures grew *Nocardia nova*. Pathology was negative for any malignancy but did show subacute osteomyelitis. The patient was started on amikacin 15 mg/kg IV daily for four weeks and then initially transitioned to trimethoprim-sulfamethoxazole for six months of treatment based on sensitivities as seen in Table 1. Repeat MRI of the cervical spine six months into treatment showed increased height loss of C4/C5 and left C6/C7 facet enhancement with new soft tissue edema. The patient clinically felt well. Antibiotic therapy with trimethoprim-sulfamethoxazole was continued for an additional six months to complete a total of 12 months of therapy. Nuclear medicine tagged white blood cell scan at 12 months did not show any areas of increased activity. At her follow-up visit one and two years after completing antibiotic therapy, our patient continues to do well. She has had mild chronic pain in her cervical spine. Repeat MRI of the cervical spine at 2 years does not show any evidence of active infection. (Fig. 2).

Discussion

Nocardia species have been implicated in causing a variety of disease presentations. A naturally occurring bacteria in soil, it is commonly



Fig. 1. Multiplanar multi-sequence magnetic resonance imaging (MRI) of the cervical spine with evidence of discitis/osteomyelitis at the level of C4-C5 (yellow arrow). Paravertebral and epidural enhancement from C2-C7.

Table 1
Nocardia Nova sensitivity panel.

	Sensitivity	MIC (mcg/ML)
Amikacin	S	<=1.0
Ciprofloxacin	R	>4.0
Clarithromycin	S	0.06
Imipenem	S	<=2.0
Linezolid	S	<=1.0
Minocycline	I	2
Tobramycin	R	16
Trimethoprim/sulfa	S	0.25/4.8

S=Sensitive, R= Resistant, I= Intermediate

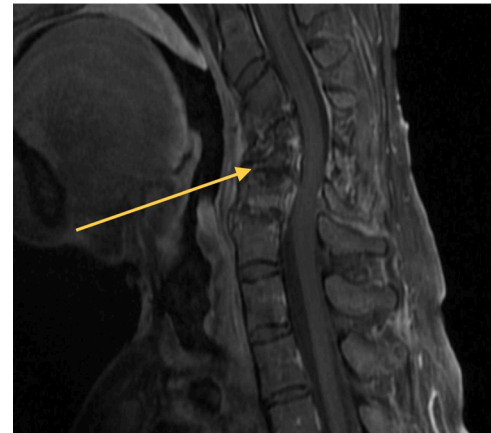


Fig. 2. : Multiplanar MRI of the cervical spine 6 months post treatment showing loss of C4/C5 and facet enhancement of C6/C7 with soft tissue swelling. No significant epidural or prevertebral soft tissue collections noted.

implicated in pulmonary infection as a result of direct inhalation of soil particles [4,5]. *Nocardia* can also spread by hematogenous route to any organ system and cases have been reported of hematogenous spread to the brain, skin, muscle, bones and lymphatics [5]. Clinically significant species included in this genus are *N. farcinica*, *N. nova*, *N. brasiliensis*, *N. asteroides* and *N. otitidiscaviarum*. The most virulent and problematic strain of the nocardia species is *N. asteroides*.⁶ Although disseminated nocardiosis infections have been reported in immunocompetent individuals, immunocompromised hosts are particularly susceptible. The pathogenesis of *N. asteroides* that makes it particularly virulent is not fully understood but a variety of mechanisms have been proposed. Studies on experimental animals revealed *N. asteroides* was able to evade host detection by inhibiting phagosome-lysosome fusion, modifying lysosomal enzymes and neutralizing the acidic environment within phagosomes [6].

Nocardia nova, although not the most virulent of the species, still poses a significant clinical threat especially if not properly identified early in the disease presentation. Given the fact that the *Nocardia spp* causes a wide spectrum of clinical diseases, diagnosis based on radiographic studies or signs and symptoms is very difficult. A sample must be obtained from the suspicious tissue and it must either be cultured on routine microbiological media, acid fast and also gram stained to improve diagnostic yield [7]. On routine and selective media such as chocolate agar, buffered charcoal-yeast extract, Thayer-Martin, or 5% sheep blood agar; *Nocardia* grows within two to seven days [7]. It is recommended that cultures be examined for up to three weeks as there are very slow growing strains of nocardia [7]. Once an identification has been made, the next step involves speciation and susceptibility studies [4,5]. This is the most clinically relevant study as it helps guide antimicrobial choice and stewardship. The first line antibiotic in treating Nocardiosis is a sulfur containing antibiotic [5–7]. The drug of choice is trimethoprim-sulfamethoxazole, although alternative antimicrobial

agents include intravenous beta-lactams such as cefotaxime and ceftriaxone. Other antimicrobial agents include minocycline, levofloxacin, linezolid, and amoxicillin-clavulanic acid [1]. The parenteral antibiotics that have shown to be most active against nocardia species are amikacin and imipenem, with amikacin showing in vitro activity against 90%–95% of all tested strains [3,8]. The duration of therapy is unknown, although there is an increased frequency of relapse and resistance in patients with shorter antibiotic courses [7]. The duration of therapy can be further guided by the location of invasion—skin, bone, brain or lungs. For example, cutaneous nocardiosis warrants a shorter course of antibiotics in comparison to nocardia osteomyelitis. Because of the involvement of the spine in this case, treatment courses run 6–12 months [7]. As such, management decisions must take into account valid concerns about drug toxicity. Monotherapy or combination therapy decisions should take into account the patient's response to treatment at subsequent assessments.

Conclusion

Osteomyelitis due to nocardia invasion is exceedingly rare such that there are limited cases that have been published in a 40 year span [4]. This is the first case of cervical spine discitis and osteomyelitis in an ostensibly immunocompetent adult. Symptoms at presentation are non-specific. In order to improve patient outcome and treatment with the appropriate antibiotics, there must be definitive isolation and identification of the species [4,5]. This poses a clinical challenge as isolation of species requires invasive methods in most cases and diagnosis cannot be made radiographically or by clinical symptoms alone [5]. In our case, the patient underwent a discectomy with intraoperative biopsies which helped guide medical management. The patient completed a total course of twelve months of antibiotics and reported improved quality of life two years post treatment. This case highlights an unusual organism that is typically difficult to diagnose, but is significant due to the unique treatment and duration of treatment.

CRedit authorship contribution statement

L. Check is the article guarantor.

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Author Statement

I have no conflict of interest to report.

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