Case Report
Second report of a *Nocardia beijingensis* infection in the United States: nodular scleritis with in vitro imipenem resistance

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Summary

We describe the case of a 52-year-old woman with scleritis caused by an imipenem-resistant strain of *Nocardia beijingensis*. The patient presented with pain, redness, and nodules on the sclera of 8 weeks’ duration. A Gram stain from a nodule on the superonasal aspect of the globe was initially negative. After empiric treatment for an autoimmune etiology, cytopathology confirmed filamentous bacteria. A presumptive diagnosis of *Nocardia* scleritis was made, and medical management was based on a literature review on treatments for *Nocardia* infections. Cultures returned confirming *Nocardia beijingensis*. Antibiotic sensitivity testing confirmed the correct initial management. The patient’s scleritis resolved with a good visual outcome.

Introduction

*Nocardia* is a genus that encompasses Gram-positive, aerobic, rod-shaped bacteria. Today, more than 30 *Nocardia* species have been shown to cause disease in humans, the most common being *N. asteroides*.1 *Nocardia* species have been implicated in a number of cases of infectious scleritis, although this occurs far less frequently than other, more common bacteria. *N. beijingensis* was discovered in 2001 and has only been previously isolated in Asia and Europe.2 *N. beijingensis* is also characteristically sensitive to imipenem. We present a case of infectious scleritis caused by a strain of imipenem-resistant *Nocardia beijingensis*. This is only the second reported infection caused by *N. beijingensis* in the United States.3

Case Report

A 52-year-old African American woman presented at the University of Florida with an 8-week history of pain, redness, and photophobia of the right eye. She had been diagnosed with a nodular, necrotizing scleritis of her right eye and had been placed on oral prednisone 40 mg daily by an ophthalmologist 4 weeks prior to presentation, with minimal improvement in symptoms. On further questioning, past medical history, family history, and review of systems was only remarkable for contact lens use. Her occupation involved substance abuse counseling, which included a high percentage of HIV-positive patients. Her vision on presentation was 20/100 in the right eye and 20/20 in the left eye. Visual inspection showed elevated, yellow-colored, subconjunctival nodules on the superonasal aspect of the sclera (Figure 1). There was no intraocular involvement. A culture and biopsy of a nodule done one week prior to presentation yielded no growth. Due to suspicion of an infectious process, another scleral biopsy and culture was performed in the operating room and yielded nonspecific inflammatory changes without isolation of organisms (Figure 2). Serology showed a positive antinuclear antibody titer (1:80). The patient was empirically treated for an autoimmune anterior nodular scleritis with a higher dose of oral prednisone (80 mg daily), topical moxiflox-
acin 0.5% twice daily, difluprednate ophthalmic drops 0.05% 4 times daily, and cyclopentolate 1% twice daily. Three weeks after presentation, culture was repeated because of nonresponse to therapy, showing filamentous bacteria on silver stain GMS. A presumptive diagnosis of *Nocardia* infectious scleritis was made, and antimicrobial therapy was initiated with trimethoprim-sulfamethoxazole 800–160 mg twice daily, amikacin 5% drops hourly, and polymyxin b/trimethoprim drops hourly.

Culture and sensitivity testing identified *Nocardia beijingensis* species sensitive to amikacin, ceftriaxone, tigecycline, trimethoprim-sulfamethoxazole, amoxicillin/clavulanate, and linezolid. The organism demonstrated intermediate sensitivity to ampicillin, clarithromycin, and minocycline but was resistant to imipenem, cipro-

flaxin, and vancomycin. The initial antibiotic regimen of Bactrim was continued unchanged.

The patient’s symptoms significantly improved within 4 months of starting antibiotic treatment with some residual visual blurring, tearing, and moderate ptosis of the right upper eyelid. After 10 months, examination showed residual anterior corneal scarring and scleral thinning at the superonasal aspect of the right eye (Figure 3). At the most recent follow-up, 3 years after initial presentation, the patient’s best-corrected visual acuity was 20/30 in the right eye. A mild cataract was noted.

### Discussion

*Nocardia beijingensis* was first isolated in 2001 by Wang et al in Beijing. It is believed to be genetically similar to *N. brasiliensis* and *N. farcinica*, sharing 16S rDNA similarity of 97% ± 6% and 97% ± 5%, respectively. A majority of *Nocardia beijingensis* infections have occurred in Asia, mainly in China, Thailand, Japan, India, and Taiwan. Isolated cases have been reported in Europe and Australia. Crozier et al wrote about the first reported infection in the United States. Historically, *N. beijingensis* is highly sensitive to treatment with imipenem, tobramycin, and kanamycin. To our knowledge, ours is the first reported case of an infectious scleritis due to *N. beijingensis* and the second human infection of *N. beijingensis* in the United States, also in an immunocompetent patient. Moreover, antibiotic susceptibility testing of this strain revealed resistance to imipenem. The patient denied travel to areas...
where *N. beijingensis* is endemic and denied contact with any individuals who had done so. The resistance to imipenem is the first report of a strain of *N. beijingensis* that does not reflect the expected drug susceptibility patterns.

Scleritis due to infectious causes is rare. In the majority of cases, scleritis is due to an autoimmune etiology. Since infectious causes are not usually suspected, the correct diagnosis is often delayed. Additionally, microbiology testing often yields negative cultures. *Pseudomonas aeruginosa* is the most commonly reported causative organism of infectious scleritis. In this case, 2 cultures were negative before the third showed the organism. Hodson et al demonstrated that scleritis due to fastidious organisms such as *Nocardia* often displays a longer time interval between symptoms and diagnosis when compared to scleritis due to other non-acid-fast Gram-positive and Gram-negative bacteria (median, 18 days and 12 days, resp.). This delay in diagnosis does not appear to ultimately affect visual acuity or the need for removal of the eye. A majority of patients with *Nocardia* scleritis present with nonspecific signs, such as pain, conjunctival injection, scleral abscess, or scleral nodule.

A high index of suspicion for *Nocardia* infection should be maintained when a patient presents with a history of ocular trauma, associated history of farm work, or a unilateral lesion. In our case, the patient’s primary risk factor included contact-lens wear. Working with HIV-positive patients may have exposed her to organisms such as *Nocardia*, which tend to affect the immunocompromised. Das et al reported a case of *Nocardia* scleritis in a patient presenting with pain and injection of the left eye with a history of a mud splash to the face 1 week prior to symptom onset. This patient was treated at the time of presentation with high-dose systemic corticosteroids, which resulted in worsening of the underlying infection. Corticosteroids are known to worsen *Nocardia* infection mainly by inhibiting the release of host lysosomal enzymes essential to destruction of the phagocytosed intracellular *Nocardia* organisms.

The treatment of *Nocardia* scleritis is complicated by the fact that the sclera is a relatively avascular structure; thus, there is reduced bioavailability of systemic antibiotics. Our patient was treated for more than 10 months. The literature confirms that surgical debridement is an essential component of treatment. Surgical intervention is employed in the majority of cases that result in complete cure. Jain et al maintain that surgical debridement is important in facilitating the penetration of antibiotics and in debulking infected tissue. Despite limited data, we believe that there could be a role for subconjunctival and sub-Tenon’s antibiotics, even though we did not use them. There are reports in the literature on the treatment of infectious scleritis and sclerokeratitis that have combined topical, oral, and subconjunctival antibiotics. Had improvement not been rapid enough with topical and oral therapy, we would have considered this option.

The prognosis of *Nocardia* scleritis is guarded. Final visual acuity in previous reports ranges from 20/20 to 20/400. In cases of infectious scleritis, poorer outcomes are associated with presenting visual acuity worse than 20/200 and concomitant keratitis or endophthalmitis.

Our case of *Nocardia* scleritis is unique in that it features *Nocardia beijingensis* as the causative organism, which further underscores the importance of maintaining a high index of suspicion for rare infectious agents even in the face of negative initial cultures. We emphasize the role of serial cultures, particularly when an atypical causative organism is suspected, or symptoms are worsening with empiric treatment. Antibiotic resistance testing is crucial in such cases, because the sensitivities of these organisms, while previously predictable, has shown some variability.

### Literature Search

A detailed literature search in MEDLINE through Ovid (1978-present) as well as LILACS (1993-present), and IMEMR (1984-present) revealed any publications with cases of in vitro resistance of *Nocardia beijingensis* to imipenem, any cases of infectious scleritis due to *N. beijingensis*, and only 1 other case of an infection in the United States caused by an *N. beijingensis* strain. Search terms included *nocardia beijingensis* and imipenem.

### References

5. Poonwan N, Mekha N, Yazawa K, Thunyaphan S, Yamanaka A, Mikami Y. Characterization of clinical isolates of pathogenic *Nocar-


