

Case report

Nocardia Arthritis Keratitis: Case Report and Review of the Literature

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Abstract

Introduction: Keratitis due to Nocardia infection is not commonly encountered in clinical practice and may therefore be mistaken for fungal or viral keratitis leading to delayed treatment and increased risk of permanent visual impairment. **Case:** An otherwise healthy 27 years old Caucasian Active Duty military member presented to the clinic with three days of light sensitivity and irritation of his right eye. He carried a history of PRK in both eyes six years prior and admitted to recent contact lens overuse. With empiric treatment for typical bacterial keratitis including corticosteroids, his condition worsened on close follow-up. While awaiting cultures, a shift to fortified topical antibiotics tobramycin, moxifloxacin and ciprofloxacin showed improvement with closure of the epithelial defect. Ulcerative relapse occurred with withdrawal of therapy. Culture proven Nocardia arthritis prompted successful treatment with topical antibiotic amikacin. On follow-up at three months, the patient was doing well with a small peripheral anterior stromal scar without permanent visual sequelae. Visual acuity returned to baseline of 20/20 in the affected eye. **Conclusion:** Keratitis caused by Nocardia species, including arthritis, responds well to amikacin. Late diagnosis and early treatment withdrawal may lead to a prolonged recovery. Current literature indicates that corticosteroids may be harmful in the treatment of Nocardia keratitis. Increased awareness of Nocardia as an ocular pathogen has the potential to reduce unnecessary morbidity related to delayed diagnosis, inadequate therapy and inappropriate use of corticosteroids.

Keywords: Nocardia arthritis, keratitis, contact lens

Introduction

Though Nocardia species can be found as saprophytes in soil, dust and water worldwide, keratitis caused by it in general is rare in clinical practice and therefore presents a challenging diagnosis and requires atypical therapy when encountered. When promptly identified and

treated with topical antibiotic amikacin, visual outcomes are good (Sridhar, et al., 2001) (Lalitha, 2009).

Since its description in 2004 (Kageyama, et al., 2004), Nocardia arthritis (NA) has been described along with other Nocardia species as a cause of keratitis in South Asia (Yin, et al., 2007). We have been unable to find case reports of keratitis due to this species from the US or Europe in the medical literature.

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Case

A 27 year old Caucasian male, active duty military member, presented to an eye clinic in the Northeastern United States in April 2015 with three days of right eye foreign body sensation and photophobia. He was otherwise healthy with no systemic or ocular disease. He provided an ocular history of bilateral PRK six years prior, with subsequent best-corrected visual acuity (BCVA) of 20/20 in each eye. He reported a 1-2 week period of constant day and night contact lens wear ending one day prior to presentation, when foreign body sensation became painful. Exam revealed a normal left eye with 20/20 BCVA. The right eye presented with 20/60 BCVA, improving with pinhole to 20/30, hyperemic conjunctiva, 1+ anterior chamber (AC) cells, corneal infiltrates and corneal ulceration. Empiric triple therapy for typical bacterial keratitis was initiated with moxifloxacin, polymyxin B sulfate/trimethoprim and erythromycin. Follow-up on day two and four revealed stable pain and photophobia with evidence of gradual epithelial closure. On day six of treatment, the patient noted continued pain and photophobia in the setting of near complete epithelial closure and 0.5+ AC cells on exam. At this time, topical prednisolone acetate 1%, four times a day, was added in an attempt to reduce inflammation and reduce scar formation.

On day 11 the patient presented with increasing pain and photophobia. Exam revealed quiet anterior chambers bilaterally, with enlargement of the ulcer. The epithelial defect measured 1.4x1.9mm. It was recognized that this was not a typical bacterial keratitis. Corticosteroid treatment was promptly discontinued after five days of use, and corneal scrapings were sent for Gram stain and culture. Initial gram stain was reported as Gram positive cocci in singles and pairs. While cultures on both chocolate and sheep blood agar were pending, empiric treatment with topical antibiotics moxifloxacin,

polymyxin B sulfate/trimethoprim and erythromycin was continued. Of note, empiric antibiotics were not held prior to obtaining this culture because it was felt that any delay in treatment was a potential additional risk in the setting of this aggressive ulcer. Four days of culture growth resulted in small, white, chalky colonies on sheep blood (Figure 1) and chocolate agar plates. Staining of cultured colonies was reported as acid fast bacilli, with lab send out required for further identification. By this time the ulcer had reached 2.1x2.0mm and showed fluffy with feathery margins and anterior stromal infiltrate. Mycobacterium was suspected and a regimen of fortified tobramycin, moxifloxacin and ciprofloxacin was substituted. On day 20 the epithelium was closed and antimicrobial therapy was discontinued. An underlying stromal opacity measuring 2.0x1.7mm remained.

Five days later his course continued with renewed pain, photophobia and a new 0.2x0.3mm epithelial defect with associated patchy and pin-head infiltration of the anterior stroma (Figure 2). Tobramycin, moxifloxacin and ciprofloxacin were restarted pending definitive identification of the pathogen. On day 27 of care, DNA sequencing revealed that the pathogen was *Nocardia arthritidis* (NA) and therapy was switched to topical amikacin 5%, polymyxin B sulfate/trimethoprim, ciprofloxacin and oral clarithromycin. Follow-up on day 33 revealed no pain, no photophobia and complete closure of epithelial defect with BCVA in the diseased eye of 20/20 -1, requiring a new, moderate astigmatic refraction. Several days later final susceptibility results were reported (Table 1) and the treatment regimen was reduced to only amikacin 5% and prednisolone acetate 1%. This dual regimen was maintained for the following two months. Three months following his initial presentation the patient felt well with visual acuity back to baseline BCVA of 20/20 bilaterally. The

ulcer heal ed well, but left behind a peripheral anterior stromal scar.

Table 1: Final sensitivities of isolated *Nocardia arthritidis*. *Note: Three separate cultures were obtained. The first two (obtained in presence of empiric antibiotics) resulted in the same *Nocardia* isolate and with identical sensitivities while a third culture obtained in presence of amikacin had no growth.

Isolated <i>Nocardia arthritidis</i> Sensitivities*		
Antibiotic	MIC	Result
Amikacin	1.0 ug/mL or less	Susceptible
Amoxicillin/CA	2/1 ug/mL	Susceptible
Ceftriaxone	4.0 ug/mL	Susceptible
Ciprofloxacin	4.0 ug/mL	Resistant
Clarithromycin	>16.0 ug/mL	Resistant
Imipenem	16.0 ug/mL	Resistant
Linezolid	1.0 ug/mL or less	Susceptible
Minocycline	1.0 ug/mL or less	Susceptible
Tobramycin	2.0 ug/mL	Susceptible
Trimethoprim/Sulfa	0.25/4.8 ug/mL	Susceptible



Figure 1: Multiple small, chalky, white colonies on sheep blood agar after four days.

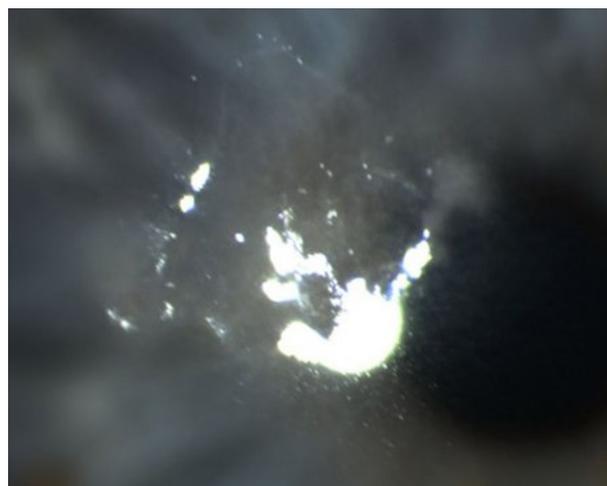


Figure 2: Re-ulceration after withdrawal of therapy. Note patch of infiltrate at right ulcer margin as well as numerous pin-point infiltrates.

Discussion

The genus *Nocardia* was first described in the late 1880's, with the first reports of *Nocardia keratitis* beginning as early as 1944 (Benedict & Iverson, 1944). Like other *Nocardia* species, NA is an aerobic, gram-positive, acid fast, nonmotile actinomycete. Since its identification in 2004 (Kageyama, et al., 2004), NA has been mentioned as an ocular pathogen in only one ophthalmologic publication (Yin, et al., 2007). Of the 11 ocular isolates reported in that article, three were found to be NA, leading the authors to conclude that it is second only to *N. asteroides* in importance as an etiology of ocular *Nocardiosis*. To our knowledge this is the first full case report of *Nocardia arthritidis keratitis*.

Nocardia species keratitis is known to present a challenging diagnosis, particularly in regions where clinicians are not familiar with the typical appearance on exam: patchy, white, and pin-head infiltrates in the anterior stroma, often arranging in a wreath pattern (Sridhar, et al., 1998), (Vemuganti, et al., 2011). This case of NA keratitis displayed similar anterior stromal infiltration with predominance of pin-

head infiltrates, both early in its course and at re-ulceration (Figure 2). Though Nocardia keratitis has been generally associated with longer duration of symptoms prior to presentation (Mascarenhas, et al., 2012), time to initial presentation in this case was less than 72 hours, and ulceration was already present. This rapid presentation and ulceration is not characteristic of Nocardia species keratitis in general. We postulate that this ulcer was likely polymicrobial with the early symptoms due to a more typical pathogen that was treated with the initial empiric antibiotic regimen, with the longer course due to Nocardia arthritis. Though less likely, it is also possible that NA keratitis has the potential to progress more rapidly than keratitis caused by other more familiar Nocardia species. Soft contact lenses have been previously associated with Nocardia keratitis. This case supports those findings and highlights the importance of maintaining a broad differential diagnosis when treating contact lens associated corneal ulcerations.

Like other Nocardia species, arthritis responded well to topical amikacin. In addition to antimicrobial therapy, we used corticosteroids at two separate times during this case. First at day six, with subsequent increase in symptoms and progression of the ulceration. Once the correct diagnosis was confirmed and amikacin started, steroids were again applied, this time without incident. However, recent research indicates that corticosteroids may actually be detrimental in Nocardia species keratitis and may lead to larger scars at 3 and 12 months (Srinivasan, et al., 2014), (Lalitha, et al., 2012), (Garg & Vazirani, 2013). In light of this recent research and our own experience with this case, we believe that corticosteroids should not be applied in the treatment of Nocardia species keratitis. Ultimately, Good outcomes can be expected when correct diagnosis and treatment are made without significant delay.

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