American Journal of Ophthalmology Case Reports 20 (2020) 100971

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Management of nontuberculous mycobacterial infections of the eye and orbit: A retrospective case series

Alice Y. Kim [a], Alexander S. Davis [a,1], Annie Moreau [a], Douglas A. Drevets [b,c], Dante P. Melendez [b,*]

[a] Ophthalmology Department, Dean McGee Eye Institute, Oklahoma University Health Sciences Center, 608 Stanton L Young Blvd, Oklahoma City, OK, 73104, USA
[b] Department of Internal Medicine, Oklahoma University Health Sciences Center, 800 Stanton L. Young Blvd. Suite 7300, Oklahoma City, OK, 73104, USA
[c] Veterans Affairs Medical Center, 921 NE 13th St, Oklahoma City, OK, 73104, USA

ARTICLE INFO

Keywords:
Nontuberculous mycobacteria
Infections
Orbit
Surgery
Management

ABSTRACT

Purpose: To provide an update on different management approaches for Nontuberculous Mycobacterial (NTM) infections of the eye and orbit.

Observations: A total of 9 eyes from 8 patients were found to meet study criteria. Of these 9 eyes, 6 eyes (66%) involved *Mycobacterium abscessus*, 2 (22%) involved *M. chelonae*, and 1 (11%) involved *M. fortuitum*. In 8 (88%) eyes, NTM infection was treated with a combination of antibiotics and removal of involved foreign body or tissue (e.g. scleral buckle, intraocular lens, orbital implant, or granuloma). One case was observed on topical therapy alone due to low suspicion for clinically significant infection. In 1 patient, a second culture-positive infection was found in the contralateral eye requiring treatment.

Conclusions and importance: Depending on the clinical presentation, optimal treatment of ocular and orbital NTM infections may require combination anti-mycobacterial antibiotics (topical and systemic), surgical removal of implanted material or tissue, or both.

1. Introduction

Nontuberculous mycobacterial (NTM) infections of the eye and orbit are an uncommon but serious complication of intraocular and orbital surgeries. Reported cases include infectious keratitis,[1,2] endophthalmitis,[3–6] and scleral buckle infections,[7] typically involving *Mycobacterium chelonae*, *M. fortuitum*, and *M. abscessus*. Published case studies and reviews report a combination of topical drops, intravitreal injections, systemic antibiotics, and/or surgical removal of foreign material if indicated as part of the management of these infections.[8] We compiled a series of patients with NTM ocular infections and present a review of the literature to help refine the management of these rare but serious infections.

1.1. Methods

All cases of ocular cultures positive for NTM between January 1, 2014, to October 1, 2018, at the Dean McGee Eye Institute and the Oklahoma University Medical Center were reviewed. This retrospective study was approved by the Oklahoma University Health Sciences Center Institutional Review Board and the study is in accordance with HIPAA regulations.

2. Findings

Nine infected eyes from 8 patients were included in the study. Table 1 lists the demographics, clinical presentation, culture results, antibiotic sensitivity and selection, surgical intervention, and clinical outcome of each case. Cases 1–4 are described in greater detail as follows.

* Corresponding author. Infectious Disease Section, Oklahoma University Health Sciences Center, 800 Stanton L. Young Blvd. Suite 7300, Oklahoma City, OK, 3104, USA.

E-mail addresses: alice-kim@dmei.org (A.Y. Kim), alexdavis008@gmail.com (A.S. Davis), Annie-Moreau@dmei.org (A. Moreau), Douglas-Drevets@ouhsc.edu (D.A. Drevets), paolo-melendez@ouhsc.edu (D.P. Melendez).

[1] Department of Surgery, Ophthalmology Division, University of New Mexico School of Medicine, MSC 10 5610, 1 University of New Mexico, Albuquerque, New Mexico, 87131, U.S.A.

https://doi.org/10.1016/j.ajoc.2020.100971
Received 3 May 2019; Received in revised form 6 August 2020; Accepted 12 October 2020
Available online 21 October 2020

2.1. Case 1

An 89-year-old Caucasian female with history of scleral buckle surgery for a right retinal detachment 4 years prior presented with chronic conjunctivitis in the same eye. Best corrected visual acuity (BCVA) was 20/500 OD at distance. Examination revealed significant tenderness over the scleral buckle sites superiorly and inferiorly as well as corneal epithelial defects (Fig. 1A). *M. abscessus* grew from 2 separate conjunctival specimens. Partial scleral buckle removal was performed which also grew *M. abscessus*. She was initially treated with oral clarithromycin 500mg PO BID and topical amikacin 10mg/mL eyedrops, 1 drop every 2 hours OD while awake. Her vision deteriorated further to count fingers over 3 weeks with persistent symptoms and corneal epithelial defects (Fig. 1B). As a result, she underwent removal of the remaining scleral buckle and received intravenous imipenem 500mg IV every 6 hours (eventually tapered to 250mg IV every 12 hours) while continuing oral clarithromycin 500mg PO BID and topical amikacin OD (eventually tapered to daily dosing prior to discontinuation) for 20 weeks. She had clinical resolution of the infection; however, the patient passed away prior to her last follow-up (unknown cause of death).

2.2. Case 2

A 57-year-old Caucasian female presented with remote history of

Table 1
Cases 1–8.

Case	Age/ Sex/ Eye	Ocular History	Exam	Diagnosis	Culture results/ source	Antibiotics for definitive treatment (susceptibility)*	Duration of antibiotics	Surgical intervention	Time to resolution**
1	89/ F/ OD	Scleral buckle for RD OD, CEIOL OU	Right conjunctival injection, discharge, and corneal haze	Scleral buckle infection	*M. abscessus*/ conjunctiva x 2 *M. abscessus*/ scleral buckle	Topical amikacin (S) PO clarithromycin (S) IV imipenem (S)	20 weeks	Removal of scleral buckle at 8 weeks	6 months
2a.	57/ F/OS	LASIK OU, CEIOL OU, endophthalmitis OS	Left hypopyon, capsular/iris fibrotic membrane with infiltrates s/p partial vitrectomy/ capsulotomy by outside provider	Endophthalmitis	*M. abscessus*/ vitreous tap, lens complex	Topical amikacin (S) & moxifloxacin (R) Intravitreal amikacin (S) & clarithryomycin (S) IV amikacin (S) PO azithromycin (S)	2 weeks	Complete extraction of intraocular lens/ capsule complex at 6 weeks, followed by enucleation after an additional 6 weeks	2 months
2b.	57/ F/ OD	LASIK OU CEIOL OU, *M. abscessus* endophthalmitis OS	Right lower lid conjunctival granuloma, diffuse epitheliopathy, hyperemia	Episcleritis, granuloma from re-inoculation	*M. abscessus*/ conjunctiva x 2	Topical amikacin (S) & clarithromycin (S) Cefoxitin (that replaced IV amikacin and imipenem) & PO clarithromycin (S)	16 weeks	Granuloma resection	4 months
3	45/ M/ OD	Evisceration OD for RD/VH	Right orbital cellulitis	Orbital cellulitis	*M. abscessus*/ orbital implant, scleral wall tissue, conjunctiva, and scleral buckle	IV amikacin (S) & imipenem (I) PO linezolid (R), *then* PO azithromycin (S)	12 weeks	Removal of right orbital sphere, scleral wall, scleral buckle hardware	2 months
4	64/ M/ OD	Evisceration OD for trauma with open globe	Right orbital implant extrusion	Orbital socket infection with implant extrusion	*M. abscessus*/ orbital socket tissue	None	N/A	Removal of implant, debridement of necrotic scleral tissue	1 month
5	81/ F/ OD	Enucleation OD for blind painful eye	Right exposed sphere implant	Orbital socket infection with exposed sphere	*M. abscessus*/ orbital socket tissue	None	N/A	Removal of implant	3 months
6	90/ F/OS	Evisceration OS for blind painful eye	Left retained scleral buckle, subcutaneous granuloma	Orbital socket infection	*M. chelonae*/ orbital socket tissue/ conjunctiva	None	N/A	Granuloma resection	1 month
7	15/ M/ OD	Congenital anophthalmos OU	Right socket discharge with ill-fitting prosthesis	Orbital socket infection	*M. chelonae*/ conjunctiva	None	N/A	None	1 month
8	77/ F/ OD	Glaucoma valve OD	Right extrusion of glaucoma implant, erosion into superior cornea	Corneal ulcer	*M. fortuitum*/ cornea	None	N/A	Corneal scleral patchgraft with tarsorrhaphy	1 month

OD: right eye; OS: left eye; OU: both eyes; RD: retinal detachment; CEIOL: cataract extraction with intraocular lens implantation; LASIK: laser in situ keratomileusis; VH: vitreous hemorrhage; PO: oral; IV: intravenous; N/A: Not applicable.
*Antibiotics used with susceptibilities in parenthesis (S: susceptible, I: intermediate; R: resistant). See text for further details of antibiotic therapy for cases 1–3.
**Time to resolution as determined by clinical and/or culture-proven resolution of infection from date of presentation.

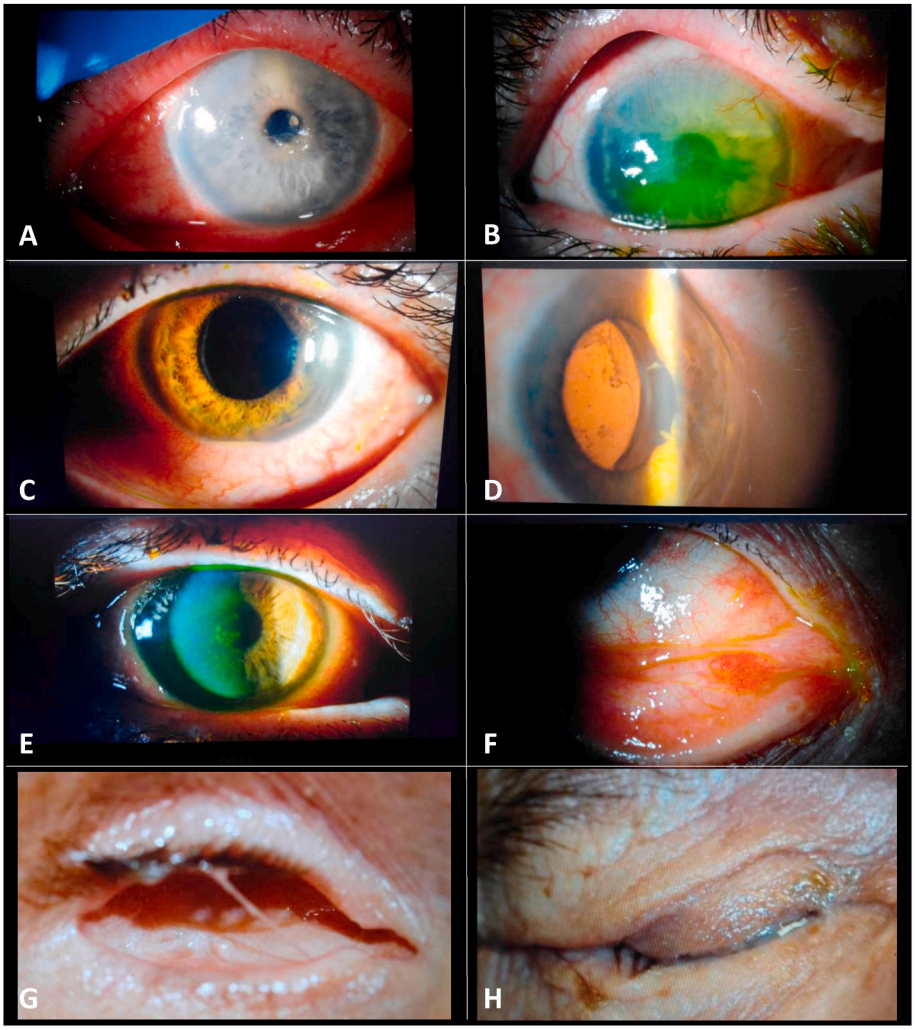

Fig. 1. Cases 1–4.
Case 1 (right eye): (A) Initial presentation with corneal epithelial defects, stromal opacity, Descemet folds; and (B) corneal appearance following partial scleral buckle removal.
Case 2A (left eye): (C) Initial presentation with hypopyon and (D) capsular/iris fibrotic membrane and multiple areas of infiltrate material on posterior capsule and anterior capsule/lens.
Case 2B (right eye): (E) Contralateral extension of infection with diffuse epitheliopathy and (F) conjunctivitis with granuloma, scleritis.
Case 3 (right eye): (G) Initial presentation with orbital cellulitis.
Case 4 (right eye): (H) Initial presentation with orbital socket infection and orbital implant extrusion.

bilateral laser-assisted in situ keratomileusis (LASIK) refractive surgery and recent bilateral cataract surgery complicated by *M. abscessus* endophthalmitis in the left eye requiring partial removal of the lens and capsule complex at an outside institution. At subsequent presentation to our clinic, her visual acuity was 20/100 OS at distance without correction. There was a hypopyon with infiltrates noted along the remaining intraocular lens and capsule complex (Fig. 1C and D), for which complete removal of the remaining complex was then performed. Both the intravitreal specimen and removed intraocular contents were positive for *M. abscessus* and were initially treated with topical amikacin 25mg/mL eyedrops, 1 drop every hour OS, and moxifloxacin 0.5% eyedrops QID OS followed by intravitreal amikacin 0.4mg/0.1mL and clarithromycin (quantity and dose not documented by administering retina specialist). Two months later, there was development of scleral abscess with exudative retinal detachment and extrascleral extension. The patient underwent enucleation and received intravenous amikacin 15mg/kg/day with oral azithromycin 500mg PO daily for 2 weeks based on *in vitro* susceptibilities, with clinical resolution.

Three months later, the patient developed contralateral conjunctivitis, scleritis, keratitis and a granuloma of the right lower eyelid (Fig. 1E and F); BCVA was 20/20 OD. Right conjunctival biopsy and cultures were both positive for *M. abscessus*. She received topical amikacin 25mg/mL eyedrops, 1 drop every 2 hours OD, and clarithromycin 1% eyedrops, 1 drop every 2 hours OD. Given monocular status, she was also started on systemic therapy including oral clarithromycin 500mg PO BID, intravenous amikacin 15mg/kg/day, and intravenous imipenem 500mg IV every 6 hours. The 2 latter antibiotics were replaced by intravenous cefoxitin 2g every 6 hours due to toxicity/rash after 4 weeks of therapy to complete a total of 16 weeks of antibiotic therapy, with complete resolution of symptoms. Eighteen months after completion of therapy, vision was 20/20 with no evidence of recurrent disease activity.

2.3. Case 3

A 47-year-old Caucasian male with prior right eye evisceration due to vitreous hemorrhage and retinal detachment with retention of the scleral buckle presented with right orbital cellulitis due to *M. abscessus*. He was treated with oral linezolid and topical moxifloxacin per initial sensitivities for 4 months at an outside institution (doses and frequency not recorded), with further worsening of the infection (Fig. 1G). At our institution, cultures confirmed *M. abscessus* growth on his right conjunctiva (now resistant to linezolid and moxifloxacin). He underwent anterior orbitotomy with removal of the silicone sphere implant and scleral wall with scleral buckle and received intravenous imipenem 1000mg/250mL IV every 6 hours and amikacin 950mg/100mL IV every day with oral azithromycin 250mg PO every day for approximately 3 months. Nine months after completion of treatment, he had no evidence of infection.

2.4. Case 4

A 65-year-old Caucasian male who sustained ocular trauma

requiring evisceration and placement of an ocular implant many years ago presented with right-sided orbital pain as well as purulent drainage and was found to have an exposed orbital sphere implant (Fig. 1H). He underwent implant removal, and cultures grew *M. abscessus* from 2 different specimens (orbital tissue specimen and conjunctival swab). Final wound closure without any implant was performed. He was only monitored off antibiotics and continues to demonstrate no signs of infection on follow-up, over 2 years after infection.

3. Discussion

Nontuberculous mycobacteria (NTM) are commonly encountered in the environment.[8] Among the rapidly-growing NTM, the most commonly encountered ocular pathogens are *M. chelonae*, *M. fortuitum*, and *M. abscessus*.[8,9] In this series, we report nine cases of ocular and orbital NTM infections from a single center, manifest in a variety of ways: scleral buckle infection (case 1), endophthalmitis with subsequent involvement of the contralateral eye as conjunctival granuloma with scleritis (case 2a and 2b), orbital cellulitis (case 3), orbital socket infection (cases 4–7), and corneal ulcer in setting of exposed glaucoma implant (case 8).

The different approaches to managing these infections are also highlighted. The first three cases demonstrate the use of both topical and systemic antibiotic therapy over long periods of time (up to 20 weeks, as in case 1) to manage ocular and orbital NTM infections. Other cases highlight how some culture-positive infections can be managed by removing the infected implant (cases 4–5 and case 8) or tissue (case 6) with minimal antibiotics on board. Lastly, case 7 was treated on non-NTM directed topical antibiotic (erythromycin 0.5% ointment nightly) as suspicion for clinically significant NTM infection was low given the patient's only complaint of increased discharge but no pain or orbital involvement on exam under anesthesia. In these cases where definitive NTM-specific antibiotic therapy was not instituted, patients were monitored as appropriate for their condition or postoperative course, with no recurrence of infection found in any of these cases.

We also present the first known case of contralateral *M. abscessus* infection after resolution of the index infection (Case 2). In this case, the patient had shown complete resolution of infection following source control via enucleation of the left eye. However, within 2 months of stopping systemic antibiotics, the fellow (right) eye became affected. The reason for this is unclear, as the patient was otherwise immunocompetent with previously normal ocular exam of the right eye. Nevertheless, given her monocular status due to prior mycobacterial infection, aggressive measures were taken as described to ensure her fellow eye remained with good vision.

Our review emphasizes the importance of a multidisciplinary approach in the management of these infections. Several important points can be highlighted from this review. First, macrolides are a mainstay of antimicrobial treatment of NTM; however, resistance can be present before, or can develop following their use. Therefore, it is crucial to obtain *in vitro* antibiotic susceptibilities before treatment as well as in the setting of treatment failure. Brown-Elliott et al. reviewed antimicrobial susceptibility of NTM ophthalmic isolates in 100 patients, noting increased susceptibility of *M. abscessus* isolates to amikacin and clarithromycin/azithromycin therapy, whereas *M. chelonae* isolates responded better to clarithromycin/azithromycin, amikacin, tobramycin, and fluoroquinolones.[10] Thus, obtaining cultures and sensitivities are important in more effectively targeting therapy for these challenging infections.

Second, antibiotic monotherapy of NTM ocular infections is not recommended since development of resistance and treatment failure are common, as illustrated by Case 3. In particular, *M. abscessus* may need to be more aggressively treated based on the clinical picture due to biofilm formation and subsequent resistance to therapy.[5,6] Although use of ocular topical antibiotics alone can potentially induce resistance, this issue has not been appropriately studied. Lastly, adequate source control through removal of infected ocular devices continues to be the most important component in management of these infections. While each of the cases presented here benefited from implant removal, Cases 1 and 2A in particular illustrate the superiority of full over partial prosthesis removal.

4. Conclusions

Although rare, NTM infections are an important differential to consider when encountering ocular infections in the setting of prior surgery and presence of ocular implants, as timely intervention can minimize morbidity. Depending on the clinical scenario, using combination antibiotics based on antimicrobial susceptibility testing and/or surgical intervention may provide definitive management of these infections. Collaboration between ophthalmology and infectious disease specialists is recommended to help elucidate the best course of action for treatment of mycobacterial infections of the eye and orbit.

5. Patient consent

Of the 8 patients included in this study, three of the patients or patient's legal guardian consented to publication of the case orally. Three patients either did not respond to phone calls despite multiple attempts, did not have a correct phone number, and/or did not have an alternative number listed to reach out to patient or family to contact regarding the study. Two patients were deceased and did not have a working contact number to reach out to family regarding the study. All documentation of phone calls and attempts was placed in each patient's electronic medical record. This report does not contain any personal information that could lead to the identification of the patients.

Funding

No funding or grant support.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

None.

Acknowledgements

None.

References

1. Dolz-Marco R, Udaondo P, Gallego-Pinazo R, Millan JM, Diaz-Llopis M. Topical linezolid for refractory bilateral Mycobacterium chelonae post-laser-assisted in situ keratomileusis keratitis. *Arch Ophthalmol*. 2012;130(11):1475–1476.
2. Kymionis GD, Kankariya VP, Kontadakis GA. Combined treatment with flap amputation, phototherapeutic keratectomy, and collagen crosslinking in severe intractable post-LASIK atypical mycobacterial infection with corneal melt. *J Cataract Refract Surg*. 2012;38(4):713–715.
3. Hsu CR, Chen JT, Yeh KM, et al. A cluster of nontuberculous mycobacterial endophthalmitis (NTME) cases after cataract surgery: clinical features and treatment outcomes. *Eye (Lond)*. 2018;32(9):1504–1511.
4. Venkateswaran N, Yeaney G, Chung M, Hindman HB. Recurrent nontuberculous mycobacterial endophthalmitis: a diagnostic conundrum. *Clin Ophthalmol*. 2014;8:837–842.
5. Hung JH, Huang YH, Chang TC, et al. A cluster of endophthalmitis caused by Mycobacterium abscessus after cataract surgery. *J Microbiol Immunol Infect*. 2016;49(5):799–803.
6. Shah M, Relhan N, Kuriyan AE, et al. Endophthalmitis caused by nontuberculous Mycobacterium: clinical features, antimicrobial susceptibilities, and treatment outcomes. *Am J Ophthalmol*. 2016;168:150–156.

7. Mohan N, Kar S, Padhi TR, Basu S, Sharma S, Das TP. Changing profile of organisms causing scleral buckle infections: a clinico-microbiological case series. *Retina*. 2014; 34(2):247–253.
8. Moorthy RS, Valluri S, Rao NA. Nontuberculous mycobacterial ocular and adnexal infections. *Surv Ophthalmol*. 2012;57(3):202–235.
9. Girgis DO, Karp CL, Miller D. Ocular infections caused by non-tuberculous mycobacteria: update on epidemiology and management. *Clin Exp Ophthalmol*. 2012; 40(5):467–475.
10. Brown-Elliott BA, Mann LB, Hail D, Whitney C, Wallace Jr RJ. Antimicrobial susceptibility of nontuberculous mycobacteria from eye infections. *Cornea*. 2012;31 (8):900–906.