European Journal of Ophthalmology / Vol. 18 no. 2, 2008 / pp. 294-296

SHORT COMMUNICATION

Mycobacterium chelonae keratitis in a patient with Sjögren's syndrome

M.T. VAN DER BEEK[1], A.T. BERNARDS[1], R. LAPID-GORTZAK[2-4]

[1]Department of Medical Microbiology, Center of Infectious Diseases
[2]Department of Ophthalmology, Leiden University Medical Center
[3]Retina-TEC Center for Refractive Surgery, Driebergen
[4]Dept. of Ophthalmology, Academic Medical Centre, University of Amsterdam, Amsterdam - The Netherlands

PURPOSE. *In this report a case of Mycobacterium chelonae keratitis in a patient without any previously described risk factors is described. The only risk factor found was a rheumatoid arthritis related Sjögren's syndrome.*
METHODS. *Case report.*
RESULTS. *A 60-year-old woman was referred to the hospital with an infectious keratitis of the left eye of 3 months duration, unresponsive to empirical therapy with ofloxacin and tobramycin drops. Her medical history included a longstanding rheumatoid arthritis and a secondary ocular surface syndrome. Upon arrival the left eye showed diffuse corneal edema and centrally several large infiltrates with fluffy edges, surrounded by several smaller satellite infiltrates. The cornea was scraped for culture and grew M chelonae and sensitivity testing showed sensitivity to ciprofloxacin, clofazimine, and clarithromycin. Systemically, ciprofloxacin 750 mg and clarithromycin 500 mg twice daily were prescribed orally. Topical therapy consisted of topical erythromycin 10 mg/mL and ofloxacin 3 mg/mL every 2 hours. Treatment was continued for a total of 10 months during which the infiltrates cleared completely, but the central cornea remained scarred.*
CONCLUSIONS. *M chelonae can be a cause of infectious keratitis in patients without known risk factors for rapidly growing mycobacterium keratitis. Especially in the case of ocular infections that show no response to regular antibacterial treatment, mycobacterial infection should be considered. Good communication between the ophthalmologist and the microbiologist is crucial for a rapid diagnosis. (Eur J Ophthalmol 2008; 18: 294-6)*

KEY WORDS. *Infectious keratitis, Mycobacterium chelonae, Rheumatoid arthritis, Sjögren syndrome*

Accepted: September 17, 2007

INTRODUCTION

Non-tuberculous mycobacteria (NTM) are a rare cause of infectious keratitis. This infection usually occurs in the setting of a surgical or other ocular trauma (1, 2). *Mycobacterium chelonae* is a rapidly growing mycobacterium (RGM) and it is known to cause keratitis after ocular trauma or surgery. For example, several case reports on mycobacterial keratitis as a complication of laser-assisted in situ keratomileusis (LASIK) have been reported in recent years (3). We describe a case of *M chelonae* keratitis in a patient without any of the previously described risk factors. The only risk factor we found was a rheumatoid arthritis related Sjögren's syndrome.

Case report

A 60-year-old woman was referred to our hospital with an infectious keratitis of 3 months duration, unresponsive to empirical therapy with tobramycin 3 mg/mL (Tobrex, Alcon, Gorinchem, The Netherlands), and ofloxacin 3 mg/mL (Trafloxal, Weesp, The Netherlands). Her medical

1120-6721/294-03$25.00/0

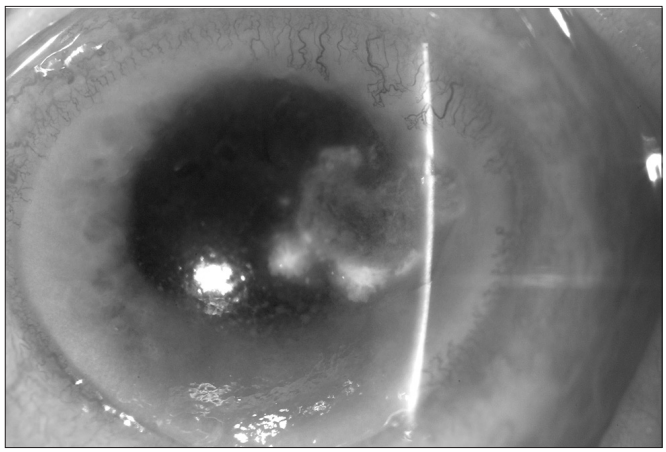

Fig. 1 - *Multiple mycobacterial infiltrates in the optical axis of the cornea.*

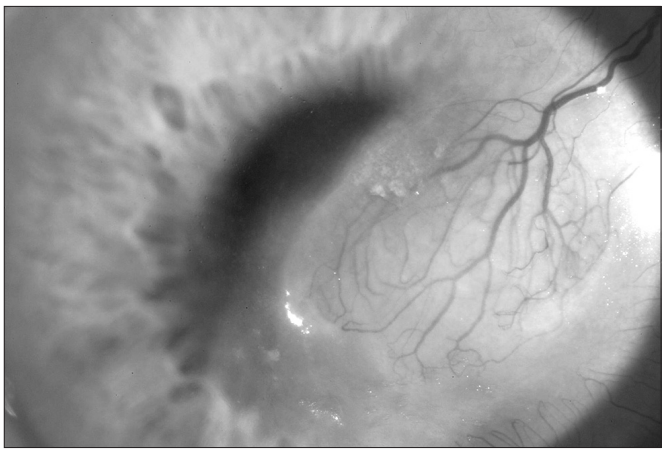

Fig. 2 - *The cornea with a paraxial scar with neovascularization. The patient has a best-corrected visual acuity of 20/40, notwithstanding the extensive scarring.*

history included a long-standing rheumatoid arthritis that was treated with hydroxychloroquine and a secondary ocular surface syndrome, for which she was treated with topical lubricants.

Upon arrival the right eye had a best-corrected visual acuity (BCVA) of 20/20 and a normal eye examination. In the left eye she had a BCVA of 20/50, with swollen rounded eyelid margins, injected and chemotic conjunctiva, and diffuse corneal edema, with centrally several large infiltrates with fluffy edges, surrounded by several smaller satellite infiltrates (Fig. 1).

The cornea was scraped for culture and the first Gram stain showed many leucocytes and Gram-positive rods, which looked like “diphtheroids”. Suspicion was raised about opportunistic infections, and another scraping was performed to get a Ziehl-Neelsen (ZN) stain, which demonstrated the presence of acid-fast rods. After 3 days of culture, very small dry white colonies were visible that were positive in ZN staining. Species determination as *M chelonae* was performed by molecular analysis of the 16s-23s ribosomal RNA spacer region using the Innolipa Mycobacteria v2 amplification kit (Innogenetics, Gent, Belgium).

The patient was started on empiric wide spectrum topical antibiotic treatment, which included cefazolin 50 mg/mL (handmade by pharmacist from IV suspension) and tobramycin 14 mg/mL hourly (handmade by pharmacist from IV suspension), and homatropine 2% twice daily. Systemically, ciprofloxacin 750 mg (Ciproxin, Bayer, Mijdrecht, the Netherlands) and clarithromycin 500 mg (Klacid, Abbott, Hoofddorp, the Netherlands) twice daily were prescribed orally. Cefazolin was stopped when allergy developed resulting in swelling and redness of the periocular skin, increased corneal hazing, and a drop in vision to hand motion (HM). At this stage, results of sensitivity testing performed by the Dutch mycobacterial reference laboratory of the National Institute for Public Health and the Environment (RIVM, Bilthoven, the Netherlands) by agar dilution assays became available and showed resistance to isoniazid, rifampicin, ethambutol, streptomycin, amikacin, tobramycin, doxycycline, imipenem, linezolid, and rifabutin and sensitivity to ciprofloxacin, clofazimine, and clarithromycin. The systemic therapy remained unchanged. Topical therapy was switched to topical erythromycin 10 mg/mL (handmade by pharmacist from IV suspension) and ofloxacin 3 mg/mL every 2 hours. Within a couple of days the skin changes disappeared and the conjunctival injection and the inflammation of the eye decreased. Within 5 months of this treatment the corneal infiltrates resolved. Treatment was continued for a total of 10 months. At the end of treatment, there was deep central corneal scarring with some loss of stroma (Fig. 2). Otherwise the ocular examination is within normal limits and BCVA is 20/40. No recurrence was detected in the first 3 months after ceasing antibiotic therapy.

DISCUSSION

Mycobacterial keratitis is a relatively infrequent cause of keratitis. It has mostly been described in patients who

had undergone ocular surgery, who had had an ocular trauma, or who had been wearing contact lenses (3, 4). In this case report we describe a patient in whom none of these previously mentioned risk factors were present. An ocular sicca syndrome with concomitant use of topical ocular lubricants was identified as a risk factor in our patient. In patients with rheumatoid arthritis or Sjögren's syndrome, keratitis caused by *M chelonae* has not been described previously.

RGM are ubiquitous in nature and are present in soil, plants, animals, and water, and many of them are considered nonpathogenic. Keratitis caused by RGM probably results from direct inoculation of a previously damaged cornea from a reservoir, e.g., water or soil. In the case of infections after medical procedures, reservoirs have been found in tap water, saline, disinfecting solutions, ice machines, and other medical supplies (3). The direct source in our patient remains unknown. Probably, epithelial microtrauma due to the sicca syndrome formed a port of entry for *M chelonae*.

Because it is rarely encountered, the diagnosis of mycobacterial keratitis can be delayed if the clinician or the medical microbiologist is not aware of the possibility of this diagnosis. As described in previous reports, Gram-staining and colony morphology can lead to confusion with *Nocardia* or even "diphtheroids" (3, 4). As was done in our case, acid-fast or fluorochrome staining should be performed when Gram-positive rods are found in significant numbers in the Gram stain. For rapidly growing mycobacteria, such as *M* chelonae, no special culture media are required and RGM can be isolated within 7 days from regular culture media.

Clinically, mycobacterial keratitis is characterized by a "snowflake" or "cracked windshield" appearance. Its clinical appearance shares resemblance with fungal keratitis. Sometimes, satellite lesions are present. Usually, mycobacterial keratitis shows an insidious course. However, *M chelonae* is one of the most resistant RGM. The majority of *M chelonae* strains is susceptible to amikacin, clarithromycin, gatifloxacin, linezolid, and tobramycin, whereas fewer strains are susceptible to ciprofloxacin, doxycycline, or imipenem (5). Due to its relative rarity, no controlled clinical trials exist that have investigated treatment options for mycobacterial keratitis. Based on the susceptibility profile of the isolate in our patient and because MIC-values of clarithromycin and ciprofloxacin are generally lower compared to other quinolone and macrolide antibiotics, we would have preferred topical therapy with clarithromycin and ciprofloxacin. Nevertheless, erythromycin was chosen because clarithromycin is not available in a topical formulation in The Netherlands and ofloxacin was chosen because of the risk of corneal deposits associated with topical ciprofloxacin and the recent corneal hazing due to cefazolin. Response to antibiotic treatment is frequently insufficient and often visual outcome is poor, necessitating penetrating keratoplasty to either decrease mycobacterial load to treat the infection or restore the vision (3, 4). In our patient visual acuity is good, and corneal transplantation is not indicated clinically.

In conclusion, *M chelonae* can be a cause of infectious keratitis in patients without known risk factors for RGM keratitis. Especially in the case of ocular infections that show no response to regular antibacterial treatment, mycobacterial infection should be considered. Good communication between the ophthalmologist and the microbiologist is crucial in rapid diagnosis.

Proprietary interest: None.

Reprint requests to:
Dr. A.T. Bernards
Department of Microbiology
Center of Infectious Diseases
Postal zone E4-P
P.O. box 9600
NL-2300 RC Leiden, The Netherlands
a.t.bernards@lumc.nl

REFERENCES

1. Bullington RH, Jr., Lanier JD, Font RL. Nontuberculous mycobacterial keratitis. Report of two cases and review of the literature. Arch Ophthalmol 1992; 110: 519-24.
2. Ford JG, Huang AJ, Pflugfelder SC, Alfonso EC, Forster RK, Miller D. Nontuberculous mycobacterial keratitis in south Florida. Ophthalmology 1998; 105: 1652-8.
3. Freitas D, Alvarenga L, Sampaio J, et al. An outbreak of Mycobacterium chelonae infection after LASIK. Ophthalmology 2003; 110: 276-85.
4. Khooshabeh R, Grange JM, Yates MD, McCartney AC, Casey TA. A case report of Mycobacterium chelonae keratitis and a review of mycobacterial infections of the eye and orbit. Tuber Lung Dis 1994; 75: 377-82.
5. Brown-Elliott BA, Wallace RJ, Jr. Clinical and taxonomic status of pathogenic nonpigmented or late-pigmenting rapidly growing mycobacteria. Clin Microbiol Rev 2002; 15: 716-46.