Case Report

Rapid diagnosis of *Mycobacterium abscessus* endophthalmitis

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Nontuberculous mycobacteria are widely distributed in the environment and have the potential to cause a wide spectrum of infections including pulmonary, bone, soft tissue or ocular infections. They are a rare cause of endophthalmitis, a potentially devastating condition, which may be acquired through contamination of water or antiseptic solutions. Diagnosis is often delayed due to low clinical suspicion, resulting in poor clinical outcomes. Newer laboratory techniques such as real-time PCR can be used for rapid detection, identification and speciation of mycobacteria and allow for initiation of focused antibiotic therapy. We describe a case of *Mycobacterium abscessus* endophthalmitis that developed 30 years after traumatic loss of cornea in a patient with diabetes mellitus.

Case Report

A 56-year-old woman with a history of non-insulin dependent diabetes mellitus presented to the emergency room with a 1 week history of worsening right eye pain with purulent drainage, headache, nausea and fever. Thirty years ago, she had suffered a traumatic injury to the right eye while living in India, which resulted in a blind eye. After a failed corneal transplant, she was fitted with a cosmetic lens (prosthesis) that fitted over her natural residual eye. She reported that she removed the prosthesis each night and stored it in a glass of tap water. The patient denied any prior upper respiratory infections or recent travel.

On physical examination, the patient was afebrile. Examination of the eye revealed proptosis, uveal prolapse, conjunctival infection and yellowish discharge (Fig. 1). White blood cell count was $16.1 \times 10^3 \text{ ml}^{-1}$, sedimentation rate was 37 mm h$^{-1}$ and haemoglobin A1c was 6.8%. Initial Gram stain of the drainage showed few polymorphonuclear cells and no organisms. Computed tomography (CT) scan of the orbits showed a 1.7 × 1.0 × 1.3 cm fluid collection with gas in the preseptal soft tissues raising concern about an abscess; multiple metallic foreign bodies were also present (Fig. 2). The right globe appeared proptotic. The patient was hospitalized and treated empirically with vancomycin and piperacillin–tazobactam, as well as trimethoprim–polymyxin ophthalmic solution.

On hospital day 2, culture of the eye drainage grew few colonies of *Staphylococcus aureus*; piperacillin–tazobactam was discontinued. Despite treatment with vancomycin the patient continued to have persistent pain and drainage.

On hospital day 5, Lowenstein–Jensen agar revealed one colony of a beaded, non-branching, Gram-positive bacillus which was Kinyoun stain positive. Initial PCR was positive for mycobacterial species. Given the speed of culture growth and PCR findings, it was felt that the organism was probably in the *Mycobacterium fortuitum* or *M. abscessus–M. chelonae* group of bacteria. Single-tube multiplex, real-time PCR testing (Richardson et al., 2009) for *Mycobacterium tuberculosis* complex, *M. avium* complex, the *M. fortuitum* group and the *M. chelonae–M. abscessus* group were performed. Results of this assay suggested *M. abscessus*.

Antibiotics were changed to treat nontuberculous mycobacteria (NTM) infection and included imipenem–cilastatin, amikacin and clarithromycin. Because of the persistence of infection and painful blind eye, the patient was taken to the operating room for right enucleation. Erythromycin ophthalmic ointment was placed inside the sclera shell at the time of surgery. Because of the high risk of recurrent infection with this group of organisms, it was recommended that reimplantation of the prosthetic device be held for 6 weeks while she completed a full course of antibiotics.

Following enucleation, the patient had rapid clinical improvement with decrease in pain and drainage. She

Abbreviations: NTM, nontuberculous mycobacteria; RGM, rapidly growing mycobacteria.
was discharged on hospital day 11 with plans to complete a 6 week course of intravenous imipenem–cilastatin and a 6 month course of oral clarithromycin. Cultures had been sent to a reference laboratory for identification and susceptibility testing. High performance liquid chromatography (HPLC) was performed and mycolic acid profile most closely resembled the *M. chelonae–M. abscessus* group; final culture results revealed *M. abscessus*. Six weeks following discharge from the hospital, susceptibility testing from the reference lab was received and showed the organism to be sensitive to clarithromycin (MIC $\leq 0.25 \mu g \text{ml}^{-1}$) and amikacin (MIC $\leq 8.0 \mu g \text{ml}^{-1}$), but resistant to imipenem (MIC $16 \mu g \text{ml}^{-1}$). The patient’s local physician was contacted regarding imipenem resistance; however, given prior surgical drainage of the abscess and removal of the hardware along with the renal toxicity of amikacin, the decision was made to continue the patient on macrolide therapy. Seven months after surgery, the patient remains on clarithromycin, 500 mg twice daily, and is without evidence of infection.

**Discussion**

Rapidly growing mycobacteria (RGM) are saprophytes found in the air, dust and soil. They differ from other nontuberculous organisms in that they form mature colonies on Lowenstein–Jensen agar within 7 days. Although relatively uncommon, they are emerging as important human pathogens that can cause a wide spectrum of infections including pulmonary, ocular, soft tissue and bone infections; they may also disseminate. The vast majority of ocular infections are caused by the Ruynon group IV organisms *M. fortuitum*, *M. chelonae* and *M. abscessus* (Brown-Elliott & Wallace, 2002). The poor prognosis of infections due to RGM is partially due to a delay in establishing a diagnosis. Recent guidelines on diagnosis and treatment of RGM strongly recommend rapid identification of RGM to the species level to assist with choosing the most effective empiric antimicrobial therapy (Griffith *et al.*, 2007). HPLC of mycobacterial wall mycolic acids and PCR are often used in laboratories to identify RGM and are useful in ruling out *M. fortuitum*. They are not, however, able to differentiate isolates of the *M. abscessus* and the *M. abscessus–M. chelonae* group. Based on methods previously published by Richardson *et al.* (2009), we used a real-time PCR assay in which primers target the internal transcribed spacer of the *M. abscessus–M. chelonae* group and used a melting temperature analysis to distinguish *M. chelonae* from *M. abscessus*. This is more cost effective than sequence analysis, which is limited to reference laboratories and subject to amplicon contamination (Guarin *et al.*, 2010).

*M. abscessus* causes skin and soft tissue infections, but it is also a cause for more than 80 % of chronic lung disease caused by rapidly growing mycobacteria (Brown-Elliott & Wallace, 2002). It is widely distributed in nature, particularly in water and it may be resistant to some disinfectants. Ocular infections by *M. abscessus* are typically acquired through surgical trauma or contamination of prosthetic material, corneal metallic bodies, water or antiseptic solution. They have been associated with keratitis, corneal transplant and endophthalmitis (Marı́n-Casanova *et al.*, 2003).

Endophthalmitis caused by *M. abscessus* is a rare and potentially devastating ocular infection, and is generally associated with poor outcomes with loss of eyesight (Matieli *et al.*, 2006). The diagnosis and treatment of RGM infections is often delayed because physicians do not consider it in the differential diagnosis. Only 18 cases of endophthalmitis caused by NTM have been reported, five (28 %) of which were caused by *M. abscessus* (Moorthy

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**Fig. 1.** Patient with right orbital proptosis, uveal prolapse, and conjunctivitis.

**Fig. 2.** Computer tomography of right orbit demonstrates fluid collection and gas concerning for abscess.
et al., 2012). Trauma, metallic corneal foreign bodies, and surgical procedures are the most common predisposing factors (Garg, 2012). Patients usually present with pain, decreased vision and erythema. Loss of vision is typically the most concerning, and usually first, sign. Because our patient was without vision in this eye, presentation to a medical professional was probably delayed.

Treatment of these infections requires surgical debridement, removal of foreign bodies and prolonged antibiotic therapy. To reach and maintain adequate antibiotic concentration within the vitreous humour can be very difficult with this group of organisms (Matieli et al., 2006). Nearly all ocular infections require a prolonged course of parenteral antibiotics in combination with clarithromycin (Griffith et al., 2007). Antimicrobial therapy varies depending on the nature of the disease and specific RGM. The choice of antibiotic is based on in vitro antimicrobial susceptibility studies which have shown that amikacin, clarithromycin, azithromycin and cefoxitin have the greatest efficacy in treating these infections. M. abscessus is usually resistant to oral antibiotics except for macrolides (Moorthy et al., 2012). Amikacin is the aminoglycoside of choice when treating rapidly growing NTM, but its use may be limited by renal or ototoxicity, particularly in the diabetic patient. Despite the use of antibiotics, many patients do not respond to medical treatment and require surgical intervention. Failure of medical therapy is largely attributed to the organism’s propensity to form a biofilm (Moorthy et al., 2012). With early diagnosis and treatment, there may be a higher success rate in eradicating RGM infections. Long-term control of NTM requires 6 weeks to 6 months of systemic antibiotic therapy using regimens containing antibiotics with different modes of action. In our case, the patient’s organism was susceptible to amikacin but we chose to avoid extended combination treatment with this aminoglycoside due to risk of renal toxicity in this diabetic patient. Additionally, surgical drainage of the abscess along with removal of vitreal tissue and foreign bodies was a crucial step in eradicating the infection. This case, however, is very unusual in that the patient was already blind and, in most cases, physicians are trying to preserve eyesight and will not remove vitreal tissue.

NTM infections can pose a difficult diagnostic and therapeutic challenge. Investigation of atypical mycobacteria should be included in the microbiological workup of ocular infections. Early diagnosis is possible with the use of rapid identification laboratory techniques such as real-time PCR, giving clinicians the opportunity to start focused antibiotic therapy that may result in improved outcomes for patients.

References


