



Case report

# Autoimmune keratitis in mycobacterium tuberculosis

Parviz Rafiezadeh, Ingo Schmack, Mehdi Shajari, Thomas Kohnen\*

Department of Ophthalmology, Goethe-University, Frankfurt, Germany

Received 9 July 2017; revised 14 March 2018; accepted 19 March 2018

Available online 18 May 2018

## Abstract

**Purpose:** To report a case of autoimmune keratitis in a patient with mycobacterium tuberculosis (MBT).

**Methods:** An 84-year-old male with pulmonary tuberculosis (TB) was admitted with chronic, non-healing bilateral ulcerations of the inferior peripheral cornea associated with stromal and subconjunctival nodules.

**Results:** Clinical examination revealed circumscribed peripheral corneal ulceration with whitish nodules in adjacent stromal and subconjunctival tissue. Microbiological cultures of the corneal tissue were negative for MBT and other microbial pathogens; however, enzyme-linked immunosorbent assay (ELISA) of blood and corneal samples showed significantly elevated levels of IgM and IgA against MBT. In addition to systemic anti-tuberculosis therapy, the patient was treated topically with Polyspectran<sup>®</sup> eye drops, Dexamethasone eye drops, and Bepanthen<sup>®</sup> ointment, for 2 weeks. Both eyes showed dramatic improvement after 2 weeks.

**Conclusion:** The present report demonstrates that MBT is able to initiate delayed autoimmune response within the corneal tissue during an intensive phase of anti-tuberculosis treatment.

Copyright © 2018, Iranian Society of Ophthalmology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Keywords:** Ocular tuberculosis; Scrofulous keratitis; Phlyctenule; Autoimmune response

## Introduction

Tuberculosis (TB) remains a global public health issue with nearly 8 million new cases per year and more than 1 million deaths per year.<sup>1</sup> Ocular TB with a mean prevalence of about 6.8%<sup>2</sup> can be observed in nearly every ocular structure resulting in a variety of vision-threatening complications, such as phlyctenulosis, granulomatous uveitis with synechia formation, vitritis, posterior uveitis, panuveitis, retinitis, and retinal vein

occlusion as well as choroidal and scleral tuberculoma.<sup>3–5</sup> Overall, cases of secondary keratitis with underlying TB are rare. To the best of our knowledge, no case report on peripheral corneal ulceration secondary to autoimmune response against mycobacterium tuberculosis (MBT) during intensive anti-tuberculosis treatment has been published previously.

## Case report

An 84-year-old man was referred with bilateral chronic keratitis, not responding to topical and systemic antibiotic therapy. The patient complained about foreign body sensation, epiphora, photophobia, and visual impairment in both eyes. Ocular history was unremarkable; ocular trauma or previous infections were denied. The patient consented to submission of this case report to the journal.

At initial consultation, the patient presented with best corrected visual acuity of 20/25 in both eyes. Slit-lamp examination revealed mild to moderate hyperemia of the

Disclosure of proprietary or commercial interest: The authors have no proprietary or commercial interests in any concept or product discussed in this article.

Financial support: None of the authors has a financial or proprietary interest in any mentioned product, method, or material.

Conflicts of interest: None.

\* Corresponding author. Department of Ophthalmology, Goethe-University, Theodor-Stern-Kai 7, Haus 8B, D-60590, Frankfurt, Germany.

E-mail address: [kohnen@em.uni-frankfurt.de](mailto:kohnen@em.uni-frankfurt.de) (T. Kohnen).

Peer review under responsibility of the Iranian Society of Ophthalmology.

<https://doi.org/10.1016/j.joco.2018.03.001>

2452-2325/Copyright © 2018, Iranian Society of Ophthalmology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

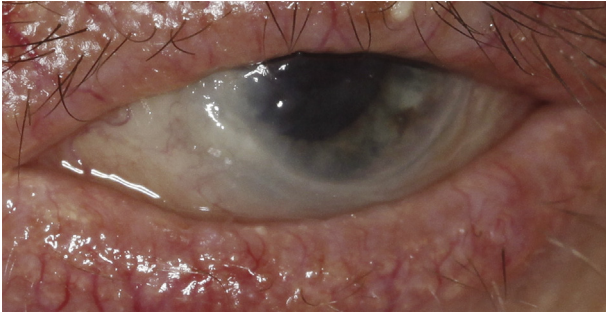


Fig. 1. Slit-lamp photo of the right eye. The patient revealed mild injection of the conjunctiva, a circumscribed corneal ulceration close to the limbus, and small reddish nodules of lymphoid tissue (Phlyctenule) within the anterior stroma of the corneal peripheral zone and limbal area.

conjunctiva, circumscribed peripheral corneal ulceration close to the limbus, and nodular thickening of the surrounding stromal and subconjunctival tissue of both eyes (Figs. 1 and 2). The anterior chamber was unremarkable and without signs of inflammation.

Past medical history was positive for arterial hypertension, chronic obstructive pulmonary disease (COPD). Recently diagnosed pulmonary TB with positive purified protein derivative (PPD) tine test and nodules in the pulmonary upper lobes were evident on the chest x-ray. Furthermore, sputum acid-fast bacilli (AFB) stains and cultures were positive for MBT. The patient was under a 4-drug anti-tuberculosis treatment with ethambutol (1 g/day), isoniazid (300 mg/day), rifampicin (600 mg/day), and pyrazinamide (1.5 g/day). Microbiological cultures of the corneal tissue on agar-based media of Middlebrook 7H10 were negative for MBT and other microbial pathogens. Enzyme-linked immunosorbent assay (ELISA) of blood and corneal samples showed significantly elevated levels of IgM and IgA for MBT. ELISA testing was performed using highly purified A 60 antigen-kits extracted from mycobacteria with 1/1000 diluted serum and corneal samples. Other ocular tissues such as uvea or retina were spared.

Based on the conjunctival and corneal findings, the patient was treated topically with Polyspectran® eye drops

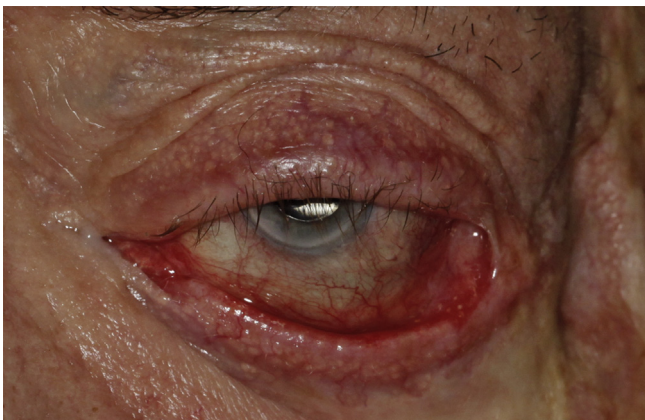


Fig. 2. Slit-lamp photo of the left eye shows moderate conjunctival hyperemia and superficial peripheral corneal ulceration in the lower nasal quadrant.

(polymyxin-B-sulfat + neomycin sulfat + gramicidin) q.i.d. (4 times a day), coupled with DEXA EDO® eye drops (Dexamethasone dihydrogenphosphat-Dinatrium) q.i.d. and Bepanthen® ointment (sodium hyaluronat + dexpanthenol) at night for 2 weeks on both eyes. During that time, signs of inflammation completely resolved.

## Discussion

MBT can be considered a direct and indirect (primary and secondary) pathogen to the eye and other organs/structures, such as skin and joints.<sup>6,7</sup> Ocular lesions can be caused by a direct invasion of microorganisms (active infection) or result from immunologic reactions (delayed hypersensitivity type IV) in absence of the infectious agent.<sup>8</sup> Overall, corneal involvement is rare. There are some reports of active conjunctival and corneal TB. Lahiri and colleagues reported a child with phlyctenular conjunctivitis in the presence of an active tuberculosis infection.<sup>9</sup> In addition, Honarvar et al. described a case of keratitis attributable to the non-tuberculous mycobacterium aurum.<sup>10</sup> Patients with immunologic reactions to MBT usually present with unilateral peripheral ulcerative keratitis (PUK) or immune stromal interstitial keratitis; however, bilateral central interstitial or disciform keratitis has also been described.<sup>11,12</sup> The differential diagnosis includes infectious diseases like Lyme disease, Epstein-Barr virus, herpes simplex virus, varicella-zoster virus or syphilis, and non-infectious conditions such as rheumatoid arthritis.<sup>11,12</sup>

Polymerase chain reaction (PCR) is a rapid technique for the diagnosis of TB with a high specificity for pulmonary (98% if AFB positive, 40–77% if AFB negative)<sup>13</sup> and extra-pulmonary TB (93.7–100%).<sup>14</sup> However, culture still remains the gold standard of MBT laboratory diagnosis (National Institute for Health and Clinical Excellence, 2006). In secondary autoimmune-induced forms, ELISA is the standard technique for diagnosis of ocular TB.

In conclusion, the present report demonstrates that MBT is able to initiate a delayed autoimmune response within the conjunctival and corneal tissue during an intensive phase of anti-tuberculosis treatment. Therefore, ocular TB should be considered in the differential diagnosis of chronic, atypical ulcerative, or interstitial keratitis. The favorable outcome was achieved in spite of the devastating nature of the infection and its autoimmune response is attributed to rapid diagnosis using ELISA and appropriate treatment with the combination of topical steroids and antibiotics, along with precise post-treatment controls.

## References

- Mjid M, Cherif J, Ben Salah N, et al. Epidemiology of tuberculosis. *Rev Pneumol Clin*. 2015;71(2-3):67–72.
- Yoo IK, Choung RS, Hyun JJ, et al. Incidences of serious infections and tuberculosis among patients receiving anti-tumor necrosis factor- $\alpha$  therapy. *Yonsei Med J*. 2014;55(2):442–448.
- Lara LP, Ocampo Jr V. Prevalence of presumed ocular tuberculosis among pulmonary tuberculosis patients in a tertiary hospital in the Philippines. *J Ophthalmic Inflamm Infect*. 2013;3(1):1.

4. Velasco e Cruz AA, Chahud F, Feldman R, Akaishi PM. Posterior scleral tuberculoma: case report. *Arq Bras Oftalmol*. 2011;74(1):53–54.
5. Mahyudin M, Choo MM, Ramli NM, Omar SS. Ocular tuberculosis initially presenting as central retinal vein occlusion. *Case Rep Ophthalmol*. 2010;1(1):30–35.
6. Purice S, Mitu S, Popescu T, Guran M, Vintila M, Sutja G. The relationship between systemic lupus erythematosus and tuberculosis. *Med Interne*. 1982;20(3):191–196.
7. Marques CD, Duarte AL, de Lorena VM, et al. Evaluation of an interferon gamma assay in the diagnosis of latent tuberculosis infection in patients with rheumatoid arthritis. *Reumatol Int*. 2009;30(1):57–62.
8. Butt T, Ahmad RN, Kazmi SY, Afzal RK, Mahmood A. An update on the diagnosis of tuberculosis. *J Coll Physicians Surg Pak*. 2003;13(12):728–734.
9. Lahiri K, Landge A, Gahlowt P, Bhattar A, Rai R. Phlyctenular conjunctivitis and tuberculosis. *Pediatr Infect Dis J*. 2015;34(6):675.
10. Honarvar B, Movahedan H, Mahmoodi M, Sheikholeslami FM, Farnia P. Mycobacterium aurum keratitis: an unusual etiology of a sight-threatening infection. *Braz J Infect Dis*. 2012;16(2):204–208.
11. Kamal S, Kuar R, Kumar S, Goel R. Bilateral interstitial keratitis and granulomatous uveitis of tubercular origin. *Eye Contact Lens*. 2014;40(2):e13–e15.
12. Yagci A. Update on peripheral ulcerative keratitis. *Clin Ophthalmol*. 2012;6:747–754.
13. Cheng VCC, Yew WW, Yuen KY. Molecular diagnostics in tuberculosis. *Eur J Clin Microbiol Infect Dis*. 2005;24(11):711–720.
14. De Benedetti ZME, Carranza LB, Gotuzzo HE, Rolando CI. Ocular tuberculosis. *Rev Chilena Infectol*. 2007;24(4):284–295.