

Case Studies of *Mycobacterium abscess* Infection after Laser *in Situ* Keratomileusis

Yixin Wang^{1,2}, Yang Zhang³, Zhirong Lin^{1,2}, Huping Wu^{1,2*}, Cheng Li^{1,2*}

¹Eye Institute & Affiliated Xiamen Eye Center, School of Medicine, Xiamen University, Xiamen, China

²Fujian Provincial Key Laboratory of Ophthalmology and Visual Science, Xiamen, China

³Beijing Institute of Ophthalmology, Beijing Tongren Hospital, Capital Medical University, Beijing, China

Email: *cheng-li@xmu.edu.cn, *wuhuping123@163.com

How to cite this paper: Wang, Y.X., Zhang, Y., Lin, Z.R., Wu, H.P. and Li, C. (2019) Case Studies of *Mycobacterium abscess* Infection after Laser *in Situ* Keratomileusis. *Case Reports in Clinical Medicine*, 8, 307-314.

<https://doi.org/10.4236/crcm.2019.812038>

Received: November 29, 2019

Accepted: December 21, 2019

Published: December 24, 2019

Copyright © 2019 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Background: Infectious keratitis after refractive surgery is uncommon, and mycobacterium abscess has never been observed in corneal infections in China. **Purpose:** To propose an unusual presentation of two cases about *Mycobacterium abscess* infection after laser *in situ* keratomileusis (LASIK). **Participants:** Both cases 1 and 2 were females who exhibited a corneal ulceration after LASIK in the same hospital. **Methods:** The first patient in the study was a 28-year-old woman who underwent Epi-LASIK surgery in both eyes. She developed an infectious corneal ulcer in one eye after 50 days post-surgery. She was referred to our out-patient clinic 3 months post-surgery with corneal perforation, and was treated with a therapeutic penetrating keratoplasty. The second patient was a 27-year-old woman who developed infectious keratitis in one eye after 2 months after bilateral LASIK and was referred to us 3 months later. **Results:** Cultures in both the cases were identified as a *Mycobacterium abscess*, and case 1 was treated with penetrating keratoplasty eventually, while case 2 recovered after sensitive treatment. **Conclusions:** Infectious keratitis after refractive surgery is uncommon, and *Mycobacterium abscess* has never been observed in corneal infections. An accurate diagnosis and identification of the causative agent is very important.

Keywords

LASIK, *Mycobacterium abscess*, Infection

1. Introduction

In recent years, with the extensive development of excimer laser *in situ* keratomileusis (LASIK), the incidence of postoperative complications of LASIK is in-

*Corresponding author.

creasing, and the reported incidence of postoperative infectious keratitis is 0.1% to 0.2% [1], but the true incidence may be much higher than the reported cases. *Non-tuberculous mycobacterium* (NTM) is one of the main pathogenic microorganisms leading to postoperative infectious keratitis, among which *Mycobacterium turtle* (34.72% [2]) and *Sporadic mycobacterium* are the most common. In 1965 Turner and Stinson [3] reported the first case of non-tuberculous mycobacterial keratitis (NTMK) occurring after the removal of the foreign body in the cornea, and identified as an incidental mycobacterial infection. The first case of NTM keratitis after LASIK was reported by Reviglio [4] in 1998, and the first case of NTM keratitis in China was reported by Qingfeng Liang *et al.* in 2005 [5].

However, the clinical case reports of *Mycobacterium abscess keratitis* (MAK) following LASIK (*Mycobacterium abscessus keratitis*), are still very few, when related to etiology and pathology research [6]. *Mycobacterium abscess* (MA) is a type of the mycobacterium tuberculosis (*non-tuberculous mycobacteria*, NTM), widely distributed in the soil, water and animals. MA can cause infectious diseases of the eyes as an opportunistic pathogen.

To the best of our knowledge, there are a few reports about *Mycobacterium abscess* bacterial keratitis after LASIK. We received two cases of *Mycobacterium abscess* infection leading to keratitis after LASIK, and the reports are as follows.

2. Case 1

A 28-year-old woman was referred for gradually decreased visual acuity and sustaining pain in her right eye after 50 days after her LASIK from another hospital. She was treated with systemic antiviral drugs and antibiotics for 20 days in the local hospital, but her symptoms didn't disappear after the treatment. Her left eye vision decreased from 20/20 to 10 cm in front of her eyes.

Examination: The vision of right eye was 20/20, the vision of left eye was 10 cm in front of eye. However, the intraocular pressure was normal for both. On examination, the epithelial was found to be defected with a central infiltrate, the left eyelid had a swelling, conjunctival mixed congestion (++++), and corneal flap edema was obvious. The corneal flap slightly displaced to the nasal side, and several different sized round dense white ulcers were observed in the stroma of the corneal flap. The focal points were closely connected, gathering into a deep round infiltration, and an obvious anterior abscess was observed (**Figure 1(A)** and **Figure 1(B)**).

Confocal corneal microscope showed the presence of a large number of inflammatory cells in the lesion (highly reflective), and the density of the lesion was much higher than that of fungal corneal ulcer that have structures similar to mycelia, so it was suspected to be special bacterial infection (**Figure 1(C)**).

The results of corneal biopsy were negative. After routine antibiotic treatment, she was transferred to the Beijing Tongren hospital for removal of the corneal infection lesions in her left eye. After the lesions were removed, *Giemsa staining* (**Figure 1(F)**) was performed on the smears of the lesions. The lesions were cauterized with 5% iodine tincture, washed with 3% amikacin sulfate, and injected

with 0.5 ml 3% amikacin sulfate injection under conjunctiva. 1% amikacin sulfate and 0.3% levofloxacin were used to spot the eye at the frequency of 1 time/h for 48 hours. The corneal infection gradually improved. Oral clarithromycin tablets were used in the dose—100 mg each time and 3 times/d for 1 week. After 6 weeks of treatment, corneal infection was completely controlled with corneal scarring, and corrected vision of the left eye was 10 cm in front of eye (**Figure 1(D)**).

Laboratory examination: Cultures of fungal and amoebic were negative, germiculture was positive. Bacteria grew in the modified roche medium, colonies were yellow, and the smear was positive in acid-fast stain (**Figure 1(E)**). Besides, after 16 identification experiments, the results analysis confirmed as *Mycobacterium abscess* subspecies. At the same time, the bacteria were sent to the tuberculosis reference laboratory for identification, whose results were also found to be *mycobacterium abscess* subspecies.

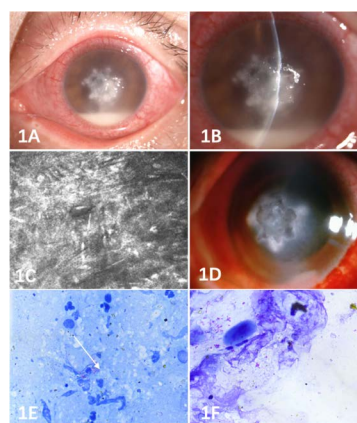


Figure 1. Case 1. A 28-year-old female was examined 50 days after LASIK. (A) and (B), Slit-lamp photograph showing a central ulcer with obvious hypopyon; (C) Multiple slender short fibrous structures were observed under confocal microscope; (D) After 6 weeks of treatment, corneal scarring can be seen through slit-lamp; (E) Smear was positive in acid-fast stain and demonstrated the presence of acid-fast bacilli; (F) Giemsa staining was performed on the smears of the lesions.

3. Case 2

A 27-year-old healthy female underwent LASIK in both eyes, and after 3 months, she had an uneventful postoperative course in her right eye. She suffered from a persistent red pain, photophobia and decreased vision in her right eye, and showed no improvement after administering glucocorticoids. Her right eye vision decreased from 20/20 to 20/200, after which she was transferred to our hospital.

Examination: The vision of left eye was 20/20, the vision of right eye was 20/200, while the binocular pressure was normal. The corneal flap of the left eye was in place. Her right eyelid exhibited a moderate swelling, with conjunctival mixed congestion (+++). The corneal flap was edematous, and several round dense gray infiltration foci were observed in the temporal side of the partial pu-

pil. Corneal ulcer lesion showed clear boundary under slit lamp, with dense sharp infiltration to 1/3 layer of cornea, with relatively clear boundary. KP (–), aqueous humor flash (–) (**Figure 2(A)** and **Figure 2(B)**).

Confocal microscope: Multiple slender short fibrous structures were observed in the lesion, slightly thinner than the fungal hyphae and corneal nerve fibers, surrounded by a large number of highly reflective infiltration of inflammatory cells, and it was suspected to be infection of special species (**Figure 2(C)** and **Figure 2(D)**).

After prescribing antibiotics, the patient was transferred to Beijing Tongren hospital to remove the corneal infection lesions in the right eye, and the lesions was smeared with *Giemsa staining* (**Figure 2(F)**), which showed presence of slim bacilli with positive acid-fast staining. The clinical diagnosis was non-tuberculous mycobacterial keratitis in the right eye after LASIK. She got the same treatment as case 1. After 6 weeks of treatment, the corneal infection was completely controlled and corneal cloud formed. The left eye had a corrected vision of 20/100.

Laboratory examination: Germiculture was positive with bacteria growing in the modified roche medium, colonies were yellow and smear was positive in acid-fast stain (**Figure 2(E)**). The 16 identification experiments showed the result of *mycobacterium abscess* subspecies infection.

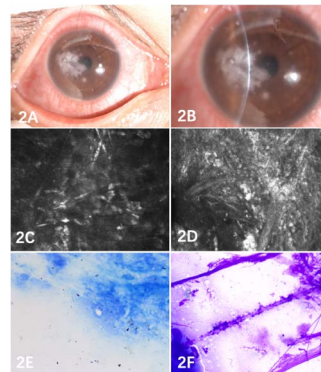


Figure 2. Case 2. A 27-year-old female was seen 3 months after LASIK. (A) and (B) Clinical photograph of stromal interface granularity; (C) and (D) Confocal microscope showed the ulcer was surrounded by a large number of highly reflective inflammatory cells infiltration and it was suspected to be infection of special species; (E) Smear was positive in acid-fast stain and demonstrated the presence of acid-fast bacilli; (F) Giemsa staining was performed on the smears of the lesions.

4. Discussion

Few reports were published relating to infectious keratitis after laser refractive surgery, and most of these cases were bacterial infection. With the increasing amounts of laser refractive procedures, the incidence of postoperative infectious cases will rise up. NTM is becoming more common than tuberculosis in external ocular infections. Also, we found that *mycobacterium abscess* was less common pathogen of infectious disease, especially in ocular surface.

Both patients suffered from an extremely rare complication after LASIK, but both patients were young women with good immunity. It shows the potential infection risk of LASIK and the necessity of strict adherence to aseptic techniques. Both the cases presented in this study showed a delayed onset *Mycobacterium abscess* keratitis after LASIK; however, the source of the infection still remains a mystery as mycobacterial infection is commonly found at the skin, lung and large-area exposure wound, etc. This is rare occurrence of a *Mycobacterium abscess* in the eye infection, and these two cases occurred in the same hospital, which has drawn great attention to the surgical procedures. With the increasing popularity of laser surgery, the incidence of postoperative infectious complications will certainly increase. Therefore, this paper reiterates the importance of postoperative care after refractive surgery. The clinical manifestations of this disease are similar to that of keratitis caused by fungi, acanthamoeba, herpes simplex virus and other bacteria, which makes an easy misdiagnosis and miss of MAK [7]. It is reported that HAIN genotyping kit and hsp65 gene sequencing method can be identified to specific subspecies, while the results of gene chip technical identification can only be identified to the level of complex group, but not to specific subspecies [8]. Therefore, the analysis and research on the etiology, histopathology and ultrastructure of MAK will be helpful for clinicians to correctly understand and diagnose the disease. It also emphasizes the importance of smear staining, pathogen culture and drug sensitivity test for corneal ulcer lesions before treatment [9].

In this study, it was found that there was a long incubation period after MAK infection, and most of them were chronic. The reason may be that the peptidoglycan layer of mycobacterium cell wall was dissolved and the cell wall was damaged and lost due to the treatment of a large number of antibiotics. It has been reported that even though the cell wall gets damaged or even completely lost, MAK still retains a certain virulence, and can evade the attack of the immune system and remain in the cornea for a long time, making the disease become chronic, prolonged and recurrent [10] [11]. This may explain the chronic and prolonged clinical manifestations of these two infected patients, which were eventually controlled by iodine tincture burning and corneal transplantation.

Nontuberculous mycobacterium keratitis is characterized by round subepithelial infiltrations or white infiltrations within the stroma at the early stage of infection, or multifocal round infiltrations under the flap with irregularly pinnate borders. With the progression of the disease, the corneal lesion gets fused into an ulceration under the flap in the later stage, and the infiltrated corneal flap can be necrotic and gets dissociated in the severe cases. Some patients with delayed corneal infection can develop crystalline keratopathy. Patients with moderate or severe disease often have significant anterior chamber reactions [12].

In laboratory examination, the incubation time of NTM is longer than that of common bacteria, and the determination result usually takes more than 1 week. Therefore, acid-fast staining of the corneal scraping is the basic method for rapid

diagnosis of NTM keratitis. The treatment of NTM keratitis after LASIK should emphasize the principle of combination of systemic treatment, combination of drugs and surgical treatment, and prohibition of glucocorticoids in acute phase [13].

Recommended treatment: 1% - 2% amikacin eye drops are preferred, one time every 30 - 60 min, continuously applied for 48 h, and then reduced appropriately. For patients with moderate or severe severity, gatifloxacin eye drops can be combined with 0.3% amikacin, sometimes 0.5 ml of 4% amikacin can be injected under the conjunctiva, if necessary. Severe patients should be treated with triple drug therapy. On the basis of above two drugs, oral clarithromycin tablets or azithromycin tablets should be given simultaneously, both at a dose of 500 mg bid [14] [15]. Loose corneal flap could be removed if the corneal flap no longer attaches to the corneal matrix. Lamellar or penetrating keratoplasty may be performed in patients who are already infected with the deep stromal layer below the flap and if drug treatment is unable to control the symptoms.

This report of two patients showed similar clinical progress. Although, sensitive antibiotics control the deterioration of the disease, transplantation still needs to be performed in patients. They face the risk of various adverse consequences, including the graft rejection, steroid related complications and graft injury [16]. Fortunately, our patients showed no signs of recurrence of keratitis during the following 6 months of follow-up.

Although the incidence of corneal infection after LASIK is rare, the epithelial barrier dysfunction and the use of anti-inflammatory drugs increase the sensitivity of the cornea to microorganisms. Corticosteroid eye drops are used to manage corneal inflammation after surgery, which lead to local immunosuppression of the ocular surface, leaving the cornea vulnerable to bacteria. In addition, corticosteroids may alter the course of infectious keratitis, leading to misdiagnosis of different types of postoperative inflammatory complications, such as diffused stratiform keratitis. Therefore, it is important to detect the corneal infection and start treatment early after refractive surgery.

Acknowledgements

The authors thank School of Medicine, Xiamen University and Xiamen Eye Center for allowing us to use their services and facilities. The content of the manuscript is solely the responsibility of the authors.

Contributors

Yixin W was chiefly responsible for concept and writing of the cases described within the article. Yang Z and Zhirong Lin provided the examination images. Huping Wu and Cheng L were responsible for planning, contributed to the discussion section and assisted final reviewing of the article.

Funding

National Natural Science Foundation of China (81770891); National Natural

Science Foundation of China (81570815); The Huaxia Translational Medicine Fund for Young Scholars (2017-A-001).

Patient Consent for Publication

Obtained.

Provenance and Peer Review

Not commissioned; externally peer reviewed.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Kouyoumdjian, G.A., *et al.* (2001) Infectious Keratitis after Laser Refractive Surgery. *Ophthalmology*, **108**, 1266-1268. [https://doi.org/10.1016/S0161-6420\(01\)00600-5](https://doi.org/10.1016/S0161-6420(01)00600-5)
- [2] Petersen, H. and Seiler, T. (1999) Laser *in Situ* Keratomileusis (LASIK). Intraoperative and Postoperative Complications. *Ophthalmologe*, **96**, 240-247. <https://doi.org/10.1007/s003470050399>
- [3] I, T.L.S. (1965) Mycobacterium Fortuitum as a Cause of Corneal Ulcer. *American Journal of Ophthalmology*, **60**, 329-331. [https://doi.org/10.1016/0002-9394\(65\)90934-7](https://doi.org/10.1016/0002-9394(65)90934-7)
- [4] Reviglio, V., *et al.* (1998) *Mycobacterium chelonae* Keratitis Following Laser *in Situ* Keratomileusis. *Journal of Refractive Surgery*, **14**, 357-360.
- [5] Liang, Q.F. (2005) A Case of Nontuberculous Mycobacterial Keratitis after LASIK. *Chinese Journal of Ophthalmology*, **141**, 2.
- [6] Yin, L., *et al.* (2010) Pathological Study of *Mycobacterium abscessus* Keratitis. *Chinese Journal of Ophthalmology*, **46**, 829-833.
- [7] Ko, J., *et al.* (2017) Delayed Onset Mycobacterium Intracellulare Keratitis after Laser *in Situ* Keratomileusis: A Case Report and Literature Review. *Medicine (Baltimore)*, **96**, e9356. <https://doi.org/10.1097/MD.00000000000009356>
- [8] Heining, A.D., *et al.* (2004) Detection and Identification of the Pathogenic Cause of a Brain Abscess by Molecular Genetic Methods. *Anaesthetist*, **53**, 830-835. <https://doi.org/10.1007/s00101-004-0729-6>
- [9] Daines, B.S., *et al.* (2003) Rapid Diagnosis and Treatment of Mycobacterial Keratitis after Laser *in Situ* Keratomileusis. *Journal of Cataract & Refractive Surgery*, **29**, 1014-1018. [https://doi.org/10.1016/S0886-3350\(02\)01613-9](https://doi.org/10.1016/S0886-3350(02)01613-9)
- [10] Chung, S.H., *et al.* (2006) *Mycobacterium abscessus* Keratitis after LASIK with IntraLase Femtosecond Laser. *Ophthalmologica*, **220**, 277-280. <https://doi.org/10.1159/000093084>
- [11] Freitas, D., *et al.* (2003) An Outbreak of *Mycobacterium chelonae* Infection after LASIK. *Ophthalmology*, **110**, 276-285. [https://doi.org/10.1016/S0161-6420\(02\)01643-3](https://doi.org/10.1016/S0161-6420(02)01643-3)
- [12] Jarzembowski, J.A. and Young, M.B. (2008) Nontuberculous Mycobacterial Infections. *Archives of Pathology & Laboratory Medicine*, **132**, 1333-1341.
- [13] Rodriguez, B., Holzinger, K.A. and Le, L.H. (2006) *Mycobacterium chelonae* Kerati-

tis after Laser-Assisted Subepithelial Keratectomy. *Journal of Cataract & Refractive Surgery*, **32**, 1059-1061. <https://doi.org/10.1016/j.jcrs.2006.03.011>

- [14] Chung, M.S., *et al.* (2000) *Mycobacterium chelonae* Keratitis after Laser *in Situ* Keratomileusis Successfully Treated with Medical Therapy and Flap Removal. *American Journal of Ophthalmology*, **129**, 382-384. [https://doi.org/10.1016/S0002-9394\(99\)00390-6](https://doi.org/10.1016/S0002-9394(99)00390-6)
- [15] Tyagi, A.K., Kayarkar, V.V. and McDonnell, P.J. (1999) An Unreported Side Effect of Topical Clarithromycin When Used Successfully to Treat *Mycobacterium avium*-Intracellulare Keratitis. *Cornea*, **18**, 606-607. <https://doi.org/10.1097/00003226-199909000-00015>
- [16] Chu, H.S., *et al.* (2015) Nontuberculous Mycobacterial Ocular Infections—Comparing the Clinical and Microbiological Characteristics between *Mycobacterium abscessus* and *Mycobacterium massiliense*. *PLoS ONE*, **10**, e0116236. <https://doi.org/10.1371/journal.pone.0116236>