American Journal of Ophthalmology Case Reports 22 (2021) 101088

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Descemet stripping endothelial keratoplasty after cytomegalovirus corneal endotheliitis and immunosuppression for Mooren's ulcer

Koji Ueda [1], Takashi Ono [1], Tetsuya Toyono, Junko Yoshida, Toshikatsu Kaburaki, Takashi Miyai [*]

Department of Ophthalmology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

ARTICLE INFO

Keywords:
Corneal ulcer
Keratitis
Corneal transplantation
Immunosuppressive agents
Visual acuity
Cytomegalovirus infections

ABSTRACT

Purpose: The aim of this report was to describe a case of cataract surgery and Descemet stripping automated endothelial keratoplasty (DSAEK) after cytomegalovirus (CMV) corneal endotheliitis and bullous keratopathy (BK) following immunosuppressive treatment for Mooren's ulcer.

Observations: A 64-year-old man was referred to our hospital because of peripheral ulcerative keratitis in his left eye. He had a history of trabeculectomy for open angle glaucoma in his left eye. He was diagnosed with Mooren's ulcer and treated with topical betamethasone and tacrolimus with systemic cyclosporine. The corneal ulcer improved, but the peripheral cornea thinned from 6 to 12 and 0–2 o'clock. Five months later, cells were observed in the left anterior chamber, and real-time polymerase chain reaction examination of the aqueous humor showed CMV-DNA-positive results. The patient was diagnosed with CMV corneal endotheliitis, and oral ganciclovir was administered. Fifteen months after the initial presentation, BK appeared with decreased vision to 20 cm/n. d. After confirmation of negative CMV-DNA in the aqueous humor, DSAEK was performed following cataract surgery. The postoperative visual acuity recovered to 0.3. Mooren's ulcer exacerbation and CMV corneal endotheliitis did not recur postoperatively.

Conclusions and Importance: This is the first report of a case in which a patient with Mooren's ulcer developed BK due to CMV corneal endotheliitis and required DSAEK. Cataract surgery and DSAEK could be performed without issue by creating the main wound and side ports in a manner that avoids the thinned parts of the cornea.

1. Introduction

Mooren's ulcer is a progressive and painful idiopathic peripheral corneal ulcer. The treatment for Mooren's ulcer includes steroids and immunosuppressive agents, and corneal transplantation is required in case of corneal perforation.[1,2] In contrast, adverse effects of long-term administration of steroids and immunosuppressive agents have also been reported, such as cytomegalovirus (CMV) corneal endotheliitis,[3,4] resulting in bullous keratopathy (BK) after anterior uveitis.[5] Furthermore, it is difficult to perform corneal transplantation in patients with Mooren's ulcer because the peripheral cornea of these patients is often very thinned and easy to perforate. Therefore, careful observation and ingenuity are required for the clinical decision of corneal transplantation for patients with Mooren's ulcer. However, our research showed that no study has reported Descemet stripping automated endothelial keratoplasty (DSAEK) performed for patients with Mooren's ulcer with BK due to CMV corneal endotheliitis. Herein, we report our experience of a case in which cataract surgery and DSAEK were successfully performed for BK owing to CMV corneal endotheliitis after immunosuppressive treatment for Mooren's ulcer.

1.1. Case report

A 64-year-old man with a peripheral corneal ulcer in his left eye was referred to our hospital. He had bilateral primary open angle glaucoma and had undergone trabeculectomy of the left eye 5 years earlier. He visited a local ophthalmologist with the chief complaint of conjunctival hyperemia and pain and afterward, our hospital for consultation. At the initial presentation, hyperemia and cells inside the anterior chamber were observed in his left eye (Fig. 1a and b). A corneal ulcer with cell infiltration in the superior cornea was also found. The best-corrected visual acuity (BCVA) of his left eye was 0.4. As a result of systemic

* Corresponding author. Department of Ophthalmology, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-8655, Japan.
E-mail address: tmiy-tky@umin.ac.jp (T. Miyai).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.ajoc.2021.101088
Received 12 May 2020; Received in revised form 21 October 2020; Accepted 4 April 2021

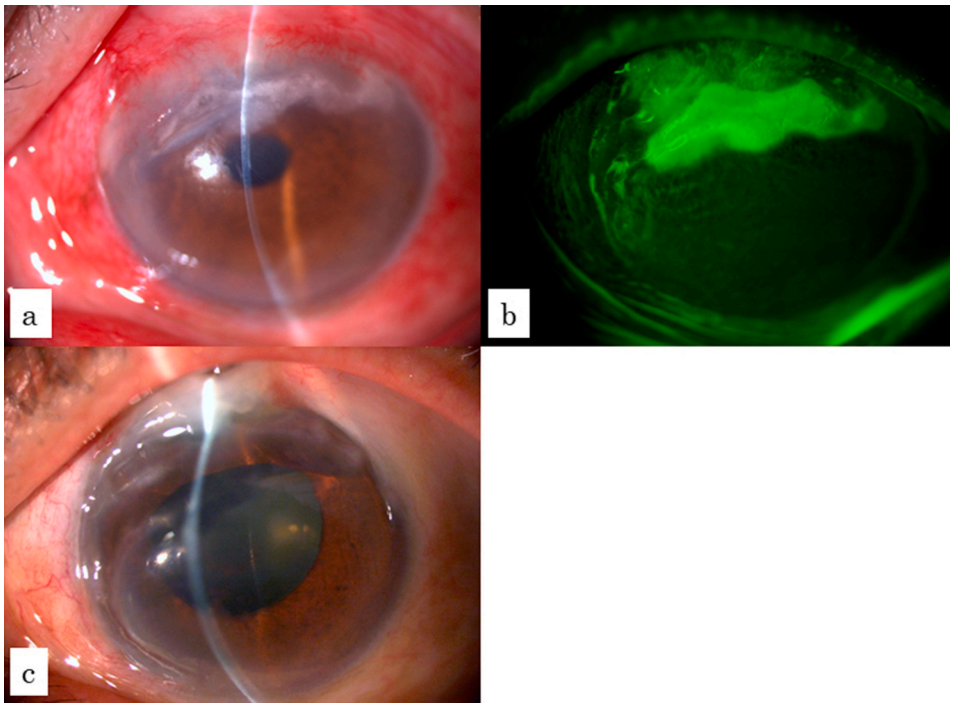

Fig. 1. Photographs of the anterior segment of the patient at the occurrence of Mooren's ulcer and of cytomegalovirus (CMV) corneal endotheliitis.
a. Photograph of the anterior segment of the patient at the occurrence of Mooren's ulcer. Hyperemia and cells inside the anterior chamber are observed in his left eye. b. Fluorescein staining image of the anterior segment at the occurrence of Mooren's ulcer. Broad corneal epithelial defect is observed in the superior cornea. c. Photograph of the anterior segment of the patient at the occurrence of CMV corneal endotheliitis. Cells and massive broad keratic precipitates in the anterior chamber are observed in the patient's left eye with hyperemia.

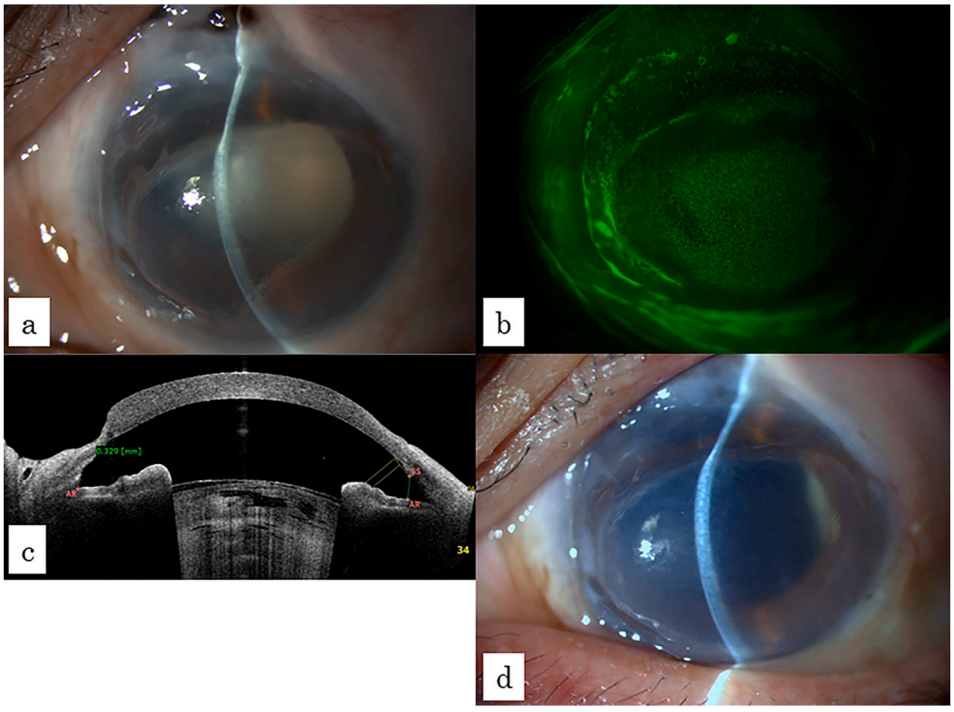

Fig. 2. Photographs of the anterior segment of the patient after the occurrence of bullous keratopathy following cytomegalovirus corneal endotheliitis.
a. Photograph of the anterior segment of the patient with bullous keratopathy. The cornea became thick and hazy owing to bullous keratopathy. No hyperemia or cells in the anterior chamber are observed. b. Fluorescein staining image of the anterior segment. Corneal edema is observed. No corneal epithelial defect is observed. c. Image of anterior-segment optical coherence tomography of the patient with bullous keratopathy. Central corneal thickness is 815 μm, and the thinnest corneal thickness is 329 μm d. Photograph of the anterior segment of the patient with bullous keratopathy after cataract surgery.

medical examination, including for collagen disease, he was diagnosed with Mooren's ulcer, and treatment was initiated with topical 0.1% betamethasone 8 times daily, 0.1% tacrolimus 4 times daily, 0.3% gatifloxacin 4 times daily, and systemic cyclosporine 400 mg/day. The corneal ulcer resolved after 3 months, although thinning of the cornea was observed at 0 to 2 and 6 to 12 o'clock.

Two months later, he complained of reduced visual acuity in the left eye. Cells and massive broad keratic precipitates (KPs) in the anterior chamber were observed in his left eye with conjunctival hyperemia (Fig. 1c). The BCVA in the left eye was 0.3. Because real-time polymerase chain reaction (PCR) examination of the aqueous humor of the left eye revealed 1.5×10^7 copies/ml of CMV-DNA, he was diagnosed with CMV corneal endotheliitis. Therefore, topical tacrolimus and systemic cyclosporine were discontinued, and oral valganciclovir (900 mg/day) was administered for 6 weeks with topical 0.1% betamethasone eye drops 6 times daily. Three months later, real-time PCR revealed remaining 4.0×10^4 copies/mL of CMV-DNA in the aqueous humor, and oral valganciclovir was administered for another 6 weeks. Four months later, CMV-DNA was not detected by real-time PCR in the aqueous humor, and no relapse of the anterior uveitis was observed with

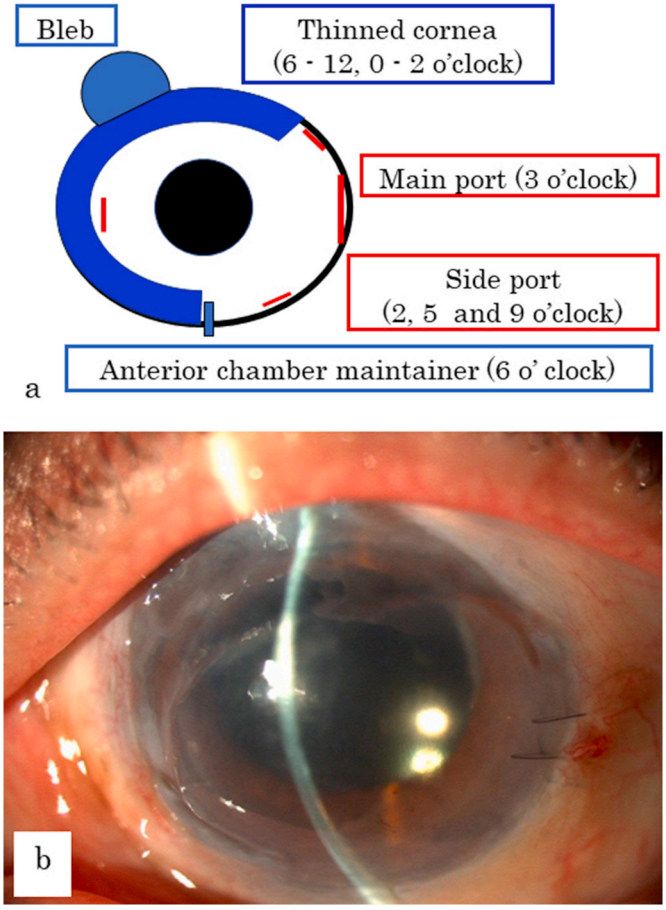

Fig. 3. Schematic diagram of Descemet stripping automated endothelial keratoplasty (DSAEK) of the patient and a photograph of the anterior segment of the patient after DSAEK.
a. Schematic diagram of DSAEK for the patient. The cornea was thinned at 6 to 12 and 0 to 2 o'clock, and conjunctival bleb after trabeculectomy existed at 11 o' clock. b. Photograph of the anterior segment of the patient after DSAEK.

use of betamethasone 6 times daily.

However, 15 months after the first presentation, corneal edema occurred in the left eye (Fig. 2a and b). Central corneal thickness was increased to 815 μm and visual acuity decreased to 20 cm/n. d. in the left eye (Fig. 2c). Because CMV-DNA was negative in the aqueous humor, the main reason of deteriorated visual acuity was considered to be BK with cataract. Therefore, cataract surgery was first performed through a 2.75-mm sclerocorneal incision at 4 o'clock with local anesthesia. Corneal epithelial removal, 0.1% trypan blue injection into the anterior chamber, and a hands-free chandelier endo-illumination system were used to help visualize the intraocular procedures. With a 27-gauge needle, two small holes were created at the 8 and 10 o' clock positions 3.5 mm from the limbus, through which the chandelier fiber optic probes (BrightStar endoilluminator, DORC International, Zuidland, The Netherlands) were inserted. After phacoemulsification and aspiration, the intraocular lens was inserted in the capsule. After cataract surgery, the BCVA increased to 0.03, and no recurrence of CMV corneal endotheliitis or Mooren's ulcer was observed (Fig. 2d).

Two months after the cataract surgery, DSAEK was performed with local anesthesia. The patient's left eye had a bleb at 11 o'clock, and peripheral corneal thinning was observed from 6 to 12 and 0 to 2 o'clock (Fig. 3a). Ingenuity was required to create the corneal incisions in a manner that would avoid the peripheral thin cornea. We made a 5 mm corneal main incision (3 o'clock) and three side ports (2, 5, 9 o'clock). The 9 o'clock side port was created at the center side from the peripheral thinning area. Leaving an anterior chamber maintainer at 6 o'clock, Descemet's membrane stripping was conducted with a reverse Sinskey hook through the 2 o'clock side port, and 8-mm endothelial graft was inserted using the pull-through technique with a Busin glide and DSAEK forceps. After two 10–0 nylon sutures at the main incision, filtered air was injected into the anterior chamber. Postoperatively, the BCVA improved to 0.3 and corneal thickness decreased to 597 μm (Fig. 3b). Corneal endothelial cell density was 938 cells/mm.[2] During the 15-month postoperative follow-up, no CMV corneal endotheliitis recurred with betamethasone and gatifloxacin 2 times daily administration.

2. Discussion

We experienced the case of a patient who had CMV corneal endotheliitis after immunosuppressive therapy for Mooren's ulcer and finally required DSAEK. There have been several previous reports of DSAEK and Descemet membrane endothelial keratoplasty (DMEK) for BK due to CMV corneal endotheliitis[6–9]; however, there has been no report of DSAEK for BK with CMV corneal endotheliitis following Mooren's ulcer. It is often technically difficult to perform DSAEK when the cornea is thinned or strongly clouded. Several technical modifications, such as removal of the recipient epithelium and biological staining of the donor and recipient tissues with trypan blue, have been reported to improve intraocular visibility under conventional microscopy.[10–12] In our case, DSAEK was performed without issue by creating a wound and side ports that avoided the peripheral thin corneal region. DSAEK was performed because DMEK had not yet been introduced in our hospital at that time. Additionally, we also safely performed phacoemulsification and aspiration with intraocular lens insertion in the capsule using a chandelier before DSAEK. Cataract surgery was performed separately because we aimed to perform the corneal endothelial transplant with less intraocular inflammation than what could be caused by combined cataract surgery. Mooren's ulcer has been reported to occur after corneal trauma and surgery.[13] A corneal ulcer starts in the periphery and may progress centrally or circumferentially to involve the entire cornea.[14–16] Furthermore, some reports have shown that cataract surgery in eyes with Mooren's ulcer is safe with no disease reactivation immediately postoperatively, and disease-free intervals of 6 months or longer before surgery have been reported along with scleral incisions with favorable outcomes.[17,18] In the current study, the trabeculectomy of the left eye that the patient had previously undergone possibly caused Mooren's ulcer. Additionally, no CMV corneal endotheliitis or Mooren's ulcer relapse was observed after cataract surgery or DSAEK.

It has been reported that most CMV anterior uveitis and corneal endotheliitis cases in immunocompetent patients show specific clinical expressions, including mild anterior chamber inflammation, coin-shaped KPs, increased intraocular pressure, and corneal endothelial cell loss,[6,19] which are likely to present as recurrent acute anterior uveitis. A previous study including 109 eyes of 106 patients with CMV endotheliitis reported that topical steroids were being used by 96.3% of patients at the time of CMV endotheliitis diagnosis.[3] It was speculated that immunosuppressive treatment using topical steroids or cyclosporine A might have facilitated CMV reactivation and the development of CMV uveitis and endotheliitis.[4,5] Continuous topical application of 0.5% ganciclovir was found to be effective for the prevention of CMV endotheliitis recurrence after DSAEK.[20] In this case, anti-CMV treatment was discontinued after DSAEK, but no recurrence of CMV corneal endotheliitis was finally observed.

Cataract surgery under conventional microscopic illumination is challenging in patients with corneal edema because of poor visibility of the lens and anterior capsule. Anterior capsule staining with indocyanine green or trypan blue is helpful for capsulorrhexis to enhance visibility.[21,22] In this case, we used anterior chamber illumination for the cataract surgery. The anterior chamber illumination technique using a light pipe has been reported to be helpful in cases with mild or moderate corneal haze.[23] Although peripheral thinning and haze were observed,

we could perform cataract surgery through a thickened and hazy cornea without issue.

3. Conclusions

We reported the case of a patient who required cataract surgery and DSAEK after CMV corneal endotheliitis following immunosuppressive treatment for Mooren's ulcer. Although it is difficult to perform DSAEK for patients with thinned corneas, it is possible to perform DSAEK unencumbered by creating the main wound and side ports in a manner that avoids the thinned parts of the cornea.

Patient consent

Written informed consent was obtained from the patient.

Funding

No funding or grant support.

Authorship

The authors who contributed to the design and conduct of the study were K.U., T.O., and T.T.; to the collection, management, analysis, and interpretation of data were K.U., T.O., T.T., and J.Y.; and to the preparation, review, and approval of the manuscript was T.T., J.Y., T.K. and T. M.

Declaration of competing interest

The authors have no financial disclosures.

Acknowledgements

None.

References

1. Zhao JC, Jim XY. Immunological analysis and treatment of Mooren's ulcer with cyclosporine A applied topically. *Cornea*. 1993;12(6):481–488.
2. Foster CS. Immunosupressive therapy for external ocular inflammatory disease. *Ophthalmology*. 1980;87(2):140–150.
3. Koizumi N, Inatomi T, Suzuki T, et al. Clinical features and management of cytomegalovirus corneal endotheliitis: analysis of 106 cases from the Japan corneal endotheliitis study. *Br J Ophthalmol*. 2015;99(1):54–58.
4. Siak J, Chee SP. Cytomegalovirus anterior uveitis following topical cyclosporine A. *Ocul Immunol Inflamm*. 2018;26(1):90–93.
5. Chee SP, Bacsal K, Jap A, Se-Thoe SY, Cheng CL, Tan BH. Clinical features of cytomegalovirus anterior uveitis in immunocompetent patients. *Am J Ophthalmol*. 2008;145(5):834–840.
6. Chee SP, Bacsal K, Jap A, Se-Thoe SY, Cheng CL, Tan BH. Corneal endotheliitis associated with evidence of cytomegalovirus infection. *Ophthalmology*. 2007;114(4):798–803.
7. Fernandez Lopez E, Chan E. Descemet stripping automated endothelial keratoplasty outcomes in patients with cytomegalovirus enodtheliitis. *Cornea*. 2017;36(1):108–112.
8. Tan TE, Tan DTH. Cytomegalovirus corneal endotheliitis after Descemet membrane endothelial keratoplasty. *Cornea*. 2019;38(4):413–418.
9. Basilious A, Chew HF. Topical ganciclovir for prophylaxis of cytomegalovirus endotheliitis in endothelial keratoplasty. *Cornea*. 2019;38(1):120–122.
10. Price Jr FW, Price MO. Descemet's stripping with endothelial keratoplasty in 200 eyes: early challenges and techniques to enhance donor adherence. *J Cataract Refract Surg*. 2006;32(3):411–418.
11. Price MO, Price Jr FW, Trespalacios R. Endothelial keratoplasty technique for aniridic aphakic eyes. *J Cataract Refract Surg*. 2007;33(3):376–379.
12. Price MO, Price Jr FW. Descemet's stripping with endothelial keratoplasty for treatment of iridocorneal endothelial syndrome. *Cornea*. 2007;26(4):493–497.
13. Mondino BJ, Hofbouer JD, Foos RY. Mooren's ulcer after penetrating keratoplasty. *Am J Ophthalmol*. 1987;103(1):53–56.
14. Lopez JS, Price Jr FW, Whitcup SM, Li Q, de Smet M, Chan CC. Immunohistochemistry of Terrien's and Mooren's corneal degeneration. *Arch Ophthalmol*. 1991;109(7):988–992.
15. Brown SI, Mondino BJ, Rabin BS. Autoimmune phenomenon in Mooren's ulcer. *Am J Ophthalmol*. 1976;82(6):835–840.
16. Gottsch JD, Liu SH, Minkovitz JB, Goodman DF, Srinivasan M, Stark WJ. Autoimmunity to a cornea-associated stromal antigen in patients with Mooren's ulcer. *Invest Ophthalmol Vis Sci*. 1995;36(8):1541–1547.
17. Sangwan VS, Surender P, Burman S. Cataract surgery in patients with Mooren's ulcer. *J Cataract Refract Surg*. 2005;31(2):359–362.
18. Das S, Mohamed A, Sangwan VS. Clinical course and outcomes in patients with Mooren ulcer who had cataract surgery. *J Cataract Refract Surg*. 2017;43(8):1044–1049.
19. Woo JH, Lim WK, Ho SL, Teoh SC. Characteristics of cytomegalovirus uveitis in immunocompetent patients. *Ocul Immunol Inflamm*. 2015;23(5):378–383.
20. Kitazawa K, Jongkhajornpong P, Inatomi T, et al. Topical ganciclovir treatment post-Descemet's stripping automated endothelial keratoplasty for patients with bullous keratopathy induced by cytomegalovirus. *Br J Ophthalmol*. 2018;102(9):1293–1297.
21. Horiguchi M, Miyake K, Ohta I, Ito Y. Staining of the lens capsule for circular continuous capsulorrhexis in eyes with white cataract. *Arch Ophthalmol*. 1998;116(4):535–537.
22. Melles GR, de Waard PW, Pameyer JH, Houdijn Beekhuis W. Trypan blue capsule staining to visualize the capsulorhexis in cataract surgery. *J Cataract Refract Surg*. 1999;25(1):7–9.
23. Oshima Y, Shima C, Maeda N, Tano Y. Chandelier retroillumination–assisted torsional oscillation for cataract surgery in patients with severe corneal opacity. *J Cataract Refract Surg*. 2007;33(12):2018–2022.