Amniotic membrane transplantation in a patient with an impending perforated corneal ulcer caused by Streptococcus mitis: a case report

CURRENT STATUS: UNDER REVIEW

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DOI: 10.21203/rs.2.434/v3

SUBJECT AREAS
Internal Medicine Specialties

KEYWORDS
Persistent corneal ulcer, amniotic membrane transplantation, Streptococcus mitis
Abstract

Background: *Streptococcus mitis* (*S. mitis*) belongs to the viridans group streptococci, which is rarely isolated as a causative pathogen of corneal ulcers. When *S. mitis* causes keratitis, penetrating keratoplasty (PK) might be necessary. Herein, we demonstrated that amniotic membrane transplantation (AMT) may be an easier procedure with acceptable outcomes and with fewer complications.

Case presentation: A 63-year-old female presented with a right persistent corneal ulcer that she had suffered from for the past nine months. The culture of a corneal scraping yielded *S. mitis*. The right eye descemetocele decreased from 3 mm in diameter to 0.8 mm in diameter after the continuous administration of topical vancomycin and ceftriaxone for two weeks. Due to the slow healing, AMT was performed. Her corneal erosion healed and gradually became clear. Her visual acuity recovered from initially counting fingers to 20/200 17 months after AMT.

Conclusion: This unusual case illustrated that antibiotics plus AMT may be an effective alternative treatment instead of PK to promote epithelialization and to reduce inflammation in corneas complicated by *S. mitis* keratitis.

Background

*Streptococcus mitis* (*S. mitis*) is an alpha-hemolytic, facultative anaerobic species of the viridans group streptococci. *S. mitis* is a commensal of the human oropharynx and is also found on the skin, in the gastrointestinal tract, and in the female genital tract. Although the low virulence and pathogenicity of this bacteria are recognized, *S. mitis* is considered an opportunistic pathogen that can lead to the development of severe infections, including endophthalmitis, infective endocarditis, bacteremia, upper respiratory tract infection and meningitis [1, 2].
Moreover, corneal ulcers caused by *Streptococcus mitis* are rare and have seldom been described. In previous reports, penetrating keratoplasty (PK) was usually adopted for the treatment of persistent corneal ulcers [3-5].

As an alternative treatment to reconstruct the ocular surface, amniotic membrane transplantation (AMT) has been proposed to promote epithelial healing and to reduce neovascularization, inflammation, and scarring, and this method has been demonstrated to be effective in promoting wound healing and in preventing corneal perforation in infectious keratitis [6-9]. In this case, we demonstrated that AMT may be successfully used to treat a patient with a nonhealing descemetocele caused by *S. mitis* rather than performing penetrating keratoplasty (PK).

**Case Presentation**

A 63-year-old Taiwanese Han female, with a history of herpes zoster ophthalmicus 18 years ago, presented to our ophthalmological clinic with the chief complaint of right eye pain. The patient had experienced right persistent corneal ulcers for nine months despite the use of biweekly therapeutic soft contact lenses along with unknown topical agents, which resulted in recurrent symptoms of ocular redness, pain, and blurred vision. Within a few years prior to the current event, she reported repeated episodes that occurred approximately two to three times yearly of right eye redness accompanied by photophobia that resolved spontaneously. Upon the initial ocular examination, her visual acuity was counting fingers and a 3 mm × 2 mm central epithelial defect with stromal infiltration and a 1 mm × 1 mm inferonasal paracentral descemetocele of right eye were documented (Figure 1). Famciclovir (250 mg, 2 tablets, TID), topical tobramycin ointment (3.5 g/tube, BID) and levofloxacin (0.5%, 25 mg/5 mL/bottle, Q1H) were prescribed. A subsequent corneal culture yielded *S. mitis* growth. Therefore, hourly topical vancomycin (25 mg/ml) and ceftriaxone (25 mg/mL) were initiated in place of the previous antiviral and
antimicrobials based on the susceptibility test.

The size of the descemetocele initially increased to 3 mm in diameter and was accompanied by the development of a 1 mm hypopyon. With the continuous administration of topical vancomycin and ceftriaxone for two weeks, the descemetocele gradually shrank to 0.8 mm × 0.8 mm, and the hypopyon resolved (Figure 2). Superficial manual keratectomy with AMT was performed [9] because of the minimal healing and the lack of further shrinkage of the descemetocele despite intensive topical antibiotic treatment (Figure 3).

During the course of the corneal ulcer treatment, the patient reported an abrupt onset of left eye redness with abundant discharge. Pterygium at eight o’clock of the cornea and 360 degree chemosis with conjunctival injection (OS) were found. Topical sulfamethoxazole (4%, TID) and fluorometholone (0.1% QID) were used, but the symptoms persisted. Therefore, the diagnostic aspiration of aqueous (OS) was performed. Fortunately, no viral DNA or organisms was identified, and the severity of the chemosis and conjunctival injection gradually improved afterwards.

In a postoperative clinic follow-up, the AM remained in situ without further epithelial defects or leakage at six months postsurgery (Figure 4). We switched the topical antibiotics to 0.5% levofloxacin and gradually tapered the dose. The cornea gradually healed and became almost clear, and visual acuity was 20/200 at the last follow-up, 17 months after the AMT was performed (Figure 5).

Discussion And Conclusions

Well-documented treatments of S. mitis keratitis are rare, and most of the reported cases had poor visual outcomes or were treated with PK [3, 5, 10]. S. mitis is a normal flora of the human oropharynx and is also found on the skin, in the gastrointestinal tract, and in the female genital tract. Despite having low virulence and pathogenicity, reports have
shown that S. mitis can cause severe infections, including endophthalmitis, infective endocarditis, bacteremia, upper respiratory tract infection and meningitis [1, 2]. This organism has been identified in patients with postsurgical endophthalmitis that resulted in poor visual outcomes [11]. In addition, the viridans group streptococci is one of the most common organisms implicated in the rare corneal infectious disease infectious crystalline keratopathy [12]. Although corneal ulcers caused by S. mitis have seldom been described, we treated the impending perforated ulcer with antibiotics and AMT.

Previously, in a 10-year review of microbial keratitis from 1972 to 1981, S. mitis was reported in 7% (3/44) of polymicrobial keratitis cases and in less than 5% of the 133 cases of monomicrobial keratitis [3]. The vision of one patient was limited to 2/200 by corneal scarring after antibacterial and antifungal therapy. The final vision of another patient was 10/200 [3]. In 2005, there was a case report of a 39-year-old female who presented with an S. mitis corneal ulcer with total corneal opacification and a 2.5 mm x 2.5 mm descemetocoele. Antibiotics were used, but eventually, it progressed to a perforated cornea and was successfully treated with PK with final visual acuity of 20/200 [4]. In 2016, another case was published of an S. mitis/oralis corneal ulcer that occurred one year after corneal transplantation. Although broad-spectrum antibiotics were given and infection was controlled, the corneal graft was complicated by scar formation. Regrafting was subsequently performed, and the new graft remained clear [5].

Giving initial topical empiric broad-spectrum antibiotics before culture data is available is the general treatment of suppurative keratitis [13]. Surgical treatment options include tissue adhesives, tarsorrhaphy, conjunctival flaps and PK [13]. The management of a perforated corneal ulcer or descemetocoele involves the repair of the mechanical disruption and the promotion of reepithelization while reducing inflammation [13, 14]. AMT is an alternative treatment for reconstructing the ocular surface, and it has been proposed to
promote epithelial healing and to reduce neovascularization, inflammation, and scarring [6, 7]. Studies have reported that AMT is effective in promoting wound healing and in preventing corneal perforation in infectious keratitis, while PK can resolve the pathology but has the disadvantage of limited source of grafts and potential complications such as astigmatism, epithelial defects, graft failure and so on [8, 9, 13].

In this case, we described the clinical and treatment course of an impending perforated corneal ulcer caused by S. mitis. We also demonstrated that treatment with antibiotics and AMT was successful, without the need for PK, and this could be considered an alternative treatment for non-healing descemetoceles induced by S. mitis, as compared to the previous treatment [3-5]. Given the current single case report, larger-scale studies are needed for AMT to become a standard treatment modality for persistent corneal ulcers prior to PK.

Abbreviations

Streptococcus mitis: S. mitis, penetrating keratoplasty: PK, amniotic membrane transplantation: AMT, BID: twice a day, TID: three times a day.

Declarations

Ethics and consent to participate:

All procedures that were performed on the patient were in accordance with the Declaration of Helsinki. This case was retrospectively reviewed, and this single case report describes the course of the diagnostics and therapy but does not include data that can identify the patient. Thus, the need for ethical approval was waived.

Consent to publish:

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.
Availability of data and material:
All data generated during this case report are included in this published article.

Competing interests:
The authors declare that they have no competing interests.

Funding:
This study was supported by Chang Gung Memorial Hospital, Linkou with an award number of CMRPG3G0031-3 and by the Ministry of Science and Technology, Taiwan with an award number of MOST 107-2314-B-182A-088-MY3.

Authors’ contributions:
HCC contributed to the conception and study design.
LKY and HCC treated and enrolled the patient.
FCH and YJM collected and interpreted the data.
FCH drafted the manuscript.
All the authors, including FCH, YJM, LKY, HYT, CHH, HKM, WCW, and HCC, were involved in the critical revision of the manuscript, supervision of the manuscript and final approval of the submission. The first two authors (Hsiao FC and Meir YJ) contributed equally to this work.

Acknowledgements:
None.

References
[1] Mitchell J. *Streptococcus mitis*: walking the line between commensalism and pathogenesis. Mol Oral Microbiol 2011;26(2):89-98.
[2] Chung JK, Lee SJ. *Streptococcus mitis/oralis* endophthalmitis management without
phakic intraocular lens removal in patient with iris-fixated phakic intraocular lens implantation. BMC Ophthalmol 2014;14(1):92.

[3] Jones DB. Polymicrobial keratitis. Trans Am Ophthalmol Soc 1981;79:153-67.

[4] Hsu VJ, Affeldt J, Blanton C. Streptococcus Mitis Corneal Ulcer. Invest Ophthalmol Vis Sci 2005;46(13):2632.

[5] Khan ID, Sati A, Arif S, Mehdi I, Bhatt P, Jain V, et al. Streptococcus Mitis/Oralis Corneal Ulcer After Corneal Transplantation. J Basic Clin Med 2016;5(1):8-10.

[6] Hick S, Demers PE, Brunette I, La C, Mabon M, Duchesne B. Amniotic membrane transplantation and fibrin glue in the management of corneal ulcers and perforations: a review of 33 cases. Cornea 2005;24(4):369-77.

[7] Kim JS, Kim JC, Hahn TW, Park WC. Amniotic membrane transplantation in infectious corneal ulcer. Cornea 2001;20(7):720-6.

[8] Chen JH, Ma DH, Tsai RJ. Amniotic membrane transplantation for pseudomonal keratitis with impending perforation. Chang Gung Med J 2002;25(3):144-52.

[9] Chen HC, Tan HY, Hsiao CH, Huang SC, Lin KK, Ma DH. Amniotic membrane transplantation for persistent corneal ulcers and perforations in acute fungal keratitis. Cornea 2006;25(5):564-72.

[10] Nicula C, Szabo I. Complicated corneal ulcer. Case report. Rom J Ophthalmol 2016;60(4):260-3.

[11] Durand ML. Endophthalmitis. Clin Microbiol Infect 2013;19(3):227-34.

[12] Khater TT, Jones DB, Wilhelmus KR. Infectious Crystalline Keratopathy Caused by Gram-negative Bacteria. Am J Ophthalmol 1997;124(1):19-23.

[13] WHO Regional Office for South-East Asia. Guidelines for the management of corneal ulcer at primary, secondary and tertiary care health facilities in the South-East Asia region. 2004.
At the initial ocular examination, a 3 mm × 2 mm central epithelial defect with stromal infiltration and a 1 mm × 1 mm inferonasal paracentral descemetocele (OD) were observed.
After the continuous administration of topical vancomycin and ceftriaxone for two weeks, the descemetocele gradually shrunk to 0.8 mm × 0.8 mm, and the hypopyon resolved.
With superficial manual keratectomy with AMT, the descemetocoele was successfully repaired with smooth epithelialization.
During the postoperative follow-up, the AM remained in situ without further epithelial defects or leakage at nine months.
Figure 5

After 17 months of follow-up, the patient’s right cornea was almost clear with visual acuity of 20/200.

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