# World Journal of *Clinical Cases*

World J Clin Cases 2022 April 26; 10(12): 3639-3968





Published by Baishideng Publishing Group Inc

W J C C World Journal of Clinical Cases

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#### **RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Ying-Yi Yuan; Production Department Director: Xu Guo; Editorial Office Director: Jin-Lei Wang,

NAME OF JOURNAL World Journal of Clinical Cases	INSTRUCTIONS TO AUTHORS https://www.wjgnet.com/bpg/gerinfo/204	
ISSN	GUIDELINES FOR ETHICS DOCUMENTS	
ISSN 2307-8960 (online)	https://www.wjgnet.com/bpg/GerInfo/287	
LAUNCH DATE	GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH	
April 16, 2013	https://www.wjgnet.com/bpg/gerinfo/240	
FREQUENCY	PUBLICATION ETHICS	
Thrice Monthly	https://www.wjgnet.com/bpg/GerInfo/288	
EDITORS-IN-CHIEF	PUBLICATION MISCONDUCT	
Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku	https://www.wjgnet.com/bpg/gerinfo/208	
EDITORIAL BOARD MEMBERS	ARTICLE PROCESSING CHARGE	
https://www.wjgnet.com/2307-8960/editorialboard.htm	https://www.wjgnet.com/bpg/gerinfo/242	
PUBLICATION DATE	STEPS FOR SUBMITTING MANUSCRIPTS	
April 26, 2022	https://www.wjgnet.com/bpg/GerInfo/239	
COPYRIGHT	ONLINE SUBMISSION	
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World J Clin Cases 2022 April 26; 10(12): 3923-3929

DOI: 10.12998/wjcc.v10.i12.3923

Provenance and peer review:

reviewed.

Unsolicited article; Externally peer

Peer-review model: Single blind

Peer-review report's scientific

P-Reviewer: Dai Q, China; Khan I, Pakistan; Salvadori M, Italy

Received: September 21, 2021 Peer-review started: September 21,

First decision: December 27, 2021

Revised: February 3, 2022

Accepted: March 6, 2022

Article in press: March 6, 2022 Published online: April 26, 2022

quality classification Grade A (Excellent): A

Grade B (Very good): B

Grade C (Good): 0 Grade D (Fair): D

Grade E (Poor): 0

2021

ISSN 2307-8960 (online)

CASE REPORT

# Amniotic membrane transplantation in a patient with impending perforated corneal ulcer caused by Streptococcus mitis: A case report and review of literature

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## Abstract

#### BACKGROUND

Streptococcus mitis (S. mitis) is an opportunistic pathogen that can lead to severe ocular infections. In previous reports, penetrating keratoplasty (PK) was usually adopted for the treatment of persistent corneal ulcers. This report describes an unusual case of nonhealing descemetocele caused by S. mitis treated by antibiotics plus amniotic membrane transplantation (AMT).

#### CASE SUMMARY

A 63-year-old woman presented with a right persistent corneal ulcer that she had suffered from for the past 9 mo. The culture of a corneal scraping yielded *S. mitis*. The right eye descemetocele decreased in diameter from 3 to 0.8 mm after the continuous administration of topical vancomycin and ceftriaxone for 2 wk. 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 100/200 at the last follow-up, 67 mo after AMT.

#### CONCLUSION



Antibiotics plus AMT may be an effective alternative treatment other than PK to promote epithelialization and to reduce inflammation in the corneas complicated by S. mitis keratitis.

Key Words: Persistent corneal ulcer; Amniotic membrane transplantation; *Streptococcus mitis*; Case report

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Core Tip: In this case, we described the clinical and treatment course of an impending perforated corneal ulcer caused by Streptococcus mitis (S. mitis). We also demonstrated that treatment with antibiotics and amniotic membrane transplantation was successful, without the need for penetrating keratoplasty, and this could be considered an alternative treatment for nonhealing descemetoceles induced by S. mitis, as compared to the previous treatment.

Citation: Hsiao FC, Meir YJJ, Yeh LK, Tan HY, Hsiao CH, Ma DHK, Wu WC, Chen HC. Amniotic membrane transplantation in a patient with impending perforated corneal ulcer caused by Streptococcus mitis: A case report and review of literature. World J Clin Cases 2022; 10(12): 3923-3929 URL: https://www.wjgnet.com/2307-8960/full/v10/i12/3923.htm

DOI: https://dx.doi.org/10.12998/wjcc.v10.i12.3923

#### INTRODUCTION

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 S. 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 PK.

#### CASE PRESENTATION

#### Chief complaints

A 63-year-old Taiwanese Han woman presented with right eye pain for 9 mo.

#### History of present illness

The patient had experienced right persistent corneal ulcers for 9 mo 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.

#### History of past illness

This patient had a history of herpes zoster ophthalmicus 18 years ago and an underlying disease of hypertension.

#### Personal and family history

The patient denied any known family history.

#### Physical examination

Upon the initial ocular examination, her right visual acuity (VA) was counting fingers. A 3 mm × 2 mm



central epithelial defect with stromal infiltration and a 1 mm × 1 mm inferonasal paracentral descemetocele were noted at her right eye (Figure 1A). The VA change is listed in Table 1.

#### Laboratory examinations

A corneal culture yielded S. mitis growth.

Imaging examinations

Not applicable.

#### FINAL DIAGNOSIS

An impending perforated corneal ulcer was caused by *S. mitis*.

#### TREATMENT

Famciclovir (250 mg, two tablets, TID), topical tobramycin ointment (3.5 g/tube, BID), and levofloxacin (0.5%, 25 mg/5 mL/bottle, Q1H) were prescribed initially. 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. AMT was performed after 2 wk of topical vancomycin and ceftriaxone.

#### OUTCOME AND FOLLOW-UP

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 2 wk, the descemetocele gradually decreased to 0.8 mm × 0.8 mm, and the hypopyon resolved (Figure 1B). Superficial manual keratectomy with AMT was performed[9] due to the minimal healing and the lack of further shrinkage of the descemetocele despite intensive topical antibiotic treatment (Figure 1C).

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° 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, neither viral DNA nor organism was identified, and the severity of the chemosis and conjunctival injection gradually improved afterwards.

In a postoperative clinic follow-up, the amniotic membrane remained in situ without further epithelial defects or leakage at 6 mo post-AMT (Figure 1D). We switched the topical antibiotics to 0.5% levofloxacin and gradually tapered the dose. The cornea gradually healed with faint subepithelial haze as demonstrated by slit lamp biomicroscopy (Figure 2A) and anterior segment optical coherence tomography (Figure 2B), and best corrected VA was 100/200 at the last follow-up, 67 mo after the AMT was performed.

#### DISCUSSION

Well-documented treatments of S. mitis keratitis are rare, and most of the reported cases had poor visual outcomes or were treated with PK that were reported several years ago[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 for 2 wk before performing 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 therapies. The final vision of another patient was 10/200[3]. In 2005, there was a case report of a 39-yearold woman who presented with an S. mitis corneal ulcer with total corneal opacification and a 2.5 mm ×

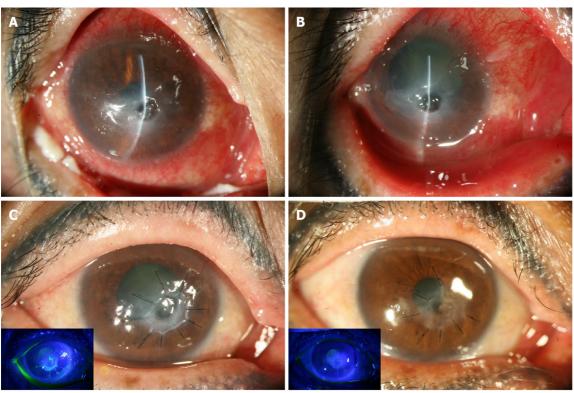


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#### Hsiao FC et al. AMT for perforated Streptococcus mitis keratitis

Table 1 Visual acuity change 2 wk before and after amniotic membrane transplantation					
Weeks after AMT		OD	OS		
-2	VA	CF/15 cm	0.5		
1.6	VA	CF/10 cm	0.4-2		
3.6	VA	HM/60 cm	0.3		
6.6	VA	CF/80 cm	0.3		
12.6	VA	CF/30 cm	0.5		
20.6	VA	CF/20 cm	0.5		
29.6	VA	CF/10 cm	0.7-2		
37.6	VAcPG	0.05	1		
54.6	VAcPG	CF/30 cm	1		
63.6	VAcPG	CF/20 cm	0.8		
73.6	VA	0.08	0.3		
268.0	VA	100/200	0.5		

AMI: Amniotic membrane transplantation; VA: Visual acuity; VAcPG: Visual acuity with glasses; OD: Oculus dexter; OS: Oculus sinister.



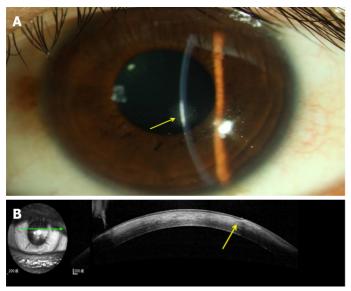
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Figure 1 External eye photograph of the cornea before and after treatment. A: At the initial ocular examination, a 3 mm × 2 mm central epithelial defect with stromal infiltration and a 1 mm × 1 mm inferonasal paracentral descemetocele were observed; B: After the continuous administration of topical vancomycin and ceftriaxone for 2 wk, the descemetocele gradually decreased to 0.8 mm × 0.8 mm, and the hypopyon resolved; C: After manual superficial keratectomy combined with amniotic membrane transplantation (AMT), the descemetocele was successfully repaired with smooth epithelialization; D: During the postoperative follow-up, the AM remained in situ without further epithelial defects or leakage at 9 mo.

> 2.5 mm descemetocele. Antibiotics were used, but eventually, it progressed to a perforated cornea and was successfully treated with PK with a final VA of 20/200[4]. In 2016, another case was published of an S. mitis/oralis corneal ulcer that occurred 1 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].



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Figure 2 Anterior segment imaging of the cornea 67 mo after amniotic membrane transplantation. A: The patient's right cornea was intact with subepithelial opacity, of which a close-up view is shown in an insert (arrow); B: On anterior segment optical coherence tomography, there was hyperreflectivity in the anterior stroma (arrow).

> Giving initial topical empiric broad-spectrum antibiotics before available culture data is the general treatment of suppurative keratitis. Surgical treatment options include tissue adhesives, tarsorrhaphy, conjunctival flaps, and PK[13]. The management of a perforated corneal ulcer or descemetocele involves the repair of the mechanical disruption and the promotion of reepithelization while reducing inflammation<sup>[13]</sup>. AMT is an alternative treatment for reconstructing the ocular surface, and it has been proposed to be antimicrobial, to promote epithelial healing, and to reduce neovascularization, inflammation, and scarring[6,7].

> AM is the innermost layer of the placenta composed of epithelium, basement membrane, and stroma. It was first used in ocular surface reconstruction in 1940 by de Rötth[14]. Later, few ophthalmologists adopted AM for surgery until Batlle and Perdomo used it for conjunctival reconstruction in the 1990s [15]. AMT can provide a physical barrier against infection and retention of antibiotics[16] and has antimicrobial properties via human beta-defensins[17], elafin[18], leukocyte protease inhibitor[19], and cystatin E[20]. In a rabbit model, AM was proven to subside pseudomonas keratitis[21]. A previous report also showed the effectiveness of AM in the treatment of infectious corneal ulcer[22].

> As for mechanism of epithelial healing, the basement membrane of AM is similar to the conjunctiva that is mainly composed of type IV, V, and VII collagen that help the adhesion, migration, growth, and differentiation of epithelial progenitor cell<sup>[23,24]</sup>. The AM stroma contains several growth factors such as epidermal growth factor, hepatocyte growth factor, and basic fibroblast growth factor supporting epithelization [25-27]. In addition, protease inhibitors and heavy chain-hyaluronan/pentraxin 3 decrease the local inflammation and scarring[28,29]. In a recent meta-analysis, adjuvant AMT for infectious keratitis showed the promotion of corneal healing and the improvement of uncorrected VA[30].

> The documented treatment for corneal ulcer caused by S. mitis was PK. While PK can resolve the pathology, it has the disadvantage of limited source of grafts and potential complications such as astigmatism, epithelial defects, and graft failure[8,9]. Considering the mechanism and effectiveness of AMT in infectious keratitis though not in S. mitis, we adopted AMT to treat the patient's chronic infectious corneal ulcer. The patient's final VA was good.

> Comparing to documented treatment, PK for corneal ulcer caused by S. mitis, several studies have reported that AMT is effective in promoting corneal ulcer healing and in preventing corneal perforation in infectious keratitis though not in S. mitis. We presented a case of corneal ulcer caused by S. mitis treated by topical antibiotics with adjuvant AMT.

#### CONCLUSION

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 nonhealing 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.

#### ACKNOWLEDGEMENTS

The authors thank the advice from Dr. Scheffer CG Tseng at the Ocular Surface Center, Miami, FL, United States.

### FOOTNOTES

Author contributions: Hsiao FC conducted the literature search, collected the data, interpreted the data, and prepared the manuscript; Meir YJ and Yeh LK collected the data and interpreted the data; Tan HY and Hsiao CH interpreted the data and edited the manuscript; Ma HK and Wu WC interpreted the data and critically revised the draft; Chen HC designed the study, interpreted the data, edited the manuscript, and critically revised the draft.

Informed consent statement: Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

**Conflict-of-interest statement:** The authors have no conflicts of interest relevant to this article.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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S-Editor: Ma YJ L-Editor: A P-Editor: Ma YI

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