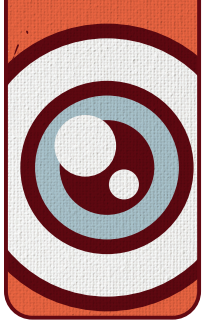

AN OD'S GUIDE TO INFECTIOUS KERATITIS


Once you have the diagnosis, these treatment pearls can help you protect patients' vision.

BY SAM LEE, OD, AND KUNIYOSHI KANAI, OD, FAAO

Infectious keratitis is a vision-threatening condition that requires prompt identification and treatment to maximize patient outcomes. Contact lens wear remains one of the most common risk factors, but others include ocular trauma, ocular surface diseases, post corneal surgery, and systemic diseases.[1] Most cases that present to the office will be bacterial, but practitioners must remain vigilant, as fungal, viral, or protozoal (eg, *Acanthamoeba*) infections may be more aggressive and will require different treatment strategies.[1] Optometrists can successfully treat infectious keratitis, but it is important to know when to change the treatment course and when to refer.

NAILING THE DIAGNOSIS

Early presentation of infectious keratitis may be nonspecific and share similar symptomatology, such as redness, pain, irritation, and photophobia. A thorough case history is imperative, because a history of injury with vegetative matter or contact lens exposure to nonsterile tap water may suggest a nonbacterial etiology (Figure).[1] Fungal infections may present with infiltrates that have feathery borders and satellite lesions; viral infections may have dendrites or pseudodendrites and *Acanthamoeba* typically causes pain that exceeds the presenting signs.[2]

When a patient presents with a round corneal infiltrate, certain characteristics can help practitioners differentiate between a sterile and infectious corneal ulcer. Sterile corneal ulcers are generally smaller and peripheral with minimal anterior chamber reaction, pain, discharge, and overlying epithelial staining.[3] On the contrary, infectious corneal ulcers are generally larger and central with greater anterior chamber reaction, pain, discharge, and overlying epithelial staining.[3] Regardless, corneal ulcers are initially treated as infectious as a precaution until proven otherwise.

TO CULTURE OR NOT TO CULTURE

In 2007, Vital et al proposed the "1, 2, 3" rule as an objective way to predict which bacterial corneal ulcers would result in vision loss after resolution of the infection.[4] Their study concluded that ulcers classified as potentially sight-threatening accurately predicted loss of best spectacle-corrected visual acuity.[4] A follow-up study at Massachusetts Eye and Ear found that this rule was beneficial in borderline cases where the clinician was unsure if the case required culture.[5] To be classified as potentially sight-threatening, any one of the following criteria must be met:[4]

- 1+ cells or 10 cells in the anterior chamber in a 1-mm beam
- 2 mm dense infiltrate in the greatest linear dimension
- Edge of infiltrate 3 mm from the center of the cornea

According to the Bacterial Keratitis Preferred Practice Pattern published

by the American Academy of Ophthalmology in 2018, culture should be performed if any of the following criteria are met:[1]

- Central and large and/or any appearance of stromal melting
- Unresponsive to broad-spectrum antibiotic therapy
- Past history of corneal surgery
- Clinical appearance suggesting fungal, amoebic, or mycobacterial etiology
- Multiple infiltrates on the cornea

In general, atypical-appearing, severe, large, and central corneal ulcers require culture to ensure appropriate treatment is initiated to minimize the risk of vision loss.[1] When faced with this type of ulcer, it may be advisable to refer to a cornea specialist for treatment, considering most optometric offices are not equipped with culturing capabilities.

TREATMENT APPROACH

Most cases of mild bacterial keratitis are managed without culture and resolve with broad-spectrum topical antibiotics such as fluoroquinolones.[1] Although broad-spectrum fluoroquinolones have revolutionized the way practitioners approach the treatment of bacterial keratitis, the growing risk of antibiotic resistance remains a challenge. The Antibiotic Resistance Monitoring in Ocular Organisms study released 10-year data that continue to show the prevalence of methicillin resistance and multidrug resistance in *Staphylococcus aureus* and coagulase-negative *staphylococci*, more so in older patients.[6] Failure to respond to treatment should trigger a culture or re-culture because it suggests antibiotic resistance or a nonbacterial origin.[6,7] Luckily, fortified vancomycin remains highly sensitive for all species, making it an excellent treatment option for high-risk corneal ulcers.[5,6]

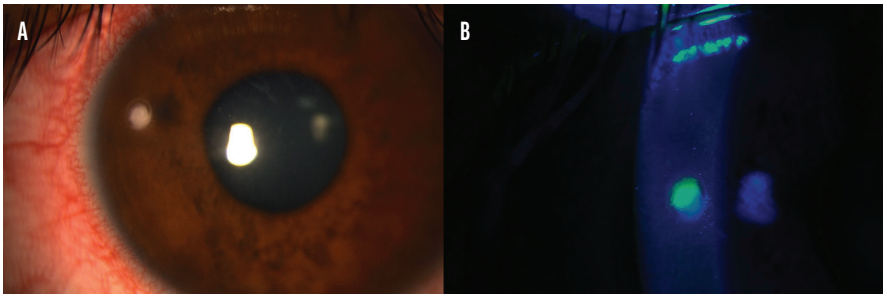

Figure. This patient has a contact lens-related infectious peripheral corneal ulcer, seen here in white light (A) and with sodium fluorescein staining (B).

The fluoroquinolone moxifloxacin is also a popular choice for many practitioners. However, a retrospective case review found a 1.26 increased odds of culturing a moxifloxacin-resistant organism every year since they began tracking in 2005.[8] The University of Pittsburgh Medical Center showed a significant increase in resistance to fourth-generation fluoroquinolones such as moxifloxacin for both methicillin-resistant *S. aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) isolates during a 20-year review.[9] The observed increase is possibly due to moxifloxacin's widespread use over time.[9] Close monitoring for clinical improvement and timely action is imperative.

The addition of topical corticosteroids in the treatment of bacterial keratitis remains controversial. These therapies have the potential benefit of reducing tissue damage and scarring by decreasing inflammation, but they could exacerbate the infection by dampening the immune system.[7,10] The Steroids for Corneal Ulcers Trial in 2012 was the first randomized, placebo-controlled, double-masked multicenter clinical trial that concluded that adding adjuvant prednisolone sodium phosphate to topical moxifloxacin had no overall benefit or harm in the treatment of bacterial keratitis.[11] When managing simple corneal ulcers without culture, the literature supports no clear benefit of adding a topical corticosteroid, and the risk is generally greater compared with any potential benefit.[1]

THE FUTURE

Corneal collagen crosslinking (CXL) is commonly performed as a treatment to slow the progression of corneal ectasias such as keratoconus. In addition, riboflavin and ultraviolet A have been shown to have antimicrobial activity and resist proteolytic enzymes secreted by infective microorganisms, making CXL a viable treatment option for infectious keratitis.[12] The Steroids and Crosslinking for Ulcer Treatment Trial is a randomized, double-masked, sham- and placebo-controlled clinical trial designed to determine the efficacy of CXL as a therapy for bacterial keratitis.[13] The group is currently enrolling participants

AT A GLANCE

- Corneal ulcers are initially treated as infectious as a precaution until proven otherwise.
- In general, atypical-appearing, severe, large, and central corneal ulcers require culture to ensure appropriate treatment is initiated to minimize the risk of vision loss.
- Most cases of mild bacterial keratitis are managed without culture and resolve with broad-spectrum topical antibiotics.

and expects to finish enrollment at the end of 2023.[13] Patient enrollment is still active at this time.

CXL using rose bengal with green light (RGX) instead of UV light has also been studied for the treatment of infectious keratitis.[14,15] Unlike UV-CXL, RGX not only delays the growth of methicillin-resistant *S. aureus* strain cultures, similar to riboflavin plus UV, but it also hinders the growth of fungal cultures.

CLINICAL PEARLS

Optometrists are at the front lines when it comes to treating infectious keratitis. Broad-spectrum antibiotics are the mainstay of treatment, although antibiotic resistance should always be in the back of the practitioner's mind. Ulcers with high-risk characteristics should be cultured, and referral to a cornea specialist is warranted if in-office culturing is not available and for patients who are refractory to treatment.

Take the appropriate steps and act speedily to maximize success and minimize long-term sequelae. ■

1. Lin A, Rhee MK, Akpek EK, et al. Bacterial keratitis preferred practice pattern. *Ophthalmology*. 2019;126(1):P1-P55.
2. Gerstenblith AT, Rabinowitz MP. The Wills Eye Manual: office and emergency room diagnosis and treatment of eye disease. 6th ed. Wolters Kluwer/Lippincott Williams & Wilkins; 2012.
3. Stein RM, Clinch TE, Cohen EJ, Genvert GI, Arentsen JJ, Laibson PR. Infected vs sterile corneal infiltrates in contact lens wearers. *Am J Ophthalmol*. 1988;105(6):632-636.
4. Vital MC, Belloso M, Prager TC, Lanier JD. Classifying the severity of corneal ulcers by using the "1, 2, 3" rule. *Cornea*. 2007;26(1):16-20.
5. Ung L, Wang Y, Vangel M, et al. Validation of a comprehensive clinical algorithm for the assessment and treatment of microbial keratitis. *Am J Ophthalmol*. 2020;214:97-109.
6. Asbell PA, Sanfilippo CM, Sahm DF, DeCory HH. Trends in antibiotic resistance among ocular microorganisms in the United States from 2009 to 2018. *JAMA Ophthalmol*. 2020;138(5):439-450.
7. Carmichael TR, Gelfand Y, Welsh NH. Topical steroids in the treatment of central and paracentral corneal ulcers. *Br J Ophthalmol*. 1990;74(9):528-531.
8. Peng MY, Cevallos V, McLeod SD, Lietman TM, Rose-Nussbaumer J. Bacterial keratitis: isolated organisms and antibiotic resistance patterns in San Francisco. *Cornea*. 2018;37(1):84-87.
9. Chang VS, Dhaliwal DK, Raju L, Kowalski RP. Antibiotic resistance in the treatment of staphylococcus aureus keratitis: A 20-year review. *Cornea*. 2015;34(6):698-703.
10. Srinivasan M, Lalitha P, Mahalakshmi R, et al. Corticosteroids for bacterial corneal ulcers. *Br J Ophthalmol*. 2009;93(2):198-202.
11. Srinivasan M, Mascarenhas J, Rajaraman R, et al. Corticosteroids for bacterial keratitis: The Steroids for Corneal Ulcers Trial (SCUT). *Arch Ophthalmol*. 2012;130(2):143-150.
12. Subasinghe SK, Ogbuehi KC, Dias GJ. Current perspectives on corneal collagen crosslinking (CXL). *Graefes Arch Clin Exp Ophthalmol*. 2018;256(8):1363-1384.
13. Radhakrishnan N, Prajna VN, Prajna LS, et al. Double-masked, sham and placebo-controlled trial of corneal cross-linking and topical difluprednate in the treatment of bacterial keratitis: Steroids and Cross-Linking for Ulcer Treatment Trial (SCUT II) study protocol. *BMJ Open Ophth*. 2021;6(1):e000811.
14. Halili F, Arboleda A, Durkee H, et al. Rose bengal- and riboflavin-mediated photodynamic therapy to inhibit methicillin-resistant staphylococcus aureus keratitis isolates. *Am J Ophthalmol*. 2016;166:194-202.
15. Arboleda A, Miller D, Cabot F, et al. Assessment of rose bengal versus riboflavin photodynamic therapy for inhibition of fungal keratitis isolates. *Am J Ophthalmol*. 2014;158:64-70.

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