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CASE REPORT

Contact-lens-related microbial keratitis: case report and review

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KEYWORDS

Keratitis;
Ulcer;
Fortified antibiotics;
Biofilm

Abstract Bacterial keratitis is a serious, potentially blinding, complication most often involving overnight contact lens wear. This case report reviews the management of a patient with bacterial keratitis and discusses the etiology, differential diagnosis, classification and risk factors associated with the condition.

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PALABRAS CLAVE

Queratitis;
Úlcera;
Antibióticos reforzados;
Biofilm

Queratitis microbiana relacionada con lentes de contacto: caso clínico y análisis

Resumen La queratitis bacteriana es una complicación grave que puede causar ceguera y a menudo se asocia con el uso de lentes de contacto durante toda la noche. En este caso clínico se analiza el tratamiento de un paciente con queratitis bacteriana y se aborda la etiología, el diagnóstico diferencial, la clasificación y el tratamiento de la enfermedad.

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Introduction

Bacterial keratitis (corneal ulcer) is a sight-threatening contact lens complication.¹⁻¹² Either untreated or severe bacterial keratitis may result in perforation and endophthalmitis.^{10,13}

Contact lens (CL) wear is the main risk factor,^{3,6,14,15} and sleeping in contact lenses is the major risk factor among

contact lens wearers.^{4,8,9} Estimates put the number affected annually by bacterial keratitis in the U.S. at 30,000 and higher.^{10,15,16}

A corneal ulcer is defined by a corneal infiltrate associated with an overlying epithelial defect.^{12,14,15} Corneal ulcers generally occur when the normal eye's natural resistance to infection has been compromised from either trauma or

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contact lens wear.¹⁰ Bacterial infection accounts for approximately 90% of microbial keratitis.⁹ Microbial keratitis increased in prevalence following the introduction of soft lenses in the 1970s.³ The most common pathogens implicated are staphylococci and pseudomonas.^{5,6,11,13,14,17-19} While most corneal ulcers in North America are bacterial in origin (accounting for approximately 90% of cases of microbial keratitis) and are most often caused by contact lens wear, trauma (often fungal) is the leading cause of ulcers in developing countries.^{2,5,8,9}

Case report

A twenty-six-year-old female presented to our clinic on May 21, 2009 with a painful right eye which was swollen shut. The patient had been seen in our clinic for routine eye exams in 2006 and 2007 and was a wearer of contact lenses (O₂ Optix -2.75 D OU, BC 8.6 DIA 14.2). She had been referred back to us by her family physician, who believed she had either a foreign body trapped in her right eye or a corneal ulcer. The patient had slept in her contact lenses the previous night. She denied using water either to clean or to store her lenses and claimed to have changed her multipurpose solution on a nightly basis. The patient also replaced her lenses fortnightly. There was no history either of swimming with the contact lenses or of injury to the eye involving vegetation.

The young woman's ocular and medical history was negative, and she denied either taking medication or having allergies. Her presenting visual acuity was 20/20 in each eye with glasses at distance. Slit lamp evaluation revealed diffuse conjunctival injection and a small circular epithelial defect with underlying stromal infiltration in the midperiphery of the right eye. The patient had a trace anterior chamber reaction and small amounts of mucopurulent discharge.

The differential diagnosis considered in this case includes the following:

- Bacterial keratitis (corneal ulcer) represents the overwhelming majority of contact-lens-related microbial keratitis (CLMK)⁹ and is defined by stromal loss with an overlying epithelial defect.¹⁸ The ulcer is associated with overnight contact lens wear.^{4,8} Pain, redness, mucopurulent discharge, photophobia and an anterior chamber reaction may be present.¹⁰
- Fungal keratitis is associated with traumatic corneal injury, especially from vegetable matter.^{11,13} The fungal lesion generally has feathery borders and may be surrounded by satellite infiltrates.¹⁸ This condition is more common in developing countries.^{2,5,6,8}
- Acanthamoeba keratitis manifests as an extremely painful ring-shaped infiltrate possibly associated with either swimming while wearing contact lenses^{12,18} or generally poor contact lens disinfection (the use of either tap water or saline instead of multipurpose solution).¹³ The patient usually has severe pain disproportionate to clinical findings.¹² The condition develops over a period of several weeks.¹⁸
- Herpes simplex keratitis is due to the reactivation of latent Herpes simplex virus-1 (HSV-1) which migrates down the axon of the branch of the trigeminal nerve to

the cornea.¹³ Dendrites with true terminal bulbs may be present on the cornea,¹² and corneal sensitivity may be decreased.¹⁸

- Herpes zoster keratitis may involve pseudodendritic lesions present on the cornea.¹² Typically, painful skin vesicles are present along a dermatomal distribution not crossing the midline.¹⁸ The condition is due to a reactivation of Herpes zoster virus (HZV) and migration to the first division of the trigeminal nerve to the skin and eye.¹³ Herpes zoster keratitis is most common in the aged and the immunocompromised.¹⁸
- Marginal keratitis is a reaction to staphylococcal exotoxins.¹³ Marginal keratitis generally occurs with coexisting conditions of either blepharitis or ocular rosacea and is usually accompanied by multiple subepithelial marginal infiltrates separated from the limbus by a clear zone.¹⁸ The condition is often bilateral and recurrent.¹⁸ Corneal staining is also possible.¹² Conjunctival injection is usually localized.¹⁸

The patient's skin was clear, and she had neither dendrites nor pseudodendrites on her cornea. There was no history of either "cold sores" or an immunocompromised state. She had not used either tap water or saline instead of multipurpose solution to clean her contacts. The ulcer was round with neither feathery borders nor a ring shape, and the pain seemed proportional to the size of the disturbance. There was no history of either blepharitis, acne rosacea or an eye injury involving vegetation. The patient had slept in her lenses and was exhibiting the classic signs and symptoms of contact-lens-related microbial keratitis (CLMK). The patient was diagnosed with bacterial keratitis.

A drop of Cyclopentolate 1% was instilled in the right eye to help to control pain and to prevent synechia formation. With a letter explaining her condition, the patient was sent to Western Hospital Emergency Department for treatment.

In the emergency room, the diagnosis of a corneal ulcer was confirmed and Vigamox was prescribed: one drop in the right eye every two hours. A follow-up was scheduled in the ophthalmology department for the next day.

Follow-up #1

The patient was seen by staff at Western Hospital Ophthalmology on May 22, 2009. Her presenting visual acuity with spectacle correction for distance was 20/20 OD and OS. Pupils were equal and reactive to light and accommodation. Slit lamp examination revealed a small corneal infiltrate with mild staining overtop. There was marked improvement in the patient's condition and the dose of Vigamox was subsequently reduced to one drop four times daily for five days. The small ulcer was attributed to contact lens noncompliance, and she was instructed not to wear contact lenses until her follow-up in one week.

Follow-up #2

The patient returned to Western Hospital Ophthalmologist on June 15, 2009. (Unclear is why, after one week, the patient had not returned as scheduled.) The attending ophthalmologist instructed the patient never to sleep in her contact lenses and informed the patient of the risks of

contact lens noncompliance. The examination was unremarkable, and "eyes all clear" was written in the record. Neither was the ulcer present nor were the symptoms of discharge, redness and pain from the first visit.

Discussion

Contact-lens-related microbial keratitis (CLMK) is a severe and potentially blinding condition requiring urgent treatment to contain damage and to improve prognosis.^{6,9,10,11} Microbial keratitis affects approximately 5 in 10,000 wearers.⁴ (One 2010 study gives a ratio of more than double that.)¹⁵ The use of contact lenses overnight is the single most common risk factor in the developed world.^{6,9}

There are approximately 125 million contact lens wearers globally.⁷ Corneal ulcers are a major cause of vision loss worldwide.² Considering the large number of contact lens wearers, there are important public health consequences for microbial keratitis and other deceptively rare diseases with significant morbidity.⁴

Though the introduction of silicone hydrogels has allowed physiological levels of oxygen to reach the ocular surface, the incidence of corneal ulcers has not dramatically decreased.^{3,4,9,17,20} In fact, there has been an upward trend in ulcers in the U.S.⁶

Mechanism behind ulceration

Although progressive research continues to make inroads into a fuller understanding of the mechanism of ulceration,²⁰ several factors play a role in contact-lens-related keratitis. They include bacterial adherence to the lens, formation of biofilm on the lens and in the storage case, resistance of microorganisms to disinfection systems, stagnation of tear film behind contact lenses and reduced resistance of the cornea to infection.^{9,20}

In bacterial keratitis, bacteria accessing the corneal stroma cause damage and an inflammatory response which result in loss of transparency.³ Although some bacteria can invade a healthy cornea, most enter through either an abnormality or a defect in the corneal surface.¹⁰

Corneal ulceration is mercifully less common than the presence of bacteria on ocular surfaces.^{11,20} Clearly, under normal conditions, the cornea's countermeasures are highly effective against invaders.^{3,20} Hypoxia may increase bacterial binding, compromise corneal integrity and impair wound healing.⁴ These effects are reduced but not eliminated with silicone hydrogel lenses.⁹ Hypoxia, which is unlikely to be the sole factor in corneal ulceration, is most likely a contributor.³

Changes to ocular surface biochemistry underneath the contact lens may be why contact lens wearers are more susceptible to infection.²⁰ Interaction with contact lenses can override the cornea's defence mechanism and increase the rate at which pathogens adhere to the ocular surface and allow progression to microbial keratitis.^{9,17,20} The adhesion of bacteria to contact lenses is considered a major risk factor for serious corneal problems (particularly *Staphylococcus epidermidis* and *Pseudomonas aeruginosa*).^{17,20} Contact lenses are a suitable surface for bacterial adhesion and biofilm formation.²⁰ They sustain a large quantity of

organisms in prolonged contact with the cornea.^{9,17} Rougher contact lenses surfaces are prone to more extensive bacterial adhesion and microbial colonization from imperfections in the lens surface, where deposits may form.¹⁷

Gram negative bacteria may survive at the upper inner rim of the case where, due to the air-liquid interface, biofilms have a higher likelihood of occurring.⁷ Therefore, a patient making contact with that area of the case while handling a lens before its insertion may be severely re-infecting the lens.⁷

Contamination of the contact lens case has been associated with microbial keratitis.⁹ The case has been shown to be more heavily contaminated than either lens or solution.⁷ The same strains have been isolated from a corneal ulcer and the contact lens case.⁷ Level of contamination is associated with the age of the lens case.⁴

The elimination of "rub and rinse" may decrease the amount of microorganisms removed in the cleaning process and create a "carry-over effect" (from lens to case) which allows the remaining pathogens to form a biofilm in the case and to increase their virulence and rate of survival.^{7,9,10,20}

Contact lens wear seems to reduce tear exchange; the mean elimination rate in eyes wearing conventional contact lenses is about half of that observed in normal non-wearers of contact lenses.^{9,20} However, silicone hydrogels may allow significantly higher levels of tear exchange than conventional lenses.²¹ The impact of tear exchange on the risk of microbial keratitis is not fully understood.^{3,20,21}

Risk of contact lens microbial keratitis varies widely with the type of contact lens and pattern of wear.¹⁰ The rate of progression of microbial keratitis is dependent on the virulence of the offending pathogen and host factors.^{10,11} *Pseudomonas aeruginosa*, one of the more common pathogens in CLMK, is highly destructive and difficult to neutralize because of its virulent structure, adaptability and high rate of survival under different conditions.^{3,20} Another highly common pathogen in CLMK, *staphylococcus*, may account for 45% of all bacterial keratitis.^{11,17}

The role of laboratory culture

Because no clinical features of microbial keratitis may be considered pathognomonic, the identification of the pathogen is critical.¹ In the U.S., the most common practice begins treatment empirically and only investigates the offending pathogen if initial treatment fails.^{1,2,10} One U.S. study has shown that approximately half of American ophthalmologists routinely culture and only 17.5% gram stain.¹⁶ The same study showed that only 13% perform cultures more than fifty per cent of the time.¹⁶

A restrained approach to cultures may be justified when we consider that over 90% of ulcers in the U.S. are bacterial in nature and respond to antibiotics.² The policy that all ulcers be cultured before treatment be initiated is, for practical reasons of time and cost, not followed by most specialists.^{2,22} Before initiating treatment, cultures are indicated in either sight-threatening or severe keratitis.¹⁰ Smears and cultures are indicated either when the infiltrate is large, when it is central, when there is no response to broad spectrum antibiotics or when the observation of

atypical clinical features suggests a more exotic pathogen (such as either fungus or acanthamoeba).^{10,18}

Cultures can also decrease toxicity by eliminating the use of unhelpful medications.¹⁰ Culture yields can be improved by avoiding anaesthetics with preservatives.¹⁰ Cultures of either the contact lens, its case or the solution may also be helpful.^{10,18} The best approach is to culture and to treat lesions as potentially infective.²²

Management

CLMK is assumed to be bacterial until proven otherwise.^{12,18} The goal of treatment is the rapid eradication of the pathogen.¹ Currently the “gold standard” of treatment for corneal ulceration is the use of fortified antibiotics: either cefazolin 5% and tobramycin 1.3% or monotherapy with second generation fluoroquinolones (either ciprofloxacin or oxacin).^{8,19}

Frequency of re-evaluation depends on severity of disease but microbial keratitis should initially be monitored on a daily basis.^{10,12} If pain decreases and the epithelial defect, inltrate size and anterior chamber reaction improve, the treatment may be considered to be effective.¹⁸

Treatment should be re-evaluated after 48 hours if there is no sign of improvement (although pseudomonas and other gram negative bacteria may show increased inflammation despite appropriate therapy within the first 24 to 48 hours).¹⁰ When ulcers are either atypical or unresponsive to medication, a mixed bacterial and fungal infection should be considered.¹¹ Ciprofloxacin ointment at bedtime (optionally tobramycin in less severe cases) may be useful.¹⁸ Cycloplegic drugs decrease synechia formation, reduce pain and manage anterior chamber reaction.^{12,13}

While some experts advocate the use of topical corticosteroids in concert with topical antibiotics,²² the value of topical steroids remains controversial.^{12,13} There is no conclusive evidence that corticosteroids alter clinical outcome.^{10,13} Consequently, the amount of corticosteroids used to achieve control of inflammation should be minimized.¹⁰ Subconjunctival antibiotics may be used in patients with poor compliance with topical treatment.¹³ Systemic antibiotics are rarely used but may be considered for severe infections.^{10,13}

Keratoplasty may be considered when aggressive microbial keratitis doesn't respond to medical therapy.^{11,18} The procedure aims to eliminate the infectious disease process and to establish the integrity of the globe.^{11,23} The procedure offers a microbial cure rate of 90 to 100%.²³ With the emergence of more potent antimicrobial agents, therapeutic keratoplasty is required less often.²³ A recent study in Bahrain found that only 1% of CLMK patients needed therapeutic keratoplasty.⁶

After their introduction in the 1990s, second generation fluoroquinolones quickly became an accepted alternative to fortified antibiotics.¹⁶ Ciprofloxacin was the most frequently used topical medication –prescribed to approximately 90% of patients in the Portsmouth study.¹⁴

Relative ease of dosing and higher potency are among the factors increasing interest in fourth generation fluoroquinolones, which are also without the recent resistance some bacteria have developed to Ciloxan (ciprofloxacin) and Ocuflox (ofloxacin).^{8,10} The suggested

initial dose of either Vigamox (moxifloxacin) or Zymar (gatifloxacin) is one drop every one to two hours.^{12,18} In less severe cases, a regime with less frequent dosing is appropriate.¹⁰

Moxifloxacin and gatifloxacin both have improved potency and impede growth of organisms resistant to the second and third generation antibiotics.^{8,10,19} In a recent study, moxifloxacin and gatifloxacin were found to have lower minimum inhibitory concentrations (MIC) than fortified antibiotics and second generation fluoroquinolones.⁸ The inhibitory property of DNA topoisomerase IV reduces the likelihood that pathogens shall develop resistance to moxifloxacin and gatifloxacin.^{8,10} Fourth generation fluoroquinolones require two mutations to establish resistance while the second generation only needs one mutation for resistance to occur.¹⁹ They have better penetration of the cornea and aqueous and therefore may lead to more effective therapeutic levels and better prognosis.⁸

One study by Hsu et al. has found that corneal specialists and comprehensive ophthalmologists by overwhelming majority (76% and 88% respectively) use fourth generation fluoroquinolones as the initial treatment of choice in corneal ulcers.¹⁶ Several studies have found no difference in efficacy between the fourth generation fluoroquinolones and the generally accepted alternatives.^{8,19} Emerging evidence of resistance to fourth generation fluoroquinolones is isolated,⁸ and they can therefore be considered just as effective as, if not more effective than, the currently accepted treatments.^{10,12,13,16,18,19} However, fourth generation fluoroquinolones are not yet FDA-approved for treatment of bacterial keratitis.^{8,10}

Risk factors, prevention and innovations in care

The problem of contact lens care is a common one; studies suggest that 40 to 70% of patients are noncompliant.²⁴ Healthy contact lens wear depends on many factors. They include age, sex, lens brand, smoking habits, cleaning regime and wearing regime.²⁵ Higher rates of complications were associated with men, with youth, with smokers, with longer periods of wear and with a lack of hand-washing.^{7,17,24,25} (Internet purchase, possibly due to attitudes and behaviours associated with it, was also recently identified as a risk.)⁴

Noncompliance with the manufacturer's recommended frequency of replacement of contact lenses is highest among teenagers and among the wearers of non-silicone hydrogels.²⁴

Microbial contamination of contact lens case and poor contact lens hygiene are also associated with microbial keratitis.⁴ Recent studies also suggest noncompliance is a factor in corneal infections related to CL solution.²⁴ Patients using hydrogen peroxide solutions were found to be more compliant with the contact lens replacement schedule, perhaps because the care regime is more complex and demanding.²⁴

Daily disposables were found to be associated with the lowest rate of complications in general.²⁴ They also have lower risks for severe CLMK and associated vision loss.^{4,20} Because neither a case nor a cleaning regime is at issue with daily disposables, their use may both reduce the risk of microbial keratitis and decrease its severity.^{4,7} Studies

suggesting that daily wear decreased the risk of microbial keratitis remain controversial.^{9,15,20,26}

Early treatment can limit the scarring and vision loss caused by CLMK.^{8,27} Even a slight delay in assessment and treatment can increase the risk of a poorer outcome.^{11,25} Recent studies show that treatment delayed by more than 12 hours increases the risk of vision loss.⁹ Therefore, timely recognition and treatment is of paramount importance.^{1,10} This would suggest that countries should follow the American model and expand the scope of practice of optometrists to enable more immediate access to crucial care.²⁵

Although the risk to the individual is low, the group at risk is a vital one, including the young, healthy and of working age who are at low risk of infection in the absence of overnight contact lens wear.^{4,6,9} Though lenses may be approved for overnight wear, informing patients of the associated risks of such use may decrease the incidence of corneal ulcers.¹⁵ Risks include the destructive nature of microbial keratitis and the potential for rapid, painful and permanent vision loss.^{10,27} There is evidence that overnight contact lens wearers are at greater risk of microbial keratitis especially in the early days of their wear experience.⁴ Patients should be particularly cautioned never either to sleep or to nap in their contact lenses.¹⁰ Teenaged and young adults should be especially educated on proper contact lens procedures and the potential for complications. Demographically common behaviours such as poor hygiene, binge drinking and contact lens overuse put them at higher risk.²⁵

Confocal microscopy is a promising tool in the diagnostic arsenal and may be used in the differential diagnosis of infectious keratitis, particularly where it involves acanthamoeba and fungus.^{1,10,12}

Collagen crosslinking (CXL) with riboflavin and ultraviolet-light A, has been used successfully to halt the progression of Keratoconus^{28,29} by increasing the biomechanical strength of the tissue and has shown potential as a treatment for severe cases of bacterial keratitis^{29,30,31,32}. Photoactivation of riboflavin (a naturally occurring vitamin^{32,33}) is thought to damage the RNA and DNA of bacteria, viruses and parasites^{31,33} and to inactivate them.^{29,31,32,33} CXL may also increase the collagen defence against enzymatic degradation.²⁹ This technique could potentially be used as an alternative to keratoplasty when ulcers do not respond to either systemic or topical therapy.^{29,30,31} A crosslinked cornea is also more resistant to corneal melting.³¹ Further investigation is needed to determine the ideal role of corneal crosslinking in the treatment of bacterial keratitis.^{29,31} The use of this technique is not yet widespread.³² Due to possible cytotoxic effects, CXL should be considered only in keratitis resistant to therapy and not as a first line of treatment.²⁹

Better lens storage design, frequent replacement of the case (every 3 to 6 months) and improved hygiene may decrease the incidence of corneal ulceration.⁷ Rubbing contact lenses when cleaning should be encouraged because that method may be superior to the "no rub" alternative.^{9,10,34}

A recent study by Hua Zhu et al. found that "rub and rinse" removed bacteria more effectively than did rinsing

alone, without regard to either the multipurpose solution used or the type of contact lens.³⁴ Interestingly, with "rinse only" multipurpose disinfection, a regime containing Polyquad solution removed more bacteria than did those with PHMB (polyhexamethylene biguanide), and Gaty Icon was more resistant to bacterial adhesion (with rinse only) than were other silicone hydrogel lenses.³⁴

A better understanding of the mechanism behind microbial keratitis will help eye care professionals to recommend and ultimately to create better lenses and to suggest ways to decrease the risks.²⁰ For the present, the fitting of patients in silicone hydrogels and daily disposables while absolutely advocating against sleeping in the lenses appears to be the best form of prevention.

Conclusions

This case of bacterial keratitis demonstrated how rapid diagnosis and effective management in the initial stages of the condition resulted in quick resolution and prevented vision loss. Continued research into the pathogenesis of bacterial keratitis as well as patient education on proper contact lens procedures will hopefully decrease the incidence of this potentially devastating infection.

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