



CASE REPORT

Good Outcome of Corneal Ulcer with Hypopyon After Long Use of Contact Lens

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**Abstract**

Introduction: Microbial keratitis is a corneal infection caused by microorganisms and is characterized by a profound corneal epithelial defect that infects the cornea and causes severe and progressive visual loss. In recent years, the incidence of microbial keratitis has increased. One of the critical risk factors for increasing this incidence is using contact lenses. As the number of contact lens users increases, the number of corneal ulcers associated with contact lenses also increases. **Case Presentation:** A 25-year-old man was admitted to the emergency department with a complaint of gradually blurry vision in his left eye four days after using contact lenses for overnight uses since the previous few days and did not routinely clean contact lenses or replace contact lens cleaning fluid. The visual acuity of the patient's left eye was hand movement with conjunctival and pericorneal injection in the conjunctiva and 6 x 7 mm stromal level infiltrate, blurred margin, and whitish color in the center of the cornea. After 28 days of treatment, an examination showed the patient's left eye improvement. Visual acuity was 3/60, conjunctival injection disappeared, corneal swelling significantly resolved, hypopyon disappeared, and ulcer completely re-epithelialized. **Conclusions:** Empirical therapy with broad-spectrum antibiotics and other adjunctive therapy has a good outcome in treating contact lens-related corneal ulcers.

Keywords: contact lens; corneal ulcer; microbial keratitis; bacterial keratitis

Introduction

The incidence of contact lens-related complications is rising due to increasing contact lens usage. The most frequent contact lens-related complications include dry eye, pinguecula, corneal neovascularization, microbial keratitis, and giant papillary conjunctivitis.^[1] An overlying corneal epithelial defect and corneal infiltrates are the hallmarks of microbial keratitis, which bacteria, fungi, amoebas, or viruses can cause. The incidence rates for contact lenses associated with microbial keratitis range from 2 to 20.9 per 10,000 people globally and seem to increase as more people use them.^[2] This medical condition is severe, progressive, and sight-threatening.^{[3],[4]} Here, we discuss the case of a 25-year-old man who first presented with a significant corneal ulcer caused by contact lens wear and how the ulcer progressed after treatment.

Case presentation

A 25-year-old man had been referred by an eye clinic in East Java to the emergency room, complaining of his left eye's vision being gradually blurrier four days prior. The complaint is accompanied by red eye, watering, difficulty opening the eye, glare, and pain. The patient said that white patches have appeared on the cornea of the left eye since three days ago. Complaints arose after the patient used extended-wear contact lenses for overnight use for the previous few days and did not routinely clean contact lenses and replace the contact lens cleaning fluid. The patient has routinely used contact lenses daily for the last two months to correct myopia.

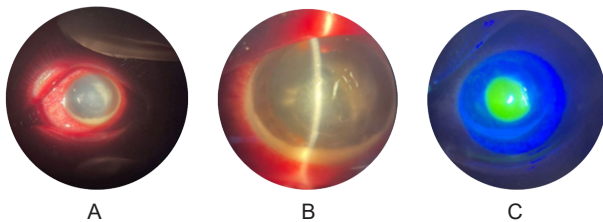


Figure 1. Left eye clinical presentation. (A) Infiltrate size 6×7 mm with blurred margins, whitish center surrounded by corneal swelling; (B) infiltrate at stroma level, and (C) positive 5×5 mm fluorescent test.

His examination at the first visit revealed typical vital signs. The left eye's visual acuity was hand movement, and the right eye was 6/60, increased by pinhole to 6/18. Intraocular pressure in both eyes was normal palpation. Examination of the left eye showed minimal swelling of the eyelid. Meibomian gland expression showed cloudy fluid in all eyelids. There was conjunctival and pericorneal injections in the conjunctiva. The cornea was hazy with an infiltrate of the 6×7 mm stromal level, a blurred margin, whitish color in the center, and surrounded by swelling of the cornea. The fluorescent test was positive with a size of 5×5 mm. There were no feathery edges, satellite lesions, descemetocoele, or corneal thinning. The anterior chamber had a hypopyon as high as 2 mm. Iris, pupil, lens, and posterior segment were difficult to be evaluated. The right eye's anterior and posterior segments were otherwise normal. Ocular ultrasonography was conducted, and no abnormalities in the posterior segment of the left eye were discovered. Corneal scraping was ordered and showed no form of bacteria or fungi in gram and KOH staining. Also, no fungal growth or aerobic bacteria were found in the culture.

The patient was assessed with contact lens-related corneal ulcer with hypopyon and started to get ceftriaxone

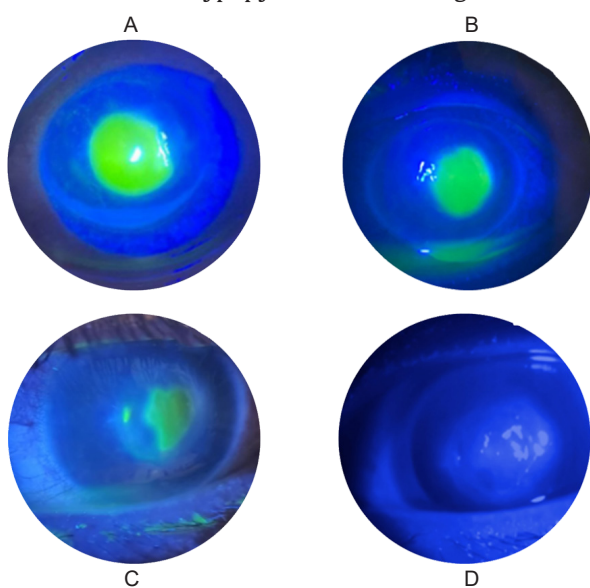


Figure 2. The size of the corneal ulcer was getting smaller, starting from 5×5 mm on the first day of treatment until it became negative after the 28th day of follow-up. (A) First day; (B) Seventh day; (C) 14th day; and (D) 28th day.

one gram intravenous injection every 12 hours for five days, moxifloxacin eyedrop one drop every five minutes for 30 minutes as a loading dose, then followed by one drop every hour for the left eye. Atropine eyedrop one drop every 12 hours for the left eye, artificial tears mini dose eyedrop one drop every two hours for both eyes, doxycycline 100 mg every 12 hours, vitamin C 500 mg every 12 hours, and mefenamic acid 500 mg every eight hours. After seven days of treatment, an examination showed the patient's left eye improvement. Visual acuity was 3/60, and eyelid spasm reduced, hypopyon disappeared, and infiltrate size 4×5 mm with positive fluorescent test size 3×3 mm. On the 14th day of follow-up, conjunctival injection significantly disappeared, and the size of the fluorescent positive area decreased to 2×3 mm. Corneal swelling resolved significantly at the last follow-up on day 28, and the ulcer was re-epithelialized entirely.

Discussion and conclusions

Microbial keratitis is a corneal infection caused by microorganisms characterized by an overlying epithelial defect and corneal infiltrates with severe and progressive vision loss.^[4] The usage of contact lenses is one of the significant risk factors for increasing this incidence. As the number of people who wear contact lenses grows, so does the number of corneal ulcers.^[3] Corneal ulcers caused by contact lenses have been linked to bacterial, fungal, and protozoan infections, most ulcers are caused by bacteria.^{[3],[5],[6]} A study conducted for five years in Japan revealed that 88.6% of microorganisms found in patients' culture is bacteria, followed by fungi (8.6%) and acanthamoeba (2.9%).^[7] *Pseudomonas aeruginosa* is the most prevalent bacteria involved in corneal infection (44%).^[7] Studies conducted^[8] in Asian countries show that in addition to *Pseudomonas aeruginosa*, *Fusarium* is the most common cause of fungal keratitis associated with contact lenses.^[9] *Acanthamoeba* is the less common but well-known protozoan that causes contact lens-related corneal ulcers. Contact lens use is one of the major risk factors for *Acanthamoeba* keratitis (more than 90%).^[5] Several studies^{[9],[10]} have found that overnight wear, poor contact lens case hygiene, infrequent contact lens case replacement, smoking, male sex, ocular surface disorder, and lower socioeconomic status are risk factors for contact lens-associated microbial keratitis. In our case, the patient has several conditions that can become risk factors for developing contact lens-related corneal ulcers, including male sex, overnight use of contact lenses, ocular surface disorder, poor contact lens hygiene, and infrequent contact lens fluid replacement.

There are various types of contact lenses according to the duration of wearing, including extended, overnight, and daily wear. This variation of use lies in the difference in oxygen permeability of the contact lens material used.

Good oxygen permeability allows soft lenses to be used longer. On the other hand, daily-wear contact lenses use hydrogel material and have poor oxygen permeability, making them impossible for long-term use.^[11] The patient has used extended-wear contact lenses for overnight use for the previous few days. Extended-use contact lenses can be used for longer than daily, often one to four weeks, including at night. The risk of developing ulcerative keratitis is ten to fifteen times greater with extended-wear contact lenses than with daily lenses.^{[12],[13]} The night time usage of this type of contact lens, as was the situation with our patients, is associated with a high incidence of extended-wear contact lenses. Long-term contact lens use can cause hypoxic stress on the cornea. When the eyes are open, oxygen from the atmosphere is delivered directly to the cornea. At the sea level, the oxygen concentration in the atmosphere is approximately 21%, corresponding to a partial pressure (PO₂) of 155 mmHg. When the eyes are closed while sleeping, the oxygen supply received by the cornea only comes from the capillary plexus of the palpebral conjunctiva but with a much lower pressure (PO₂ = 55-60 mmHg). Using overnight contact lenses will further reduce the partial pressure of oxygen to the cornea. Consequently, the cornea's oxygen supply is much reduced and can cause the cornea to fall into a hypoxic stage and induce the corneal metabolism to turn anaerobic. Furthermore, on repeated and prolonged exposure, these two end products can also cause damage to the corneal epithelial cells and promote defects to this layer which can be a part of the entry of microorganisms invasion.^[14] Due to the high incidence of keratitis in overnight contact lens wearers, the American Academy of Ophthalmology (AAO)^[12] recommended using contact lenses with extended wear. The usage of contact lenses overnight was only advised once a week.^[12]

Physical examination showed that the expression of the meibomian glands found cloudy secretions. This can indicate the possibility of meibomian gland dysfunction in the patient, an ocular surface disorder that can be a risk factor for contact lens-related corneal ulcer. Deficiencies in the meibomian glands can cause disturbances in the lipid layer of tears, which causes evaporative water loss from the exposed surface of the eye, inducing dry eyes, and can cause corneal epithelial defect.^[15] The corneal epithelium comprises 4-6 layers of epithelial cells. It is 40-50 m thick, and the epithelium and tear film create an optically smooth surface. Tight junctions between superficial epithelial cells stop pathogens from accessing more profound layers of the cornea.^[16] The contact lenses are generally contraindicated in cases of dry eye. Wearing contact lenses may result in insufficient or irregular tear production. This will reduce the stability and volume of tears, causing dry eyes to get worse. Therefore, it is essential to rule out the possibility of dry eye in a patient

before recommending a contact lens. Assessing the ocular surface and tear film of every person who wears contacts is crucial.^[17]

Poor contact lens cleanliness and infrequent replenishment of contact lens fluid are the patient's additional risk factors. There is evidence that contact lens cases, unhygienic storage cases, and infrequent replacement are relevant to the formation of microbial keratitis.^[18] The contact lens storage case frequently contaminates the pathogen organisms. The storage case was where the causative organisms for microbial keratitis were found, and they can also spread to the contact lens during lens insertion. The microorganisms move on to the cornea while being handled and worn.^{[19],[20]} The following hygiene and compliance risk factors contribute to the microbial contamination of contact lens cases, failure to allow the storage case to air dry, failure to rinse the case with a multipurpose solution after removing the lenses, mismatch between the multipurpose solution and storage case, extended lens wear history, infrequent replacement of the disinfection solution, type of disinfection system, use of tap water to rinse the case, and use of an older storage case.^[4]

The slit lamp examination found that the patient's cornea was hazy with a large area of infiltrate, a blurred margin, and a whitish color in the center, surrounded by swelling of the cornea and hypopyon in the anterior chamber. The characteristics of these lesions are typically similar to infections caused by bacteria. Bacterial corneal ulcers often include a single infiltration, a prominent epithelial demarcation, and a thick, suppurative stromal inflammation beneath that has ill-defined boundaries and is encircled by edema. *Pseudomonas aeruginosa*, the most frequent bacterium to cause corneal ulcers associated with contact lenses, frequently results in stromal necrosis, which has an uneven surface and adherent mucopurulent pus, hypopyon, a noticeable anterior chamber response, and endothelial inflammatory plaque. Fungal infections tend to have fewer signs of inflammation but with more intense pain during the initial infection period than bacteria. Gray-white lesions, a raised corneal surface, a dry, rough, or gritty texture, uneven feathery or filamentous edges, and on occasion, multifocal or satellite infiltrates may also be observed are characteristics of the lesions.

On the other hand, *Acanthamoeba* infection is often characterized by severe pain, non-suppurative gray-white infiltrate, and central partial or complete ring infiltrates in the central cornea are often observed.^{[16],[21]} *Pseudomonas aeruginosa* can form biofilms during infection and attach to molecular receptors on damaged epithelial cells. Bacteria will multiply and enter the stroma once bound. Inflammation starts with the release of many cytokines and chemokines, the recruitment of

inflammatory cells from the tear and limbal arteries, and the secretion of matrix metalloproteinases that lead to corneal necrosis, frequently with the support of bacterial-specific proteases.^{[2],[16],[22],[23]}

Standard examination of microbial keratitis includes corneal scraping. The AAO^[16] recommends an infiltrate culture that extends to the center of the cornea, deep in stroma or involves a large area of the cornea (>2 mm), and for patients with a history or clinical presentation suggesting a possibility of fungal, protozoan, mycobacterial, or other drug-resistant organism infection as the causal agent. We ordered corneal scraping but found no form of bacteria or fungi in the gram and KOH staining. Also, no fungal growth or aerobic bacteria were found in the culture. The negative result after corneal scrapings of suspected microbial keratitis has been reported to be 23% and 53%. The unfavorable results of corneal scraping may be caused by previous antibiotic treatment before the procedure. The same finding was made in the study by Das et al.^[24], which showed that the patient's prior use of broad-spectrum antibiotics may have contributed to the reduced positive corneal scraping culture results. Antibiotics should be stopped 12 to 24 hours before scraping, according to the AAO^[16], to improve culture sensitivity. When a corneal scrape culture gives a negative result, a contact lens cast or cleaning liquid culture can offer some crucial hints.^{[16],[24]}

The healing in patients is relatively fast, indicating the success of using a combination of empirical therapy given to patients. We treated the patient with the broad spectrum antibiotics, moxifloxacin eyedrop, and ceftriaxone intravenous, as the empirical therapy without waiting for the corneal scraping result and showing the excellent result with the improvement of the patient's visual acuity and decreasing of infiltrate size. Because it responds effectively to the administration of antibiotics, it suggests that the possible infectious agent is bacteria. Numerous studies demonstrate that microbial keratitis is typically treated empirically, without getting cultures, with a single broad-spectrum antibiotic.^{[25],[26]} Currently, moxifloxacin, fourth-generation fluoroquinolones, is increasingly being accepted and replacing fortified antibiotic therapy, which used to be the standard for managing microbial corneal ulcers. There was no difference in the healing rate or visual acuity at three months in a randomized trial comparing the effectiveness of fourth-generation fluoroquinolone monotherapy with supplemented antibiotics in treating bacterial corneal ulcers.^[27] Fluoroquinolones act by inhibiting DNA topoisomerase involved in bacterial DNA synthesis; this enzyme is not present in human cells and is essential for bacterial DNA replication, thus allowing fluoroquinolones to have specific and bactericide effects.^[28]

In our case, antibiotics were intended to lessen the amount of bacteria and the ensuing inflammatory

reactions, but they did not address the continued corneal melting process. Therefore, using anti-metalloproteinases like doxycycline to treat persistent stromal necrosis and stop corneal melting may be advantageous. A broad-spectrum antibiotic such as doxycycline works by preventing the formation of bacterial proteins. They also have anti-collagenolytic activity through the ability to inhibit MMP9, including collagenase.^[29] The ability of doxycycline as an anti-collagenase is related to its ability to chelate calcium and zinc ions. Collagenases and other metalloproteinase enzymes need cations like calcium, zinc, or magnesium to remain active. Therefore, doxycycline's chelation of these ions can lower the activity of these enzymes.^[30]

The patient was also given vitamin C. Vitamin C has been shown to have a protective effect on the epithelial and stromal layers of the cornea in patients with corneal ulcers. Vitamin C is an essential modulator of collagen production. Proline and lysine residues in procollagen are hydroxylated by vitamin C, which boosts the formation of various collagen forms. Additionally, vitamin C can inhibit the angiogenic factors, vascular endothelial growth factor, and mucous membrane pemphigoid (MMP), preventing corneal neovascularization. Another action of vitamin C is that it can act as a cofactor for extracellular matrix synthesis to help the tissue recovering from corneal stromal damage tissue recovers normally. Vitamin C also has antioxidant effects. It can protect the eye from the inflammatory response by scavenging reactive oxygen radicals. Therefore, it is expected to prevent the surrounding stromal and epithelial tissue from being damaged. All these effects make vitamin C able to promote accelerated healing of the corneal epithelium and reduce corneal opacity.^[31]

We also give the patient an atropine eyedrop. The parasympatholytic drug atropine can cause the pupil to dilate by acting directly on it. The chance of developing posterior synechiae is lower when the pupil dilates. Atropine additionally reduces the exudation of proteins and cells into the anterior chamber by restoring the integrity of the blood-water barrier. Finally, it can reduce the level of inflammation in the anterior chamber.^[32] Administration of carboxymethylcellulose (CMC) as artificial tears aims to reduce dry eyes and promote healing of the corneal epithelium in patients. CMC is a polymer of glucopyranose subunits, the predominant form of glucose in solution. The viscous and mucoadhesive qualities of the CMC found in artificial tears help explain their prolonged retention on the ocular surface. Transient extracellular matrix proteins like fibronectin are used in the first stage of epithelial wound repair. To create CMC-fibronectin or collagen complexes, CMC can bind to the matrix proteins fibronectin or collagen, making it easier for epithelial cells to adhere and promoting epithelial corneal repair.^[33]

The patient presented with a visually threatening lesion because it was centrally located, large, and ulcerated as deep as the cornea's stroma. This presentation is comparable to specific studies that indicate a rise in the severity of corneal ulcers caused by contact lenses. Larger ulcers, the development of hypopyon, and an increase in central or paracentral ulcers are all related to the more severe ulcers becoming a vision-threatening condition.^{[7],[34]} Damage that occurs deeper than Bowman's membrane will cause scarring of the cornea and potentially cause visual impairment if it is significant and the location covers the visual axis.^[16] A severe injury that damages Descemet's membrane and causes a delay in basement membrane regeneration causes profibrotic cytokines like transforming growth factor (TGF) 1, TGF 2, and platelet-derived growth factor (PDGF) to penetrate the tissue for an extended time. These cytokines encourage the growth of mature smooth muscle actin alpha (SMA)+ myofibroblasts, which then secrete large amounts of fragmented extracellular matrix components to cause stromal fibrosis.^[35]

Never sleep in contact lenses, wash hands with soap and water before handling lenses, keep water away from lenses and contact lens case, avoid swimming or taking a shower while wearing contact lenses, recommended by the eye care provider, replace contact lens case at least once every three months, and remove contact lenses immediately are all recommended prevention measures by the centers for disease control (CDC).^[5] Before disinfecting contact lens that will be reused. Rubbing the contact lens as part of the cleaning step is essential. Rubbing improves cleaning performance by removing loosely bound deposits, including bacterial colonies or biofilms that can grow in contact lenses or solutions.^[12]

Education to patients, because currently, the patient has a history of failure to care for contact lenses and monoculars, which is a relative contraindication to using contact lenses so that to correct myopia, the patient is advised to wear glasses. Other relative contraindications that we should consider when suggesting contact lenses for patients include diabetes mellitus, mainly if poorly controlled, use of immunosuppression agent, long-term use of topical ocular medications such as corticosteroids, high-risk exposure of occupational chemical or foreign body, abnormal eyelid function severe dry eye, and corneal neovascularization.^[16]

In conclusion, contact lens-related corneal ulcers are severe, progressive, and sight-threatening medical conditions. The prevalence of corneal ulcers caused by contact lenses likewise rises as more people use them. Bacterial, fungal, and protozoan infections are all related to corneal ulcers caused by contact lens wear. Several risk factors for contact lens-associated microbial keratitis include overnight wear, poor contact lens case

hygiene, infrequent replacement of contact lens cases, smoking, male sex, and lower socioeconomic level. Corneal scraping is a standard part of the examination for microbial keratitis. The use of antibiotics prior to corneal scraping may be the reason for the procedure's negative result. In this situation, contact lens culture can provide some critical clues. Fourth-generation fluoroquinolones are increasingly being accepted and replacing fortified antibiotic therapy, which used to be the standard treatment of microbial corneal ulcers.

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