Contact Lens-Related Corneal Ulcer: A Teaching Case Report

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Abstract

Corneal ulcer, or ulcerative keratitis, is essentially an open wound to the eye. It is characterized by disruption of the corneal epithelium and stroma and can be either inflammatory or infectious. This teaching case report reviews the diagnosis and management of a specific contact lens-related corneal ulcer case and includes a discussion of the differential diagnosis, risk factors, and pharmacological treatments for corneal ulcers. This topic is important because of the potentially severe ocular complications that can arise from overwear of contact lenses.

Key Words: *corneal ulcer, infectious keratitis, ulcerative keratitis, contact lens, fluoroquinolone*

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Background

Corneal ulcer, also known as ulcerative keratitis and infectious keratitis, is most often associated with contact lens use or misuse. The following case report involves a 30-year-old African-American female who developed a corneal ulcer after falling asleep in her contact lenses. It discusses the differential diagnosis, risk factors and pharmacological treatments for corneal ulcers as well as the educational component necessary to transfer the information from a didactic to a clinical setting. The case is appropriate as a teaching guide for second- third- and fourth-year students. While second-year students may benefit from a review of ocular anatomy and pharmacology, third- and fourth-year students can learn the sequence of care for a contact lens-related corneal ulcer ranging from initial diagnosis to treatment and proper patient education for the prevention of future episodes. This topic is important to teach because of the potentially sight-threatening consequences of corneal ulcers.

Student Discussion Guide

Case description

Patient GG, a 30-year-old African-American female was referred from the urgent care clinic at a neighborhood community health center on Jan. 28, 2006 for pain in her right eye (OD). She reported falling asleep in her contact lenses (CLs) two nights prior to the visit and waking the next morning with no ocular problems. She continued to wear her CLs until she removed them at noon, when the eye started to bother her. She noted burning, redness, tearing and sensitivity to light OD and stated that it "feels as if there is something in it." She had not used any eye drops and reported no discharge from her eyes. She denied any recent trauma or surgery to her eye, and confirmed she had not traveled recently to a warm and moist environment. She had not been swimming in her CLs or using tap water to clean them.

The patient was on her last pair of CLs and did not know the brand of CLs or solution used. Since she had not saved any of the blister packs, she was not able to bring them to the next visit. She did

not recall the name or location of her last eye doctor or the date of her last visit. She typically wore her CLs for 10 hours a day and replaced them every two months. This was the second incidence of falling asleep in her CLs.

The patient's medical history was positive for asthma, depression, eczema, and chronic allergic rhinitis. She was taking indomethacin, hydrocortisone cream, albuterol and hydroxyzine hydrochloride tablets. She was a nonsmoker and denied any allergies to medications. She reported no history of ocular disease, eye surgery, diabetes or collagen vascular disease. Entering distance visual acuity with her spectacle lenses was 20/25 OD and 20/20 OS. She reported the OD was blurrier than usual. The pupils were equally round and reactive to light with negative afferent pupillary defect noted OU. Anterior segment evaluation by slit lamp examination revealed clear lashes OU, meibomian gland stasis OU, grade 1 conjunctival hyperemia OD and clear conjunctiva OS. An approximately 0.5-mm, round, deep, well-demarcated white epithelial defect with stromal excavation slightly inferior nasal to the visual axis was seen OD. (A depiction of this defect is seen in **Figure 1**. It is not the actual photo of this patient.)

Use of a 0.6-mg fluorescein sodium strip OD/OS highlighted the area of the defect OD. There was also grade 2 corneal edema affecting the epithelial layer that was slightly larger than 0.5 mm OD but no hypopyon OD/OS. The anterior chamber revealed grade 2 cells and flare OD but was clear OS. The iris, angle (on Von Herrick estimation) and lens were normal OU. One drop of fluorescein sodium/benoxinate ophthalmic solution (Fluress) was instilled OD/OS, and intraocular pressures measured at 10:10 a.m. by Goldmann applanation tonometry were 13 mmHg OD and 13 mmHg OS. The tentative diagnosis at this time was corneal ulcer OD. Data from the examination on Jan. 28, 2006 are listed in **Table 1.**

Follow-up #1: Jan. 31, 2006

The patient missed her 24-hour follow-up appointment but returned on Jan. 31, 2006, three days after her initial visit. She reported a 50% improvement in redness, pain and irritation OD. As prescribed at the initial visit, she had

Figure 1
Example of a corneal ulcer (reprinted with permission from Dr. Joseph Sowka).

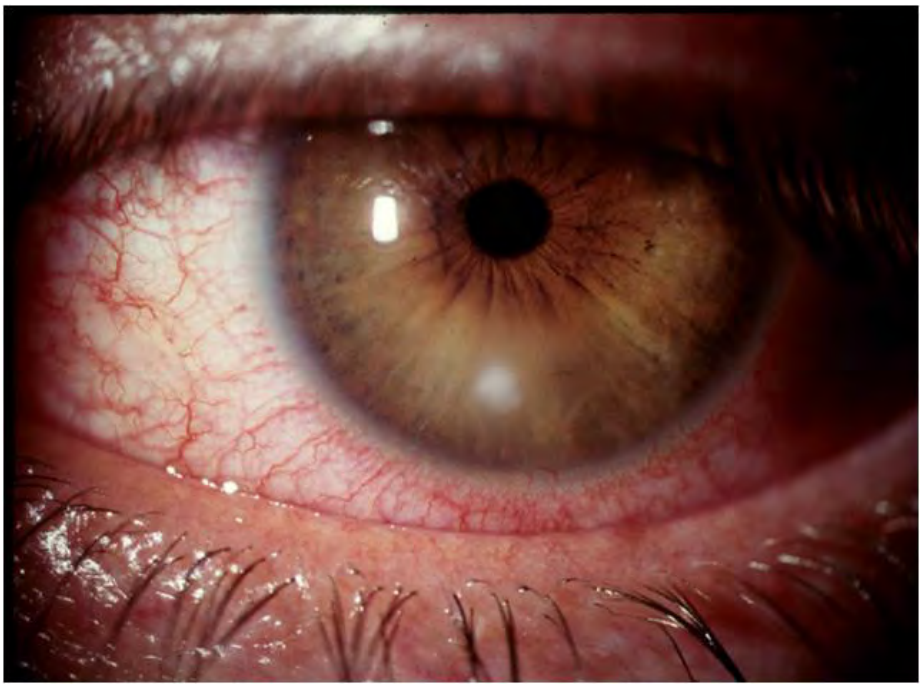

Table 1
Initial Presentation: Jan. 28, 2006

	OD	OS
Distance VA with glasses	20/25	20/20
Pupils	Pupils equal, round and reactive to light (PERRL) Negative afferent pupillary defect (APD)	PERRL Negative APD
Significant anterior segment findings	Grade 1 conjunctival hyperemia Round, deep, well-demarcated white epithelial defect with stromal excavation ~ 0.5 mm in size slightly inferior nasal to visual axis Grade 2 corneal edema No hypopyon	Clear
Fluorescein staining	Positive staining depicted an excavated corneal defect	Clear
Anterior chamber	Grade 2 cells and flare	Clear
Intraocular pressures (GAT) @ 10:10 a.m.	13 mmHg	13 mmHg

been using moxifloxacin (Vigamox) five times per day OD and cyclopentolate (Cyclogyl) bid OD. She had also been using over-the-counter Walgreen's artificial tears three times per day, which had been recommended by the store pharmacist. The patient reported no changes to vision or health since the last eye exam.

Distance visual acuity with spectacle correction was 20/30+2 OD and 20/20 OS. Pupils were equally round and reactive to light with negative afferent pupil defect noted OU. Anterior segment evaluation with slit lamp revealed clear lashes OU, mild meibomian gland stasis in the lids OU, grade 1+ hyperemia in the inferior conjunctiva OD and no hyperemia OS. A corneal scar, approximately 0.5 mm, was present slightly inferior nasal to the visual axis OD. A 0.6-mg fluorescein sodium ophthalmic strip was instilled OD/OS, which revealed inferior punctate epithelial erosion (PEE) OU and no staining in the area of the ulcer OD. All other structures, including the iris, angle and lens were unchanged from the previous visit. The secondary anterior chamber reaction had resolved. One drop of fluorescein sodium/benoxinateophthalmic solution was instilled OD/OS and revealed intraocular pressures of 12 mmHg OD and 12 mmHg OS at 9:30 a.m. by Goldmann applanation tonometry. Data from this examination is shown in **Table 2**.

Table 2
Follow-Up #1: Jan. 31, 2006

	OD	OS
Distance VA with glasses	20/30+2	20/20
Pupils	Pupils equal, round and reactive to light (PERRL) Negative afferent pupillary defect (APD)	PERRL Negative APD
Significant anterior segment findings	Grade 1+conjunctival hyperemia Corneal scar ~0.5 mm slightly inferior nasal to visual axis	Clear
Fluorescein staining	Inferior punctate epithelial erosion (PEE) No staining in area of ulcer	Inferior punctate epithelial erosion (PEE)
Anterior chamber	Clear	Clear
Intraocular pressures (GAT) @ 9:30 a.m.	12 mmHg	12 mmHg

Table 3
Follow-Up #2: Feb. 3, 2006

	OD	OS
Distance VA with glasses	20/25+1	20/20
Pupils	Pupils equal, round and reactive to light (PERRL) Negative afferent pupillary defect (APD)	PERRL Negative APD
Significant anterior segment findings	Corneal scar ~ 0.5 mm in size inferior nasal to visual axis	Clear
Fluorescein staining	Clear	Clear
Anterior chamber	Clear	Clear
Intraocular pressures (GAT) @ 1:20 p.m.	10 mmHg	10 mmHg

The assessment was that the patient had a resolving corneal ulcer OD with resultant stromal scar and resolved secondary uveitis OD. The patient was instructed to continue moxifloxacin fives times per day OD and to discontinue the cyclopentolateas her pain had subsided. The patient was also instructed to discontinue the Walgreen's artificial tears and to start using preservative-free artificial tears (TheraTears) tidOU to treat the superficial punctate keratitis. She was to return in three days for follow-up or sooner with worsening symptoms or pain.

Follow-up #2: Feb. 3, 2006

The patient returned three days later on Feb. 3, 2006. She reported improved vision with no pain, redness, tearing or discharge OD. The patient was still using moxifloxacin five times per day, last dosed a half hour prior to the visit. She was also using preservative-free artificial tears as instructed tid OU. She reported no changes to vision or health since the last eye exam.

Distance visual acuity with spectacle correction was 20/25+1 OD and 20/20 OS. Pupils were equally round and reactive to light with negative afferent pupillary defect noted OU. Anterior segment evaluation by slit lamp revealed clear lashes OU, meibomian gland stasis OU, and clear conjunctiva OU. A corneal scar approximately 0.5 mm in size was seen inferior nasal to the visual axis OD. One 0.6-mg fluorescein sodium ophthalmic strip was instilled OD/OS and revealed mild inferior PEE OU and instantaneous tear break-up time (TBUT) OD/OS. All other structures including iris, angle, anterior chamber and lens remained unchanged OU. One drop of fluorescein sodium/benoxinate ophthalmic solution was instilled OD/OS and revealed intraocular pressures of 10 mmHg OD and 10 mmHg OS at 1:20 p.m. by Goldmann applanation tonometry. Lensometry indicated a prescription of -5.25 sphere OD and -5.00 sphere OS. Data from this examination are shown in **Table 3**.

The diagnosis was stromal scar resulting from corneal ulcer due to CL overwear OD and meibomian gland stasis with secondary dry eye OU. The patient was instructed to discontinue moxifloxacin and to continue the preservative-free artificial tears tid OU. She was advised on warm compresses bid and lid scrubs bid OU for the meibomian gland stasis. The patient was asked to return in two weeks for a comprehensive eye exam and CL fitting. She was instructed to discontinue CLs until her next visit. She was educated on the risks of extended wear and the need for proper lens care. She was to return to the clinic sooner than two weeks if any of the symptoms of pain, redness or decreased vision resurfaced. Unfortunately the patient did not return.

Learning objectives

At the conclusion of the case discussion, students should be able to:

1. Describe the corneal ocular anatomy and metabolism in relationship to microbial infection and its consequences.
2. Describe the etiology and differential diagnosis of a corneal ulcer.
3. Describe the evidence needed to diagnose an infectious corneal ulcer.
4. Identify the risk factors associated with a corneal ulcer.
5. Identify treatment options, including standard of care, implications of the management plan and evidence-based medicine.
6. Determine appropriate contact lens fitting options after corneal ulcer resolution.
7. Differentiate between inflammatory and infectious corneal ulcers.

Key concepts

1. The pathophysiology of a corneal ulcer, including bacteria invasion of cells and tissue response.
2. The body's natural immunological response to bacterial invasion.
3. The role of medication in enhancing the body's response to an invading organism.
4. The role of CL wear in influencing corneal metabolism and increasing susceptibility.

Discussion topics

1. Ocular anatomy of the cornea
   a. layers of the cornea
   b. blood supply to the cornea
   c. metabolic activity of the cornea
   d. scarring in the cornea
2. Etiology and differential diagnosis of corneal ulcers
   a. differentiating between bacterial, fungal, acanthamoebic and herpes types
   b. how bacteria invade tissue
   c. signs and symptoms
3. Evidence needed to diagnose
   a. history of CL wear
   b. physical exam and signs of corneal ulcer
   c. staining pattern of corneal ulcers
   d. culture use, e.g., when to culture and what to do when not equipped to culture
   e. inflammation vs. infection
4. Risk factors for corneal ulcer
   a. decreased oxygen related to CLs, DK, materials, oxygen exchange of CLs vs. oxygen demand of cornea
   b. care of CLs and case disposal, including improper disinfection with water
   c. role of dry eye, blepharitis, being immunocompromised, etc., in increasing risk of corneal ulcer
   d. role of environmental and other factors, such as age, gender and tobacco use, in increasing risk of corneal ulcer
   e. soft CLs vs. gas permeable CLs
5. Treatment options
   a. pharmacological treatment, including off-label use, mode of action of drug, use of steroids, dosage and standard of care, differences between the fluoroquinolones
   b. patient education
   c. complications and implications
6. Contact lens use after corneal ulcer resolution
   a. when to restart CLs, when to refit CLs
   b. patient education
   c. gas permeable CLs vs. soft CLs

Educational Guidelines

Literature review

Corneal ulcers, although debilitating and potentially sight-threatening, are quite a rare disease entity. The incidence of ulcerative keratitis caused by contact lenses is believed to be approximately 71,000 cases per year, with an average of 1.7 ulcerations annually per practitioner[1]. A corneal ulcer is caused by a break in the corneal epithelium and/or stroma and can lead to the entrance of a micro-organism through the break[2]. Although more common unilaterally, it can present bilaterally and can vary in size and severity[1]. Patient demographics include younger patients and those living in developed nations, both who are more likely to wear contact lenses[3]. Corneal ulcers are more common among males due to their greater likelihood of sustaining ocular trauma[6,9]. The etiology can be bacterial, fungal, parasitic or viral and will determine the course of treatment. Other less common risk factors for corneal ulcers include trauma, dry eye, exposure keratopathy and lid abnormalities[4]. With delays in treatment, or when left untreated, corneal ulcers, especially those centered along the visual axis, can be quite serious and sight-threatening[5].

A major risk factor for developing a corneal ulcer is overnight use of soft contact lenses, and the risk increases with each consecutive night of continuous wear[6,7]. The closed-eye environment causes metabolic stress on the cornea by trapping bacteria from tear stasisand allowing pathogenic bacteria to invade the vulnerable and compromised cornea[8]. It appears that lens to cornea interactions during lid closure contribute more to corneal hypoxia than the actual characteristics of a contact lens such as oxygen permeability[6,9]. Thus, new contact lens materials such as silicone hydrogel (which have higher DK) have been developed in recent years to increase oxygen permeability and reduce corneal hypoxia that contributes to corneal ulcer formation[9,12].

In addition to overnight contact lens wear, other risk factors for corneal ul-

cers include poor lens hygiene, use of homemade saline solutions, reuse of contact lens solutions, the use of tap water without proper drying, poor case hygiene such as not replacing cases regularly and delayed lens replacement[11,15,16]. In addition, environmental factors, such as climate and temperature, affect the risk for corneal ulcers. For example, the higher incidence of Gram-positive organisms in temperate zones[13] and higher incidence of CL wearers in developed nations have likely resulted in a greater number of microbial keratitis cases here[2]. A study has indicated a 30% increase in microbial keratitis in developed countries[2].

In addition to risk factors, it is important to understand the relationship between corneal anatomy and ulcers. The cornea is a multi-layered epithelial sheet broken down into five distinct layers: epithelium, Bowman's layer, stroma, Descemet's membrane and endothelium[17]. Of these, the stroma, which makes up 90% of the cornea, is the largest. The cornea has an arsenal of defenses, including the antimicrobial properties of the tear film and the physical tight cellular junctions of the corneal epithelium. In order for microbial keratitis to occur, an organism must penetrate through the stromal layer[11]. Scarring can ensue when the defect affects the stromal layer or beyond. A corneal ulcer can vary in size, depth and severity. It is best viewed with different illuminations on the slit lamp. Initially, a wide diffuse illumination is used to locate and obtain a gross view of the lesion. A parallelopiped illumination allows for a more three-dimensional view of the lesion, and an optic section can be used to assess the depth of the lesion. Sodium fluorescein dye is used to highlight the area of epithelial defect. Positive fluorescein staining often contours to the shape of the lesion.

A corneal culture is indicated in certain scenarios. A culture is warranted when the corneal ulcer is large (>2 mm), greater than one-third the thickness of the cornea, centered along the visual axis, occurs in "at risk" populations (i.e., elderly, immunocompromised or monocular patients), or does not respond to antibacterial treatment[7]. Corneal scrapings and cultures are needed in many cases to determine the causative organism. Cultures should also be taken of the patient's contact lenses and solutions[1,15]. A study found that 67% of negative corneal scraping cases showed a positive contact lenses culture[1].

Although new multi-purpose solutions and no-rub formulations have been developed in recent years to improve patient compliance, they have not been as effective against certain microbes such as *Acanthamoeba* and *Fusarium*. The outbreak of *Fusarium* keratitis in the United States between June 2005 and July 2006 resulted in 164 confirmed cases and was linked to the use of MoistureLoc multi-purpose solution[13,16]. Studies have also found that most CL-related corneal ulcers are bacterial in origin (60%) followed by fungal (38%) and *Acanthamoeba* keratitis (2%)[5]. The overwhelming majority have found *Pseudomonas aeruginosa* to be the main causative bacterial organism[1,17,18,19]. *Pseudomonas* thrives because it survives the moist environment of contact lenses storage cases and solutions and can quickly cause destruction of the cornea[1]. Other less common bacterial isolates include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Serratia marcescens* and *Moraxella* species[20].

The differential diagnosis of ulcerative keratitis includes: contact lens associated red eye (CLARE), infiltrative keratitis, corneal ulcer, contact lens peripheral ulcer (CLPU) and microbial keratitis.

- CLARE is an acute unilateral inflammatory sterile keratitis associated with colonization of Gram-negative bacteria on contact lenses (usually *Pseudomonas*). The typical patient wears extended-wear hydrogel lenses and awakens with ocular pain, tearing, variable decreased vision and photophobia. There are mid-peripheral corneal infiltrates in severe cases. Cases are usually resolved by discontinuing CL wear[11,15]. Hence, sterile keratitis is more benign and is not usually associated with vision loss.The incidence of sterile keratitis linked to contact lens wear is in the range of 1% to 7% of soft lens wearers annually[6].
- Infiltrative keratitis is a cellular response in which corneal infiltrates or multiple discrete aggregates of gray or white inflammatory cells invade the cornea. They usually occur near the limbus but can present anywhere. They are commonly associated with contact lens overwear and usually present later in the day. Management is best achieved by discontinuing CL wear[15].
- Corneal ulcer is an umbrella term for an inflammatory or infectious event that is characterized by redness, pain and sometimes decreased vision. Examples of corneal ulcers include inflammatory CLPU or infectious microbial, fungal or *Acanthamoeba* keratitis. In infectious corneal ulcers, both Gram-positive and Gram-negative bacteria can colonize the corneal surface. Symptoms can vary from mild to severe. Treatment is best with a broad-spectrum antibiotic[7].
    - o CLPU is a unilateral inflammatory event usually associated with extended-wear silicone hydrogel lenses. It is characterized by a small, sterile whitish gray ulcer typically located at the corneal-limbal border. It is usually caused by colonization of the contact lens surface by pathogenic Gram-positive bacteria, usually *Staph aureus* or *Staph epidermidis*. It is usually limited to the epithelium and not associated with much anterior chamber reaction or significant pain. Symptoms may range from mild to moderate. Discontinuing CL wear usually helps to resolve the condition[11,15]. It can also be treated with topical antibiotics or steroids[6].
    - o Microbial keratitis is a serious infection of the cornea characterized by excavation of the corneal epithelium, Bowman's layer and stroma with infiltration and necrosis of tissue[15]. It can cause vision loss with a risk of 0.3 to 3.6 per 10,000[8]. The incidence ranges from 1.8 to 2.44 per 10,000 CL wearers per year[13]. The risk is higher with soft contact lenses compared to rigid gas permeable lenses (2/3 compared to 1/3)[13]. Approximately 10% of infec-

tions result in the loss of two or more lines of visual acuity[14]. Symptoms are typically severe and the condition can become sight-threatening. It is most often associated with *Pseudomonas spp*, a Gram-negative bacteria. Treatment is best with a broad-spectrum antibiotic, such as a fourth-generation fluoroquinolone[15].

Treatment for corneal ulcers includes removing the offending agent, which in many cases means discontinuing CL wear. Cool compresses may be applied for symptom relief. Patients should be counseled to not touch or rub their eyes and to engage in proper visual hygiene, including frequent hand-washing. They may take over-the-counter medications such as acetaminophen or ibuprofen for pain[14].The most effective treatment is an ophthalmic eye drop. In the past, aminoglycosides such as gentamicin and tobramycin were readily used[14]. Although they demonstrated good Gram-negative bacterial coverage, they also revealed significant hypersensitivity in documented cases[14]. Today, fluoroquinolones (second-, third- and fourth-generation) are more popular. A dilation drop such as cyclopentolate may be administered to relieve pain or inflammation[14]. The use of steroids in bacterial keratitis is controversial[18]. While some advocate topical steroids to reduce tissue damage and scarring, others fear that steroids will reduce the cornea's immune response and prolong infection[21]. A study found that steroid treatment delayed corneal re-epithelialization but did not cause a significant difference in visual acuity or scar size[20]. In worst-case scenarios, a surgical corneal transplant may be indicated if the ulcer perforates the cornea[19].

The second-generation fluoroquinolones, ciprofloxacin 0.3% (Ciloxan) and ofloxacin 0.3% (Ocuflox), were introduced in the 1990s and are FDA-approved for the treatment of bacterial conjunctivitis and keratitis[22]. Although these broad-spectrum antibiotics target both Gram-positive and Gram-negative organisms, their effectiveness has been steadily decreasing due to bacterial resistance[22]. Ciprofloxacin has demonstrated the greatest effectiveness against Gram-negative bacteria such as *Pseudomonas aeruginosa* and multi-drug resistant Gram-negative organisms[14]. The third-generation fluoroquinolone levofloxacin 0.5% (Quixin) was introduced in 2000 and is more water-soluable than ofloxacin at a neutral pH, meaning it demonstrates higher ocular concentrations and thus greater clinical efficacy. Levofloxacin also has increased activity against *Streptococci* compared to second-generation fluoroquinolones. A newer formulation of levofloxacin with ahigher 1.5% concentration (Iquix) has also been approved by the FDA[24]. Although the minimum inhibitory concentration (MIC) for both concentrations of levofloxacin is the same, the increased concentration of levofloxacin 1.5% improves its ability to penetrate ocular tissue[22]. The MIC is the lowest concentration of an antimicrobial that will inhibit the growth of a micro-organism after overnight incubation. Two newer fluoroquinolones, introduced in 2003, moxifloxacin 0.5% (Vigamox) and gatifloxacin 0.3% (Zymar) are statistically more potent than Quixin against Gram-positive organisms and similar in potency in most cases of Gram-negative bacteria.A study found that moxifloxacin had significantly lower median MICs for nearly all types of Gram-positive isolates than gatifloxacin[24]. However, moxifloxacinand gatifloxacin demonstrated equal susceptibility to Gram-negative isolates[22]. Although moxifloxacin and gatifloxacin are not FDA-approved for the treatment of bacterial corneal ulcers, they are typically used as "standard of care" treatment[23]. A major difference between these fluoroquinolones is that the second- and third-generation fluoroquinolones act on a single DNA-replicating enzyme while the fourth-generation fluoroquinolones target two DNA-replicating enzymes, thus lowering the likelihood of bacterial resistance[24].

There are numerous reasons moxifloxacin seems to be more effective and was chosen for treatment (in this case) over gatifloxacin and the second-generation fluoroquinolones. Studies show that moxifloxacin penetrates the cornea and aqueous humor significantly better than gatifloxacin[6]. Likewise, moxifloxacin was found to have 10 times the MIC for an organism, while gatifloxacin did not[25]. This means that moxifloxacin is more bactericidal and can penetrate into the aqueous humor with four times daily dosing[25]. Moxifloxacin is also 8-16 times more potent against Gram-positive organisms than previous-generation fluoroquinolones[26]. Moxifloxacin has been found to be resistant against methicillin-resistant *Staph aureus* (MRSA). Moxifloxacin has broad-spectrum coverage and excellent activity against Gram-negative organisms, such as *Pseudomonas aeruginosa*. Although ciprofloxacin has historically been the fluoroquinolone of choice for the treatment of *Pseudomonas*, it does not penetrate the cornea as well as moxifloxacin[26]. Moxifloxacin differs from gatifloxacinin that it is a biphasic molecule, meaning it is soluble in both lipid and aqueous solutions[26]. This allows it to achieve very high concentrations in the eye. Lastly, moxifloxacin has less corneal and conjunctival toxicity than the other fluoroquinolones, including gatifloxacin and Quixin[22].

Since this patient was treated, a new fluoroquinolone, besifloxacin 0.6% ophthalmic suspension (Besivance), has become available. It is a fourth-generation fluoroquinolone that was approved by the FDA in 2009 for the treatment of bacterial conjunctivitis[27]. It is the first fluoroquinolone developed specifically for ophthalmic use. In other words it has no systemic counterpart[28]. With no systemic use, studies have shown that besifloxacin is less likely to develop bacterial resistance than other fluoroquinolones[29]. Because this drug is still relatively new, more studies need to be conducted to determine drug resistance and efficacy.

Discussion

Gathering information

In the case presented, the young woman reported generic symptoms of eye pain and redness in one eye. The astute clinician should ask probing questions about the circumstances surrounding the symptoms as well as CL use and recent ocular trauma. If CL wear is established, specific questions regarding the history of CL wear should be addressed.The clinician should inquire about the type of CLs worn as well as the type of CL solution used as these factors can contribute to the type of

infection presented. In this case unfortunately, the patient did not know the type of CLs worn or the CL solution used. Although this information can be useful, clinical decision-making often requires the clinician to make reasonable judgments based on the information available.

Confirmation of diagnosis

The diagnosis at first visit was corneal ulcer with secondary uveitis from CL overwear OD. This was determined mainly from the patient's report of sudden onset redness and pain after falling asleep in her CLs along with the presence and location of a paracentral circumscribed corneal infiltrate with stromal excavation producing positive staining. Other differentials were considered and ruled out. For instance, herpes simplex was ruled out because fluorescein staining did not show a typical dendritic pattern. Fungal keratitis was ruled out because the patient denied any recent ocular trauma and the lesion did not present a feathery border. *Acanthamoeba* keratitis was ruled-out because the patient did not swim in her CLs and did not recently travel to a warm and moist environment. The process of clinical decision-making involves justification of diagnosis as well as ruling out other potential diagnoses.

Management

Treatment with antibiotics should be aggressive and immediate in most cases to eradicate the potential microbe. The patient was advised to return in 24 hours but because the clinic was not open on the weekend, she returned the following Monday[30]. The patient was advised to go to the emergency room if symptoms worsened over the weekend. A culture was not taken in this case because the corneal ulcer was small, not on the visual axis and responded to treatment. Although obtaining a corneal scraping is recommended before prescribing antibiotics, standard of care as stated in American Optometric Association guidelines does not require obtaining a corneal culture[30].

Patient education

The patient was counseled to throw away her current CLs and to stay out of them until the condition resolved. Close follow-up care is crucial to prevent rapid visual deterioration from any potential microbe or organism. At the first visit, a prescription was given for moxifloxacin 0.5% ophthalmic solution to be used every 30 minutes OD that day and then every hour OD for the next two days. Cyclopentolate 1% bid OD was also prescribed to temper the anterior chamber reaction, to prevent a posterior synechiae, and to reduce eye pain. Moxifloxacin was chosen over the second-generation fluoroquinolones because of its greater spectrum of coverage, lower antibacterial resistance and ease of dosage. It was chosen over gatifloxacin because of its longer half-life (and thus less-frequent dosing schedule) and greater penetration into the cornea[24]. Also, it has a lower incidence of toxicity and is preservative-free[31]. Besifloxacin may be a good choice due to its lower dosing schedule.

Follow-up

The patient was instructed to go to the emergency room with any increased pain or decrease in vision over the weekend. An appointment was scheduled for the following Monday because the clinic was not open on the weekend. The patient was warned about the potential for a slight vision reduction after resolution of the ulcer. Her primary care physician was notified of the findings.

Resolution of ulcer

CL wear can resume only after the corneal ulcer has healed. It is important to choose CLs with high oxygen permeability (DK), such as silicone hydrogel lenses. Many variables, such as oxygen content and replacement schedule, must be considered when selecting new CLs. Acuvue Oasys, PureVision, or Ciba Night & Day would be suitable options for refitting because they are all silicone hydrogel lenses that allow for greater oxygen permeability and all are approved for overnight wear[6,11]. Although sleeping in contact lenses is still not recommended despite labeling for overnight wear, patient noncompliance is common. Therefore, it is advantageous to fit more highly oxygen permeable CLs. In this case, Acuvue Oasys was the desired lens because it is not only made of silicone hydrogel but also has a two-week replacement schedule (as opposed to the monthly replacement schedule for the other two silicone hydrogels). A suitable alternative, if the patient is willing to try a different modality, is a daily disposable CL. One example is 1-Day Acuvue TruEye, the first daily disposable silicone hydrogel lens, which debuted in June 2010 in the United States. Frequent replacement of CLs helps to prevent long-term buildup of proteins and deposits on the lens surface. Therefore, it is important to educate patients on the replacement schedule for their CLs. In addition to selecting the most suitable CLs, it is important to educate patients on proper hygiene, including lens cleaning and care regimens and frequent case replacement. Patients must be counseled extensively to not overwear CLs and to not sleep in them. Rigid gas permeable CLs are another alternative to soft contact lenses but they are often less desirable for patients who are already accustomed to the comfort of a soft CL. Rigid lenses also allow favorable oxygen permeability to the cornea.

As illustrated by this case, corneal ulcer therapy involves not only removal of the offending agent but also use of topical agents including antibiotics, a culture when warranted, a change in CL materials and fit, and modification of CL maintenance and care.

Conclusion

This case demonstrates the role of taking a careful history and the role of close clinical observation in the diagnosis of corneal ulcers. In milder cases, diagnosis can be made by clinical observation. However, in moderate cases, presentations along the visual axis or situations that do not respond to initial treatment, a corneal culture is necessary. The prognosis is better with earlier diagnosis and treatment. Treatment should be aggressive and can be modified as the ulcer begins to heal. Clinicians must be able to revise treatment if the corneal ulcer does not heal within 24 hours or within an appropriate time frame. Patient noncompliance is an important issue that must be considered not only in prescribing medication but also in refitting the patient with new CLs. Clinicians must educate patients on the potential causes of corneal ulcers, and if they are contact lens wearers stress the importance of not overwearing their CLs. Specifically, clinicians should review lens care

regimens, including recommended replacement schedule, frequent replacement of storage cases, not swimming in CLs, adequate lens disinfection, and avoidance of tap water for cleaning and soaking lenses[7]. Hopefully, with proper patient education and advances in CL technology, materials and solutions, there will be a significant reduction in the number and severity of ulcerative keratitis cases.

Lead Questions for Evaluating Knowledge and Stimulating Discussion

1. Which of the following is the most likely diagnosis based on the patient's presenting symptoms?
   a. corneal ulcer
   b. contact lens-induced acute red eye
   c. primary anterior uveitis
   d. infiltrative keratitis
2. Which of the following is the most likely diagnosis?
   a. fungal keratitis
   b. amoebic keratitis
   c. viral keratitis
   d. bacterial keratitis
   e. primary anterior uveitis
3. Which of the following is most likely associated with this condition?
   a. history of recent trauma
   b. swimming in CLs
   c. improper care of CLs
   d. systemic diagnosis of ulcerative colitis
   e. sleeping in CLs
4. The most appropriate initial treatment option for this patient is:
   a. moxifloxacin 0.5% (Vigamox) one drop every 30 minutes for the first four hours then one drop every hour for the next 18 hours and cyclopentolate 1% (Cyclogyl) bid
   b. prednisolone acetate 1% (Pred Forte) one drop every four hours and cyclopentolate 1% (Cyclogyl) bid
   c. trifluridine 1% (Viroptic) one drop every hour and cyclopentolate 1% (Cyclogyl) bid
   d. natamycin 5% (Natacyn) one drop every hour and cyclopentolate 1% (Cyclogyl) bid
   e. ciprofloxacin 0.3% (Ciloxan) two drops every 15 minutes for six hours, then two drops every 30 minutes for 18 hours and cyclopentolate 1% (Cyclogyl) bid
   f. polymyxin B sulfate/trimethoprim sulfate (Polytrim) one drop every hour and cyclopentolate 1% (Cyclogyl) bid
5. The most appropriate follow-up for this patient is:
   a. 24 hours
   b. 48 hours
   c. 1 week
   d. 3 days
   e. return if symptoms worsen
6. Which of the following is the most likely potential sequel of this patient's condition?
   a. corneal scar
   b. corneal transplant
   c. anterior synechiae
   d. posteriorsynechiae
   e. glaucoma
7. Which of the following is a defense mechanism of the cornea?
   a. tight cellular junctions of the corneal epithelium
   b. corneal endothelial pump
   c. tight cellular junctions of stroma
   d. epithelial regeneration
8. The most common reason for a corneal culture in this case would be:
   a. size of epithelial defect
   b. location of defect
   c. poor response to therapy on follow-up
   d. age of patient
   e. history of CL use
9. Which of the following best describes the pathophysiology of this patient's condition?
   a. increased metabolic stress on the cornea
   b. inability of endothelial pump to remove fluid
   c. tear film instability
   d. hyperosmolarity on the cornea
10. Which of the following is the most likely etiology of this condition?
    a. Fusarium
    b. Acanthamoeba
    c. Pseudomonas
    d. Herpes simplex
    e. Staphylococcus

Answer key: 1(a), 2(d), 3(e), 4(a), 5(a), 6(a), 7(a), 8(c), 9(a), 10(c)

To initiate discussion, "why" each answer was chosen should be elicited from students. Question #4 should involve a discussion of the off-label use of medication.

References

1. Mela EK, Giannelou IP, John KX, Sotirios GP. Ulcerative keratitis in contact lens wearers. Eye & Contact Lens. 2003;29(4):207-209.
2. Bharathi MJ, Ramakrishnan R, Meenakshi R, Kumar CS, Padmavathy S, Mittal S.Ulcerative keratitis associated with contact lens wear. Indian J of Ophthalmol. 2007;55:64-67.
3. Green M, Apel A, Stapleton F. Risk factors and causative organisms in microbial keratitis. Cornea. Jan 2008;27(1):22-27.
4. Kaiser P, Friedman N, Pineda R.The Massachusetts Eye and Ear Infirmary Illustrated Manual of Ophthalmology 2nd Ed. Philadelphia: Saunders 2004.
5. Sirikul T, Prabriputaloong T, Smathivat A, Chuck R, Vongthongsri A. Predisposing factors and etiologic diagnosis of ulcerative keratitis. Cornea. April 2008;27(3):283-287.
6. Keay L, Stapleton F, Schein O.Epidemiology of contact-lens related inflammation and microbial keratitis: a 20-year perspective. Eye & Contact Lens. 2007;33(6):346-353.
7. Mah-Sadorra JH, Yavuz GA, Najjar DM, Laibson PR, Rapuano CJ, Cohen EJ. Trends in contact lens-related corneal ulcers. Cornea. Jan 2005;24(1)51-58.
8. Holden BA, Sweeney DF, Sankaridurg PR, Carnt N, Edwards K, Stretton S, Stapleton F.Microbial keratitis and vision loss with contact lenses. Eye & Contact Lens. 2003;29:131-134.
9. Das S, Sheorey H, Taylor HR, Vajpayee RB. Association between cultures of contact lens and corneal scraping in contact lens-related mi-

crobial keratitis. Arch Ophthalmol. Sept 2007;125(9):1182-1185.
10. Pinna A, Usai D, Sechi L, Molicotti P, Zanetti S, Carta A. Detection of virulence factors in pseudomonas aeruginosa strains isolated from contact lens-associated corneal ulcers.Cornea. April 2008;27(3):320-326.
11. Sweeney D, Naduvilath T. Are inflammatory events a marker for an increased risk of microbial keratitis? Eye & Contact Lens. 2007;33(6):383-387.
12. Morgan PB, Efron N, Hill EA, Raynor MK, Whiting MA, Tullo AB. Incidence of keratitis of varying severity among contact lens wearers. Br J Ophthalmol. 2005;89:430-436.
13. Moriyama AS, Hofling-Lima AL. Contact lens-associated microbial keratitis. Arq Bras Oftalmol. 2008;71(6 supl):32-36.
14. Mills TJ. Corneal ulceration and ulcerative keratitis. Retrieved Sept 15, 2008 http://emedicine.medscape.com/article/798100-overview.
15. Silbert, JA. Corneal infiltrative complications associated with contact lens wear. Review of Optometry. April 2004;141(04):1CE-8CE.
16. Patel A, Hammersmith K. Contact lens-related microbial keratitis: recent outbreaks. Current Opinion in Ophthalmology. July 2008;19(4):302-306.
17. Robertson DM, Cavanagh HD. The clinical and cellular basis of contact lens-related corneal infections. ClinOphthalmol. 2008;2(4):907-917.
18. Ali N, Ali M.Bilateral simultaneous infectious keratitis secondary to contact lens wear: An unusual case report with rare organisms. Eye & Contact Lens. 2007; 33(6):338-340.
19. Keay L, Edwards K, Naduvilath T, Forde K, Stapleton F. Factors affecting the morbidity of contact lens-related microbial keratitis:A population study. Ophthalmology and Vision Science. Oct 2006;47(10):4302-4308.
20. Green MD, Apel AJ, Naduvilath T, Stapleton FJ. Clinical outcomes of keratitis. Clinical and Experiemental Ophthalmology. 2007;35:421-426.
21. Srinivasan M, Lalitha P, Mahalakshmi R, Prajna NV, Mascarenhas J, Chidambaram JD, Lee S, Hong KC, Zegans M, Glidden DV, McLeod S, Whitcher JP, Lietman TM, Acharya NR. Corticosteroids for bacterial corneal ulcers.Br. J. Ophthalmol. 2009;93;198-202.
22. Scoper S.Review of third and fourth generation fluoroquinolones in ophthalmology: in-vitro and in-vivo efficacy. AdvTher. 2008;25(10):979-994.
23. Sowka JW, Gurwood AS, Kabat AG. Fourth generation fluoroquinolones and bacterial keratitis. Handbook of Ocular Disease Management. March 2006;25A-26A.
24. Duggiral A, Joseph J, Sharma S, Nutheti R, Garg P, Das T. Activity of newer fluoroquinolones against Gram-positive and Gram-negative bacteria isolated from ocular infections: an in vitro comparison. Indian J Ophthalmol. 2007;55:15-19.
25. McCulley JP, Surratt G, Shine W. 4th generation fluoroquinolone penetration into aqueous humor in humans. InvestOphthalmol Vis. Sci. 44 Abstract 4927-B251 Vol 2.
26. Katz, HR. Vigamox safely treats corneal ulcers. Retrieved April 16, 2009 http://www.eyeworld.org/ewweeksupplementarticle.php?id=12.
27. Chang MH, Fung HB. Besifloxacin: a topical fluoroquinolone for the treatment of bacterial conjunctivitis. ClinTher. March 2010;32(3):454-471.
28. Comstock TL, Karpecki PM, Morris TW, Zhang JZ. Besifloxacin: a novel anti-infective for the treatment of bacterial conjunctivitis. ClinOpthalmol. April 2010;4:215-225.
29. McDonald M, Blondeau JM.Emerging antibiotic resistance in ocular infections and the role of fluoroquinolones. J Cataract Refract Surg. Sept 2010;36(9):1588-1598.
30. American Optometric Association; Optometric Clinical Practice Guideline: Care of the Contact Lenses Patient. St.Louis, MO. Retrieved December 14, 2010 Available http://www.aoa.org/documents/CPG-19.pdf 40-46.
31. Kabat AG. How to manage ocular infection. Review of Optometry April 2007;144(11):100-101.