Herpetic Keratitis in Practice: Diagnosis, Considerations, and Treatment Across Various Patient Types

Four experts in herpetic keratitis management gathered to discuss their perspectives at the American Academy of Ophthalmology 2022 Annual Meeting in Chicago, IL.

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Participants in this discussion are paid consultants of Bausch + Lomb.

Background

Corneal infections caused by herpes simplex virus (HSV) are primarily mild and self-limiting, lasting from 2 to 3 weeks depending on severity and treatment.[1] Nevertheless, HSV keratitis can become quite problematic without proper management. Recurrent keratitis can lead to corneal scarring, thinning, and neovascularization.[1] These effects help explain why herpetic keratitis is a major cause of visual morbidity. Therefore, a shared goal among all physicians treating herpetic keratitis should be to properly identify and appropriately manage the infection in the hopes of reducing the risk of recurrence.[1]

Identifying herpetic keratitis

When a physician sees a patient presenting with symptoms suggestive of herpetic keratitis, the diagnosis is not always obvious at first glance. Accurate diagnosis requires a detailed review of the patient's history and thorough examination of the ocular surface.[1] Even when a case is clear in its presentation, understanding the patient's previous response to treatments, history of recurrence, and overall expectations is necessary to overcome potential barriers.

"A lot of times we will see the patients primarily, and they'll come in with an untoward lesion on the corneal surface. It doesn't always have to be a beautiful dendrite; it could be a pseudodendrite that's emerging into a dendrite, or it could be a confluence of SPK—superficial punctate keratitis," said **Dr. Parekh**. "If they're very early, then we'll follow the patient. By day 3, we'll observe them; now there's a confluence, the dendrite is emerging, and so forth."

A patient case of Dr. Parekh's proved to be a textbook example of disease identification and treatment.

Dr. Parekh | Patient Case 1	
PRESENTATION	**62-year-old male** complaining of red eye for 3 days
VISION	20/40 with normal intraocular pressure, mild infection, fresh dendrite on the central cornea with some SPK, anterior chamber shows no cells or flare, mild cataract
HISTORY	Viral eye infection 15 years ago • Treated with trifluridine (7 times/day), experienced some loss of vision and foreign body sensation • Compensated with preservative-free tears and gels/ointments to bring vision back • Baseline dry eye in the previously affected eye

In this particular case, **Dr. Parekh** suspected herpetic keratitis and determined that treatment with ZIRGAN® (ganciclovir ophthalmic gel) 0.15% was the appropriate option. Given the patient's prior experience with trifluridine, they were understandably hesitant toward this course of treatment and did not want to face similar obstacles. After consultation and discussion of attributes of ZIRGAN, including its targeted eradication and control of the herpetic lesion in a soothing gel formulation,[2] the patient agreed and experienced improvement of the lesion within 5 days.

Dr. Koreishi confirmed that she would handle this case in a similar manner. "I think the easy point is that when the disease is unilateral, HSV is on your list as a possibility, even if you're uncertain as to why it happened. In terms of treatment, if there is a clearly stained dendrite, I'll always use ZIRGAN and avoid the toxicity that may be associated with other options." The general group consensus was that the patient's prior use of trifluridine likely compounded the process of herpetic keratitis itself, resulting in not only a poor experience but a worsening of the irritation of the disease.

As previously mentioned, not all cases of herpetic keratitis provide clear-cut symptoms for diagnosis. A closer clinical examination by the physician may be required to adequately assess the situation.

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>
> **–Dr. Koreishi**

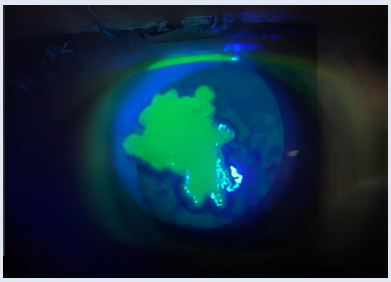
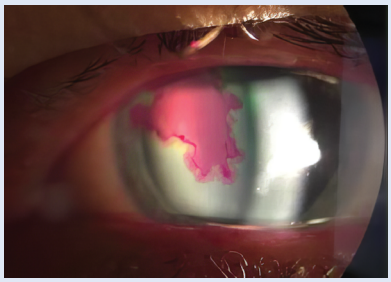
IMPORTANT SAFETY INFORMATION (CONT'D)

- Patients should not wear contact lenses if they have signs or symptoms of herpetic keratitis or during the course of therapy with ZIRGAN.

Please see full Prescribing Information for ZIRGAN here.

Dr. Al-Mohtaseb offered a patient case with a more complex presentation of herpetic keratitis.

Dr. Al-Mohtaseb | Patient Case 2	
PRESENTATION	**37-year-old female** with left eye pain and decreased vision for 2 weeks
VISION	BCVA: OD, 20/20; OS: 20/50 • Pupils: no relative afferent pupillary defect OU • Extraocular motility: full, orthophoria • Intraocular pressure: 14 mmHg, 12 mmHg
HISTORY	Treated by the emergency room with tobramycin/dexamethasone 5 days prior and feels worse • No trauma, systemic infection, contact lens wear, or previous red eye

Staining imagery courtesy of Zaina Al-Mohtaseb, MD.

The diagnosis determined in this case was a geographic ulcer, which was HSV epithelial keratitis that was initially treated with corticosteroids. **Dr. Al-Mohtaseb** explained that through treatment of an actively replicating virus with a corticosteroid, the disease process was worsened, resulting in a large epithelial defect.[3] The 2 keys to making this diagnosis were: 1) the rose bengal staining—the darker reddish appearance outlining the epithelial defect—with knowledge that those areas have elevation above the epithelial plane; 2) the appearance of the dendrite itself—which was more of a circular epithelial defect.

In this case, the recommended course of treatment was to immediately stop use of tobramycin/dexamethasone and begin treatment with ZIRGAN® (ganciclovir ophthalmic gel) 0.15% to specifically treat the active epithelial keratitis. This avoided damaging the normal/healthy corneal cells that assist with the healing of the epithelial defect itself.[4]

Managing misdiagnosis

As discussed previously, proper diagnosis can take time and may include an initial misdiagnosis to arrive at a confirmed case of herpetic keratitis. With a condition that can be misinterpreted as it evolves, it is oftentimes necessary to rule out other conditions to reach an accurate diagnosis.

> *"Sometimes it's not that physicians aren't treating with the appropriate medication, but rather that the disease itself is often misdiagnosed."*
>
> **—Dr. Al-Mohtaseb**

"Sometimes, it isn't that we as physicians aren't treating with the appropriate medication, but rather that the disease itself is often misdiagnosed. This accounts for a nontrivial patient population," **Dr. Al-Mohtaseb** stated. The key is not only to minimize the likelihood of misdiagnosis, but also to recognize those patients who have been misdiagnosed by a previous physician and come in for a consultation under preconceived notions.

IMPORTANT SAFETY INFORMATION (CONT'D)

- Most common adverse reactions reported in patients were blurred vision (60%), eye irritation (20%), punctate keratitis (5%), and conjunctival hyperemia (5%).

Zirgan®
(ganciclovir ophthalmic gel) 0.15%

"I've seen an *Acanthamoeba* infection treated as HSV early on, but then the diagnosis became *Acanthamoeba* keratitis because of the dendritic pattern of epithelial involvement," confirmed **Dr. Koreishi**. "I talk to the patient and say, 'This looks like different things. That's why you're here and you're frustrated.'"

One of Dr. Malhotra's patients is an example of prior misdiagnosis who required extra attention to reveal an accurate diagnosis and eventually receive proper treatment.

Dr. Malhotra | Patient Case 3	
PRESENTATION	**43-year-old male** with recurrent erosion in the right eye with increasing frequency; first episode resolved after 3-day duration, then erosions occurred 3 times per month, then 1-2 times per week
VISION	BCVA: OD, 20/25; OS: 20/20 • Eyelids have 1+ meibomian gland dysfunction • Conjunctiva/sclera white and quiescent • Cornea OD has interior temporal deep and superficial vascularization 0.5 mm over a 0.5-mm area anterior stromal scar/haze with 1+ keratitis in a faint dendriform pattern with overlying epithelial defect • Anterior chamber deep/quiet, lens clear, fundus normal
HISTORY	Recurrent erosion OD over the past year • Denies history of trauma to the affected eye

This patient did not have the appearance of a classic dendrite (as seen with the previous cases) but showed constellation in a linear pattern as SPK with an overlying epithelial defect. However, their previous physician treated them for recurrent erosions, and the course of treatment included a sodium chloride hypertonicity ophthalmic ointment, artificial tears, and intermittent use of antibiotics as flare-ups occurred. **Dr. Al-Mohtaseb** added, "I think recurrent erosion is one that is commonly misdiagnosed when it's actually herpes."

Dr. Malhotra further clarified, "This was one of those masqueraders where my radar turned on, and I thought this patient likely had herpetic keratitis. We stopped the previous course of treatment and, instead, prescribed ZIRGAN® (ganciclovir ophthalmic gel) 0.15% five times per day. The patient's symptoms resolved. After we treated the acute disease, we put him on an oral antiviral, and the patient has not had any recurrent erosions for years."

"A lot of physicians will suspect herpes later on when they bounce around the system for a second or third professional opinion." **Dr. Parekh** added, "In general, educating the patient is key because it's a recurrent disease. Sometimes a patient will come to me as their third or fourth doctor and by then they're so frustrated. Taking the time to educate a patient and let them know that 1) herpetic keratitis can be a hard disease to diagnose and 2) they weren't initially treated correctly. Now, the diagnosis is obvious and we're on the right track."

Setting expectations

Patients rarely enter the exam room without preconceived notions. In fact, many patients are hesitant to start treatment due to a negative previous experience (as discussed above), continued prophylaxis, or even perceived cost. However, explaining the advantages of treatment and how they outweigh the alternatives can help shift the mindset and create better outcomes.

IMPORTANT SAFETY INFORMATION (CONT'D)

- Safety and efficacy in pediatric patients below the age of 2 years have not been established.

Dr. Parekh added, "Herpes is a lifelong journey. It's rare for us to see this type of patient only once. We know that the herpes virus lives in the ganglion and can come back due to stress and so forth."[1] The objective is always to prioritize the diagnosis and assure that the patient's short- and long-term goals are aligned to their best possible outcome.

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>
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A seemingly simple case can often bring its own set of complications that require additional context and conversation with a patient, as with Dr. Koreishi's case.

Dr. Koreishi | Patient Case 4	
PRESENTATION	**46-year-old male** with a 3-week history of red/blurry vision
VISION	20/40
HISTORY	Treated with fluoroquinolone without resolution • Mild corticosteroid was added, with no improvement

In further describing the case, **Dr. Koreishi** shared, "This patient came in after a few different diagnoses, and he was very upset during our first consultation, as no one was able to accurately determine the appropriate resolution for the case." **Dr. Koreishi** stopped all prior medications and prescribed ZIRGAN® (ganciclovir ophthalmic gel) 0.15% every 3 hours while awake. This proved to be effective, as the patient's dendrites had disappeared and the patient was feeling better within a week.

After resolving the redness and tapering off the antiviral, the patient returned for a follow-up visit with complaints of light sensitivity. Upon examination, **Dr. Koreishi** discovered a subepithelial infiltrate with no active staining, which was treated with a topical corticosteroid. This new finding warranted a thorough discussion of the potential for recurrence and the importance of early symptom reporting. Managing expectations will be key for this patient's long-term success.

As mentioned, there can be many hurdles to overcome with patients experiencing herpetic keratitis—most of which can be approached with patient education and awareness. **Dr. Koreishi** highlighted the common hurdle of cost, noting, "I tell patients that I understand ZIRGAN is not an inexpensive drop, but it provides benefits that I feel are worth the cost."

"There's a misconception that trifluridine is less expensive," added **Dr. Malhotra**. "In fact, even though it is generic, trifluridine can be expensive. The other alternatives to treatment are orals such as valacyclovir or acyclovir. However, my preference would be to use a topical therapy like ZIRGAN, which unlike a pill is administered directly onto the ocular surface. This topical mode of administration makes ZIRGAN cost-effective."

> *"This topical mode of administration makes ZIRGAN cost-effective."*
>
> —Dr. Malhotra

Dr. Parekh agreed and pointed out the greater price of not addressing a patient's concerns or working with them to resolve the issue: "It's the disease burden. The cost of the patient not getting better is burdensome to them too, as they often need to take more days off from work, more frustration, more time off, etc. Usually, they're escorted by a family member, and so forth. There's a burden for the whole system. This is a recurrent disease."

Treatment with ZIRGAN® (ganciclovir ophthalmic gel) 0.15%

While there are currently 2 FDA-approved topical options for the treatment of herpetic keratitis—trifluridine ophthalmic solution and ZIRGAN[1]—this group articulated multiple reasons why ZIRGAN is their preferred option.

Dr. Koreishi confirmed, "We don't want to irritate the corneal surface. Finally, there's a treatment for herpetic keratitis that can actually protect the ocular surface at the same time." When treating this disease, it is imperative that the integrity of the corneal surface is preserved.

ZIRGAN is a topical ophthalmic antiviral treatment that is indicated for the treatment of acute herpetic keratitis.[2] ZIRGAN targets virus-infected cells (not healthy cells) and effectively resolved 77% of dendritic ulcers at day 7.[2] With a convenient storage and dosing schedule,[2] patients can more easily follow through with their prescribed course of treatment.

SCAN TO LEARN MORE ABOUT
ZIRGAN AND ITS BENEFITS

INDICATION

ZIRGAN® (ganciclovir ophthalmic gel) 0.15% is a topical ophthalmic antiviral that is indicated for the treatment of acute herpetic keratitis (dendritic ulcers).

IMPORTANT SAFETY INFORMATION

- ZIRGAN is indicated for topical ophthalmic use only.
- Patients should not wear contact lenses if they have signs or symptoms of herpetic keratitis or during the course of therapy with ZIRGAN.
- Most common adverse reactions reported in patients were blurred vision (60%), eye irritation (20%), punctate keratitis (5%), and conjunctival hyperemia (5%).
- Safety and efficacy in pediatric patients below the age of 2 years have not been established.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see full Prescribing Information for ZIRGAN here.

References: 1. Labib BA, Chigbu DI. Clinical management of herpes simplex virus keratitis. *Diagnostics (Basel)*. 2022;12(10):2368. **2.** ZIRGAN. Prescribing Information. Bausch & Lomb Inc. **3.** Chodosh J. The Herpetic Eye Disease Study: topical corticosteroid trial for herpes simplex stromal keratitis: a paradigm shifting clinical trial. *Ophthalmology*. 2020;127(4S):S3-S4. **4.** Raizman MB, Hamrah P, Holland EJ, et al. Drug-induced corneal epithelial changes. *Surv Ophthalmol*. 2017;62(3):286-301.

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