Photographic Monitoring of Herpes Simplex Virus Keratitis During Anti-inflammatory Treatment

In the course of the Herpetic Eye Disease Study, we validated digital photomicrography and computer-assisted image analysis for evaluating the severity of stromal keratitis and endotheliitis due to herpes simplex virus. We have now conducted a nested prospective cohort study to investigate how corneal imaging can track the geometric metamorphosis of herpetic keratitis among 62 patients during the systematic administration of a topical corticosteroid and antiviral agent.

Methods. Individuals with herpes simplex virus stromal keratitis or endotheliitis gave informed consent under protocols approved by institutional review boards and were assigned to a Herpetic Eye Disease Study treatment regimen of prednisolone sodium phosphate, 1%, tapered from 8 times per day to once daily over 5 weeks and trifluridine, 1%, 4 times per day for 3 weeks and then twice daily.2,3 Standardized corneal photographs were obtained at baseline, and 62 patients had repeated photography taken a mode of 35 days (range, 32-38 days) later. Diapositives archived at the Herpetic Eye Disease Study Photography Reading Center were later scanned, converted to grayscale equivalents, and calibrated to linear and luminance scales.1 Interactive image processing by one of us (B.M.M.), who was masked to slitlamp biomicroscopic measurements, estimated paired morphometric, cartographic, and densitometric values for area (in millimeters squared), shape factor \( (4\pi \times \text{area} / \text{perimeter}^2) \), location (polar coordinates on a corneal template), and relative intensity (average pixel-based gray level) of corneal inflammation and opacification at baseline and at 5 weeks.

Results. The area of corneal opacification contracted significantly \((P < .001)\) during 5 weeks of topical treatment with prednisolone and trifluridine. Inflammatory signs resolved with the prescribed treatment schedule in 43 eyes, while 19 eyes had lingering corneal inflammation that decreased in area by a median of 38% (interquartile range, 15%-49%) using image planimetry. The median shape factor of 0.68 (interquartile range, 0.53-0.79) of the zone of stromal infiltration and edema at baseline did not significantly differ \((P = .61)\) from that of 0.70 (interquartile range, 0.54-0.83) 5 weeks later, at which time the geometric center of the corneal opacity remained within a median distance of 0.8 mm (interquartile range, 0.5-1.1 mm) of its initial position. Neither a larger \((>20 \text{ mm}^2)\) initial area of stromal keratitis \((P = .48)\) nor the presence of iritis \((P = .89)\) at baseline was associated with the relative severity of residual corneal opacification measured on corneal photographs captured 5 weeks after enrollment. However, eyes with an initially whiter intensity \((>81 \text{ gray-value units})\) of inflammation and edema were more likely \((P < .001)\) to end up with a denser opacity. On completing 5 weeks of treatment, eyes having visual acuity worse than 20/100 on a modified Bailey-Lovie chart averaged a whiter opacity than those with better visual outcome \((P = .03)\).

Comment. Slitlamp photography is able to monitor dynamic alterations of corneal disease. In managing herpes simplex virus keratouveitis and endotheliitis, the examiner strives to adjudicate treatment responses during dosage adjustment of corticosteroids and antivirals. We found that digitized photographs can supplement the clinical follow-up of patients with herpetic keratitis and could potentially contribute to therapeutic decision making.

Photoanalysis demonstrated how the disciform contour of stromal inflammation and edema fades and shrinks with treatment while retaining an ellipsoidal shape centered at its initial topographic position. Image processing also confirmed that a greater intensity of stromal inflammation predisposes to a whiter corneal opacity that in turn contributes to poorer vision.

New modalities in documenting conditions of the anterior segment are leading to improved representation and quantitative interpretation of ocular disorders. The integration of bioimaging and other ophthalmic metadata into a comprehensive electronic record offers the prospect of enriching patient management and facilitating teleconsultation in corneal practice.

Kirk R. Wilhelmus, MD, PhD
Bradley M. Mitchell, PhD
Dan B. Jones, MD
for the Herpetic Eye Disease Study Group

Author Affiliations: Cullen Eye Institute, Baylor College of Medicine, Houston, Texas.

Correspondence: Dr Wilhelmus, Sid W. Richardson Ocular Microbiology Laboratory, Department of Ophthalmology, Baylor College of Medicine, 6565 Fannin St, Houston, TX 77030 (kirkw@bcm.edu).

Author Contributions: Dr Wilhelmus had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.


Financial Disclosure: None reported.

Funding/Support: This work was supported by grants EY07479, EY07480, EY07482, EY07483, EY07486,
An Unusual Manifestation of Herpes Simplex Virus–Associated Acute Iris Depigmentation and Pigmentary Glaucoma

Herpes simplex virus (HSV) has been established as a cause of acute anterior uveitis with sectoral iris atrophy and has been demonstrated to occur in patients without history of keratitis.1,2 We report a case of acute, diffuse iris depigmentation, anterior uveitis with a significant amount of pigmented cells, and associated pigmentary glaucoma without any distinctive herpetic corneal findings. Immunostaining results for HSV were positive in a histopathologic specimen obtained during an urgent trabeculectomy.

Report of a Case. A 61-year-old man had redness and irritation in his right eye for 3 days. Visual acuity was 20/25 OD and intraocular pressure was 16 mm Hg OD. The conjunctiva was white and quiet. The cornea showed Descemet membrane folds without any epithelial or stromal abnormalities. The anterior chamber was deep with 3+ cells, consisting mostly of pigmented cells and granules. There was mild nuclear sclerosis and the anterior vitreous was clear. The optic nerve showed a cup-disc ratio of 0.5 with normal color and sharp margins. The remainder of the posterior segment was normal with no signs of retinitis. Anterior uveitis was diagnosed and the patient began treatment with prednisolone, 1%, eye-drops 4 times a day and atropine sulfate, 1%, twice a day.

On return examination 4 days later, diffuse transillumination defects were noted, 3+ pigmented cells were again observed in the anterior chamber, pigment was noted to be peppering the surface of the iris, and intraocular pressure was 48 mm Hg (Figure 1). Gonioscopy showed an angle open to scleral spur for 360° with extensive pigment deposition throughout. In addition to treatment with brimonidine tartrate, 0.15%, the patient began treatment with timolol maleate, 0.5%, and brinzolamide, 1%, as well as oral prednisone, 60 mg/d, and acyclovir, 800 mg 5 times a day, for suspected herpetic uveitis.

Despite maximal topical medical therapy, the patient’s intraocular pressure further elevated and remained greater than 50 mm Hg for 4 days. An urgent trabeculectomy was performed 10 days after the patient's initial visit. The optic disc appearance 1 day prior to the trabeculectomy was not significantly changed from the appearance at the initial visit. Aqueous humor, iris from the iridectomy, and a small corneoscleral specimen from the deep sclerectomy were sent for HSV polymerase chain reaction (PCR) and histopathologic analysis. The quali-