To our knowledge, this is the first clinicopathological report demonstrating the histological scleral changes composing fusion of scleral collagen to seal the sclerotomy site. We believe this technique to be an easy and effective way to seal leaking sclerotomies in small-gauge sutureless vitrectomy (Video).

Yoreh Barak, MD
Elizabeth Summers Lee, BA
Shlomit Schaal, MD, PhD

Author Affiliations: Department of Ophthalmology and Visual Sciences, University of Louisville, Louisville, Kentucky.

Corresponding Author: Shlomit Schaal, MD, PhD, Department of Ophthalmology and Visual Sciences, University of Louisville, 301 E Muhammad Ali Blvd, Louisville, KY 40202 (s.schaal@louisville.edu).


Author Contributions: Dr Schaal 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. Study concept and design: All authors. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: All authors. Critical revision of the manuscript for important intellectual content: All authors. Administrative, technical, or material support: All authors. Study supervision: Schaal.

Conflict of Interest Disclosures: None reported.

Funding/Support: The work was supported in part by an unrestricted grant from Research to Prevent Blindness, Inc.

Role of the Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.


**Epstein-Barr Virus–Positive Polymorphous Lymphoplasmacytic Infiltrate of the Lacrimal Glands in a Patient With Acute Lymphoblastic Leukemia**

An atypical inflammatory infiltrate of the orbital tissues in the setting of a patient with a known history of treated leukemia presents the clinician with the daunting task of having to establish whether a relapse of the leukemia has occurred, which would necessitate reintroduction of toxic chemotherapeutic agents. Herein, we report such a case.

**Report of a Case** | A boy in his early teens presented to the hospital with a 3-day history of painless swelling and erythema of bilateral upper and lower eyelids. He had had high-risk acute lymphoblastic leukemia that was in remission with maintenance chemotherapy. The upper eyelids exhibited temporal fullness (Figure 1A and B). Computed tomography revealed preseptal edema with bilaterally enlarged lacrimal glands and no bony destruction or globe compression (Figure 1C and D).

After admission to the hospital, blood cultures and viral cultures were obtained and were negative for cytomegalovirus, influenza, respiratory syncytial virus, and adenovirus. Of note, Epstein-Barr virus (EBV) IgG was positive and IgM was negative, with a serum viral load greater than 100 000 copies/mL. Lacrimal gland biopsies revealed that the lacrimal gland lobules were preserved (Figure 1E). The acini and ducts were splayed apart by polymorphous lymphoplasmacytic cells displaying mildly enlarged and irregularly shaped nuclei with modest amphophilic cytoplasm (Figure 1E, inset). There was no fibrosis of the lacrimal gland or spillover of the infiltrate into the adjacent orbital connective tissues.

Immunohistochemical staining revealed the following results: CD10+ and CD20+ lymphocytes; a small focus of CD21+ and CD23+ dendritic cells; CD56 predominantly negative except for some natural killer cells; CD138 strongly positive for plasma cells; BCL2 dimly positive; BCL6 negative; terminal deoxynucleotidyl transferase negative for leukemic cells; and Ki-67 positive in 70% of cells (Figure 2A). Immunoglobulin staining disclosed IgG greater than IgM greater than IgA. Many CD3+ and CD5+ T cells were dispersed throughout the lesion (Figure 2B). Flow cytometry did not reveal any abnormal B-, T-, or plasma-cell populations. The T cells showed an inverted CD4 to CD8 ratio, which would most likely represent a T-cell response to EBV-infected B cells. In situ hybridization to test for EBV-associated RNA expression was strongly positive in lymphocytes but was negative in the acini (Figure 2C). In situ hybridization for K+ immunoglobulin light chain (Figure 2D) was slightly more positive than that for lambda immunoglobulin light chain (Figure 2E). Polymerase chain reaction testing revealed a clonal heavy-chain gene rearrangement, indicating the presence of a small clonal B-cell population considered to be of no clinical significance.

**Discussion** | The central dilemma in this case was to determine whether the lacrimal gland infiltrates represented a relapse of the acute lymphoblastic leukemia, an inflammatory infiltrate, or a B- or T-cell neoplasm caused by EBV-positive lymphocytes. The clinical picture was confusing because the patient was receiving maintenance chemotherapy. The bilaterality of the process and its rapid evolution appeared ominous, as did the infiltrates composed of intermediate lymphocytes with somewhat irregular nuclei displaying a high Ki-67 proliferative index of 70%. Immunohistochemical studies, however, disclosed EBV infection of B lymphocytes with in situ hybridization and showed approximately equal K and lambda light-chain expression. Polymerase chain reaction disclosed a small clonal immunoglobulin heavy-chain gene rearrangement, which was not interpreted as evidence of a malignant cell population.1,2

In light of the absence of peripheral blood and bone marrow abnormalities of leukemia and the results of the lacrimal gland biopsy, it was decided not to treat the patient for a
relapse of leukemia. The patient’s routine prednisone dose was discontinued. During the ensuing 3 months, the lacrimal gland swellings subsided spontaneously and the serum EBV viral load fell to less than 300 copies/mL from greater than 100 000 copies/mL.

Epstein-Barr virus has been implicated in the pathogenesis of a number of orbital conditions, including Burkitt B-cell lymphoma, CD57+ natural killer cell lymphoma, and EBV-positive T-cell lymphoma as well as immunodeficiency and autoimmune disorders.3–6

Alia Rashid, MBChB
N. Grace Lee, MD
Frederick A. Jakobiec, MD, DSc
Suzanne K. Freitag, MD

Author Affiliations: David G. Cogan Laboratory of Ophthalmic Pathology, Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston (Rashid, Jakobiec); Ophthalmic Plastic Surgery Service, Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston (Lee, Freitag).

Corresponding Author: Frederick A. Jakobiec, MD, DSc, David G. Cogan Laboratory of Ophthalmic Pathology, Massachusetts Eye and Ear Infirmary, Ste 328, 243 Charles St, Boston, MA 02114 (fred_jakobiec@meei.harvard.edu).

Author Contributions: Drs Rashid and Jakobiec had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: All authors. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Rashid, Lee, Jakobiec. Critical revision of the manuscript for important intellectual content: Jakobiec, Freitag. Statistical analysis: Jakobiec.

Administrative, technical, or material support: Rashid, Jakobiec. Study supervision: All authors.

Conflict of Interest Disclosures: None reported.


Figure 1. Lacrimal Gland Inflammatory Infiltrates

A, Clinical photograph shows bilateral eyelid erythema with lacrimal gland enlargement producing an S-shaped upper eyelid configuration. B, Several days later, a fine, flaky scaling was observed in the skin, signifying rapid epidermal turnover due to inflammatory stimulation. C and D, Computed tomographic studies show bilateral lacrimal gland enlargement. C, Axial view demonstrates oblong enlargement of the lacrimal glands with involvement of the palpebral lobes anterior to the orbital rim (arrowhead) with molding to the globe and absence of bone destruction. D, Coronal view displays intact orbital bones and elongated enlargement of the lacrimal glands (arrowhead), without indentation of the globe, rather than the oval shape of an epithelial tumor.

E, Histopathologic studies show enlarged lobules without spillover of inflammation into surrounding connective tissue. The pale-staining small foci correspond to surviving parenchyma (hematoxylin-eosin, original magnification ×40). Inset, The acini of the gland are separated by intermediate-sized, mildly atypical lymphoplasmacytic cells (hematoxylin-eosin, original magnification ×400).

Figure 2. Immunohistochemistry of Infiltrating Inflammatory Cells in Lacrimal Gland

A, Ki-67 immunostains the nuclei of 70% of the infiltrating cells (original magnification ×200). B, CD3+ T lymphocytes are diffusely distributed between the pale-staining acini (original magnification ×100). C, Inflammatory cells with Epstein-Barr virus-positive nuclei surround pale-staining acini (original magnification ×200). In situ hybridization discloses a polyclonal population of B lymphocytes with roughly equal numbers of cells staining for κ (D) and λ (E) cytoplasmic light chains (original magnification ×200).


Novel Telemedicine Device for Diagnosis of Corneal Abrasions and Ulcers in Resource-Poor Settings

Corneal ulcers are a significant cause of corneal blindness worldwide. Normally, traumatic corneal damage and secondary infections are diagnosed by an ophthalmologist via slitlamp examination. However, limited health care resources in developing regions may delay diagnosis and treatment, increasing the risk of vision loss.2 Mobile phones are widely available even in resource-limited settings and therefore could potentially be used to aid in diagnosis of corneal epithelial defects with a smartphone.

Methods | We designed a smartphone attachment to provide magnified images of the cornea with controlled illumination. The attachment consisted of a +25-diopter lens and external light-emitting diode (LED) light sources that were aligned with the smartphone camera for image acquisition (Figure 1).

In one configuration, white LEDs (correlated color temperature of a 5250-K lamp) were used to capture white-light corneal photographs. In a second configuration, blue LEDs (472-nm peak wavelength) were used with a 550-nm/50-nm emission filter to capture fluorescein-stained corneal photographs. The attachments, which we refer to as Corneal CellScopes, slide on and off unmodified smartphones, allowing a single smartphone to take both white-light and fluorescein photographs.

To validate the smartphone attachments, we used an iPhone 4S (Apple Inc) to photograph 17 eyes from 17 patients at Chiang Mai University Hospital, Chiang Mai, Thailand. Participants had a slitlamp examination by an ophthalmologist, followed by photography with the white-light smartphone attachment. Fluorescein was then administered, followed by slitlamp examination and photography with the fluorescein smartphone attachment. Three off-site ophthalmologists graded all 34 photographs masked to the diagnosis, first as 34 independent photographs and then as 17 pairs of white-light and fluorescein photographs from the same eye. We calculated the agreement between the various assessments of an epithelial defect with Cohen κ. We estimated the sensitivity and specificity of smartphone photography vs the on-site ophthalmologist using the grades of all 3 graders and constructed 95% confidence intervals by percentile bootstrap, resampling eyes to account for nonindependence between grades of the same eye (10 000 repetitions). Analyses were performed with Stata version 12.0 statistical software (StataCorp LP). Institutional review board approval was obtained from the University of California, San Francisco. Written informed consent was obtained from all participants.

Results | The on-site ophthalmologist detected an epithelial defect in 6 of 17 eyes (Figure 2 and eFigure in the Supplement). The consensus diagnosis (agreement of ≥2 of the 3 graders) detected an epithelial defect in 5 eyes—all of which also had an epithelial defect diagnosed by the on-site ophthalmologist. Agreement between the 3 graders for the diagnosis of epithelial defect was good (κ = 0.73; 95% CI, 0.53-0.91). Agreement between the consensus diagnosis and the on-site ophthalmologist’s diagnosis for epithelial defect was excellent (κ = 0.87; 95% CI, 0.61-1.00). Compared with the on-site ophthalmologist’s examination, the sensitivity of photographic diagnosis of an epithelial defect was 83.3% (95% CI, 61.1%-100%) and specificity was 97.0% (95% CI, 90.9%-100%). When the white-light and fluorescein photographs were assessed as a pair, the sensitivity of photographic diagnosis of an epithelial defect improved to 88.9%