AMERICAN ACADEMY™ OF OPHTHALMOLOGY

Report

Long-term Management of Panuveitis and Iris Heterochromia in an Ebola Survivor

The 2013−2016 West African Ebola virus (EBOV) disease (EVD) outbreak was the largest in history with 28 616 cases and 11 310 deaths in the highest transmission countries (Sierra Leone, Guinea, and Liberia).[1] Reports of uveitis have emerged in EVD survivors.[2,3] We discuss clinical features, multimodality imaging, and long-term management of aggressive, sight-threatening panuveitis in an EVD survivor, providing insight into the pathogenesis of this condition.

A 43-year-old physician developed EVD in Kenema, Sierra Leone. After 40 days of hospitalization at Emory University, he was discharged with serum and urine testing negative by quantitative reverse transcription-polymerase chain reaction (qRT-PCR) assay for EBOV RNA.[4] One month after discharge, he experienced blurred vision, sacroiliitis, enthesitis, and word-finding difficulties. Ophthalmic evaluation showed visual acuities (VA) of 20/15 in both eyes and multiple peripheral chorioretinal scars with hypopigmented haloes bilaterally, consistent with inactive chorioretinitis requiring no intervention (Fig S1; available at www.aaojournal.org).

Fourteen weeks after EVD diagnosis, the patient presented with acute, left hypertensive anterior uveitis with VA of 20/20 and intraocular pressure (IOP) of 44 mmHg in the left eye.[2] Treatment was initiated with topical prednisolone acetate 1% (Pred Forte 1%) 4 times daily, brimonidine 0.2%, and dorzolamide 2%/timolol 0.5%, and acetazolamide. Serologies for syphilis, cytomegalovirus, herpes simplex virus-1 and -2, and *Toxoplasma gondii*. His HLA-B27 was negative.

Left anterior chamber paracentesis yielded aqueous humor positive for EBOV by qRT-PCR with a cycling threshold of 18.7 and a positive EBOV culture. Before and 24 hours after the procedure, conjunctival swab and tear film tested negative for EBOV RNA.[2]

On day 5 of the acute ocular illness, left VA decreased to 20/60 and the IOP was 15 mmHg. Diffuse anterior scleritis and intermediate uveitis prompted addition of oral prednisone 80 mg, with the topical Pred Forte 1% every 2 hours, timolol 0.5%, and atropine 1% (Fig S2; available at www.aaojounral.org).

Left VA decreased to 20/150 at day 6 of illness, and examination revealed grade 2+ anterior chamber (AC) cell, a 0.5-mm hypopyon, and grade 1 to 2+ vitreous haze. An OCT scan showed mild left retinal thickening (Fig S2; available at www.aaojounral.org).

Despite symptomatic improvement, left VA worsened to 20/250 at day 9, and IOP decreased to 6 mmHg. Corneal edema followed hypotony, with grade 2+ AC cell and grade 3+ vitreous haze (Fig S2; available at www.aaojounral.org). Difluprednate 0.05% every 2 hours was initiated.

Left VA deteriorated to 20/500 and IOP decreased to 2 mmHg at day 10. A left relative afferent pupillary defect developed, indicating optic neuropathy. Iris heterochromia developed at day 11, with a change from blue to green (Fig 1). Left anterior segment OCT revealed iris stromal thickening (502 μm) compared to the right (376 μm). Ultrasound biomicroscopy showed ciliary body edema. A dense grade 3+ vitreous haze persisted, prompting B-scan ultrasonography, which revealed shallow peripheral, choroidal effusions and optic nerve head edema (Fig 1).

Owing to clinical worsening, a 21-day course of oral favipiravir (T-705, Toyama Chemical, Tokyo, Japan) was initiated. After 2 loading doses of 2000 mg, favipiravir was administered 1200 mg twice daily. Three days after starting favipiravir (day 18 of illness), VA had decreased to finger counting at 2 feet and IOP was 3 mmHg. A periocular triaminolone acetonide injection (40 mg/ml) was administered in the Emory University Hospital Serious Communicable Diseases Unit. A postprocedure conjunctival swab tested negative for EBOV RNA.

One day after the injection, left VA was hand motions, but IOP increased to 9 mmHg. The patient was discharged on a course of favipiravir, and oral prednisone was tapered, decreasing by 10 mg/d every 2 weeks. Topical difluprednate 0.05% and atropine 1% were continued.

Forty-five days after initial onset of acute ocular illness, the patient completed favipiravir and remained on oral prednisone 15 mg/d and topical difluprednate 0.05%. Visual acuity had improved to 20/15 with resolution of relative afferent pupillary defect and IOP of 10 mmHg. Slit lamp examination showed resolved corneal edema, endothelial pigment without keratic precipitates, and trace AC pigment. Posterior segment examination showed grade 0.5+ vitreous haze. The iris thickness had decreased to 452 μm by day 32, with resolution of heterochromia (Fig 1).

At 1-year follow-up, left VA returned to 20/20 with IOP of 11 mmHg. After 18 months, VA had decreased to 20/60 with diffuse posterior capsular cataract. Anterior uveitis was observed with diffuse stellate keratic precipitates, 1+ AC cell, and stable posterior segment. Repeat AC paracentesis tested negative for EBOV by qRT-PCR. The PCR testing was negative for cytomegalovirus, herpes simplex virus, and varicella zoster virus DNA. Topical prednisolone acetate taper was given over 4 weeks with resolution of anterior uveitis.

Clinical and multimodal imaging features of this aggressive spectrum of ophthalmic pathology highlight the mechanisms of inflammation and infection, which improved after the administration of corticosteroids and antiviral medication.

Iris heterochromia coincided with iris and ciliary body edema by anterior segment OCT and ultrasound biomicroscopy; this was suggestive of heavy leukocyte infiltration and/or massive protein exudation related to an extreme inflammatory response associated with active EBOV replication. Immediate improvement of IOP and recovery of ciliary body anatomy after the corticosteroid injection supported the key role of appropriately timed anti-inflammatory therapy.

Although the precise role of favipiravir, a pyrazinecarboxamide derivative that inhibits viral RNA replicase,[5] was unclear, our patient's disease process worsened initially on topical and systemic corticosteroid. After the initiation of favipiravir, a

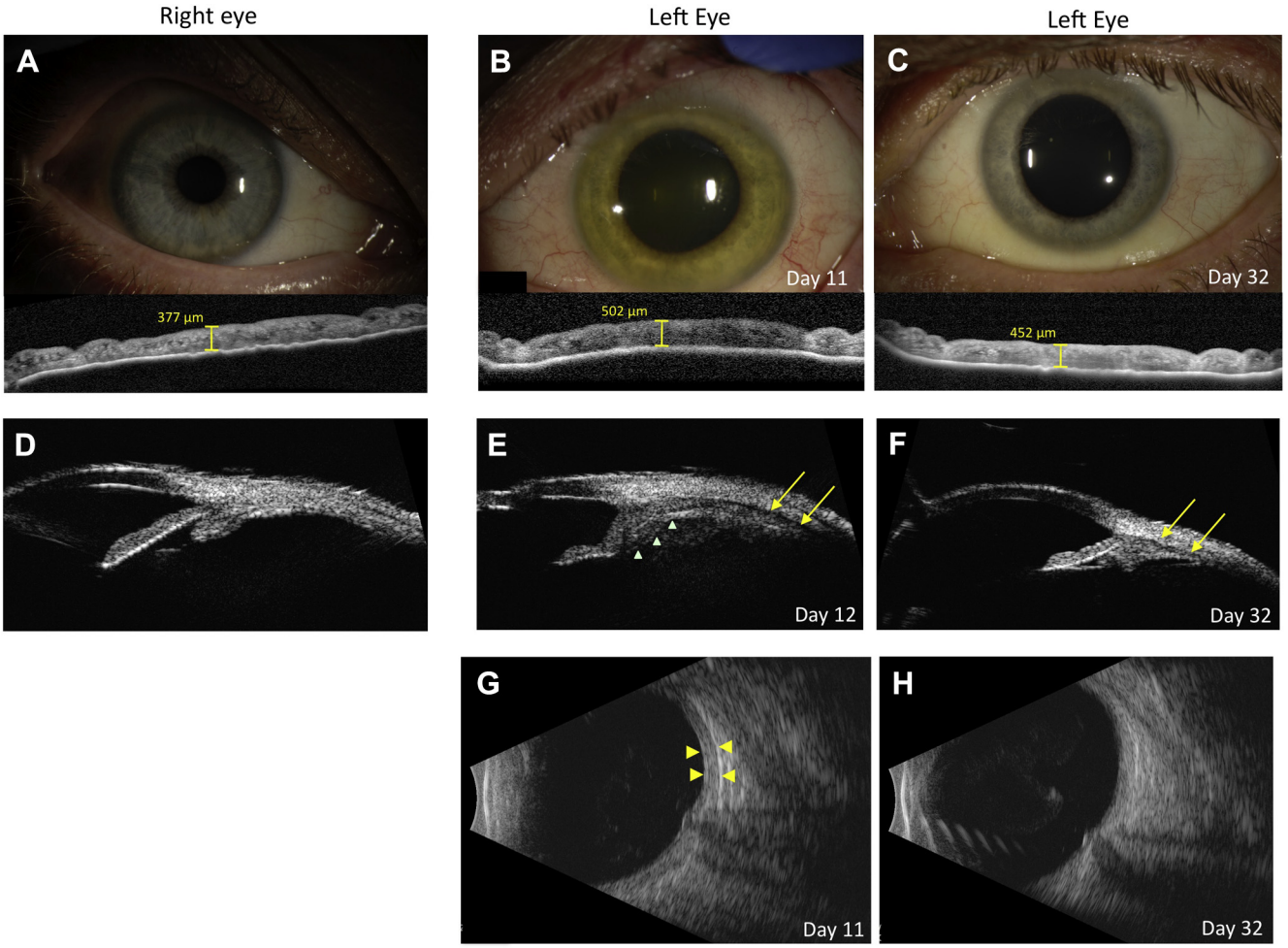

Figure 1. Anterior segment photographs and digital imaging. **A**, Slit lamp photograph of right eye with corresponding anterior segment optical coherence tomography (OCT) at baseline shows iris thickness of 377 µm. **B**, Slit lamp photograph and anterior segment OCT at day 11 show a green iris color with iris thickening at 502 µm. **C**, By day 32, slit lamp photography shows reversal of iris color to original blue color and corresponding decrease in iris edema to 452 µm. **D**, Ultrasound biomicroscopy (UBM) shows normal ciliary body anatomy of the right eye. **E**, At day 12, UBM of the left eye shows ciliary body swelling (*green triangles*) and supraciliary/choroidal effusion (*yellow areas*) consistent with progressive panuveitis, choroiditis, and evolving hypotony. **F**, Repeat UBM shows decreased ciliary body swelling and resolution of supraciliary/choroidal effusion (*yellow arrows*) by day 32. **G**, B-scan ultrasound imaging shows choroidal thickening at day 11 and repeat at day 32. **H**, Resolution of choroidal thickening.

periocular corticosteroid injection was administered because of concerns for recalcitrant hypotony, ciliary body shutdown, and irreversible vision loss. The patient's clinical improvement paralleled the anatomic reduction in iris thickening by anterior segment OCT.

Diagnostic ophthalmic imaging highlighted the anatomic and pathologic changes that occurred during our patient's sight-threatening panuveitis. The imaging findings suggested severe reactive inflammation in the presence of EBOV viral replication, emphasizing the need for consideration of management strategies that target infectious and inflammatory processes in post-Ebola uveitis. Potential for uveitis recurrence mandates long-term monitoring.

Jessica G. Shantha, MD[1]
Ian Crozier, MD[2]
Jay B. Varkey, MD[3]
Colleen S. Kraft, MD[3,4]
G. Marshall Lyon, III, MD, MMSc[3]
Aneesh K. Mehta, MD[3]
Renee Donahue Carlson, MD[3]
Charles E. Hill, MD, PhD[4]
Gokul Kumar, MD[1]
Matthew R. Debiec, MD[1]
Purnima S. Patel, MD[1]
Timothy W. Olsen, MD[1]
Robert B. Nussenblatt, MD, MPH[5]
Daniel F. Martin, MD[6]
Ute Ströher, PhD[7]
Timothy M. Uyeki, MD, MPH, MPP[7]
Bruce S. Ribner, MD, MPH[3]
Justine R. Smith, FRANZCO, PhD[8]
Steven Yeh, MD[1]