OBSERVATION

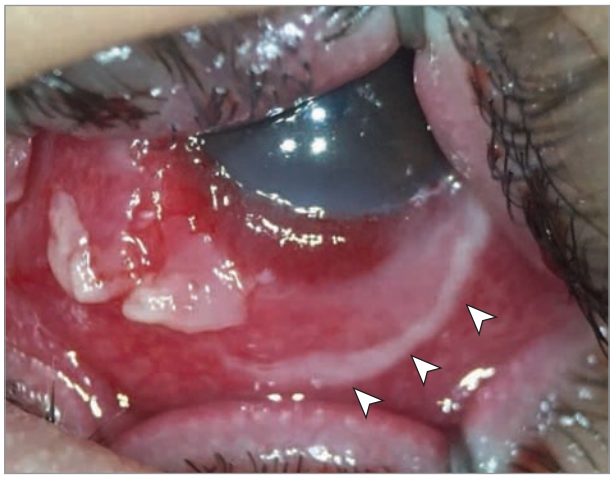
Conjunctival Biopsy of a Patient With Mpox

Mpox, caused by a zoonotic orthopoxvirus, is an emergent infectious disease that has drawn global attention since 2022.[1] Commonly reported signs and symptoms include skin rash or lesions, fever, lethargy, myalgia, headache, and lymphadenopathy.[2] Rare cases of conjunctivitis associated with *Monkeypox virus* are in the literature.[3-5] In this article, we share the results of a conjunctival biopsy of a patient with mpox.

A male patient in his late 20s presented with severe pain, photophobia, and visual changes in his left eye for the past 2 weeks. His medical history was significant for AIDS, with past infections including syphilis, cytomegalovirus, *Pneumocystis jiroveci* (formerly *Pneumocystis carinii*) pneumonia, giardiasis, and condyloma acuminata. In the past year, a diagnosis of mpox was treated with tecovirimat over 24 days (10 days intravenously and 14 days orally). The patient's symptoms improved while taking treatment. One month posttherapy, the patient noted recurrence of the prior skin lesion and left eye symptoms and a new 2-cm ulcerated forehead lesion. Results of the forehead lesion swab polymerase chain reaction were positive for *Orthopoxvirus*.

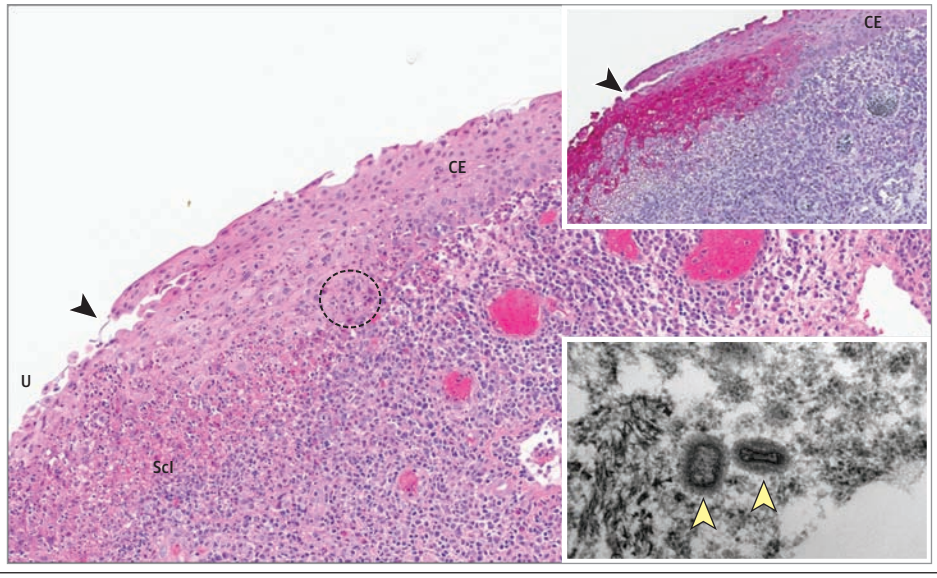
Initial ophthalmic evaluation was significant for severe hyperemia of the left eye with demarcation lines suggestive of necrosis (**Figure 1**). The patient had severe pain in the left eye, and visual acuity was counting fingers OS. CD4 lymphocyte count was 12 cells/μL at the time of admission. A full-thickness conjunctival biopsy was performed due to the profound CD4 lymphopenia necessitating exclusion of opportu-

Figure 1. Photograph of the Left Eye on Presentation



Inflamed conjunctiva with a white, necrotic demarcation line (arrowheads).

Figure 2. Pathology Findings of Superior Conjunctival Biopsy



The superior conjunctival ulcer with glassy eosinophilic nuclear pseudoinclsuions at the margins is indicated by the dotted circle (hematoxylin-eosin, original magnification ×10). The black arrowhead indicates the edge of the ulcer with loss of conjunctival epithelium (CE). There was also subconjunctival infiltrate (SCI) of mixed acute and chronic infiltrate of neutrophils, lymphocytes, karryorhectic debris, and macrophages. Top inset, Immunohistochemistry staining with vector red lower power using an immune alkaline phosphatase technique performed at the US Centers for Disease Control and Prevention, Atlanta, Georgia. The rabbit polyclonal antibody used was generated against *Monkeypox virus* but is broadly reactive with *Orthopoxvirus*, including various (smallpox) virus, vaccinia virus, and cowpox virus. It is not known to cross-react with bovine parapoxvirus or orf virus. The ulcer edge showed diffuse, strong, positively stained viral antigen throughout the ulcerating epithelial cytoplasm epithelium (black arrowhead; hematoxylin-eosin, original magnification ×10). Bottom inset, Electron microscopy of formalin-fixed paraffin-embedded biopsy. Cytoplasmic viral particles consistent with pox virus (yellow arrowheads) with dumbbell-shaped cores (original magnification ×30 000).

nistic infections and potential concerns regarding medication compliance for HIV and mpox infections.

On hematoxylin-eosin staining, the inferior conjunctival sample showed acute conjunctivitis with subconjunctival edema and hemorrhage, mild acute neutrophilic infiltrates throughout the conjunctiva, and mild perivascular lymphoplastic infiltrate. The superior conjunctival sample showed acute ulcerative conjunctivitis with necrosis and exudate, karyorrhectic neutrophilic debris, rare eosinophilic glassy nuclear pseudoinclusions, and mixed acute and chronic infiltrate and subconjunctival edema (**Figure 2**). There were no cytoplasmic inclusions visible on hematoxylin-eosin stains. Results of immunohistochemical testing were positive for *Orthopoxvirus* antigen in the cytoplasm of cells in the ulcerated area, and electron microscopy demonstrated viral particles in the cytoplasm with none in the nucleus, typical of orthopox virus species (Figure 2). Differential diagnoses included ulcerating infections in the conjunctiva, including varicella-zoster virus, herpes simplex virus I and II, cytomegalovirus, and *Treponema pallidum*, for which results of all immunohistochemical stains were negative. The eye biopsy showed a necro-inflammatory ulcer with loss of conjunctival epithelium, while the skin biopsy showed acanthotic thickening with central necrosis. These pathologic differences manifested as an injected ulcerating conjunctival lesion and a pearly umbilicated centrally ulcerating skin papule, respectively.

The patient was treated systemically with intravenous tecovirimat, 200 mg, every 12 hours and oral valacyclovir, 1000 mg, every 8 hours. Left ocular treatment consisted of tobramycin-dexamethasone eye drops, a 10-day course of ganciclovir, 0.15%, ophthalmic gel, and 10-day course of ciprofloxacin, 0.3%, ophthalmic ointment. A few months posttreatment, the patient developed stromal scarring in the left eye and was treated with prednisolone acetate, 1%. Final visual acuity was 20/40 OS.

Conjunctivitis may present after treatment of mpox, as seen in this patient. Recurrence was noted by prior skin lesions, a new 2-cm forehead lesion, and left eye inflammation. While only a single case, full-thickness conjunctival biopsy of the eye lesion showed infection with positive results on immunohistochemical staining for orthopox. Though management can be challenging, an acceptable visual outcome can be achieved. Biopsy and laboratory examinations were instrumental in this case to determine *Monkeypox virus* in the conjunctiva and helped guide aggressive treatment to restore the patient's vision.

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Published Online: January 11, 2024. doi:10.1001/jamaophthalmol.2023.5780

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank Jana M. Ritter, DVM (US Centers for Disease Control and Prevention, Atlanta, Georgia), and Jon Charlesworth, MA (Mayo Clinic, Rochester, Minnesota), for providing the immunohistochemistry and electron microscopy images on Figure 2B and C, respectively. Neither contributor was compensated for their work.

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Optical Coherence Tomography Feature of Retinoschisis in *CRB1*-Associated Maculopathy

CRB1-associated macular dystrophy (CAMD) presents initially with macular retinoschisis and in more advanced disease with degeneration of the macular outer retina.[1-5] CAMD differs clinically and genetically from otherwise retinawide *CRB1*-associated degeneration: it usually develops when 1 allele harbors the in-frame deletion c.498-506del that solely affects the CRB1-A isoform, thereby still allowing for full-length expression of the more abundant CRB1-B isoform.

Here, we describe a phenotypic feature on optical coherence tomography (OCT) imaging that appears to be characteristic for CAMD-associated macular retinoschisis: hyperreflective columns in the outer nuclear layer. In 2 patients, OCT imaging showed macular retinoschisis with hyperreflective linear structures crossing the outer nuclear layer. The ellipsoid layer facing 1 end of these hyperreflective columns appeared interrupted.

Figure 1 presents longitudinal observations on OCT scans of a 39-year-old male patient who initially presented with unilateral macular changes, which allowed for monitoring of the evolution of the macular schisis and hyperreflective columns in the subsequently affected fellow eye. Schitic changes started in the paracentral inner nuclear layer and later involved the foveal outer nuclear layer. Visual acuity was 20/36 at baseline and 20/80 at 25 months' follow-up in the right eye and 20/20 at baseline and 20/60 at follow-up in the left eye. Genetic testing revealed the *CRB1* variant c.2490_2491del, p.(Tyr831fs) in trans with the in-frame deletion c.498-506del.

Figure 2 shows OCT scans of a an 11-year-old female patient. The hyperreflective columns that were present at baseline examination remained partially visible after spontaneous resolution of the macular retinoschisis 10 months later. Visual acuity was 20/36 at baseline and 20/30 at 10 months' follow-up in the right eye and 20/40 at baseline and 20/25 at follow-up in the left eye. Genetic testing revealed the *CRB1* variant c.2234C>T, p.(Thr745Met), in trans with the in-frame deletion c.498-506del.

A literature review revealed hyperreflective columns in other early-stage CAMD cases with macular schisis[2,5] but not in late-stages with macular degeneration.[1,4] The hyperreflective