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NOVEL ID CASES

A Case of Sustained Viral Shedding of Mpox With Ocular Involvement Resulting in Vision Loss

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Mpox, caused by infection with *Monkeypox virus*, usually presents as a mild, self-limited illness in immunocompetent persons that resolves within 2–4 weeks. Serious complications have been reported when mpox lesions involve vulnerable anatomic sites, such as the eye, and in those with substantial immunosuppression. We describe a patient with advanced human immunodeficiency virus infection and sustained viral shedding of mpox with ocular involvement, which resulted in vision loss.

Keywords. Ocular MPOX; MPOX; HIV.

Mpox is caused by *Monkeypox virus*, a DNA virus in the orthopoxvirus (OPXV) family [1]. Prior to 2022, sporadic cases in the United States (US) occurred from contact with imported animals [2]. In May 2022, a global outbreak of mpox with clade IIb was first recognized in Europe and the US [3], with the majority of cases in men who have sex with men.

Transmission occurs primarily through contact with infected lesions and the majority of patients experience a mild, self-limiting illness that resolves within 2–4 weeks. However, as cases increased through the 2022 outbreak, serious complications were recognized when lesions involved vulnerable anatomic sites, such as the eye, and in those with substantial immunosuppression (eg, human immunodeficiency virus [HIV] infection with CD4 count <50 cells/μL) [4]. Ophthalmic complications are rare, occurring in <5% [5, 6] of patients, but can cause irreversible blindness. We describe a case of mpox with sustained shedding and ocular involvement that resulted in vision loss.

CASE PRESENTATION

In July 2022, a 29-year-old man with HIV infection (CD4 count 12 cells/μL and viral load [VL] 34 200 copies/mL), poor antiretroviral treatment (ART) adherence, and housing insecurity presented to his primary care physician with a rash on the face, trunk, and extremities after a sex partner was diagnosed with mpox. A skin swab from 1 of the lesions was negative for OPXV polymerase chain reaction (PCR) testing (Centers for Disease Control and Prevention [CDC]). On day 10 of illness, he developed increasing conjunctival redness for which he was given a course of doxycycline and prednisone eye drops and referred to ophthalmology. A swab of a second skin lesion was obtained, which returned positive for OPXV (CDC PCR). Oral tecovirimat (TPOXX) and trifluridine eye drops were prescribed; however, due to progressive left eye pain, and blurred vision, he was hospitalized on day 21 of illness.

On admission to hospital A, he had excessive tearing, vision loss, and pain in the left eye with photophobia that limited evaluation. A superficial 4 mm × 2 mm corneal ulcer was seen at the 6 o'clock limbus with conjunctival injection. Intravenous (IV) tecovirimat, IV ganciclovir, and ophthalmic drops with ofloxacin, trifluridine, and erythromycin were started. Ganciclovir was discontinued after cytomegalovirus (CMV) immunoglobulin G (IgG) returned negative. Over the next 3 days, the corneal ulcer decreased in size to 1 mm × 2 mm, visual acuity remained stable, and the skin lesions started to involute. With improvement of constitutional symptoms, eye pain, and photophobia, he was discharged on hospital day 5 with trifluridine eye drops, erythromycin ointment, and a 14-day course of oral tecovirimat. Testing for other pathogens returned negative, including serum *Cryptococcus* antigen, syphilis screen, *Toxoplasma* IgG, *Coccidioides* (enzyme immunoassay), CMV PCR and IgG, and urine gonococcus and chlamydia nucleic acid amplification test.

Over the next 4 weeks, the patient developed new facial lesions and decreased left eye vision with increased pain. He presented to hospital B where he was noted to have left eye conjunctivitis, keratitis, and a conjunctival ulcer (Figure 1). He reported nonadherence to oral tecovirimat provided by the prior hospital. A conjunctival swab tested positive for

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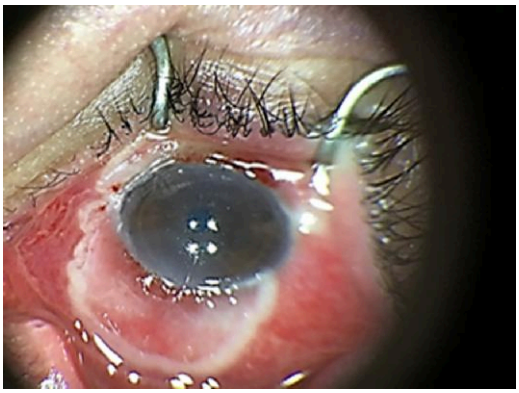

Figure 1. Slit light exam of left eye on admission to hospital B showing conjunctival edema, chemosis, hemorrhage with ring infiltrate circumferentially, episcleral injection temporally, and stromal edema of the cornea.

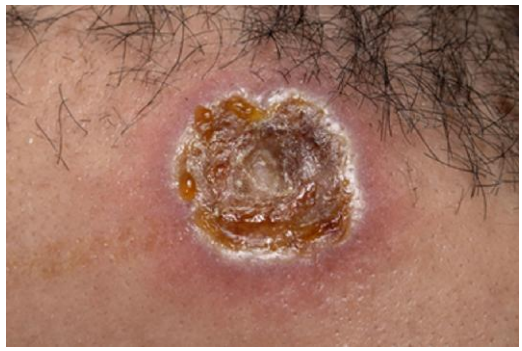

Figure 3. Papular skin lesion with central ulceration and brown debris with a yellow, pearly border, and circumferential rim of erythema.

OPXV PCR (CDC PCR), and biopsy showed necroulcerative conjunctivitis with extensive intralesional orthopoxviral antigen detected by immunohistochemistry (Figure 2). A swab and biopsy of a new skin lesion (Figures 3 and 4) was also positive for OPXV; varicella zoster virus and herpes simplex virus PCR results were negative. After CDC consultation, IV tecovirimat was started. Topical trifluridine and povidone-iodine were also applied to the eye. Tecovirimat resistance testing was negative. Over the next week, he experienced waxing and waning left eye pain and photosensitivity. Intraocular and IV cidofovir were administered on hospital day 10. After 23 days of IV tecovirimat, the conjunctivitis significantly improved, and he was transitioned to oral tecovirimat. On hospital day 25, he developed new skin lesions, which were biopsied and found to be molluscum contagiosum and a secondary infection with methicillin-resistant *Staphylococcus aureus*. By the end of his 5-week hospitalization, he had received 59 days of oral and IV tecovirimat and 3 weekly doses of IV cidofovir, with resolution of cutaneous lesions and improvement in the left eye conjunctivitis, although he continued to have vision loss. Due to a reported history of possible resistance, his HIV therapy was intensified by adding Prezcobix (darunavir/cobicistat) to Biktarvy (bictegravir/tenofovir alafenamide/emtricitabine). HIV resistance testing showed a M184V and an E157Q mutation. Prezcobix was continued in the setting of his profound immunosuppression and severe mpox. At the time of discharge, his CD4 count was 30 cells/μL and HIV VL was 30 copies/mL. He was discharged on oral tecovirimat to complete a total course of 64 days in addition to Biktarvy, linezolid for the skin and soft tissue infection, and prophylactic acyclovir. He received inhaled pentamidine for pneumocystis prophylaxis in the setting of gastrointestinal intolerance to trimethoprim-sulfamethoxazole. Prezcobix was stopped at this time.

Three days later, he presented to hospital C for myalgias and progressive rash for which he received another 14-day course of IV tecovirimat with resolution of symptoms. No repeat

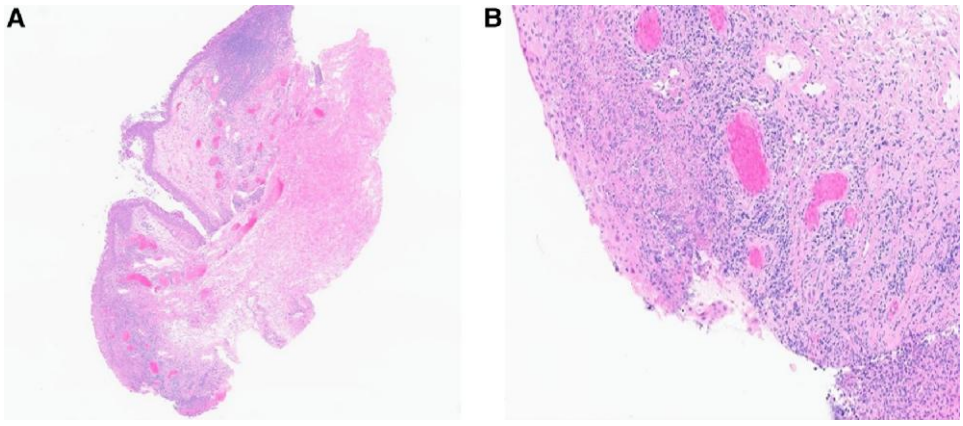

Figure 2. Superior left conjunctiva biopsy. *A*, Acute and chronic ulcerative conjunctivitis with necrosis, exudate, dense lymphoplasmacytic subconjunctival infiltrate, and edema. *B*, Ulceration is seen at higher magnification on the right. Staining for orthopoxviral antigen was positive within ulcerated epithelium.

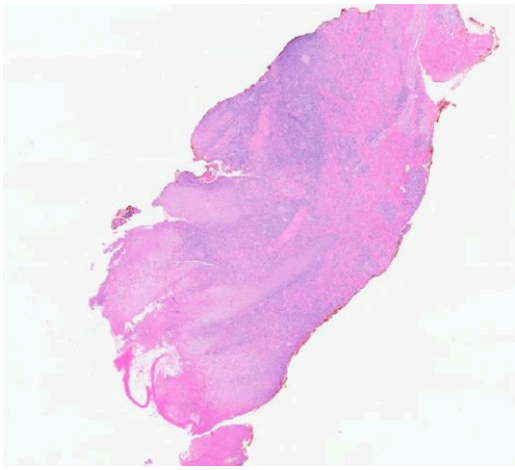

Figure 4. Left lateral neck skin biopsy. Acantholysis, ulceration, central necrosis with surrounding dense exudate/infiltrate of lymphocytes, histiocytes, neutrophils, karyorrhectic debris, and eosinophils. The thickening in the epidermal layer seen in this skin biopsy, not seen in the conjunctival specimen, accounts for the pearly border often seen in such skin lesions (see Figure 3).

mpox testing was obtained. By the end of this third hospitalization, his CD4 count was 16 cells/μL and HIV viral load was <20 copies/mL. Nine months postdischarge, he remains stable with corneal scarring limiting his vision in the involved eye.

DISCUSSION

Many mpox cases are self-limited [7]; however, those who are immunosuppressed are at risk of severe manifestations and death [4]. To date, there have been 42 deaths attributed to mpox [8]. The majority of these patients had advanced HIV with low CD4 counts [4]. Data on the immune response to mpox are limited, but as this case highlights, it plays an integral role in the severity and clinical course of the disease.

Both innate and adaptive arms of immunity, especially T cells, are necessary in mpox viral clearance [9]. Histologic studies show that the immune response to mpox skin lesions involves infiltration of $CD3^+$ T cells [10]. In addition, cytotoxic T-lymphocyte responses are associated with improved viral control in vaccinated rhesus macaques [11]. An mpox cohort showed a significantly higher case fatality rate of 14.9% in children aged 0–4 years, suggesting that a mature functioning adaptive immune response plays an important role in disease control [12].

$CD4^+$ T cells enhance both cytotoxic activity and virus-specific B-cell antibody production. Vaccination with vaccinia virus (VACV) can increase interferon gamma (IFN-γ)–producing $CD4^+$ and $CD8^+$ T cells [13]. In addition, $CD4^+$ T cells upregulate cytolytic activity genes in humans infected with VACV, and $CD4^+$ cytolytic T cells have been seen in participants vaccinated with VACV [14, 15]. In a study of 528 patients with mpox, those with a history of smallpox vaccination comprised only 9% of the group [16]. In contrast, macaques infected with simian immunodeficiency virus and $CD4^+$ T-cell counts <300 did not mount VACV-specific IgG and died when challenged with mpox virus [11]. These observations support the crucial role of $CD4^+$ T cells in mpox immunity and suggest that immune reconstitution may reduce severe disease and enhance recovery.

Multiple case reports of mpox in people living with HIV with $CD4^+$ count <200 cells/μL not on ART show higher risk of hospitalization and severe disease, including progression to skin and ocular necrotic and gangrenous lesions instead of the expected pustular response [17]. In 1 severe case, T lymphocytes were absent in a punch biopsy of necrotic skin [17]. T-cell deficiency in HIV infection may thus lead to progressive evolution of disease via viremia and contiguous intradermal spread.

To date, there have been a total of 31 published cases of ocular mpox during the 2022 outbreak [18–20]. Due to a lack of data, treatment of published cases varied widely [18]. Recently, the CDC published guidance for the management of ocular mpox [21]. Tecovirimat inhibits orthopoxvirus VP37 envelope wrapping protein, thus blocking cellular transmission of the virus [22]. It should be given to those with ocular mpox, with consideration for IV administration if there are absorption concerns, including if a patient is unable to consume a high-fat meal (600 calories and 25 g fat) with each dose [21]. IV tecovirimat should also be given to those with diffuse and disseminated infection [21]. Tecovirimat is typically administered for a 14-day duration; however, those with severe immunocompromise, such as our case, may benefit from extended treatment [21]. The recommendation is to extend treatment in short, defined intervals (eg, 7 days) with close monitoring for safety and clinical response [21]. Due to tecovirimat's low barrier to resistance, the CDC has been monitoring for tecovirimat-resistant virus since the start of the 2022 outbreak. In November 2022, 2 patients were confirmed to have tecovirimat-resistant viruses [23]. Resistance testing is recommended for those who develop new lesions after they have received 7 days of tecovirimat [21]. Our patient did have a prolonged course and severe manifestations. As tecovirimat does not stop viral replication, and rather only inhibits viral exit from the cell, our patient's inability to take tecovirimat twice daily as prescribed led to increased viral spread. In the setting of his profound T-cell deficiency, this led to significant progression of disease. Furthermore, he likely required such a prolonged course of treatment until he was reliably on antiretrovirals to help control his HIV and allow for CD4 recovery. Trifluridine eye drops are recommended in cases of mpox virus keratitis [21] and may be given up to 4 weeks [21]. Continued administration beyond 4 weeks is not recommended due to the risk for corneal epithelial toxicity [24]. Topical lubricants and/or antibiotics should also be considered in the setting of corneal disease to help prevent bacterial superinfection [25].

The efficacy of vaccinia immune globulin intravenous (VIGIV) for mpox is unknown. However, it has been recommended for immunosuppressed patients unable to mount a sufficient immune response to clear the virus, as it may provide protective IgG [21]. It is thought to have a favorable side effect profile; however, there are limited data based on 2 animal models, 1 of which suggested an increased risk for corneal scarring [21]. We opted not to give our patient VIGIV because of unknown efficacy and risk of corneal scarring.

Brincidofovir or cidofovir may be used in conjunction with tecovirimat for those with, or at risk of, severe mpox [21, 26]. It is not recommended to use brincidofovir or cidofovir without tecovirimat, unless there is a contraindication to tecovirimat; nor is it recommended to use brincidofovir and cidofovir within 1 week of each other due to the prolonged duration of the active metabolite, cidofovir diphosphate, and the potential for overlapping side effects [21].

There are 2 available vaccinations that may be used in the prevention of mpox: a replication-deficient modified vaccinia Ankara vaccine (JYNNEOS in the US), and a replication-competent smallpox vaccine (ACAM2000) [27]. Peak immunity is expected 14 days after the second dose of vaccine [28]. Among those who developed mpox after vaccination; the majority of cases developed mpox within the first 14 days from receipt of their first dose [29]. There are also rare breakthrough cases that occurred >14 days from the second dose [29]. The patient in the case above did not receive vaccination prior to his acquisition of mpox. In the setting of uncontrolled HIV, vaccination may have been protective. Per the Advisory Committee on Immunization Practices and the CDC, it is recommended for those 18 years and older at risk of mpox to receive the 2-dose JYNNEOS vaccine series [30].

While the number of mpox cases has declined since peaking in August 2022, there has been persistent low-level transmission [31]. Between 18 March and 15 May 2023, there was a cluster of 21 cases in Chicago, 17 of whom were vaccinated (11 with 2 doses of JYNNEOS, 1 with ACAM2000, 5 with 1 dose of JYNNEOS) [32]. Five had well-controlled HIV infection, and none were hospitalized [32]. There is concern for a possible resurgence of mpox with the warmer-weather months and group gatherings [32].

CONCLUSIONS

Patients with advanced HIV infection have an increased risk for severe, disseminated mpox infection as well as a higher mortality rate. This case report elucidates the impact of mpox ocular infections on patients with advanced HIV infection. In addition to prompt evaluation and initiation of systemic antiviral therapy with tecovirimat and topical trifluridine eye drops, optimizing immune function is essential for recovery in those with advanced immunosuppression.

Notes

Patient consent. The patient's written consent was obtained.

Potential conflicts of interest. All authors: No reported conflicts of interest.

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