Received: 2 March 2024 | Accepted: 24 April 2024

DOI: 10.1111/hiv.13656

SHORT COMMUNICATION

Severe ocular Mpox in person living with advanced HIV treated with extended course of tecovirimat

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Abstract

Background: People living with HIV are disproportionately represented among people with severe mpox. Mild and self-limiting conjunctival involvement has been well-documented, and severe ocular complications, including keratitis, corneal scarring, and the associated loss of vision, are increasingly recognized. Tecovirimat is the first-line antiviral therapy for severe mpox, but data around the efficacy of systemic antiviral agents for mpox are limited, particularly in cases of ocular mpox.

Case Report: Here, we describe a case of sight-threatening necrotic blepharo-keratoconjunctivitis in a person with advanced HIV, requiring an extended course of tecovirimat due to persistent mpox viral shedding for nearly 5 months.

KEYWORDS

corneal ulcer, immune reconstitution, keratitis, monkeypox, Mpox, ocular complications, ophthalmology, viral infection

BACKGROUND

Since the 2022 multi-country outbreak of mpox (formerly known as monkeypox), over 93 000 cases have been reported globally. People living with HIV account for 38%–50% of these cases and are disproportionately represented among those with severe disease [1]. Mild and self-limiting conjunctival involvement has been well-documented, and severe ocular complications, including keratitis, corneal scarring, and the associated loss of vision, are increasingly recognized [2–6]. Tecovirimat is the first-line antiviral therapy for severe mpox, but data around the efficacy of systemic antiviral agents for mpox are limited, particularly in cases of ocular mpox. Here, we describe a case of sight-threatening necrotic blepharo-keratoconjunctivitis in a person with advanced HIV.

CASE REPORT

A man in his late 20s with advanced HIV (CD4 10/mL, viral load 9004 copies/mL) who had restarted antiretroviral therapy (ART) 6 weeks previously was admitted to hospital with a 2-week history of left eyelid swelling and subsequent headache, fever, and non-productive cough. On examination, the patient was unable to open the left eye and had severely limited ocular movements in all positions of gaze and, consequently, diplopia in the primary

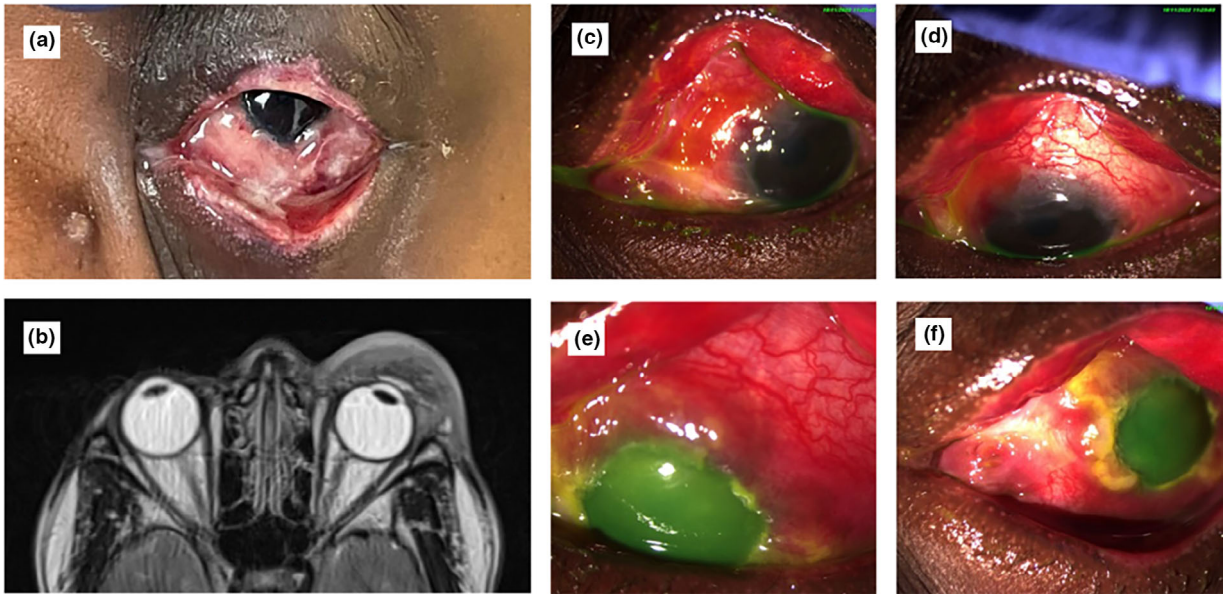

FIGURE 1 (a) Photograph of eye on day 12, (b) MRI orbit captured on day 7 of first admission. There is extensive left preseptal cellulitis with dacryoadenitis and conjunctivitis, with enhancement and thickening along the ciliary body, iris, and levator palpebrae superioris. (c–f): Extensive bulbar, tarsal conjunctival, and limbal inflammation with gross thickening and areas of necrotic change at the limbus associated with a total corneal epithelial defect evident on staining with fluorescein 2%. MRI, magnetic resonance imaging.

position. Slit lamp examination demonstrated macerated, necrotic lid margins alongside a cicatrizing conjunctivitis with an associated lower lid symblepharon and clear cornea with an unaided visual acuity (VA) reduced to 6/12 (Figure 1). One week later, he developed a corneal epithelial defect. At presentation, he had over 100 papular skin lesions, including in the peri-anal region and oral cavity. Widespread lymphadenopathy was present. No lesions were observed at the eyelid margin, although pox lesions were present on the face and scalp. Mpox DNA polymerase chain reaction (PCR) from skin, vesicle, and conjunctival swabs were positive. He was initially treated both with intravenous antibiotics (ceftriaxone) for preseptal cellulitis and dacryoadenitis and with topical antibiotics in the form of guttae moxifloxacin 0.5% four times daily. When mpox was confirmed by PCR, oral tecovirimat (14 days) was commenced alongside a course of topical trifluridine five times per day and guttae dexamethasone 0.1% 2 hourly with topical lubricants. An additional course of tecovirimat (14 days) was required because of persistent rectal swab positivity and concern that the corneal epithelial defect was slow to heal.

After 36 days in hospital and clinical improvement, the patient was discharged home where he remained under regular ophthalmic review and was clinically stable. Following this, a decision was made to cease ongoing swabbing for mpox because of the prompt improvement in his clinical picture.

He re-presented to the eye casualty 4 weeks later with eye pain, photophobia, and a worsening unaided VA of 6/24; topical steroid had been ceased 3 weeks prior. He had a large 15 × 13 mm epithelial defect associated with limbal stem cell failure, and topical lubricants and antibiotics were commenced. At this time, the patient reported non-adherence to his ART. Conjunctival and skin swabs (taken from dry lesions that appeared healed) were persistently positive for mpox DNA. A third course of oral tecovirimat (14 days) and a second course of trifluridine 1% drops were commenced, and topical dexamethasone, guttae moxifloxacin, and chloramphenicol ointment were restarted. Corneal scrapings were negative for bacteria/fungi. He remained on topical intraocular pressure-lowering therapy throughout because of an associated steroid-induced pressure rise. Although the patient was clinically improving, conjunctival swabs remained positive for mpox DNA and only became negative following a fourth and final course of tecovirimat (28 days). In total, the patient received 10 weeks of tecovirimat and 4 weeks of trifluridine eye drops.

Cycle threshold (Ct) values on PCR of conjunctival swabs had decreased slightly at representation to eye casualty then increased over the following weeks (indicating a decreasing concentration of viral material). Mpox DNA remained detectable for a total of almost 5 months after symptom onset (Figure 2). Although the patient remained stable for 3 months, he later presented again with another epithelial defect following cessation

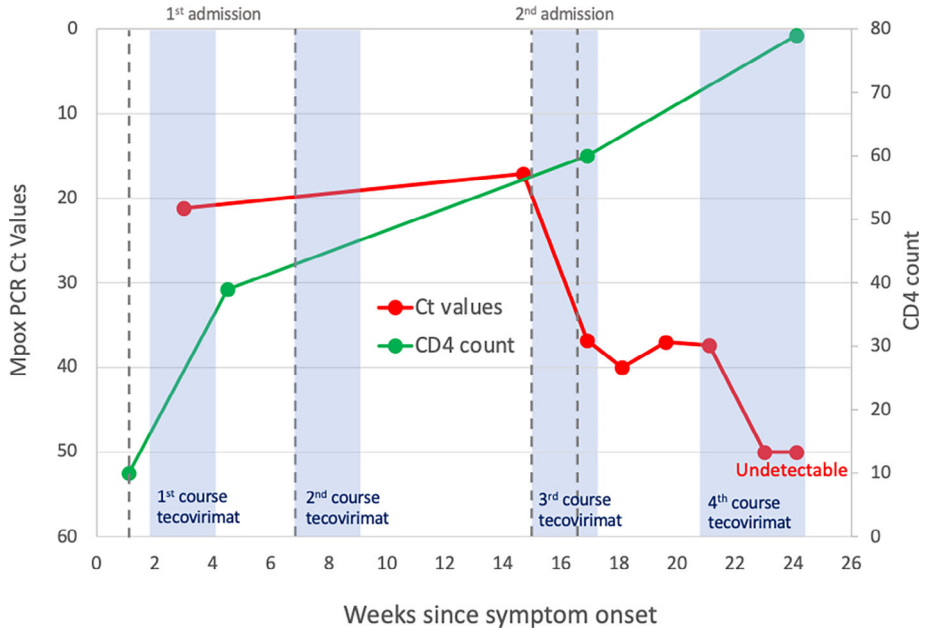

FIGURE 2 Changes in the mpox cycle threshold (Ct) values of in-house Viasure real-time polymerase chain reaction (PCR) assay on conjunctival swab samples. Where duplicate samples were collected on the same day, the lowest Ct value is presented.

of topical steroid, was negative for mpox DNA on PCR testing, and has responded well to topical steroid and antibiotic, with a slower taper of topical steroid initiated to avoid further ocular complications.

DISCUSSION

Immunosuppression due to advanced HIV may have contributed to the very prolonged viral shedding of almost 5 months observed in our patient, beyond viral shedding from skin lesions. Clinicians should be aware of the possibility of disease recurrence and prolonged infectiousness from the inflamed ocular surface and secretions. This is shown by the low Ct value on day 1 of second admission (Figure 2), highlighting the importance of continuing active treatment until Ct values are no longer detected. Persistent viral shedding and potential for prolonged infectiousness posed additional challenges for navigating infection prevention control measures and directing the patient regarding self-isolation and returning to work, especially without formal government guidance.

The patient originally presented 6 weeks after restarting ART and demonstrated immune reconstitution (increase in CD4 from 10 to 40/mL). The possibility of immune reconstitution inflammatory syndrome contributing to the subsequent ocular inflammation and initiation of systemic corticosteroids was considered but thought unlikely given the disease reoccurred during a period of non-adherence to ART, the relatively low Ct value on eye swabs at re-presentation (suggesting active viral replication rather than the virus being cleared by an overly exuberant immune response), and the prompt clinical improvement on reinstating ART. Ct values from mpox PCR analysis of further eye swabs indicated persistent low viral concentrations and an inability to clear the virus for nearly 5 months, which was the more likely cause of persistent ocular inflammation. Systemic corticosteroids were avoided to prevent further systemic immune suppression. Our patient had not received the smallpox vaccine before their presentation, which may have prevented or reduced the severity of mpox infection [7].

The medical management of our patient included oral tecovirimat, topical trifluridine, and topical steroids. At the start of the mpox outbreak in the UK, the use of tecovirimat was tightly restricted, with national oversight of use limiting treatment courses to 14 days in the absence of severe features or active infection. Antibiotics were added to treat and prevent bacterial co-infection. Data around the efficacy of systemic antiviral agents for mpox are limited, particularly in cases of ocular mpox. The systemic antiviral tecovirimat has been demonstrated to be effective in reducing mortality associated with mpox in animal models and to have a good safety profile in phase I and II human studies [8]. On this basis, the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) recommend a standard 14-day course of tecovirimat in severe mpox

including ocular involvement, which may be extended up to 90 days depending on response. Phase III randomized controlled trials investigating the efficacy of tecovirimat for the treatment of human mpox in adult cohorts in the UK and USA are ongoing [9, 10]. Importantly, the ophthalmic bioavailability of tecovirimat has not yet been characterized. Experimental and early observational data suggest there may be a low barrier to developing resistance to tecovirimat [1, 11]. Prolonged courses of tecovirimat without close supervision and monitoring could result in subtherapeutic drug levels and promote resistance [12]. The WHO and the CDC recommend trifluridine as an adjunctive treatment for human mpox alongside tecovirimat. Trifluridine, a US Food and Drug Administration-licensed treatment for herpes virus keratitis, has demonstrated efficacy against orthopoxviruses in vitro and in animal models [13–15]. There is a risk of corneal toxicity with prolonged use, so a maximum duration of 21 days is advised. A recent in vitro study demonstrated the efficacy of trifluridine against strains of mpox resistant to tecovirimat and an additive effect of trifluridine and tecovirimat in conjunctival epithelial cells [16]. In our patient, the duration of topical trifluridine was limited by its availability in the UK.

Importantly, neither tecovirimat nor trifluridine are virucidal agents; they merely inhibit viral replication, whereas an effective immune response is likely to be necessary to clear the virus. In our case, it is possible that immune reconstitution was necessary to control the infection. Arguments have been made against the use of topical steroids, as they are known to prolong viral shedding and may lead to persistent infection. In our case, it was felt that this risk was outweighed by the need to control surface inflammation, protect limbal stem cell populations, and prevent the sequelae leading to corneal scarring. We recommend careful use of topical steroids under specialist guidance of ophthalmology. Management of any corneal epitheliopathy may include application of intensive preservative-free topical lubricants and empirical broad-spectrum topical antibiotic therapy. Further investigation and management – such as corneal scrapes for microscopy, culture, and sensitivities – may be required if ulceration develops. In this case, late, recurrent corneal epithelial breakdown was attributed to limbal stem cell deficiency resulting from mpox-driven limbitis; this responded to treatment with topical steroid, and a tapering course of this was continued.

AUTHOR CONTRIBUTIONS

ID.M, EA, SR, RK, GO'H and SD were senior clinicians responsible for leading patient management in this case. LB, PS, MI, CD, AH were clincians contributing to patient management. LB wrote the first draft of the manuscript. ID.M, EA, SR, PS and MI revised the first draft of the manuscript. All authors discussed the findings and reviewed the final manuscript.

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How to cite this article: Brown L, Sargent P, Islam M, et al. Severe ocular Mpox in person living with advanced HIV treated with extended course of tecovirimat. *HIV Med*. 2024;1-5. doi:10.1111/hiv.13656