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Ocular manifestations and treatment course of monkeypox virus in two males with acquired immunodeficiency syndrome

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ABSTRACT

Introduction: Mpox (formerly monkeypox) is a previously endemic virus that has become a global concern.

Case Report: In this case series, we present two cases of ocular mpox in men with acquired immunodeficiency syndrome (AIDS), highlighting their clinical presentation, diagnosis, and management. Treatment involved the use of antiviral medications, tecovirimat and ganciclovir, based on limited existing data and recommendations from the Center for Disease Control (CDC).

Conclusion: These cases highlight the variability in presentation among AIDS patients with extensive corneal and conjunctival involvement and the potential for immune reconstitution inflammatory syndrome upon re-initiation of anti-retroviral therapy during active mpox infection. These cases emphasize the importance of early recognition, involvement of ophthalmology, and a multidisciplinary approach to prevent vision-threatening complications.

Keywords: AIDS, HIV, Monkeypox, Mpox, Ocular mpox, Ophthalmology, Orthopoxvirus, Tecovirimat

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INTRODUCTION

Mpox (formerly known as monkeypox) is a virus that was once endemic to certain areas but has now become a worldwide concern, creating a significant public health challenge. Recognizing its severity, the World Health Organization (WHO) declared mpox a Public Health Emergency of International Concern in July 2022 [1]. Overall, prognosis has been favorable, with the CDC reporting 184 deaths out of 95,912 cases worldwide; however, vulnerable populations such as the immunocompromised are at a heightened risk for complications [2, 3].

Mpox is a large double-stranded DNA-virus belonging to the Orthopoxvirus genus within the Poxviridae family, sharing its genus with variola virus, the causative agent of smallpox [4]. The primary hosts of mpox include rodents,

rabbits, bats, and non-human primates. Transmission from these hosts to humans can lead to human-to-human transmission mainly through contact with body fluids, skin lesions, respiratory droplets, and contaminated clothing of infected individuals, causing a smallpox-like illness [4]. Mpox is further divided into genetic clades I and II, endemic to Central and West Africa, respectively. Genomic sequencing suggests that the current clade, clade IIb, likely derived from the West African clade [5].

While smallpox has been eradicated since 1980, cases of mpox have been reported since its initial isolation from monkeys in 1958 in Copenhagen. The first documented human infection with mpox occurred in 1970 in the Democratic Republic of Congo, with the first human outbreak reported in 1997–1998 [6]. In 2003, an outbreak in the United States was linked to contact with infected prairie dogs. Since then, sporadic outbreaks have been infrequently reported outside of Central and West Africa [7]. Interestingly, the ongoing epidemic has defied the epidemiology of the disease, with 90% of cases occurring in the Americas and Europe [8].

While mpox typically manifests as self-limiting skin and mucosal lesions, ocular involvement can occur in rare cases. The most common ocular manifestation is a characteristic rash in the periorbital and eyelid regions [9]. Conjunctivitis resulting from mpox can present as conjunctival ulcers, widespread blistering or papular lesions on the conjunctiva, conjunctival follicular reactions, and pseudomembranous or subconjunctival nodules [9]. The most severe complication of ocular involvement is corneal infection, which can lead to permanent vision loss and corneal scarring [9].

Ocular mpox lacks clear guidelines regarding standard-of-care treatment. Nevertheless, early recognition and collaboration with ophthalmologists play a crucial role in guiding treatment and preventing the progression of vision-threatening complications. Herein, we report two cases of ocular mpox in men with acquired immunodeficiency syndrome (AIDS), detailing their associated clinical presentation, diagnosis, and management.

CASE SERIES

Case 1

A 28-year-old male with AIDS and polymerase chain reaction (PCR)-confirmed mpox status post treatment with tecovirimat one month prior presented to the emergency room with left eye pain and a worsening genital ulcer. The patient's last CD4 count was 30 (normal range 500–1500 cell/mm^3) despite reported adherence to anti-retroviral therapy (ART). The patient was non-compliant with tecovirimat as prescribed after initial discharge. Ophthalmology was consulted and eye examination revealed a single circular lesion on the supratemporal bulbar conjunctiva OS without corneal or lid involvement (Figure 1A). The patient was restarted on oral tecovirimat; ocular involvement was managed with artificial tears (q2h), moxifloxacin (4× daily), trifluridine 1% (5× daily for a maximum of 14 days due to cornea toxicity), and ganciclovir (5× daily). Therefore, in total, he underwent 2 courses of tecovirmat 600 mg by mouth (PO) and twice daily (BID) for 14 days initially and then continued the medication as his lesions progressed. Conjunctival staining improved to 25% of the original lesion after treatment for eight days (Figure 1B and C). On follow-up, the patient's genital lesion had improved. In addition, the patient experienced full resolution of the conjunctival lesion (Figure 1D) and had a visual acuity of 20/20. He was lost to follow-up upon discharge.

Figure 1: Case 1: External photograph of the left eye revealing diffuse conjunctival injection and an elevated ulcerative lesion on the bulbar conjunctiva extending from 1 to 2 hours (A) with improvement of lesions after eight days of treatment (B and C). After three months there was complete resolution of epithelial defect without fluorescein uptake (D).

Case 2

A 27-year-old male with AIDS presented with umbilicated lesions on the face, eyes, torso, and groin. He reported that his first signs were vesicles and pustules of the bilateral eyelids that spread to other regions of the skin. He endorsed decreased vision, pain with eye movement, and photophobia that began one week prior to evaluation. Due to the acute course and accompanying rash, mpox was suspected and confirmed with PCR of a serum sample. The patient had not taken ART in over a year, and his most recent CD4 count was 26. Due to concern for potential of immune reconstitution inflammatory syndrome (IRIS), it was decided to not start ART therapy. Ophthalmology consultation revealed multiple round, ulcerative lesions on the lower eyelids and similar lesions of the conjunctiva with severe keratoconjunctivitis oculus uterque (OU). Initially, the corneas were clear OU without staining defects, there was no ocular inflammation and dilated exam was normal. Visual acuity was 20/60 oculus dexter (OD) and 20/20 oculus sinister (OS). The patient was started on tecovirimat 200 mg intravenous (IV) BID for systemic mpox. The ocular involvement was treated with moxifloxacin (four times daily), erythromycin (four times daily), betadine 1% (four times daily), and artificial tears and lubricant gels (every hour) for ocular involvement. Over the next

week, his eyelid and conjunctival lesions worsened, and the patient developed an inferior corneal epithelial defect at the corneal limbus in the right eye (Figure 2A). It extended for 4 clock hours. A similar lesion formed in the left eye at the corneal limbus superiorly. The Center for Disease Control was consulted who recommended fluorometholone 0.1% (four times daily) which was added. In order to reduce corneal toxicity, erythromycin was discontinued, and betadine was replaced with 1% chlorhexidine. The patient was also started on oral valacyclovir 1 gram daily for viral prophylaxis. The patient's systemic, eyelid, conjunctival, and corneal lesions continued to worsen over a period of two weeks. Ganciclovir ophthalmic gel 0.15% (five times daily) and Trifluridine 1% (six times daily) were then started. Over two weeks, the corneal epithelial defects stopped progressing and began to improve. Vision improved back to 20/20 OD. Treatment with trifluridine was stopped and fluorometholone, chlorhexidine, and moxifloxacin were paused for three days intervals to prevent cornea toxicity. The cornea remained stable; however, the patient's eyelid and systemic skin lesions continued to worsen. The patient also developed superinfections of his systemic skin ulcers. Antibiotics were escalated and Cidofovir 5 mg/kg IV was started without improvement. There became concern that the infection would soon be fatal due to the severity of his groin, buttock, and torso lesions. Multidisciplinary discussions were held, and the patient was started on ART therapy in an attempt to reverse the course of the disease. Unfortunately several days after re-initiating ART, the patient experienced worsening facial and eyelid edema and progression of all pox lesions (Figure 2B). The corneal involvement did not recur; however, the patient's conjunctival and eyelid lesions continued to worsen. Over the next several weeks the eyelid lesions severely progressed (Figure 2C). His cardiac and respiratory status began to decline. The patient was transferred another hospital where he passed away from complications of his illness.

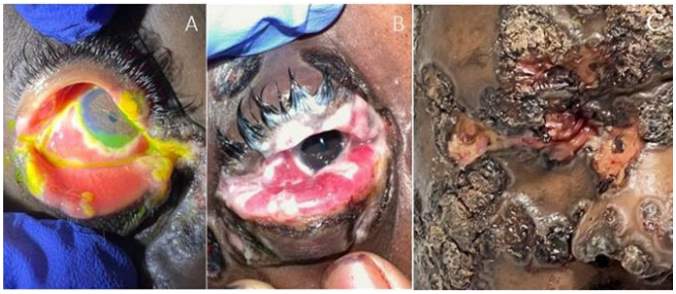

Figure 2: Case 2: External photograph of the right eye showing ulcerative lesions affecting the eyelid margin, conjunctiva, limbus, and inferior corneal epithelial defect with fluorescein staining (A). Progression of skin and ocular lesions following re-initiation of anti-retroviral therapy (B) and five weeks later (C). The lesions initially began as small, flat eschars that progressed to large, thickened plaques with adjacent fissures.

DISCUSSION

In the 2022–2023 outbreak of mpox, conjunctivitis had been reported in less than 1%, compared to 7–30% of cases in previous outbreaks. Corneal involvement was even less reported [10]. Historically, keratitis has occurred in approximately 3.6–7.5% of mpox cases and is of particular concern due to its potential to cause corneal scarring and irreversible vision loss [11]. Based on the available information, ophthalmic comorbidity and ocular complications appear to have been less frequent during the recent epidemic. We hypothesize this is because the outbreak from 2022–2023 was caused by a clade IIb strain virus. Bilious et al. report ophthalmic comorbidity primarily stems from clade I outbreaks [12].

Currently, there are no standardized treatment guidelines for ophthalmic disease related to mpox. The management of the two cases discussed in this study relied on recommendations from the Center for Disease Control (CDC) and a limited number of existing case reports available at the time [9, 13–16]. In these cases, treatment involved administration of antiviral medications, specifically tecovirimat and ganciclovir. However, it is important to note that the use of these antivirals has typically been reserved for complicated cases, and there is limited data on their efficacy [9, 13]. To address the epidemic, the CDC has granted non-research expanded access for the use of tecovirimat [17]. In addition, the CDC recommended the use of trifluridine 1%, an FDA-approved ophthalmic agent used against herpes simplex keratitis, for ocular mpox in 111 cases. Generous topical lubrication and topical antibiotics were also employed to protect the cornea and prevent bacterial superinfection [13]. Determining the appropriate treatment approach for these cases required careful consideration of the potential risks of corneal toxicity associated with topical treatment compared to the risk of viral seeding of the cornea [18].

The current outbreak exhibits several unique characteristics, primarily affecting unvaccinated men against smallpox and men who have sex with men. Approximately 93% of mpox patients had sexual preference for members of the same sex, with 44% of them living with HIV or AIDS [3]. The mode of transmission is also distinct, with sexual contact being linked to the spread of the virus [5]. Current data from the CDC suggests autoinoculation as the primary mechanism of ocular involvement (CDC), although there is support for the theory of bloodstream infection seeding into conjunctival secretions as well [19, 20]. It is likely that cases, including the ones presented in this study, are caused by a combination of these proposed mechanisms.

Those at substantial risk for disease are the immunocompromised, pediatric patients, and pregnant women [17]. The risk of severe disease is particularly elevated in individuals with advanced HIV, as seen in our cases where CD4 counts were ≤30 [21]. Literature regarding management of co-existing HIV and mpox is

limited. In case 2, our patient was non-adherent to ART, and re-initiation of ART during his hospitalization led to rapid clinical deterioration, progression of pox lesions, and eventual death. We believe that patient 2 possibly experienced IRIS as a result of ART re-initiation during active infection. Immune reconstitution inflammatory syndrome following ART initiation or re-initiation in mpox has appeared in the literature involving other organ systems but not with extensive ocular involvement [22]. It is also plausible that patient 2 succumbed from progressive disseminated mpox instead. The external lesions in Figure 2C are quite severe and suggest that disseminated mpox could have contributed. Furthermore, steroids have been shown in multiple cases and in orthopoxvirus animal model to lead to poorer ocular mpox outcomes [23–26]. The use of fluorometholone (FML) here could have contributed to clinical worsening to some degree.

This case report presents an exceptional scenario involving two AIDS patients who experienced distinct trajectories upon contracting mpox. By delving into these cases, we aim to contribute to the currently scarce literature on mpox-related ophthalmic disease and offer guidance on managing the condition in the absence of established protocols. These findings emphasize the importance of vigilance among clinicians and ophthalmologists in promptly identifying ocular involvement to prevent irreversible vision loss in individuals affected by mpox.

CONCLUSION

These cases demonstrate that AIDS patients with a similar disease burden can have a highly variable presentation. In addition, clinicians should be aware that initiating anti-retroviral treatment during an acute infection may lead to IRIS and allow the infection to systemically proliferate. Our cases highlight that disease management can involve a complicated treatment course with the aim of preventing infection-related ocular complications while minimizing treatment-related corneal toxicity.

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Author Contributions

Nikolas Hopkins – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.