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Mpox Keratitis: A Case Report and Review

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Purpose: Mpox is a rare infectious disease. Lack of knowledge among eye care professionals regarding mpox keratitis greatly reduces the likelihood of diagnosis and effective management. This report and review seek to increase the knowledge of mpox keratitis among eye care professionals.

Methods: We report a patient with mpox keratitis who underwent successful penetrating keratoplasty, with 20 years of follow-up. A systematic literature search and review of cases of mpox keratitis from 1970 to 2024 was performed.

Results: A total of 24 articles and 2 abstracts reporting 35 cases of mpox keratitis were identified. A frequency of 0.5% to 1.0% may be the lower range of mpox keratitis among symptomatic patients with a confirmed mpox diagnosis. Mpox keratitis occurred with and without systemic mpox. Initial misdiagnoses were common (40%). Polymerase chain reaction results aided clinical diagnosis. Corneal disease ranged from mild epitheliopathy to fulminant ulcerative keratitis. Outcomes ranged from 20/20 acuity to no light perception. In the absence of fulminant systemic disease, tecovirimat was associated with clinical improvement of mpox keratitis in almost all cases. Our case is the only known report of successful penetrating keratoplasty for mpox keratitis and the only case whereby *monkeypox virus* was cultured from the corneal surface.

Conclusions: Mpox keratitis is rare but can result in severe vision loss and blindness. Systemic tecovirimat seems to be effective in treating mpox keratitis, although the low frequency of keratitis precludes clinical trials. Topical steroids may extend virus survival in the cornea. Polymerase chain reaction may help confirm mpox corneal involvement.

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Key Words: mpox, mpox ocular disease, mpox keratitis, mpox related ocular disease

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pox is a systemic disease caused by *monkeypox virus* (MPXV), an *orthopoxvirus* related to *variola virus*, the causative agent of smallpox.¹ Ocular involvement can result in vision loss and blindness, typically from keratitis.² The infrequency of severe ocular involvement and the absence of randomized clinical trials require that treatment strategies draw from past experiences with smallpox and vaccinia, case reports from the recent mpox outbreak, and knowledge from other viral ocular conditions.^{3–5}

To collate and organize the literature on mpox keratitis, we reviewed all English-language publications on human mpox from 1970 through 2023. We report the only known successful penetrating keratoplasty for mpox keratitis, which occurred during the 2003 US outbreak and reinterpret the clinical findings and course considering reports from the 2022–2023 outbreak. Features of mpox keratitis are summarized, and diagnostic and treatment considerations are discussed.

METHODS

Report of a Case

The first mpox outbreak outside of Africa occurred in 2003 in the United States.⁶ The patient described herein was a confirmed case.^{6,7} An immunocompetent 32-year-old veterinarian developed tender cervical lymphadenopathy and right eye (OD) conjunctivitis 12 days after an mpoxinfected prairie dog was treated at her workplace. She was not involved in the animal's care but handled the leather gloves contaminated by the animal and potentially inoculated her eye during surgical mask donning.

On day 2 after symptom onset, she presented to an urgent care center for eyelid swelling and was treated for conjunctivitis with oral amoxicillin. On day 3, topical ofloxacin was added and she was referred to an ophthalmologist. On day 4, ophthalmic examination noted 20/30 visual acuity (VA) OD, with severe lid swelling and conjunctival injection. The cornea was clear, and the anterior chamber was without inflammation. The left eye was normal with 20/20 VA and remained unaffected. Swab specimens from the OD conjunctiva and a skin lesion (Fig. 1A) were sent on day 5 for culture and polymerase chain reaction (PCR) to the Poxvirus Section of the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. PCR and viral culture were

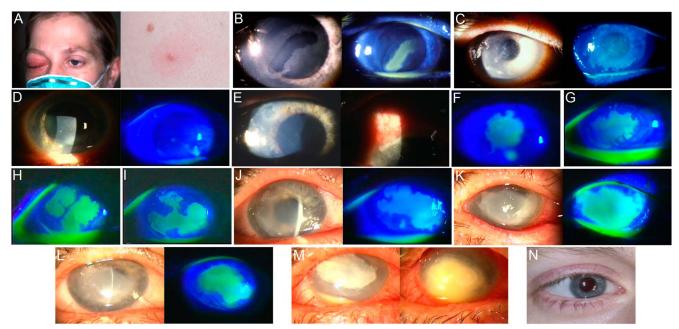


FIGURE 1. Clinical progression of case patient ocular findings. A, Day 2 after symptom onset with right eyelid swelling and left eyebrow and back mpox lesions. B, Day 27, on referral to cornea service with a new corneal epithelial defect. C, Day 41, showing an enlarged irregular epithelial defect. D, Day 48, a week after increasing prednisolone acetate; the epithelial defect was almost resolved. E, Day 52, new limbitis with an associated corneal epithelial defect. F, Day 55, enlargement of the corneal epithelial defect. G–I, Over the following 2 weeks (days 62–76) with changing geographic epithelial ulcers. J, Day 88, pan-cultures, PCR, and lateral tarsorrhaphy performed. K, Day 100, initiation of trifluridine after positive MPXV culture, increasing stromal opacification. L, Day 119, trifluridine stopped after 2 consecutive weeks of negative MPXV cultures, with the epithelial defect persistent since day 50. M, Day 132, new-onset hypopyon with stromal infiltrate grows *Streptococcus pneumoniae*; corneal perforation occurs despite appropriate response to antibiotics. N, 20 years later with a clear corneal graft.

MPXV-positive, and she was quarantined per public health protocols.

On day 18, fever, malaise, lymphadenopathy, and pox lesions were resolved, but she had worsening eye discomfort and VA of 20/50. Slit-lamp examination revealed a corneal arcuate immune line, punctate epithelial fluorescein staining, and mild iritis. Prednisolone acetate 1% qid and a cycloplegic were initiated. On day 20, keratic precipitates (KP) were noted and PA1% was increased to q2 hours. On day 25, VA was 20/100 with a central corneal epithelial defect, and she was referred to the cornea service.

On day 27, the initial cornea service examination, VA was 20/400, with 3+ lid edema, a peripheral corneal immune ring, and central corneal epithelial defect (Fig. 1B). A bandage contact lens (BCL) was placed, with PA1% qid and atropine 1% daily. A topical antibiotic was used throughout the treatment.

On day 30, the epithelial defect and stromal inflammation were unchanged; PA1% and atropine were stopped, and oral prednisone 60 mg daily was begun to minimize topical medications and attempt better inflammation control. On day 41, the epithelial defect had enlarged (Fig. 1C) and significant stromal inflammation remained, so PA1% q2 hours was resumed. Corneal surface specimens were sent to CDC. MPXV culture was negative, and MPXV PCR remained positive.

On day 48, the epithelium had a small defect, with less stromal inflammation (Fig. 1D). PA1% was reduced to q3 hours, but 4 days later, limbitis developed (Fig. 1E), so PA1% was increased. This reduced pain and inflammation, but the associated epithelial defect enlarged (Fig. 1F). Preservative-free PA1% was obtained to reduce preservative toxicity and used thenceforth. In the following 2 weeks, stromal inflammation remained stable, but geographic epithelial defects developed with changing morphology at each visit (Figs. 1G–I). Another BCL was placed, without improvement. The BCL was removed, and taped lid closure was performed for 5 days, without improvement.

On day 88 (Fig. 1J), a 50% tarsorrhaphy was performed with corneal scraping for bacterial and Acanthamoeba culture and PCR and culture for viruses (MPXV, herpes simplex virus, and varicella zoster virus). On day 96, all results were negative except for MPXV detection, which was culture- and PCR-positive. Confirmatory scrapings on day 97 for MPXV culture and PCR were also positive.

On day 100, topical trifluridine 6x daily was initiated. Tecovirimat did not yet exist. Preservative-free PA1% was decreased to bid but not discontinued because of pain and worsening stromal opacification (Fig. 1K). Trifluridine was used for 16 days, with weekly corneal swabs sent to CDC for MPXV culture and PCR. On day 109, culture was negative

(PCR remained positive). On day 116, trifluridine was discontinued after 2 weeks of negative cultures. From day 50, until subsequent keratoplasty, an epithelial defect and stromal inflammation persisted (Fig. 1L).

On day 130, after 4 weeks of negative MPXV cultures (PCR remained positive), the weekly surveillance culture became positive and trifluridine was restarted. Days later, *Streptococcus pneumoniae* keratitis developed (Fig. 1M). Steroids were stopped, and topical vancomycin was started. Trifluridine was continued for 15 days; vancomycin was tapered as the infiltrate improved, but perforation occurred requiring tectonic penetrating keratoplasty on day 145. Postoperatively, standard (with preservatives) PA1% and antibiotic were administered, but not trifluridine. A week after keratoplasty, the eye showed minimal inflammation and intact epithelium. Subsequent recovery was uneventful. The corneal graft remains clear after 20 years with 20/20 acuity (Fig. 1N).

Literature Reviewed

A systematic literature search was performed on PubMed, Embase, and EBSCO to identify published reports of mpox keratitis from 1970 to January 5, 2024 (Table 1). Articles were excluded if they were not available in English or did not provide either a description or photograph of mpox keratitis with a clinical history. Abstracts and text were reviewed and excluded if there were no reports of keratitis. In total, 24 articles and 2 abstracts reporting 35 cases of mpox keratitis were identified and their results summarized (Table 2).

RESULTS

The Changing Epidemiology of Mpox

Until the 2022–2023 global outbreak, mpox was a rare zoonotic disease that occurred sporadically in rural Africa.³⁴ The mode of infection often involved direct interaction with infected rodents and nonhuman primates.³⁵ In 2014, the number of cases in Africa surpassed the number of cumulative cases from the previous 40 years.³⁶ A 2017 outbreak in Nigeria raised concern about the role of men having sex with men (MSM) as a new mode of transmission.^{36,37} Sexual contact was the primary mode of transmission in the 2022–2023 global outbreak involving more than 115 countries.³⁸

Frequency of Mpox Keratitis

Determining mpox keratitis frequency is hampered by its low occurrence rate and probable underdiagnosis and underreporting. Potential explanatory factors include poor health care access and possible cultural and legal risks related to MSM.³⁹ To accurately determine frequency, each patient within an mpox cohort would need to undergo an eye examination to confirm lack of corneal involvement, which has not been reported. However, an estimate of minimum mpox keratitis frequency can be made from published series (Table 3).

Two series with keratitis cases are reported before 2022: a 1980s World Health Organization Democratic Republic of Congo mpox surveillance report, where 12 (4%) of 338 patients had keratitis, and the 2003 US outbreak, where 1 (2%) of 47 patients had keratitis. In both, presumably, only symptomatic patients received eye examinations. Two series without reported keratitis include a 2011-2015 Democratic Republic of Congo surveillance report of 1057 mpox cases in which conjunctivitis occurred in 20% and photophobia in 30%. Is Given that keratitis is a common cause of photophobia, a 30% photophobia prevalence without any occurrence of keratitis underscores potential underdiagnosis without ocular examination of all patients. Similarly, a 2017-2018 outbreak of 122 cases in Nigeria recorded facial rash in 96%, with conjunctivitis in over 20%, but no keratitis.

Among 5 series from the 2022–2023 outbreak, keratitis was reported in 1 (0.4%) of 264 patients⁴¹ and 2 (0.3%) of 588 in France,¹⁴ 10 (6%) of 160 patients in Nigeria,⁴² in 4 (0.5%) of 880 patients in Spain,²¹ and 1 (1.0%) of 100 patients in Mexico.²⁶ In the Spanish and Mexican reports, patients with ocular symptoms underwent examination by an ophthalmologist.^{21,26} Based on these latter 2 series, an estimated frequency of 0.5% to 1.0% may be the lower range of mpox keratitis among patients with a confirmed mpox diagnosis *and ocular symptoms* (Table 3).

Diagnostic Considerations

Diagnosis of mpox keratitis by the ophthalmologist may be delayed because of lack of awareness of disease manifestations. Clinical manifestations of mpox typically include a prodromal fever, lymphadenopathy, and vesiculopapular rash. Dermatologic manifestations are the most common sign, reported in 90% of cases in the 2022–2023

TABLE 1. Search Terms	T	ABL	E.	1.	Search	Terms
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Database	Search Terms
PubMed	("Monkeypox virus" [Mesh] OR "Monkeypox" [Mesh] OR monkeypox [tw] OR mpox [tw] OR "monkeypox virus*" [tw] OR "mpox virus*" [tw] AND ("eye diseases" [Mesh] OR "Ophthalmology" [Mesh] OR ophthalmology [tw] OR "eye diseases*" [tw] OR "eye lesion*" [tw] OR "ocular infection*" [tw] OR "ocular inflammation*" [tw] OR uveitis[tw] OR scleritis [tw] OR conjunctivitis [tw] OR keratitis [tw] OR "corneal ulcer" [tw] OR eye [tw] OR "monkeypox-related ophthalmic disease" [tw] OR MPXROD [tw])
EBSCO	("monkeypox"/exp OR "monkeypox" OR "monkeypox virus"/exp OR "monkeypox virus") AND ("ophthalmology"/exp OR "ophthalmology" OR "eye disease" OR "eye injury" OR "eye infection" OR "eye inflammation" OR "uveitis" OR "scleritis" OR "conjunctivitis" OR "keratitis" OR "cornea ulcer")
Embase	(Monkeypox OR mpox OR monkeypox virus OR mpox virus) AND (ophthalmology OR eye disease OR eye lesion OR ocular inflammation OR uveitis OR scleritis OR conjunctivitis OR keratitis OR corneal ulcer OR eye OR monkeypox-related ophthalmic disease OR

TABLE 2. Reported Cases of Mpox Keratitis

Year	Reference	Age, Sex	Key Corneal Findings	Nonocular MPOX Lesions	Ocular PCR	Immune Compromise	Topical Therapy	Systemic Antivirals or Corticosteroid	Final Acuity, Outcome
Published mar	nuscripts								
2022	Lamas- Francis et al ⁸	45 yr Male	Geographic epithelial ulcer Limbitis AC cell	Genital Perioral	+MPXV Cornea, conjunctiva	HIV+ On ART "poor adherence" CD4 873 cells/mm ³	Ganciclovir Povidone iodine Moxifloxacin	PO-tecovirimat	20/25 Resolution with faint subepithelial haze
2022	Cash- Goldwasser et al ⁹	20–29 yr Male	Peripheral keratitis	Buttocks Chest Arms Hands Face	+OPXV Conjunctiva	HIV+ Off ART CD4 25 cells/ mm ³	Trifluridine	PO-tecovirimat (failed) IV-tecovirimat PO-tecovirimat (failed) IV-tecovirimat	20/800 "Profound visual impairment"
		30–39 yr Male	Nonspecific epithelial defect/ulcer	Chest Legs Perianal Face Medial canthus	+OPXV Face/scalp	HIV+ Off ART CD4 78 cells cells/mm ³	Trifluridine Antibacterial drops	PO-tecovirimat (recurred) PO-tecovirimat	"Regression of the eye lesion"
2022	Bacorn et al ¹⁰	47 yr Male	Perforation Fulminant disease	Extremities Trunk Face Eyelids Fulminant systemic disease	No info	HIV + Off ART CD4 28 cells/ mm ³	Trifluridine Moxifloxacin	Tecovirimat	No light perception Death
2022	Alexis et al ¹¹	38 yr Male	Superficial punctate epithelial erosions	Anogenital Upper limb(s) Lower limb(s)	+MPXV Conjunctiva	No	Chloramphenicol	PO-tecovirimat	Acuity not reported Resolution
2023	Vasquez- Perez et al ¹²	63 yr Male	Corneal edema Geographic epithelial ulcer Stromal keratitis	Face Arms Back Groin	+MPXV Conjunctiva	HIV+ On ART CD4 495 cells/mm ³	Trifluridine Moxifloxacin Chloramphenicol Dexamethasone	PO-tecovirimat	Count fingers "Corneal scarring with a negative effect on vision."
2023	Finamor et al ¹³	27 yr Male	Serpiginous/ arcuate epithelial keratitis Stromal infiltrates Keratic precipitates AC cell	Genitals Face Upper back Hands Feet Eyelid	+MPXV "Eye swab"	No	Sodium hyaluronate Moxifloxacin Fluorometholone	PO- valacyclovir (progressed) PO-tecovirimat	20/30 Resolution with "superficial corneal opacities and residual keratic precipitates"
2023	Doan et al ¹⁴	34 yr Male	Serpiginous/ arcuate epithelial keratitis	Penis Perineum Eyelid	+MPXV Cornea	No	Offoxacin Dexamethasone Trifluridine	PO- valacyclovir (failed) Prednisone (self-admin)	"Normal" vision Resolution with limbal neovascularization
		30 yo Male	Limbitis Serpiginous/ arcuate	Penis Eyelid	+MPXV Cornea	No	Ganciclovir Dexamethasone Trifluridine	IV-cidofovir (progressed) IV-cidofovir PO-tecovirimat	20/32 Linear corneal scar, limbal stem cell deficiency, corneal

TABLE 2. (Continued) Reported Cases of Mpox Keratitis

Year	Reference	Age, Sex	Key Corneal Findings	Nonocular MPOX Lesions	Ocular PCR	Immune Compromise	Topical Therapy	Systemic Antivirals or Corticosteroid	Final Acuity, Outcome
2023	Alsarhani	36 yr	epithelial keratitis Serpiginous/	Face	+MPXV	No	Prednisolone	PO-tecovirimat	neovascularization, hazy epithelium 20/40
2023	et al ¹⁵	Male	arcuate epithelial keratitis disciform edema Keratic precipitates AC cell	Scalp Torso Genitals Arms Legs	Conjunctiva	110	Tedissione	10-tecoviiiiia	"Small subepithelial corneal opacity"
2023	Androudi et al ¹⁶	50 yr Male	Serpiginous/ arcuate epithelial keratitis geographic epithelial ulcer AC cell	Eyelid Body	+MPXV Tears	HIV + "Highviral load"	Artificial tears Moxifloxacin Cyclopentolate Dexamethasone PF- dexamethasone Levofloxacin	PO- valacyclovir (worsened) PO- tecovirimat	20/200 "Hazy cornea"
		31 yr Male	Keratic precipitates Geographic epithelial ulcer AC cell	Face Eyelid Neck	+MPXV Tears	No	Dexamethasone "antiglaucoma drops" Vitamin A ointment Trifluridine Autologous serum	PO- valacyclovir (worsened) PO- tecovirimat	20/20 Resolution
2023	Bhamray- Sanchez et al ¹⁷	28 yr Male	Stromal keratitis Peripheral ulcerative keratitis Nonspecific opacification	Penis Back Shoulder	+OPXV Cornea	HIV + On ART CD4 951 cells/mm ³	Cyclopentolate Erythromycin Trifluridine	PO- valacyclovir (worsened) PO-tecovirimat	Hand motions "Keratitis and ulceration healed"
		36 yr Male	Stromal keratitis	Face	+OPXV Cornea	HIV status not reported Initiated ART during treatment course	Moxifloxacin Vancomycin Tobramycin Trifluridine Tobramycin Prednisolone Erythromycin	PO- valacyclovir PO- tecovirimat	"Vision did not improve" "Photophobia, tearing, and eye pain resolved after 6 wk of treatment"
2023	Carrubba et al ¹⁸	33 yr Male	Perforation Fulminant disease	Face Torso Extremities Fulminant systemic disease	+OPXV Crystalline lens (possible eyelid contamination)	HIV+ Off ART CD4 55 cells/ mm ³	Not reported	PO-tecovirimat IV-tecovirimat Vaccinia IVIG	Bilateral globe rupture Death
2023	Quites et al ¹⁹	32 yr Male	Serpiginous/ arcuate epithelial keratitis Geographic epithelial ulcer Immune ring	Genital Body	+MPXV Cornea, conjunctiva	No	Ciprofloxacin Gatifloxacin Diclofenac	PO-Acyclovir (worsened) IV-Acyclovir (worsened) PO-tecovirimat	20/100
2023	Nguyen et al ²⁰	53 yr Male	Keratic precipitates	None (semen		Lymphopenia	Erythromycin ointment		Light perception

(Continued)

TABLE 2. (Continued) Reported Cases of Mpox Keratitis

Year	Reference	Age, Sex	Key Corneal Findings	Nonocular MPOX Lesions	Ocular PCR	Immune Compromise	Topical Therapy	Systemic Antivirals or Corticosteroid	Final Acuity, Outcome
			Geographic epithelial ulcer Limbitis Perforation Fulminant disease	deposition into affected eye)	+MPXV (RNA sequence) Aqueous +MPXV Cornea Sclera Conjunctiva	Chronic lymphocytic leukemia	Moxifloxacin Prednisolone Voriconazole (route not specified) Trifluridine Betadine	PO- valacyclovir (worsened) PO-prednisone (worsened) PO-tecovirimat (worsened) IV-tecovirimat IV-cidofovir	Opacified vascularized cornea
2023	Pazos et al ²¹	24 yr Male	Geographic epithelial ulcer Peripheral ulcerative keratitis	Genital Proctitis	+MPXV Conjunctiva	No	0.6% Povidone iodine Erythromycin ointment Lubrication	PO-tecovirimat	"No significant vision loss" Peripheral corneal scarring
		36 yr Male	Serpiginous/ arcuate epithelial keratitis Stromal keratitis AC cell	Genital	+MPXV Conjunctiva	HIV On ART	0.6% Povidone iodine Erythromycin ointment Lubrication	PO-tecovirimat	No vision loss
		46 yr Male	Nonspecific epithelial defect/ulcer	Chest Peri-rectal	+MPXV Conjunctiva	No	0.6% Povidone iodine Erythromycin ointment Dexamethasone Lubrication	PO-tecovirimat	No vision loss
		35 yr Male	Nonspecific epithelial defect Stromal keratitis Endotheliitis	Skin	+MPXV Conjunctiva	No	0.6% Povidone iodine Erythromycin ointment Dexamethasone Lubrication	PO-tecovirimat	No vision loss
2023	Uner et al ²²	47 yr Male	Geographic epithelial ulcer	Groin Back Feet Face Eyelid	+OPXV Conjunctiva	No	Artificial tears Erythromycin Moxifloxacin Prednisolone	PO-tecovirimat	20/25 Resolution with symblepharon
2023	Raccagni et al ²³	35 yr Male	Geographic epithelial ulcer Stromal infiltrate	Hand	+MPXV Conjunctiva +MPXV Conjunctiva (after relapse) +MPXV Conjunctiva (after s relapse)	No	Moxifloxacin Tobramycin Polymyxin "Topical steroids" Dexamethasone	PO-Acyclovir PO-tecovirimat (relapsed) PO-tecovirimat (relapsed) PO-tecovirimat IV-cidofovir	20/30 Resolution with stromal opacity
2023	Ditta et al ²⁴	8 yr Female	Limbitis Stromal infiltrate	Eyelid	Eye not tested (skin lesions +MPXV)	No	Erythromycin Trifluridine	IV-Acyclovir Clindamycin PO-tecovirimat	Resolution with "subepithelial and stromal infiltrates"
2023	Arteaga- Rivera et al ²⁵	24 yr Female	Serpiginous/ arcuate epithelial keratitis AC cell	Hands Face Armpits Abdomen	+MPXV Cornea, conjunctiva	No	Prednisolone acetate Moxifloxacin Interferon alpha 2b	PO-prednisone PO-Acyclovir	20/30 Resolution

TABLE 2. (Continued) Reported Cases of Mpox Keratitis

Year	Reference	Age, Sex	Key Corneal Findings	Nonocular MPOX Lesions	Ocular PCR	Immune Compromise	Topical Therapy	Systemic Antivirals or Corticosteroid	Final Acuity, Outcome
			5	Right foot		•	Prednisolone acetate Tropicamide/ phenylephrine		
2023	Rodríguez- Badillo et al ²⁶	19 yr Male	Corneal edema Stromal infiltrate Peripheral ulcerative keratitis	Face Chest Abdomen	+MPXV Cornea, conjunctiva	Not reported	"Topical analgesics" "Antibiotics" "Topical corticosteroids" Interferon alfa- 2b	PO- corticosteroids	"Decreased visual acuity"
2023	Bloom et al ²⁷	38 yr Male	Superficial punctate epithelial erosions	Eyelid Face	Eye sample error	HIV+ ART/immune status not reported	Moxifloxacin	Acyclovir Azithromycin Tecovirimat	Lost to follow-up
2023	Oprea et al ²⁸	42 yr Male	Nonspecific epithelial defect/ulcer	Face Limbs Inguinal area Scrotum	+MPXV Conjunctiva	HIV+ on ART	"Ocular drops prescribed by the ophthalmologist"	Tecovirimat	Not reported
2023	Trawally Flores et al ²⁹	37 yr Male	Peripheral ulcerative keratitis	Hands Feet Chest	+MPXV Conjunctiva	No	Tobramycin Dexamethasone Artificial tears Povidone iodine Ozonized oil Ofloxacin Ganciclovir Serum tears Fluorometholone	PO-tecovirimat	20/200 Corneal leukoma, symblepharon
2023	Malciolu- Nica et al ³⁰	41 yr Male	Peripheral ulcerative keratitis	Skin Oral	+MPXV "Eye lesions"	HIV+ ART/immune status not reported	Chloramphenicol Dexamethasone Lubricants Acyclovir Antibiotics Mydriatic	"Systemic" tecovirimat	20/25 Corneal scarring, peripheral pannus
2023	Avila and Gallego- Suarez ³¹	24 yr Male	Limbitis AC cell Corneal edema	Eyelid	+MPXV Conjunctiva	No	Ganciclovir Lubrication Prednisolone Ice	IV-Acyclovir IV-ceftriaxone	20/50 Resolution
2024	This report	32 yr Female	AC cell with keratic precipitates Geographic epithelial ulcer Limbitis Stromal keratitis	Eyebrow Torso Limbs	+MPXV Cornea	No	Ofloxacin Mydriatic Moxifloxacin Prednisolone acetate Trifluridine	PO-prednisone	20/20 Stromal opacification, secondary bacterial keratitis, perforation Penetrating keratoplasty
Abstracts 2023	Cuppari et al ³²	28 yr Male	Peripheral ulcerative keratitis Stromal keratitis	Not reported	+MPXV Cornea	HIV+, syphilis	Trifluridine	"Systemic" tecovirimat	Count fingers at 2 feet "Healed ulcer"

(Continued)

TABLE 2. (Continued) Reported Cases of Mpox Keratitis

Reference	Age, Sex	Key Corneal Findings	Nonocular MPOX Lesions	Ocular PCR	Immune Compromise	Topical Therapy	Systemic Antivirals or Corticosteroid	Final Acuity, Outcome
	36 yr Male	Nonspecific epithelial defect/ulcer	Not reported	+MPXV Cornea	HIV+, latent TB, syphilis	Trifluridine	PO-tecovirimat	20/70 Subepithelial and stromal opacities
Carrubba	NR	Stromal infiltrate "Limited	Not	Not reported	No	Trifluridine	Tecovirimat	Not reported
et al ³³	NR	keratouveitis" Fulminant disease	reported Not reported	Not reported	HIV+ CD4 < 200	Steroids Not reported	Not reported	Not reported
		Reference Sex 36 yr Male Carrubba et al ³³ NR	ReferenceSexFindings36 yr MaleNonspecific epithelial defect/ulcerStromal infiltrateStromal infiltrateCarrubba et al33NR Keratouveitis"NRFulminant	ReferenceAge, SexKey Corneal FindingsMPOX Lesions36 yr MaleNonspecific epithelial defect/ulcerNot reportedStromal infiltrateStromal infiltrateNot reportedCarrubba et al33NR "Limited keratouvcitis" reportedNotNR FulminantNot	Reference Age, Sex Key Corneal Findings MPOX Lesions Ocular PCR 36 yr Male Nonspecific epithelial defect/ulcer Not reported +MPXV Cornea Stromal infiltrate Stromal infiltrate Not Not reported Carrubba et al ³³ NR "Limited keratouveitis" reported Not Not reported NR Fulminant Not Not reported	Reference Age, Sex Key Corneal Findings MPOX Lesions Ocular PCR Immune Compromise 36 yr Male Male Equithelial defect/ulcer Not epithelial defect/ulcer Not reported Cornea HIV+, latent TB, syphilis Carrubba et al ³³ NR "Limited keratouveitis" Not reported reported Not reported No reported NR Fulminant Not Not reported HIV+	ReferenceAge, SexKey Corneal FindingsMPOX LesionsImmune CompromiseTopical Therapy36 yr Male epithelial defect/ulcer Stromal infiltrateNot reported et al33+MPXV HIV+, latent CorneaTrifluridine TherapyCarrubba et al33NR FulminantNot reported Reatouveitis"Not reported SteroidsNot reported HIV+Not reported	Reference Age, Sex Key Corneal Findings MPOX Lesions Immune Compromise Topical Therapy Antivirals or Corticosteroid 36 yr Male Male Equithelial defect/ulcer Nonspecific epithelial defect/ulcer Not reported HIV+, latent TB, syphilis Trifluridine PO-tecovirimat Carrubba et al ³³ NR "Limited keratouveitis" Not reported Not reported No Trifluridine Steroids Tecovirimat NR Fulminant Not Not reported HIV+ Not reported Not reported

AC cell, iritis, anterior uveitis; IV, intravenous; PO, oral; TB, tuberculosis.

outbreak.⁴⁴ Mpox-related ocular disease (MPXROD) may rarely be the only or first presenting sign of mpox,²⁰ but it more often presents in a patient with known mpox who subsequently develops ocular complaints. In reported cases, mpox keratitis presented at a median of 17.5 days after systemic manifestations (range, 0–60 days) and was not associated with systemic manifestations in 2 cases.^{20,29}

Among the 35 patients with mpox keratitis from the 2022–2023 outbreak, 31 (89%) were male, 2 (6%) were female, and sex was unreported in 2 (6%). Fifteen patients (43%) had HIV infection (Table 2). MSM was the primary mode of transmission (83%) during the 2022-2023 outbreak⁴⁵; if MPXROD is suspected, a sexual history should be obtained.

Misdiagnosis of mpox keratitis occurred initially in 14 patients (40%) because of lack of known mpox exposure, lack of nonocular signs or symptoms, or findings suggestive of

other conditions. ^{12,16,17,19,20,22–25,27,29–31} The 16 patients (46%) initially diagnosed with mpox keratitis had a diagnosis of systemic mpox before presentation to the eye clinic. ^{8–11,13–15,17,18,21,30} No diagnostic history was provided for 5 patients. ^{26,32,33} Misdiagnoses included bacterial preseptal cellulitis, syphilis, adenoviral conjunctivitis, and, frequently, herpetic keratitis. ^{12,16,17,19,20,22–25,27,29–31} PCR of skin, corneal, or conjunctival samples was instrumental in revising the diagnosis for patients with mpox keratitis who were initially misdiagnosed. ^{12,16,17,19,20,22–25,27,29–31}

Current CDC and World Health Organization guidelines recommend use of real time (RT)-PCR for diagnosis of acute mpox infection, either by 2-stage testing with nonvariola orthopoxvirus (OPXV), followed by MPXV, or if available, with MPXV initially. PCR detects viral DNA, which may not reflect the presence of infectious virus. Thus, its role in guiding treatment is undetermined. Serial

TABLE 3. Number and Percentage of Patients With Mpox Keratitis and Vision Loss in Published Case Series*

Reference Number	Country	Years	Total Number of Mpox Cases	Mpox Diagnostic Laboratory methods	No. (%) of Men	Age Range	No. (%) of Patients With Keratitis	No. (%) of Patients With Vision Loss
1	Zaire (Democratic Republic of Congo)	1981– 1986	338	Electron microscopy (EM), chorioallantoic membrane inoculation, serology	182 (54%)	3 month– 69 yrs	12 (3.6%)	12 (3.6%)
40	United States	2003	47	Polymerase chain reaction (PCR), culture, immunohistochemical staining, EM	22 (47%)	1–51 yrs	1 (2.1%)	1 (2.1%)
41	France	2022	264	PCR	262 (99%)	30–41 yrs	1 (0.38%)	Not reported
14	France	2022	588	PCR	Not available (NA)	NA	2 (0.34%)	0
21	Spain	2022	880	PCR	880 (100%)	38 years (mean)	4 (0.45%)	0
26	Mexico	2022	100	PCR	NA	NA	1 (1.0%)	Reported but not quantified
42	Nigeria	2022- 2023	160	PCR	114 (71%)	4 month– 75 yrs	10 (6%)†	Not reported

^{*}Patients could have had unilateral or bilateral involvement.

[†]No case descriptions or photographs. 30% of patients in cohort had concomitant varicella zoster infection, raising concern for possible overdiagnosis of mpox keratitis.

quantitative PCR may help clarify clinical observations, but availability is limited. MPXV culture should not be performed routinely because of the risk of accidental occupational exposure to infectious virus.⁴⁶

Mpox Corneal Manifestations

Among reported cases of mpox keratitis, corneal disease ranges from mild epitheliopathy to fulminant ulcerative keratitis.² It is unclear whether mpox keratitis occurs as part of the primary eruption, as secondary to autoinoculation from a periocular or nonocular lesion, as contiguous spread from the involved conjunctiva, or as the primary ocular manifestation.

Thirty-five cases with sufficient clinical details were identified in the systematic search, and our added case yields 36. Based on these cases, mpox keratitis can affect the corneal epithelium, stroma, and endothelium. In most cases, mpox keratitis occurred in concert with conjunctival, eyelid, or facial lesions, but it has occurred in systemic disease without ocular or facial findings and as isolated keratitis (Table 2).

Mpox keratitis shares similarities with variola and vaccinia keratitis, which can manifest with punctate and geographic epithelial defects, dendritiform lesions, stromal keratitis, and disciform keratitis with KP (resembling herpes simplex keratitis). A.5 Review of the published cases and the case reported here provides insight into common features of epithelial, stromal, and inflammatory/endothelial manifestations of mpox keratitis. The manifestations of mpox keratitis are presented in Table 4 to show their relative frequency. Most patients had multiple manifestations.

Epithelium

Epithelial involvement was the most common mpox keratitis finding, occurring in 31 (86%) of the 36 patients as a distinct clinical manifestation and as a component of peripheral keratitis, perforation, or nonspecific "ulcer" (Table 2). As a distinct clinical manifestation, the 2 primary epithelial abnormalities were arcuate or serpiginous epithelial keratitis and geographic epithelial defects, occurring in 19 patients (Table 4). 8,9,12–16,19–23,25,30,32 Descriptions and photos of the arcuate and serpiginous keratitis show an elevated epithelial ridge stained with fluorescein, 9,13-16,19,21 located at and potentially emanating from the peripheral cornea. Progressive central migration of the ridge and coalescence was observed in 4 cases, ^{13,14,19,25} and in 2 cases, the peripheral epitheliopathy preceded a central geographic epithelial defect. 16,19 An arcuate epithelial defect was noted in our patient early in the disease course and preceded the central geographic epithelial defects. A geographic epithelial defect, which stained with fluorescein, was a major epithelial manifestation in 12 of the 19 patients. 8,12,16,19,21,23,30 Three of the 19 patients, including our patient, had both serpiginous and geographic epithelial keratitis. 16,19

With one exception, all patients with these epithelial manifestations were OPXV or MPXV PCR positive from the ocular surface^{9,13–16,19,21}; the exception was positive from a skin lesion.²⁷ PCR positivity usually persisted beyond

resolution of the keratitis and up to 46 days. 13-15,21 Our patient was still PCR-positive when last tested on day 130, with active keratitis and before penetrating keratoplasty. In contrast to current guidelines, the CDC performed MPXV cultures for our patient during the 2003 US outbreak. This is the only known report of MPXV recovery by culture from the corneal surface of human mpox keratitis. Quantitative MPXV RT-PCR values supported the clinical observations in our patient, with high values when culture-positive and decreasing values after initiation of trifluridine and when cultures were negative. The recovery of infectious virus by culture from the geographic epithelial defects of our patient is direct evidence to support that these epithelial manifestations represent mpox infectious epithelial keratitis. We suggest mpox arcuate and serpiginous epithelial keratitis and mpox geographic epithelial ulcer as the 2 primary types of mpox infectious epithelial keratitis (Table 4).

Stroma

Stromal involvement varied significantly in clinical descriptions, case photographs, and used terminology. Stromal findings were reported in 11 cases and ranged from advanced imaging findings suggestive of stromal involvement³¹ and anterior stromal infiltration without stromal thinning or significant scarring, to severe inflammation, thinning (including perforation), opacification, and visually significant scarring (Tables 2 and 4). 12,13,17,21,23,24,26,29,30,32 Our patient had prolonged stromal inflammation for 5 months, which included periods of infectious epithelial keratitis. Including the case herein, 10 cases had stromal infiltrates or opacity. 12,13,17,21,23,24,32 Seven cases showed peripheral stromal infiltrates with varying degrees of associated stromal thinning, with several reports using the terminology "peripheral ulcerative keratitis. "17,21,26,29,30,32 Four cases reported "stromal keratitis" or "stromal interstitial keratitis" without additional detail. 12,17,32 Fulminant stromal disease is also discussed below. 10,18,20

The combination of few cases, inconsistent terminology, and cooccurrence with epithelial disease limits conclusions regarding the pathologic mechanisms of stromal inflammation. Based on published reports, we are unable to distinguish stromal inflammation from MPXV particles in the stroma from stromal inflammation secondary to epithelial disease. Until such understanding may occur, *mpox stromal keratitis* may encompass the various manifestations of stromal inflammation (Table 4).

Endothelium and Other Inflammatory Manifestations

Endothelial manifestations included endotheliitis with KP, with or without anterior uveitis (Tables 2 and 4).8,13,15,16,20,21,25,33,47 These findings may accompany the epithelial manifestations,8,15,16 appear later in the disease course,¹³ or occur as an independent cornea-sparing anterior uveitis with conjunctival disease.⁴⁷ Stromal edema occurred in several cases of epithelial keratitis or inflammatory disease and thus is unlikely to be a primary manifestation of mpox.

TABLE 4. Reported Mpox Keratitis Manifestations and Recommended Nomenclature†

Type of Lesion	Reported Descriptions	Number	Reference*
Epithelial			
Mpox infectious epithelial keratitis (mpox IEK)†			
Mpox arcuate or serpiginous peripheral epithelial keratitis†			
Elevated leading edge that stains with fluorescein	"Serpiginous epitheliopathy"		Doan et al ¹⁴ (2 cases)
Usually peripheral, though location likely dependent on time	"Arcuate staining epithelial	10	Pazos et al ²¹ (1 case)
point of observation	lines"		Androudi et al ¹⁶ (1 case)
	"Arcuate corneal infiltrates which stained"		Quites et al ¹⁹ (1 case)
	"Corneal epithelial ridge which		Arteaga-Rivera et al ²⁵ (1 case)
	stained"		Cash-Goldwasser et al ⁹ (1 case)
			Finamor et al ¹³ (1 case)
			Alsarhani et al ¹⁵ (1 case)
			Case report herein (1 case)
Mpox geographic epithelial ulcer†	"0 1: 1 1 "		D (121 (1
Geographic epithelial defect which stains with fluorescein	"Geographic corneal ulcers"	12	Pazos et al ²¹ (1 case)
		12	Nguyen et al ²⁰ (1 case)
			Vasquez-Perez et al ¹² (1 case) Androudi et al ¹⁶ (2 cases)
			Quites et al ¹⁹ (1 case)
			Uner et al ²² (1 case)
			Raccagni et al ²³ (1 case)
			Malciolu-Nica et al ³⁰ (1 case)
			Lamas-Francis et al ⁸ (1 case)
			Cuppari et al ³² (1 case)
			Case report herein (1 case)
Other epithelial manifestations			1
Nonspecific defect			Pazos et al ²¹ (2 cases)
		5	Cash-Goldwasser et al ⁹ (1 case)
			Cuppari et al ³² (1 case)
			Oprea et al ²⁸ (1 case)
Punctate epithelial keratitis			Bloom et al ²⁷ (1 case)
		3	Alexis et al ¹¹ (1 case)
			Case report herein (1 case)
Stromal			
Mpox stromal keratitis†			112 (4
Description or image of stromal infiltrate and/or opacity	10		Vasquez-Perez et al ¹² (1 case)
opacity	10		Finamor et al ¹³ (1 case)
			Bhamray-Sanchez et al ¹⁷ (2 cases)
			Raccagni et al ²³ (1 case) Ditta et al ²⁴ (1 case)
			Rodríguez-Badillo et al ²⁶ (1 case)
			Cuppari ³² (2 cases)
			Case report herein (1 case)
Peripheral ulcerative keratitis			Pazos et al ²¹ (2 cases)
Description or image of peripheral stromal infiltrate	7		Rodríguez-Badillo et al ²⁶ (1 case)
and thinning			Trawally Flores et al ²⁹ (1 case)
			Bhamray-Sanchez et al ¹⁷ (1 case)
			Malciolu-Nica et al ³⁰ (1 case)
			Cuppari et al ³² (1 case)
Inflammatory/Endothelial			
Limbitis			
Peripheral or limbal epithelial ulcer			Doan et al ¹⁴ (1 case)
Limbal infiltrate which stains with fluorescein	6		Nguyen et al ²⁰ (1 case)
Uncertain if infectious			Ditta et al ²⁴ (1 case)
			Avila et al ³¹ (1 case)
			Lamas-Francis et al ⁸ (1 case)

TABLE 4. (Continued) Reported Mpox Keratitis Manifestations and Recommended Nomenclature+

Type of Lesion		Reported Descriptions	Number	Reference*
				Case report herein (1 case)
Other Inflammatory/Endothelial Manifestations				
Anterior chamber reaction	"Iritis"			Pazos et al ²¹ (2 cases)
	"Anterior uveitis"	10		Androudi et al ¹⁶ (2 cases)
				Atreaga-Rivera et al ²⁵ (1 case)
				Lamas-Francis et al ⁸ (1 case)
				Finamor et al ¹³ (1 case)
				Alsarhani et al ¹⁵ (1 case)
				Carrubba et al ³³ (1 case)
				Case report herein (1 case)
Keratic precipitates				Finamor ¹³ (1 case)
		5		Androudi et al ¹⁶ (1 case)
				Nguyen et al ²⁰ (1 case)
				Alsarhani ¹⁵ (1 case)
				Case report herein (1 case)
Stromal edema				Pazos et al ²¹ (2 cases)
		5		Rodríguez-Badillo et al ²⁶ (1 case
				Vasquez-Perez et al ¹² (1 case)
				Avila et al ³¹ (1 case)
Immune ring				Quites et al ¹⁹ (1 case)
		2		Case report herein (1 case)
Disciform edema				Alsarhani et al ¹⁵ (1 case)
		1		
Other				
Fulminant ocular disease with perforation				Bacorn et al ¹⁰ (1 case)
			2	Carrubba et al ¹⁸ (1 case)
Progressive treatment-resistant keratouveitis with st	romal melt, intraocula	r		Nguyen et al ²⁰ (1 case)
seeding			2	Carrubba et al ³³ (1 case)

One or more manifestations usually occurred in each patient.

By contrast, disciform edema was reported in one case and resolved after receiving systemic tecovirimat and topical steroids. ¹⁵ Three patients had ocular hypertension with concomitant anterior uveitis. ^{16,17} Limbal inflammation (limbitis) was described in 6 patients, including ours. ^{8,14,20,24} As with stromal inflammation, it is unclear whether these inflammatory manifestations occur because of infection or as a subsequent inflammatory response.

Fulminant Disease

Severe keratitis with perforation, loss of vision, and death was reported in 2 patients with fulminant systemic mpox and immune compromise from HIV.^{10,18} A prolonged case of severe uveitis, scleritis, and keratitis occurred in a patient exposed to direct inoculation of the eye by semen. He did not have fulminant systemic mpox but was immune compromised because of chronic lymphocytic leukemia.²⁰ Another case of severe keratitis was reported in a patient with HIV and a CD4 count <200 cells/µL but did not include significant detail.^{18,33} Patients with immune compromise and patients with severe systemic mpox seem at greater risk of severe keratitis, even with appropriate antiviral treatment.

Treatment Observations

Treatment varied significantly across cases. Different combinations of topical and systemic antibiotics, steroids, and antivirals (anti-herpes and anti-OPX) were administered, initiated at different stages of disease, and for variable durations. This fact, together with the small number of cases and absence of clinical trials, limits conclusions regarding treatment efficacy for mpox keratitis. CDC guidance recommends systemic antiviral therapy for all patients with severe mpox disease, which includes ocular manifestations.⁴⁸

Anti-OPX treatments used include systemic tecovirimat, systemic cidofovir, vaccinia IVIG, topical trifluridine, and topical interferon alpha. Thirty (83%) of 36 patients received oral or intravenous tecovirimat. Tecovirimat administration was associated with clinical improvement and resolution of mpox epithelial keratitis in almost all cases. Seven of 10 patients with arcuate or serpiginous epithelial keratitis and 11 of 12 with geographic epithelial defects received tecovirimat with disease resolution. 8,9,12–16,19,21–23,25,30 One case progressed despite intravenous cidofovir before tecovirimat administration. 4 One case of epithelial disease, 2 cases of nonspecific "keratitis," and a fulminant

^{*}Cited reports may include several patients.

[†]Recommended nomenclature

keratitis case received more than 1 course of tecovirimat because of incomplete keratitis resolution or recurrence. 9,20,23 Among cases that did not receive tecovirimat, 1 serpiginous epitheliopathy case resolved with corticosteroids and trifluridine, 14 2 cases of serpiginous epithelial keratitis resolved with topical interferon alpha, 25,26 1 case of geographic epithelial defect resolved after prolonged disease and treatment that included trifluridine, 12 1 case with predominantly inflammatory disease resolved with topical steroids, 31 and our case did not demonstrate viral clearance despite topical trifluridine until cessation of topical steroids and penetrating keratoplasty.

Use of additional systemic anti-OPX medications was also reported, but the efficacy of these agents is less clear. Cidofovir was used in 3 cases, either before or concurrent with tecovirimat, and was not given as a monotherapy. 14,20,23 Vaccinia IVIG was part of a complex treatment regimen in 1 case of severe mpox keratitis with bilateral globe rupture. 18 Acyclovir, valacyclovir, and ganciclovir antiherpes medications are not effective against orthopoxviruses; mpox keratitis worsened in patients receiving systemic antiherpetic therapy before receiving tecovirimat. 13,14,16,19,25,27

Including our case, topical trifluridine was used in 15 cases, 13 of which also received tecovirimat; thus, it is uncertain whether trifluridine monotherapy could effectively treat mpox keratitis. 9,10,12,14,16,17,20,24,32,33 Our patient demonstrated culture-positive mpox keratitis for over 4 months despite 2 courses of topical trifluridine but also received chronic steroids.

Most cases received topical steroids for stromal or endothelial inflammation or iritis at various time points (Table 2). Viral persistence in the setting of topical steroids has occurred in vaccinia keratitis in a rabbit model,⁴⁹ as well as in our patient, which is notable because orthopoxviruses do not establish latency in humans. Tecovirimat appeared to resolve infectious mpox keratitis in most patients who did not have fulimnant systemic disease, despite systemic or topical steroid use. One report described persistent keratitis for 8 months in an immunocompetent patient; topical steroids were used for 4 months, and disease resolution occurred after IV cidofovir was administered consecutively to a third course of tecovirimat.²³

Surgical intervention was rare. Two patients had amniotic membrane placement for corneal epithelial defects. 12,22 One patient with fulminant disease and perforation underwent penetrating keratoplasty with poor outcome (no light perception), 10 and corneal glue application complicated by expulsion of intraocular contents was attempted on 1 patient with fulminant disease and corneal perforation. 18 Our patient underwent successful penetrating keratoplasty.

Study Limitations

We emphasize the challenge of categorizing the various findings across highly heterogenous reports. Descriptions and nomenclature varied widely, even when referring to potentially related processes. For example, limbitis, peripheral keratitis, peripheral ulcerative keratitis, and semilunar corneal ulceration all describe peripheral corneal manifestations

whereby both epithelial and stromal abnormalities occur. These could represent various stages of the same mpox corneal disease process, or they could represent distinct subtypes of peripheral mpox keratitis, but published reports make it difficult to draw such distinctions. Regardless, the broad categories of common and shared clinical manifestations should be noted as manifestations of mpox keratitis (Table 4).

CONCLUSIONS

Mpox keratitis is a rare but potentially devastating complication of MPXROD. Underdiagnosis of mpox keratitis will likely remain a major challenge because of worldwide unfamiliarity with mpox, the sporadic nature of cases, and the rarity of mpox keratitis as a complication.

Mpox keratitis usually occurs within the context of systemic mpox at a median of 2 and a half weeks after systemic symptoms but rarely occurs in the absence of systemic disease. PCR may help confirm mpox keratitis, especially when the clinical diagnosis is ambiguous. Common features of mpox keratitis include infectious epithelial keratitis (including serpiginous/arcuate epithelial keratitis and geographic epithelial ulcer), stromal keratitis, and endotheliitis with or without anterior uveitis.

Tecovirimat tended to result in improvement or resolution of mpox keratitis. The efficacy of other anti-OPX treatments for mpox keratitis is less certain. Topical steroids should be used with caution in mpox keratitis and should generally not be used in the absence of effective systemic anti-mpox therapy.

The prognosis of mpox keratitis depends on early recognition and treatment before the development of vision-limiting sequelae. Clinicians should maintain a high index of suspicion for mpox keratitis in patients with confirmed or suspected mpox, patients at high risk of mpox, and cases of atypical or persistent keratitis, particularly in the setting of a local mpox outbreak.

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