Case Report

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Monkeypox-related ophthalmic disease

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Abstract:

Monkeypox (Mpox) is an acute febrile rash illness caused by the Mpox virus. The ongoing international outbreak since mid-2022 has spread worldwide, including Taiwan. Ocular involvement in Mpox infection is uncommon, including external and ocular surface lesions. Here, we describe a man who developed unilateral blepharoconjunctivitis and preseptal cellulitis, followed by the appearance of skin symptoms 6 days after the ocular manifestations. Samples taken from his oropharynx and skin lesions tested positive for the Mpox virus through a polymerase chain reaction test. He was hospitalized for isolation with topical lubricant, antibiotic, and acyclovir eye ointment until the skin lesions healed. However, on the day of discharge, punctate epithelial keratitis was observed in the same eye. The corneal lesion also tested positive for the Mpox virus. His keratitis progressed to dendritic ulceration, and treatment with tecovirimat was initiated. Initially, his corneal ulcer responded well to tecovirimat, but 12 days later, it deteriorated along with cells in the anterior chamber. To treat his condition, low-dose steroid and ganciclovir eye drops were administered. Eventually, the patient experienced resolution of the corneal lesion, leaving a scar.

Keywords:

Blepharoconjunctivitis, keratitis, monkeypox, uveitis

Introduction

Monkeypox (Mpox) virus is a species of the genus orthopoxvirus in the *Poxviridae* family. It was first identified in monkeys by Ladnyj *et al*. (1972). In 1970, the first human case of Mpox was reported in Congo.[1] Following the elimination of smallpox in 1980 and the discontinuation of mass vaccination programs, sporadic cases of Mpox have been reported in Central and West Africa.[2] It manifests as a skin rash, enlarged lymph nodes, and fever but with low mortality. However, in May 2022, an outbreak that originated in the United Kingdom has spread to 110 countries worldwide. The World Health Organization (WHO) declared the Mpox pandemic a public health emergency in July 2022. According to a meta-analysis, the pooled prevalence of ophthalmic lesions in Mpox patients was 9%,[3] with the highest prevalence (51%) in Congo, while the lowest prevalence was 0.57% in a recent study across 16 countries.[3-5] In Taiwan, the first Mpox case was confirmed in June 2022. As of July 3, 2023, a total of 221 cases of Mpox have been reported.[6] Herein, we describe a case of Mpox-related ophthalmic disease (MPXROD) with initial manifestation with blepharoconjunctivitis, preseptal cellulitis, and then corneal involvement. To the best of our knowledge, this is the first documented occurrence of this rare clinical presentation in Taiwan.

Case Report

A 39-year-old Taiwanese man without any systemic illness presented to our eye clinic with complaints of worsening redness, pain, and eyelid swelling in his right eye for 5 days. He denied a history of recent travel or animal exposure. He visited a local clinic first and was given topical acyclovir and an antibiotic ophthalmic solution. On ocular examination, he had

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severe erythematous swelling in his right eyelid with ulcerations at both upper and lower eyelid margins. Extraocular movement was full and free. The conjunctiva of his right eye showed severe injection with mucoid discharge. Pseudomembrane and nodule-like lesions were observed at the conjunctiva [Figure 1]. Neither corneal nor anterior chamber involvement was observed. Vision and intraocular pressure were not measured due to concerns about the contagious nature of the disease. Computed tomography of the orbit revealed right preseptal soft-tissue thickening without any retrobulbar involvement. The patient did not have fever, upper airway symptoms, or swollen lymph nodes. Laboratory work-up revealed no leukocytosis (white blood cells 6000/μL) but with an elevation in reactive lymphocyte (10%) and the level of C-reactive protein (1.41 mg/dL). Screening tests for human immunodeficiency virus and syphilis were both negative. Conjunctiva swab for bacterial culture yielded *Staphylococcus epidermidis* but negative for gonococcus. Under the impression of preseptal cellulitis, he received one intravenous (IV) curam injection immediately along with oral antibiotics (amoxicillin + clavulanic acid + doxycycline) and topical lubricant and antibiotics (levofloxacin + gentamycin).

Follow-up 3 days later, there was a modest improvement in his periorbital swelling. However, the patient reported the development of vesicles on his right face, left palm, and right knee 1–2 days after his initial presentation [Figure 2]. After consulting with an infection specialist, there was a strong suspicion of Mpox infection. Viral swabs taken from his oropharynx and skin lesion both tested positive for Mpox DNA through polymerase chain reaction (PCR) testing. The patient disclosed that he had engaged in a sexual encounter with a man 3 weeks before the onset of his ocular symptoms. He was subsequently hospitalized for isolation, receiving continuous topical therapies, and acyclovir ophthalmic ointment.

On the day of discharge (after 8 days of hospitalization), ophthalmic evaluation revealed that the cutaneous vesicles had formed crusts. The swelling and ulceration of his eyelid had almost healed, although conjunctivitis persisted. However, punctate epithelial keratitis was observed in the same eye [Figure 3a] during examination. Two weeks later, his corneal lesion progressed into a dendritic ulcer [Figure 3b]. A corneal sample was collected and sent for PCR testing for Mpox once again, which once more confirmed a positive result for the Mpox virus. Tecovirimat was then administered at a dosage of 600 mg twice daily for 14 days. His corneal ulcer showed improvement in the following 5 days after tecovirimat administration. However, during the following week's visit, an extended area of ulceration with corneal stromal edema and 1+ cells in the anterior chamber were observed [Figure 3c]. Aqueous humor PCR testing for herpes simplex, varicella-zoster, and cytomegalovirus all yielded negative results. Treatment was initiated using fluorometholone 0.02% and NaCl 5% eye drops. In addition, topical 2% ganciclovir eye drops, prepared from cymevene lyophilized IV powder, were used in place of acyclovir eye ointment. On his last visit, 2 months after his initial presentation of keratitis, the patient's best-corrected visual acuity was 0.9, accompanied by a cornea scar [Figure 3d]. Figure 4 illustrates the timeline of this patient's clinical findings and treatment course.

Discussion

Mpox virus belongs to the *orthopoxvirus* genus of the *poxviridae* family. It is a zoonotic disease, and transmission from animal to human may include direct contact with the infected animals, being scratched or bitten by

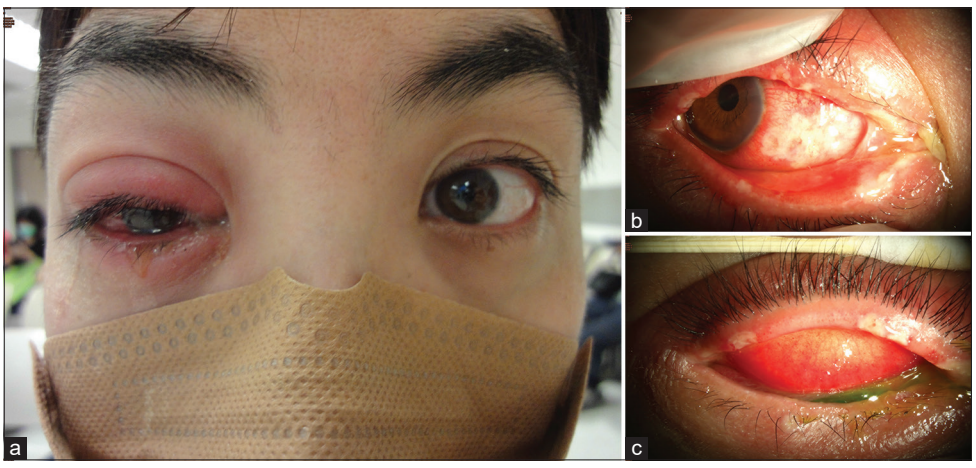

Figure 1: (a) The patient's right eyelid was severely inflamed and swollen at his first presentation. The left eye was normal, (b and c) Slit-lamp biomicroscopy revealed multiple ulcerations at eyelid margins, severe conjunctiva injection, and pseudomembrane and nodule-like lesions at the conjunctiva

animals, and coming in contact with contaminated objects. Person-to-person transmission occurs through close contact with an infected individual, including contact with respiratory secretions, body fluids, skin lesions, or genital areas. The majority of affected patients in this ongoing Mpox outbreak are men who have sex with men (MSM).

The clinical features of Mpox are similar to those of smallpox but with more subtle symptoms. Swollen lymph node, occurring in the early stage of the illness, is a distinctive feature differentiating Mpox from smallpox and chickenpox. The incubation period of Mpox is about 1–2 weeks.[7,8] Its clinical course in humans can be divided into two phases: the viral prodrome and the rash (WHO. Mpox [2022]). The prodrome includes headache, fever, sore throat, muscle ache, and lymphadenopathy. The rash appears a few days after the onset of fever and lymphadenopathy. The rash begins on the face and then spreads to the rest of the body. Disseminated vesiculopustular rash is a typical feature of Mpox. These characteristic skin lesions appear first as rash, then evolve in stages: macules, papules, vesicles, and pustules. It takes 2–4 weeks for these lesions to crust and shed.[9-11] Severe complications of Mpox include encephalitis, pneumonitis, keratitis, and sepsis.

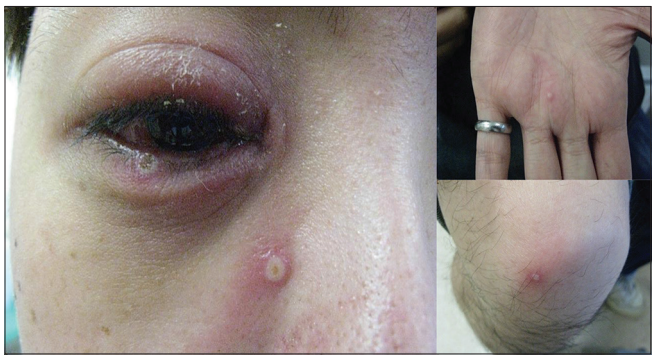

Figure 2: One–2 days after the patient's first visit, vesicles appeared at his right lower eyelid, left palm, and right knee

Ocular involvement is a potential complication for people experiencing Mpox infection. The virus may enter the eye through autoinoculation or systemic viremia. Conjunctivitis and blepharitis are the most common MPXROD. Cases of eyelid/periorbital skin lesions, preseptal cellulitis, keratitis, and corneal ulcers have also been reported. It is important to differentiate

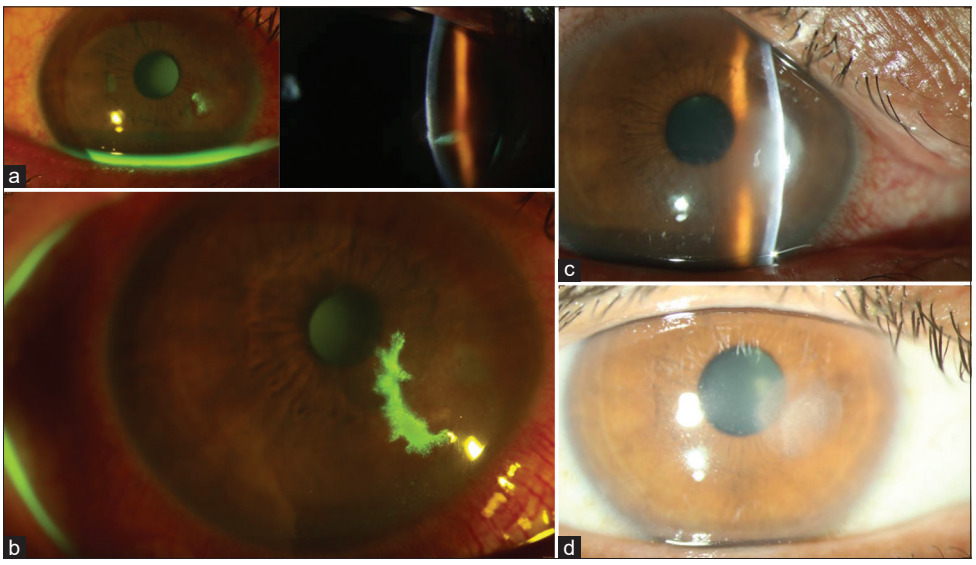

Figure 3: (a) Punctate epithelial keratitis with mild infiltration was found after 2 weeks of his initial ocular symptoms, (b) Two weeks after the appearance of keratitis, the corneal lesion progressed to dendritic-like ulceration, (c) The corneal ulceration enlarged along with stromal edema and cell in the anterior chamber, (d) The corneal lesion resolved, leaving a faint scar

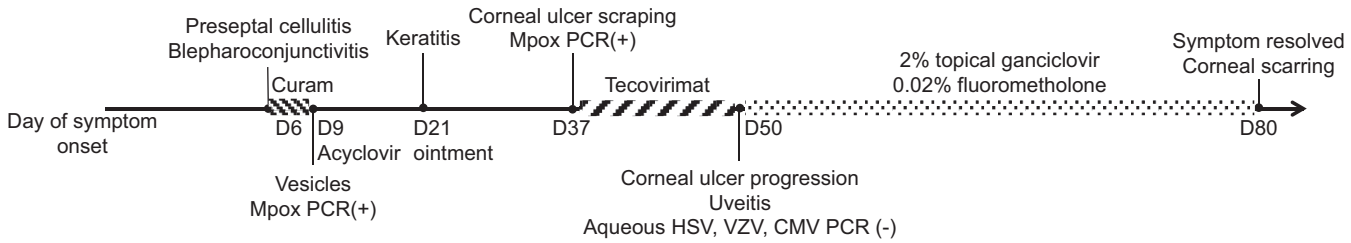

Figure 4: Timeline of this patient's clinical course. This man had an eruption of monkeypox vesicles 1 week after the manifestation of preseptal cellulitis and blepharoconjunctivitis. Sight-threatening keratouveitis was developed subsequently. He eventually recovered with a fair visual outcome after treatments. PCR: Polymerase chain reaction

Mpox from other ocular vesicular diseases, such as herpes simplex, varicella zoster, and molluscum contagiosum infections. The epidemiology of Mpox is evolving, with ongoing multicountry outbreaks exhibiting atypical clinical features. For instance, ophthalmic lesions tend to be milder and less frequent in nonendemic countries. The possible reasons why the present global outbreak is different from previous endemic outbreaks may be caused by a different Mpox clade (clade II in the present outbreak versus clade I in the historical outbreaks), or it could be attributed to a different mode of transmission.[12]

Infection with Mpox is largely a self-limited disease with symptoms lasting for 2–4 weeks. Therefore, it is recommended to provide supportive care, pain management, and prevention of complications early in the course of the illness. However, the most devastating consequences of MPXROD are corneal ulceration and subsequent corneal scarring, which can result in permanent visual impairment.[13] Corneal lesions, including ulcerations seen in 4% of unvaccinated patients and 1% of vaccinated patients and keratitis seen in 3.6%–7.5% of patients, have been reported as late presentations of Mpox infection.[12] Currently, topical antiviral agents specific for Mpox infection remain unavailable. Enhanced lubrication or topical antibiotics have been suggested for symptom relief and prevention of bacterial superinfection. Acyclovir and ganciclovir have limited effects on Mpox due to their specific spectrum of activity primarily targeting herpesviruses.[14] Tecovirimat, originally developed to treat smallpox, is approved by the European Medicines Agency for the treatment of severe Mpox infections, including those involving the eyes. In a recent study in Spain, tecovirimat was administered to five patients suffering from severe MPXROD, including corneal ulceration, corneal stromal edema, and corneal endothelitis. Their symptoms showed significant improvement after 1 week of treatment, with complete recovery observed at a median of 4 weeks, all without any reported side effects.[15] Other antiviral agents such as cidofvir and brincidofovir, along with vaccinia immune globulin, can be considered for severe cases. In cases of MPXROD, the Centers for Disease Control and Prevention of the United States suggests considering trifluridine ophthalmic solution, which is approved by the Food and Drug Administration for ocular herpes simplex keratitis.[14,16] Topical steroids may be prescribed to reduce inflammation in combination with antiviral agents. Vaccination is recommended for vulnerable demographic groups, including children, pregnant women, and health workers at high risk of exposure.

In the ophthalmic clinic setting, the use of personal protective equipment such as an N95 mask, gown, gloves, and goggles is required for safety. After gloves are removed, hands should be washed with soap and water for at least 20 s. If soap and water are not available, an alcohol-based sanitizer with at least 60% alcohol should be used. For instrument disinfection, use an Environmental Protection Agency (EPA)-registered hospital-grade disinfectant that is effective against viral pathogens. When cleaning the environment, refrain from dry dusting, or sweeping, as this may disperse dust particles containing the virus into the air. Instead, employ wet cleaning methods such as wipes, sprays, and mopping.[17]

In conclusion, we report a case of MPXROD presenting with blepharoconjunctivitis and preseptal cellulitis, which developed 6 days before the appearance of skin lesions. He later developed vision-threatening keratitis and subsequently received tecovirimat treatment. The strength of this report lies in its achievement of being the first to gain PCR approval for corneal tissue infected by the Mpox virus. However, a limitation of this study is that this single observation alone is insufficient to determine the effect of antiviral drugs on Mpox. Currently, the information on MPXROD remains limited currently. With the increasing scale of the current Mpox outbreak, ophthalmologists should be vigilant about this disease. Early diagnosis and proper intervention may not only reduce ocular and systemic morbidity but could also play a vital role in containing the further spread of the outbreak.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consents for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Nil.

Conflicts of interest

Dr. Cheng-Kuo Cheng, Editor-in-Chief at Taiwan Journal of Ophthalmology, had no role in the peer review process of or decision to publish this article. The other authors declared no conflicts of interest in writing this paper.

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