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EDITORIAL

Ophthalmic manifestations of monkeypox virus

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Monkeypox virus (MPXV), a double-stranded DNA virus belonging to the Orthopox genus of the Poxviridae family, was first reported as a zoonotic infection transmitted from animals to humans in 1958, with the first human case being reported in 1970. The first human-to-human transmission outbreak was reported in 1996–1997 in the Democratic Republic of Congo through respiratory droplets and direct contact with infected individuals [1]. Then, sexual transmission in men having sex with other men (MSM) became evident [2]. Notably, MPXV re-emerged in May 2022 in multiple countries with no evident epidemiological link between reported cases. As of July 3rd, 2022, the total number of confirmed cases reached 6178 in 56 countries, being highest in Spain ($N = 1196$), England ($N = 1185$), Germany ($N = 1054$), France ($N = 498$), and the United States ($N = 459$) (Fig. 1).

The presenting symptoms of MPXV are quite similar to those of smallpox with an incubation period ranging from 5 to 21 days [3]. However, available evidence highlights the presence of several yet frequent ophthalmic manifestations that are associated with this virus. Given the current burden of the disease, and the fact that it was declared a pandemic by the World Health Network (WHN) on June 22, 2022 [4], such symptoms should be recognized by healthcare workers, particularly ophthalmologists.

The clinical picture of the MPXV is very similar to that of the ordinary and modified forms of smallpox [5, 6]. Lymphadenopathy, occurring in the early stage of the illness, is a distinctive hallmark differentiating human monkeypox from smallpox and chickenpox [5, 6]. MXPV has been reported to have several ophthalmic manifestations which are common like other non-specific symptoms (i.e., fatigue, headache, muscle ache) [5, 6]. For instance, the characteristic lesions of MPXV usually appear as first macular, then papular, then vesicular and pustular which often involve peri-orbital and orbital skin, resembling Varicella-Zoster rash, which affect 25% of cases [7]. A full list of ophthalmological manifestations of MPXV is provided in Table 1.

Conjunctivitis and edema of the eyelids were common (approximately over 20% of affected patients) and resulted in substantial but temporary distress to the affected patients [5, 7–9]. Interestingly, Jezek Z et al. [10] showed that conjunctivitis was more common among patients affected by animal MPXV (20.3%) compared to those affected by human MPXV (16.4%). Furthermore, focal lesions on the conjunctiva and along the margins of the eyelids were seen with a greater incidence among unvaccinated patients with confirmed MPXV (nearly 25%, 68/294) [5, 11]. Hughes et al. [9] reported that patients, where "conjunctivitis" was observed, had a higher frequency of other symptoms, such as nausea, chills/sweating, oral ulcers, sore throat, general malaise, lymphadenopathy, and photophobia compared to those with no reported "conjunctivitis". In addition, conjunctivitis is likely predictive of the illness course. For example, 47% of patients with conjunctivitis reported being "bed-ridden", compared to 16% of patients where "conjunctivitis" was not reported [9].

Corneal involvement may range from mild to severe involvement. Photophobia, alone, was reported in approximately 22% of affected patients [7]. In addition, severe corneal infections that can result in severe keratitis forms (seen in 7.5% of patients in one study), corneal scarring (seen in 4% of unvaccinated, and 1% of previously smallpox-vaccinated case patients), and permanent vision loss were also reported [6–8, 10]. Based on the study of Jezek et al. [10], unilateral or bilateral blindness, and weak vision were observed in 10% of primary (who presumably were infected from an animal source) and 5% of secondary cases (in whom the rash appeared between 7 and 21 days after exposure to another human case which may have occurred due to person-to-person transmission). Of note, Trifluridine has been used to treat Orthopoxvirus-associated corneal lesions. However, there is no available evidence of its efficacy in MPXV cases specifically [9]. We should not forget to mention that MPXV causes lymphadenopathy, which may involve pre-auricular lymph nodes as seen in viral conjunctivitis [5–8, 12]. Frontal headache involving the orbits was also reported [5, 6, 8, 12]. Furthermore, one study showed that blepharitis was observed in 30% of unvaccinated, and in 7% of previously smallpox-vaccinated patients [13].

Monkeypox is usually a self-limited disease with symptoms lasting from two to four weeks [8]. The potential benefits of relatively simple therapies for ocular complications, such as enhanced lubrication or topical antibiotics, could be considered [11]. Of note, severe sequelae and complications of monkeypox occur more commonly among unvaccinated populations (74%) compared to vaccinated patients (39.5%) [5, 6, 8, 14]. Therefore, we should highlight the importance of the vaccine by increasing public awareness. However, an accidental infection may occur secondary to vaccine strains themselves [15]. In the 5 years between 1963 and 1968, ocular vaccinia was observed in 348 persons: 259 vaccinees and 66 contacts. Of these, 22 had evidence of corneal involvement, and 11 had permanent defects [14]. In addition, ophthalmologists should be aware of any new ocular complaints following confirmed MPXV. Improving the availability of ophthalmologic resources in areas endemic to the MPXV may reduce risks for significant visual sequelae among affected patients.

Since the majority of MPXV-associated ophthalmic manifestation surpass the rare event assumption (<5%), and given the continuous and rapid increase in the number of cases, we highly recommend that ophthalmologists incorporate MPXV as a part of their differential diagnosis when they come across similar cases presenting with ophthalmic manifestations like conjunctivitis, blepharitis, keratitis, or corneal lesions. And since these manifestations are more likely observed in non-vaccinated individuals, we, therefore, encourage healthcare authorities to redistribute the smallpox vaccine for high-risk groups.

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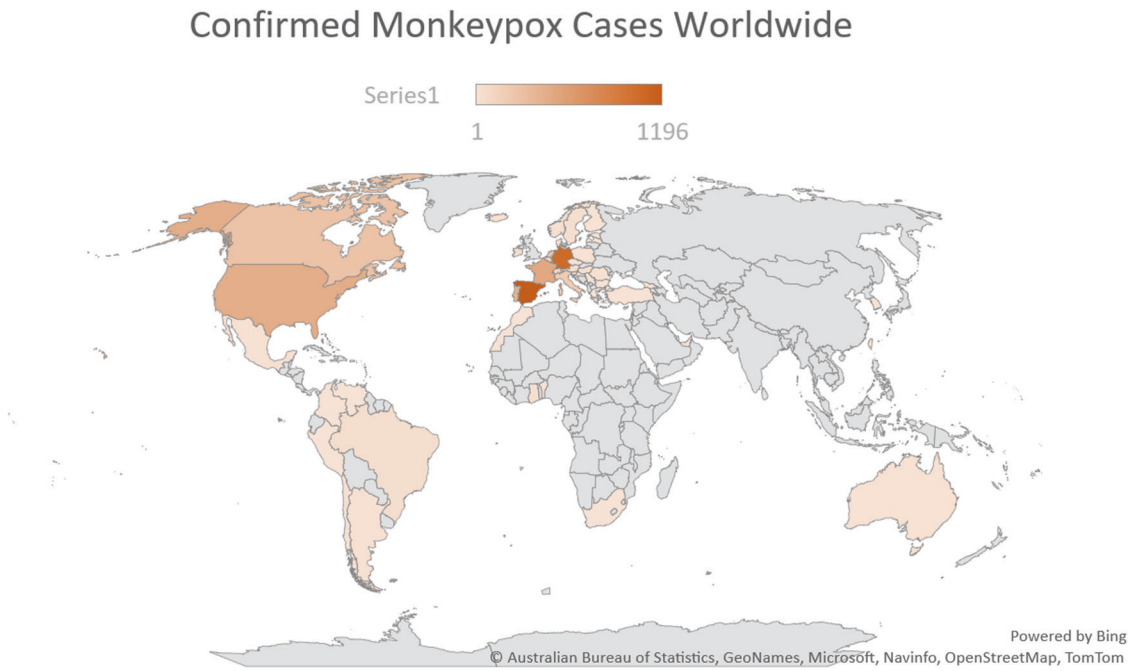

Fig. 1 Confirmed Monkeypox cases worldwide as of July 3, 2022.

Table 1. Ophthalmic manifestations of Monkeypox virus.

Ophthalmic manifestations	Frequency	Timing of presentation	Reference
Enlarged Lymph nodes including pre-auricular nodes			
	71%	Early	[12]
Vesicular rash involving orbital and peri-ocular skin			
	25%	Early	[7]
Frontal headache			
	65%	Early	[12]
Blepharitis			
	30% of unvaccinated patients	Early	[13]
	7% of vaccinated patients		
Conjunctivitis			
	30% of unvaccinated patients	Early	[13]
	7% of vaccinated patients		
Focal conjunctival lesions			
	17% of unvaccinated patients	Early	[5]
	14% of vaccinated patients		
Corneal ulcerations			
	4% of unvaccinated patients	Late	[10]
	1% of vaccinated patients		
Photophobia			
	22.5%	Late	[7]
Keratitis			
	3.6%–7.5%	Late	[7, 10]
Visual loss			
	10% of primary cases	Late	[10]
	5% of secondary cases		

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AUTHOR CONTRIBUTIONS

AA was responsible for the conceptualization of the research idea, searching the literature, making the figure, providing supervision in regards to manuscript writing, and editing and reviewing the final draft. Both RS and AJRM helped with the conceptualization of the research idea and reviewing and editing the manuscript. HAS was responsible for searching the literature, highlighting key relevant studies, making a summary table of findings, and writing the manuscript. MAM was responsible for doing literature search and writing the manuscript. All authors approved the final version of the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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