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Short Communication

Clinical manifestations and viral kinetics of people with Mpox: A case series during the 2023 outbreak in Taiwan

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Abstract Monkeypox (Mpox) has emerged as a global threat since 2022. We reported 14 cases of Mpox in 10 people with HIV (PWH) and 4 people without HIV (PWoH), of whom 64.3% had sexually transmitted co-infections. Severe complications of Mpox and prolonged viral shedding might occur in both PWH and PWoH.

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immunodeficiency syndrome;
Human immunodeficiency virus;
Tecovirimat

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Introduction

Mpox continues to spread worldwide and has affected 99,176 individuals and caused 208 deaths according to the WHO as of August 2, 2024. The WHO had declared that the outbreak was associated with sexual contact in the gay, bisexual, and other men who have sex with men (GBMSM) community as a Public Health Emergency of International Concern.[1] Previous studies have shown that 38—50% of individuals diagnosed with Mpox were people with HIV (PWH), and people with advanced HIV infection are at higher risk of developing fulminant dermatological manifestations, sepsis, or even death.[1,2]

The first imported case of Mpox in Taiwan occurred in a person with HIV who had been receiving antiretroviral therapy with viral suppression in June, 2022.[3] Vaccination program against Mpox in Taiwan was implemented on March 21, 2023, in response to a domestic outbreak of Mpox in the GBMSM community. As of July 28, 2024, 388 cases of Mpox have been diagnosed and reported to Taiwan Centers of Disease Control (CDC). Here, we present the clinical features and viral kinetics from different sites sampled of 14 patients with Mpox before the implementation of vaccine program.

Materials and methods

Study population and setting

All hospitalized adult people with laboratory-confirmed Mpox by real-time polymerase-chain-reaction (RT-PCR) assay at the National Taiwan University Hospital (NTUH) between February and October 2023 were recruited. We prospectively collected the information on demographics, presenting symptoms, date of symptom onset and evolution of the skin lesions, antiretroviral therapy, CD4 lymphocyte count, and plasma HIV-1 RNA, as well as comorbidities from the electronic medical records. The study was approved by the Research Ethics Committee of NTUH (NTUH 202303128RIND) and all participants gave written informed consent.

All participants tested for syphilis, hepatitis B and C viruses, and other sexually transmitted infections (STIs) with the use of multiplex PCR assay (Allplex™ STI Essential Assay) on the specimens collected from the throat, rectum and urethra on admission. For those without known HIV infection before presentation, a screening test for HIV antibodies and antigens was performed. Other laboratory examinations were conducted based on physicians' judgement according to the associated symptoms, including blood cultures, stool cultures and PCR assays of stool specimens for *Entamoeba histolytica*.

Management of Mpox during the hospitalization

All participants were isolated in a single room. Tecovirimat was administered based on the treatment criteria established by Taiwan CDC to persons with immunodeficiency, such as PWH with CD4 counts $<$200 cells/mm^3, pediatric populations, women who were pregnant or breastfeeding, and persons with severe Mpox according to the definitions by the U.S. Centers for Disease Control and Prevention.[4] Antibiotics were not routinely administered unless bacterial co-infections were confirmed or suspected at the discretion of treating physicians.

Laboratory investigations

Clinical specimens for PCR testing of Mpox virus (MPVX) were obtained from the skin lesions, throat, urethral, and rectal regions on admission, which were repeated twice weekly before de-isolation by fulfilling the criteria by Taiwan CDC, including (1) defervescence with improvement of presenting symptoms; and (2) desquamation of all skin and oral lesions. Specimens of the skin were sampled from the most severe lesions on admission, and newly developed skin lesions observed were sampled during follow-up. A molecular testing was established on the Bio-Rad CFX96 platform by targeting E9L, an orthopoxvirus DNA polymerase gene for detection of the non-variola Orthopoxvirus, and a MPXV-specific TNF receptor gene. Quantitative PCR assay was performed on each specimen to determine the cycle threshold (Ct) values. A negative result for MPXV was defined with a Ct value higher than 35.

Results

Fourteen people with confirmed Mpox between February and October, 2023 were diagnosed and enrolled (Table 1). All participants were MSM, with a median age of 32 years (range, 22—46). Ten (71.4%) were PWH, with four (40%) of them having CD4 counts $<$200 cells/mm^3 on presentation of Mpox. One of the other four people without HIV infection (PWoH) was followed at our hospital receiving co-formulated tenofovir disoproxil fumarate/emtricitabine as pre-exposure prophylaxis for HIV. The median duration from the first pustule observed to admission was 7 days (range, 2—21). Tecovirimat was administered to eleven participants including the four PWH with CD4 counts $<$200 cells/mm^3 and other seven participants with severe disease among whom were 2 PWoH.[4] Nine (64.3%) participants met the criteria of severe disease, including 2 of 4 PWH with CD4 counts $<$200 cells/mm^3 (Fig. S1). The most common complication was cellulitis with necrotic skin

Table 1 Clinical manifestations and concurrent sexually transmitted infections of the included participants.

Case	Age (y)/ Sex	HIV/CD4 cells/mm^3	Associated symptoms	Duration from onset to admission/ symptom onset to desquamation of all lesions (d)	Estimated peak number of skin lesions	Complications	Concurrent sexually transmitted infections	Treatment
1[a]	25/M	PWH/170	Anal pain, inguinal LAP	7/67	>100	Proctitis with anal bleeding	Syphilis, MG and UU infection, Genital warts	Tecovirimat for 14 days
2[a]	37/M	PWH/860	Malaise, Anal pain	3/11	30–50	Proctitis	UU and MH infection	Tecovirimat for 14 days
3[a]	34/M	PWH/959	Inguinal LAP	3/20	<10	None	gonorrhea, CT, UU, and MH infection, shigellosis	Tecovirimat for 14 days
4	29/M	PWH/135	Fever, inguinal LAP	2/17	<10	None	UU and MH infection	Tecovirimat for 14 days
5[a]	31/M	PWH/351	Inguinal LAP	7/17	30–50	Carbuncle and cellulitis	gonorrhea, MH infection, genital warts	Tecovirimat for 14 days
6	23/M	PWH/500	Inguinal LAP	7/12	<10	None	None	None
7	25/M	PWH/189	Fever	7/21	<10	Balanitis	UU and MH infection	Tecovirimat for 14 days
8[a]	34/M	PWH/0	Anal pain, tongue ulcer	21/50	50–100	Proctitis, IRIS with fulminant skin rash and anal pain	MH infection, amebiasis, genital warts	Tecovirimat for 14 days for 2 cycles
9[a]	40/M	PWH/758	Fever	7/15	30–50	Balanitis	Syphilis	Tecovirimat for 14 days
10[a]	46/M	PWH/616	Fever, inguinal LAP	7/14	30/50	Cellulitis and necrotic skin lesions	None	Tecovirimat for 14 days
11[a]	44/M	PWoH/NA	Fever, headache	5/18	50–100	Cellulitis and necrotic skin lesions	None	Tecovirimat for 14 days
12	22/M	PWoH/NA	Fever	7/7	<10	None	MG infection	None
13	33/M	PWoH/NA	Fever	7/12	10–20	Cellulitis	None	None
14[a]	22/M	PWoH/NA	None	7/16	>100	Cellulitis and necrotic skin lesions	None	Tecovirimat for 14 days

[a] Fulfilling the criteria of severe disease according to the definitions by the U.S Centers for Disease Control and Prevention.

Abbreviations: CT, *Chlamydia trachomatis*; IRIS, Immune reconstitution inflammatory syndrome; LAP, Lymphadenopathy; M, male; MPXV, monkeypox virus; MG, *Mycoplasma genitalium*; MH, *Mycoplasma hominis*; NA, not applicable; NG, *Neisseria gonorrhoeae*; PWH, people with HIV; PWoH, people without HIV; UU, *Ureaplasma urealyticum*.

lesions, followed by proctitis and balanitis (Table 1). One PWH (Case 8) with an extremely low CD4 count (0 cells/mm^3 on admission) developed a second wave of skin rash and anal pain 13 days after completion the first cycle of tecovirimat treatment, which required a second hospitalization for management of Mpox. Although immune reconstitution inflammatory syndrome of Mpox was suspected, another 14-day course of tecovirimat was administered after approval from Taiwan CDC. The patient's discomfort resolved within 1 month after the second course of tecovirimat. Nine (64.3%) of the 14 participants were concurrently diagnosed with other STI, including six with *Mycoplasma hominis* infection, five *Ureaplasma urealyticum* infection, two syphilis, two *Neisseria gonorrhoeae* infection, two *M. genitalium* infection, one *Chlamydia trachomatis* infection, one amebiasis, and one *Shigella* spp. infection (Table 1).

On admission, MPXV was detected from 11 (78.6%) skin specimens, 13 (92.9%) rectal specimens, 12 (85.7%) throat specimens, and 8 (57.1%) urethral specimens. Overall, MPXV viral loads were found to be higher in the specimens obtained from skin lesions (median Ct value, 23.7) than those from the rectum (26.5), throat (30.1) and urethra (33.1). Over the 10-day observation period, there were significant decreases in MPXV viral loads at all sampled sites (Fig. 1, Fig. S2). On the hospital day 14, decreases in the positive rates of specimens tested by PCR assays at all sites were observed: skin (45.5%, 5/11), rectum (33.3%, 4/12), throat (18.2%, 2/11), and urethra (16.7%, 2/12) (Table S1). Six (42.9%) participants continued to test positive for MPVX PCR assay of the specimens obtained from either skin lesion, the throat or rectum, despite the fact that desquamation of the skin lesions had developed (data not shown).

Discussion

Our study highlights a high prevalence (64.3%) of sexually transmitted co-infections among the 14 included people presenting with Mpox and a significant decrease of MPVX viral loads over the 10 days of hospitalization. MPXV might remain detectable by PCR assay despite of the desquamation of skin lesions. Moreover, severe complications of Mpox occurred not only in PWH but in previously healthy individuals.

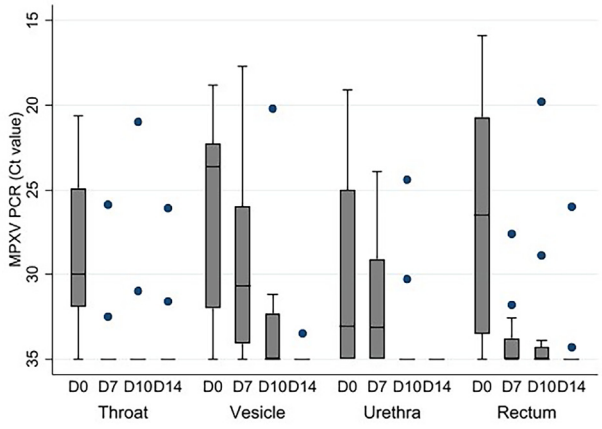

Figure 1. Viral kinetics of MPXV from different sampled sites from day 1 to day 14. Abbreviations: Ct, cycle threshold; MPXV, monkeypox virus.

In the study by Maldonado-Barrueco et al., 19.2% of the people with Mpox had concurrent STIs, and the most commonly affected site was the rectum. Herpes simplex virus, *N. gonorrhoeae*, and *C. trachomatis* were the most commonly detected etiologies by PCR assays.[5] Our study showed an even higher prevalence of concurrent STIs, probably related to the performance of an active multi-site screening using PCR assays including the throat, rectum and urethra, which echoed the findings of the study by Hiransuthikul A.[6] Skin lesions associated with Mpox might have been mistakenly diagnosed as other common STIs in previous studies.[7] Therefore, multi-site screening for STIs is essential for individuals presenting with Mpox due to the high prevalence of concurrent STIs and for accurate differential diagnosis.

Previous studies have shown that PWH with CD4 counts $<$350 cells/mm^3 were at higher risk of developing severe complications, including necrotizing skin lesions, secondary bacteremia, and respiratory failure.[3] Our study further demonstrated that severe complications, particularly fulminant skin rash, might also occur in PWoH. The finding was consistent with those of a cohort study in the United Kingdom, which showed a similar clinical presentations, duration, and hospitalization rate between virologically-suppressed PWH and PWoH.[8]

In this study, higher MPXV viral loads were found in the specimens collected from skin lesions, compared with those from the rectum, urethra and throat. However, not all skin lesions on admission yielded positive results, probably due to sampling errors. These findings are in line with those of a previous case series by Palich et al., which highlighted the necessity of collecting specimens from multiple sites for accurate diagnosis.[9] We also observed significant decreases in MPXV viral loads of all sampled sites 10 days after admission; however, MPXV viral loads appeared to decrease slower in vesicles than other sampled sites. We found that some people remained testing positive by PCR assay, especially those with CD4 counts less than 200 cells/mm^3. Moreover, those with desquamated skin lesions might continue to have detectable MPXV in the rectum or urethra. Towns et al. reported that people with Mpox might have prolonged viral shedding with positive viral cultures even after the resolution of Mpox lesions.[10] Therefore, while isolation precautions may be discontinued in people with Mpox who meet the de-isolation criteria, caution is needed for close contact with others.

In conclusion, we demonstrated the clinical manifestations of 14 people with Mpox and their trends of MPXV viral loads of specimens collected from different sites during the hospital stay. Prolonged viral shedding may be observed. Screening for STIs is imperative for all people with Mpox, regardless of their HIV status.

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CRediT authorship contribution statement

Kai-Hsiang Chen: Data curation, Formal analysis, Writing — original draft, Writing — review & editing, Conceptualization, Investigation, Methodology. **Wang-Da Liu:** Conceptualization, Funding acquisition, Methodology, Writing — review & editing. **Kuo-Chen Weng:** Investigation, Resources. **Hui-Hou Chen:** Investigation, Resources. **Shu-Yuan Ho:** Investigation, Resources. **Yu-Shan Huang:** Investigation, Resources. **Tzong-Yow Wu:** Investigation, Resources. **Guei-Chi Li:** Project administration. **Sui-Yuan Chang:** Investigation, Methodology, Resources, Supervision, Writing — review & editing. **Chien-Ching Hung:** Conceptualization, Methodology, Project administration, Resources, Supervision, Writing — review & editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2024.08.008.