CASE SERIES

Mpox Infection in People With HIV: A Case Series in a Non-endemic Country

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ABSTRACT

Introduction: Mpox is a zoonotic viral infection caused by an enveloped double-stranded deoxyribonucleic acid (DNA) monkeypox virus (MPXV). It is endemic in Central and West Africa, but global mpox outbreak has been declared by World Health Organization (WHO) as a Public Health Emergency of International Concern (PHEIC) following the escalation of cases in non-endemic countries in July 2022. This outbreak has been associated with concomitant human immunodeficiency virus (HIV) and sexually transmitted disease, involving primarily gay, bisexual and men who have sex with men (MSM). **Case series:** This is a case series of mpox in people living with HIV in a non-endemic locality, which were confirmed by detection of MPXV DNA by polymerase chain reaction (PCR) from the lesion swabs. The clinical manifestations and transmission routes of mpox virus (MPXV) infection in immunocompromised individuals, especially in non-endemic regions, remain poorly understood. The case series highlights the different clinical manifestation and routes of transmission of MPXV in immunodeficient patients, particularly in people with HIV. **Conclusion:** This case series can provide healthcare practitioners and the public with insights into identifying the clinical manifestations of mpox and the vulnerable groups, thereby improving screening efforts and helping to curb the transmission of the infection in a non-endemic country.
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INTRODUCTION

Mpox (formerly known as monkeypox) is an endemic zoonotic viral infection in Central and West Africa, first discovered in 1958 in cynomolgus monkeys in Denmark. The first human mpox infection was confirmed in the Congo in 1970. Subsequently, sporadic cases in humans were diagnosed, mainly from the spillover of zoonotic infections in rural areas and travellers who visited endemic regions. MPXV belongs to the Poxviridae family, the same as the variola virus, and manifests similarly to smallpox but with milder symptoms. Transmission occurs from animals to animals, primarily primates and rodents, from animals to humans, and from humans to humans through exposure to mucous membranes, body fluids, and tissues via close contact with an infected person or animal, contaminated materials like bedding and toilet seats, and exhaled large droplets. Once exposed, the virus enters the host through mucous membranes or broken skin, spreading through tissue-resident immune cells and draining lymph nodes. The incubation period ranges from two to four weeks before the infected person becomes symptomatic (1-8).

The global mpox outbreak in 2022 revealed important insights into the spread of the disease, particularly among immunocompromised individuals (1,2). This case series reported the possible route of transmission, clinical manifestation and outcome of mpox in people with HIV in a non-endemic country.

CASE SERIES

Patient 1

Patient 1 is a man in his mid-30s who has no significant medical history. He presented with the sudden onset of multiple painful rashes, starting from his right hand and left little finger, and spreading to the abdominal region. He reported no prodromal symptoms. Three weeks

prior to presentation, he had unprotected sex with a new partner. He denied any history of travelling outside the country in the past 3 months, but reported contact with a suspected mpox patient. On examination, skin rashes appeared as monomorphic umbilical papules with central crusting, located on the left little finger, dorsum of the right hand and fingers, suprapubic region, and penile shaft. There was no involvement of the oral mucosa. Tender, shotty right inguinal lymph nodes were also noted. The crusty lesions tested positive for MPXV by PCR.

Infectious screening revealed a reactive serological result for HIV antibody, with an HIV-1 viral RNA count of 379 copies/ml and a CD4 count of 621 cells/μL. Two days after admission, he developed dysuria and urethral discharge. Urine nucleic acid amplification testing (NAAT) detected Chlamydia trachomatis and Neisseria gonorrhoeae. Screening for syphilis by rapid plasma reagin (RPR) test was non-reactive. Additionally, he had acute paronychia over his right middle finger, diagnosed clinically and treated empirically as a secondary bacterial infection.

After undergoing treatment with oral doxycycline 100mg once daily for one week and a single dose of intramuscular (IM) ceftriaxone 500mg, the urethral discharge and paronychia resolved. Antiretroviral therapy was initiated in the ward after five days, which he tolerated well. All the lesions resolved with new epithelialization after three weeks.

Patient 2

Patient 2 is a man in his early 30s with a medical history of perianal warts. He presented with prodromal symptoms of fever, runny nose, headache, myalgia, and diarrhoea for five days, followed by the onset of a painless rash on the abdomen, which spread to the right forearm. He also experienced pain during defecation. He denied any history of travelling outside the country in the past 3 months, but reported contact with a suspected mpox patient. On examination, he had a generalized maculopapular rash on his chest and back, along with umbilicated papules on the right side of his face, right forearm and hand, and scrotal and perianal regions. There was no involvement of the oral mucosa. However, proctoscopy was not done to examine the possibility of proctitis due to the pain. He also had bilateral tender, enlarged inguinal lymph nodes and submandibular lymphadenopathy.

Confirmatory testing using PCR detected MPXV DNA from the skin lesions. Infectious screening revealed positive HIV antibody with an HIV-1 viral load of 303 copies/ml and an absolute CD4 count of 473 cells/μL. Urine NAAT for Chlamydia trachomatis and Neisseria gonorrhoeae and RPR test for syphilis were negative.

Prophylactic treatment for chlamydia and gonorrhoea was administered with oral doxycycline 100mg once daily for one week and a single dose of IM ceftriaxone 500mg, due to concern over recent diagnosis of the infection in his male partner. Antiretroviral therapy was initiated in the ward after five days, which he tolerated well. All the lesions resolved with new epithelialization after three weeks.

Patient 3

A young man in his 20s, newly diagnosed with HIV five months earlier and on antiretroviral therapy, presented with a one-week history of painful umbilicated papules. The rash had begun on his fingers and spread to his bilateral arms, face, trunk, back, and thighs in a centrifugal distribution. There were no lesions on the oral mucosa or anogenital area. The rash was preceded by a two-day fever. He also had submental lymphadenopathy. He engaged in heterosexual behaviour and last had sexual intercourse with a female partner six month ago. He denied any recent travel or contact with Mpox patients. The lesions tested positive for MPXV DNA using PCR. As he had good compliant to ART, his baseline HIV-1 viral load decreased from 48300 copies/ml to 77 copies/ml with improvement of CD4 count from 16 cells/μl to 88 cells/μl during this admission. He was treated symptomatically, discharged well on day 3 of admission, and the lesions resolved with new epithelialization during 21 days of home quarantine.

DISCUSSION

The first global mpox outbreak in 2022 demonstrated a broader geographical spread, encompassing countries without previous reported cases such as Malaysia. In July 2022, WHO declared the mpox multi-country outbreak a Public Health Emergency of International Concern (PHEIC). In 2023, Malaysia reported nine cases with no fatalities. Unlike the endemic regions where mpox clade 1 mainly infects children and young adults with equal gender distribution, this outbreak primarily affected MSM, sustaining human-to-human transmission through sexual contact. This outbreak was associated with clade IIb MPXV and presented with different clinical features than previously reported cases (1-8). Diagnosis was confirmed by PCR in the national reference laboratory, detecting MPXV from clinical samples such as lesion fluid, scab or crust during the rash phase, tonsillar tissue swab or nasopharyngeal swab, and blood during the prodromal phase.

In this case series, all patients were immunocompromised and presented with mild symptoms. Prodromal symptoms did not manifest in all patients. Patients 1 and 2 had anogenital rashes with inguinal lymphadenopathy, similar to most reported cases in the outbreak. The absence of prodromal symptoms in patients with anogenital rashes suggests sexual transmission. Typical mpox rash is monomorphic with centrifugal distribution, as seen in Patient 3. However, an atypical presentation

of a generalized maculopapular rash associated with acute mpox infection was observed in Patient 2, forming concurrently with monomorphic umbilicated papules after the prodrome. A case series of mpox infection with morbilliform rash by Bartholomew E. et al. highlighted this atypical presentation, mainly involving the trunk, with extremity involvement and sparing the face (5).

As mpox has been recognized to be transmitted sexually, coinfections with other infections such as chlamydia, gonorrhoea, and syphilis have been frequently reported, as seen in Patient 1. In patients suspected of MPXV infection with anogenital rashes, it is imperative to screen for other sexually transmitted infections and HIV to institute appropriate treatment (9-11). The MPXV infection revealed the underlying immunocompromised state in Patient 1 and 2, warranting hospitalization. Mpox emerged as HIV-associated opportunistic infection, accounting for 40% to 67% of cases in the 2022 outbreak (9,10). It mainly affects undiagnosed people who presented at advanced stage of HIV or uncontrolled disease due to suboptimal care contributed by inaccessible treatment, psychosocial barrier or lack of compliance to the ART (10-12). A global case series of mpox in people with advanced HIV reported more severe infections have been reported in HIV patients with CD4 counts below 100 cells/mm as compared with those with more than 300 cells/mm3. potentially leading to mortality. They reported that all mortality occurred in patients with CD4 counts less than 200 cells/mm , with more deaths occurring in patients with a high HIV viral load (12). In this case series, all the patients had self-limiting symptoms due to high CD4 counts of more than 300 cell/mm3 in Patient 1 and Patient 2, and the HIV was well-controlled with adherence to ART in Patient 3 (Table I).

Table I: Patients' characteristics, clinical, diagnostic and treatment information

Patient ID	Age decade	Sex	HIV status	HIV viral load during diagnosis of mpox (copies/ml)	CD4 count (cells/mm^3)	ART	Prodrome	Clinical manifestations	Concomitant tests performed	Concomitant diagnoses with mpox	Treatment
Patient 1	30	Male	Newly diagnosed	379	621	Started during this admission and well-tolerated	No prodrome	-Painful monomorphic rash over genitalia, trunk, arms and palms -Lymphadenopathy	MPXV PCR, Serology HIV Ag/Ab, HIV-1 viral load, urine NAAT for C. trachomatis and N. gonorrhoeae, RPR	HIV, chlamydia, gonorrhoea, acute paronychia of right middle finger	-Symptomatic treatment for mpox -IM ceftriaxone 500mg one dose for gonorrhoea -Oral doxycycline 100mg OD for chlamydia
Patient 2	30	Male	Newly diagnosed	303	473	Started during this admission and well-tolerated	Fever, runny nose, headache, myalgia, and diarrhoea 5 days before the rash onset	-Painless generalised maculopapular rash over trunk -Painless monomorphic rash over face, arms, palms, perianal and genitalia -Proctitis -Lymphadenopathy	MPXV PCR, Serology HIV Ag/Ab, HIV-1 viral load, urine NAAT for C. trachomatis and N. gonorrhoeae, RPR	HIV	-Symptomatic treatment for mpox -IM ceftriaxone 500mg one dose for gonorrhoea as post-exposure prophylaxis -Oral doxycycline 100mg OD for chlamydia s post-exposure prophylaxis
Patient 3	20	Male	Known case	77	88	Compliant to ART	Fever for 2 days before the rash onset	-Painful monomorphic rash over face, arms, palms, trunk and legs -Lymphadenopathy	MPXV PCR, HIV-1 viral load	HIV	-Symptomatic treatment for mpox

Transmission to immunocompromised individuals sustains the virus in humans, contributing to viral mutation and adaptation to human hosts, leading to further dissemination (4,6,7). The mode of transmission for Patient 3 was possibly through direct contact with contaminated surfaces or exhaled droplets, indicating that MPXV can be transmitted human-to-human in the environment asymptomatically. Underreporting of cases may occur due to the self-limiting and mild symptoms, posing a threat to future outbreaks involving young children, the elderly, and immunosuppressed individuals if prevention is not implemented.

WHO has published interim guidance on clinical management and infection prevention and control for mpox. For mild infections, symptomatic treatment is recommended while monitoring for signs and symptoms of severe complications such as bacterial skin and soft

tissue infections, respiratory distress, corneal infection, and severe dehydration. The use of antivirals like tecovirimat is limited to severe infections. Post-exposure prophylaxis with smallpox vaccines offers cross-protection against mpox infection (5, 9-12). Preventive measures to prevent further dissemination of MPXV include continuous surveillance of new infections, isolation of infected individuals from healthy persons, and education for healthcare workers and the public on the diverse epidemiology, risk factors, modes of viral transmission, and clinical presentations of mpox infection. This will enhance recognition and adherence to standard infection control practices (2).

CONCLUSION

Mpox infection has been diagnosed in non-endemic countries following the global outbreak in 2022. It can be transmitted sexually and screening of other sexually transmitted infections are necessary as co-infections are frequently reported in immunocompromised patients. The manifestations may vary and high index of suspicion is needed to diagnose the infection early and for infection prevention and control measures to be implemented.

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