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BRIEF REPORT

Human Monkeypox in People With HIV: Transmission, Clinical Features, and Outcome

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We describe the first 25 persons with HIV diagnosed with human monkeypox virus (MPXV) in our hospital in an ongoing outbreak in Spain. Proctitis was the predominant finding in 52%, and MPXV DNA was detected in rectal swabs from 90%. Proctitis and demonstration of MPXV in rectal swabs support the sexual transmission of MPXV.

Keywords. human monkeypox; HIV; clinical characteristics; outcome; sexually transmitted infections; transmission.

Commencing in May 2022, an emerging outbreak of human monkeypox virus (MPXV) infection is quickly spreading worldwide, primarily affecting men who have sex with men (MSM). Outbreaks of the disease reported in several countries indicate that among MSM patients with MPXV for whom HIV status in known, 28%–51% have HIV infection [1–9]. In a multinational cohort with predominately well-controlled HIV, clinical presentation was similar among persons with HIV infection (PWH) and those without HIV infection [3, 4]. However, monkeypox disease in advanced and uncontrolled HIV infection individuals could have a severe or prolonged course, as described in 2 case series in Nigeria caused by the same strain responsible for the current outbreak [10, 11]. In contrast, recent reports from European countries, where patients are under effective antiretroviral treatment, have described no evident excess in hospitalizations or deaths among PWH with MPXV [1–4]. In addition, according to a World Health Organization statement, a more severe disease course has not been reported in PWH who are receiving antiretroviral therapy (ART) and have a robust immune system [12].

We describe a series of 25 consecutive patients with HIV and monkeypox coinfection to further understand this population's clinical characteristics and transmission risks.

METHODS

In this analysis, we review the epidemiological and clinical characteristics of all consecutive individuals with confirmed MPXV infection who attended the HIV Clinic, University Hospital Ramón y Cajal, in Madrid, between May 16 (the first patient diagnosed) and June 23 (last patient included in this report). After the first 3 patients were seen on May 16, a uniform evaluation of all subsequent cases was performed for diagnosis, follow-up, and public health measures. Only patients with laboratory-confirmed MPXV were included in this series. Samples were processed at the Instituto de Salud Carlos III referral laboratory or University Hospital Ramón y Cajal laboratory.

The information collected in the clinical records constitutes the basis of our study. Samples sent for testing included a swab taken from a suspected skin lesion and rectal and pharyngeal swabs depending on clinical presentation. The microbiological diagnosis was made by real-time polymerase chain reaction (PCR). For orthopoxvirus (OPV) detection, a 231-pb polymerase gene fragment was amplified as previously described [13]. Positive samples for OPV were subsequently analyzed for specific detection of MPXV following the protocol described by Li et al. [14] using primers and probes for generic detection of both clades (West Africa and Congo Basin), which target a region within the receptor tumor necrosis factor gene. In addition, most patients were screened for sexually transmitted infections (STIs), including *Chlamydia trachomatis* and *Neisseria gonorrhoeae* from urine, pharyngeal, and rectal samples, as well as HCV and syphilis serology. Herpes virus (HSV) molecular testing was also performed when deemed clinically indicated.

RESULTS

During the study period, 25 PWH usually followed at our clinic were diagnosed with MPXV, representing a prevalence of at least 8.5 cases per 1000 population. All cases were identified as West African clade. The characteristics of the 25 cases are shown in Table 1.

Received 1 August 2022; editorial decision 17 October 2022; accepted 18 October 2022; published online 19 October 2022

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https://doi.org/10.1093/ofid/ofac557

Table 1. Characteristics of 25 MSM PWH With Human Monkeypox Virus Infection

	Patients, No. (%)
Age[a]	39.5 (33–46)
Years of HIV infection[a]	11 (9–13)
Prior AIDS	3 (12)
Years on ART[a]	9 (6–115)
Current ART regimen	
TAF/FTC/BIC	17 (68)
DTG/3TC	5 (20)
TAF/FTC//RPV	2 (8)
DRV/c + DTG	1 (4)
CD4 count, cells/mL[a]	630 (4815–923)
Reported clinical features	
Rash or skin lesions	25 (100)
Fever	14 (56)
General malaise	12 (48)
Lymphadenopathy	21 (84)
Pharyngitis	5 (20)
Myalgias	4 (16)
Proctitis or anorectal pain	13 (52)
Distribution of lesions	
Genital/perianal	14 (56)
Trunk	12 (48)
Face	10 (40)
Arms	10 (40)
Hands	5 (20)
Oral	3 (12)
Monkeypox viral DNA detected, positive/total No. (%)	
Skin/genital skin	20/22 (91)
Rectum	9/10 (90)
Oral mucosa	3/3 (100)
Pharynx	3/4 (75)
Concomitant STI[b]	6 (24)
Chlamydia trachomatis	4
Neisseria gonorrhoeae	2
Lymphogranuloma venereum	1
HSV-1	1
Syphilis	1
Documented smallpox vaccination	
Yes	5 (20)
No	9 (36)
Unknown	11 (44)
Duration of lesions, d[a]	8 (6.5–11)

Abbreviations: ART, antiretroviral treatment; DRV/c + DTG, darunavir/cobicistat plus dolutegravir; DTG/3TC, dolutegravir plus lamivudine; HSV-1, herpes simplex virus 1; LGV, lymphogranuloma venereum; MSM, men who have sex with men; PWH, people with HIV; STI, sexually transmitted infection; TAF/FTC/BIC, tenofovir alafenamide plus emtricitabine plus bictegravir; TAF/FTC/RPV, tenofovir alafenamide plus emtricitabine plus rilpivirine.

[a]Median (interquartile range).

[b]Coinfection with *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in 2 patients and *Chlamydia trachomatis* alone in 2 patients (1 resulted LGV).

All patients were MSM with a median age of 39.5 years. All were receiving antiretroviral treatment, had undetectable plasma viral loads, and their median CD4 count was 630 cells/mm^3. Most patients (76%) presented with prodromic symptoms, mainly consisting of fever, general malaise, and pharyngitis. Lymphadenopathy was a prominent finding in 84% of the patients. Of particular note, proctitis was present in 52% of the patients, in most cases (76%) with no other concomitant sexually transmitted infections. Symptoms of proctitis were predominantly local, including perianal pain, tenesmus, and rectal bleeding. Skin lesions, presented in all patients, progressed from macules to a pustular appearance with an umbilicated necrotic center and an erythematous halo. In our series, we did not observe major changes in terms of the distribution or characteristics of the lesions among patients. The genital and perianal areas were involved in 56% of cases.

MPXV DNA was detected in all patients, usually in >1 clinical specimen. Swabs from cutaneous lesions were positive in all but 2 patients, who were diagnosed by rectal samples. Of interest, MPXV was found in rectal swabs from 9 of 10 (90%) patients with proctitis. Five out of twenty-five presented with pharyngitis or odynophagia, 4 of whom were tested, and 3 were positive for MPXV. No treatment with tecovirimat was given to any of the patients.

Smallpox vaccination was confirmed in 5 of 14 cases (36%) with available information. None of the patients required hospitalization, and resolution was complete, with a median duration of symptoms of 8 days.

DISCUSSION

We describe the clinical course and microbiological findings for 25 PWH with MPXV coinfection. Clinical outcomes in this case series were reassuring. Most cases were mild and self-limited, and there were no hospitalizations or deaths. Sexual activity among this cohort of men who have sex with men was the most frequently suspected route of transmission, as evidenced by frequent detection of MPXV in rectal swabs (or genital, anal, and oral mucosal lesions).

The clinical course of monkeypox was initially described in individual cases and outbreaks of the disease in endemic countries and has been characterized by the development, after a prodromal period of systemic symptoms (fever, malaise, headache), of a monophasic vesiculopustular rash, which allows MPXV to be differentiated from other diseases such as chickenpox. Some differences have been observed in descriptions of the condition in the ongoing outbreak among MSM. Prodromal phase is sometimes absent with mucocutaneous rash as first manifestation. The rash is multiphasic, with lesions in various stages; it evolves more frequently the genital area, accompanied by lymphadenopathy. More than half of the patients reported symptoms of proctitis, including tenesmus, pain, and rectal bleeding. Our observations confirm these peculiarities and add rectal involvement as a prominent finding.

In our series, the diagnosis of monkeypox was most commonly confirmed from swab specimens taken from skin or genital lesions, with pharyngeal and rectal swab specimens being

less commonly tested. Anal or rectal swabs should be considered for those presenting with anal pain or proctitis. MPXV was detected in the rectal swabs in 36% of our patients and in 90% of those who had samples sent to the laboratory. Of note, MPXV was the only possible STI detected in rectal swabs from 5 out of 9 patients with evidence of MPXV proctitis.

The clinical outcomes of the disease were uniformly self-limiting in all of our patients. We did not detect significant systemic or local complications except rectal pain, which in some cases required prolonged analgesia. No patient required hospitalization. Our results are similar to those of a German cohort: Most PWH had good immunovirological status, and the course of the MPXV infection did not differ between MSM with and without HIV infection, with very low hospitalization rates [4]. In contrast, risk for hospitalization and more severe complications has recently been reported among PWH [3]. In an HMPX outbreak in 8 US jurisdictions, PWH with HMPX were more commonly hospitalized than persons without HIV infection (8% vs 3%) [15]. Previous reports have pointed out a higher rate of complications and mortality associated with factors such as young age (children) and viral clade (the Central Africa clade causing more severe disease than the West Africa clade) [16]. Interestingly, shotgun metagenomics allowed for the rapid reconstruction and phylogenomic characterization of the first MPXV outbreak genome sequences, showing that this MPXV belongs to clade 3 and that the outbreak most likely has a single origin [17]. In contrast to our observations, coinfection with HIV was found to be a contributory factor to the clinical course in Nigeria [11]. These differences could be explained by the control of HIV infection by ART. While in our case all patients were receiving ART with a good immunovirological status, most patients were not receiving ART in the report from Nigeria and had a detectable viral load and a low CD4 T-lymphocyte count. It may be possible, then, that advanced or uncontrolled HIV infection could lead to more severe outcomes.

Sexual activity among this cohort of men who have sex with men was the most frequently suspected route of transmission, as evidenced by frequent detection of MPXV in genital mucosal lesions. The detection of MPXV in rectal samples could explain our clinical findings, suggesting the presence of mucosal lesions caused by the virus. In the current outbreak, genital lesions are far more frequently reported than in prior studies with classical transmission from animals [18]. In addition, high rates of concomitant STIs and frequent anogenital symptoms suggest transmission through local inoculation during sexual contact. Furthermore, a previous study reported transmission of the vaccinia virus after sexual contact with a smallpox vaccinee, with a presentation similar to what is being seen in the current outbreak [19]. MPVX has been detected in genital, anal samples, and DNA was found to be positive in the seminal fluid of monkeypox patients in recent reports, with cycle threshold values in the range of those measured in their nasopharyngeal swabs [20]. Moreover, viable MPXV has been detected in culture among PCR-positive anal swabs and PCR-positive urethral swabs, which also could indicate the possibility of MPXV transmission via the sexual route [21].

The current outbreak is disproportionately affecting gay, bisexual, and other men who have sex with men; this is consistent with data reported from other countries. Public health efforts to slow monkeypox transmission among gay, bisexual, and other men who have sex with men require addressing challenges that include homophobia, stigma, and discrimination.

Several limitations must be addressed. Our findings cannot be considered definitive evidence of infectivity. Many other viruses causing viremia can be found in semen, with no direct evidence of sexual transmission, but efficiency in terms of transmission cannot be ruled out. Also, the study only includes PWH well controlled on effective ART in a single hospital, and low study subject numbers limit generalization.

In conclusion, this series of prospectively followed cases of MPXV in PWH reveals some particular clinical characteristics and the lack of influence of HIV on outcomes. Possible sexual transmission should be confirmed in further studies.

Acknowledgments

Financial support. M.J.V.-G. is supported by a grant from the Instituto de Salud Carlos III (Contratos Juan Rodés, JR19/00031).

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Patient consent. The data collection and the report were approved by the Hospital Ramón y Cajal Ethics Committee. Informed oral consent was obtained from all participants and recorded in the clinical history.

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