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Do not forget mpox!

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Dear Editor,

In 2022, a novel outbreak of mpox (formerly known as monkeypox) emerged globally, showing no apparent link to travel to regions with high endemicity. Surprisingly, the disease manifested as a sexually transmitted infection, primarily affecting men who have sex with men (MSM) and people living with HIV (PLWH). Having multiple sexual partners emerged as a significant risk factor for contracting the disease, and the human mpox virus was isolated in seminal fluid [1]. This new manifestation of mpox presented with distinct clinical features not typically seen in previous monkeypox cases. Clinical presentations included penile edema, proctitis, and lymphadenopathy, often with few or no characteristic pustular lesions. Moreover, severe cases resulting in multiorgan involvement and fatalities were documented [2]. Mpox cases declined after the peak in the summer of 2022, but a consistently low level of cases occurred since then. However, in the United States, there were higher caseloads in 2024 compared to 2023, mainly involving people who were not vaccinated or had only received one dose of JYNNEOS [3,4]. In addition, the circulation of the mpox virus in asymptomatic or paucisymptomatic forms would be responsible for the missed diagnoses and therefore for an underestimation of the real number of cases. In Italy, a few cases (n = 53) were reported from January until May 24, 2024 [3]. Here, we present an interesting case of mpox with lymphogranuloma-like presentation, involving a 54-year-old MSM with HIV infection and a history of ulcerative colitis treated with infliximab, an anti-tumor necrosis factor-α. He was compliant with antiretroviral therapy. $CD4^+$ T-cell count was 831 cells/μl and HIV viral load was 20 copies/ml. He had his last unprotected sexual intercourse with an Italian casual sexual partner, whom the patient described as healthy, about 45 days before presenting to our unit. Eleven days before the presentation, he noticed the appearance of an inguinal vesicle near the base of the penis and in a few days, he developed a purulent bleeding urethritis. Vesicular lesions were initially asymptomatic but had become painful in a few days. The right inguinal lymph nodes were tender and swollen, and penile edema occurred (Fig. 1). Simultaneously, he complained of rectal bleeding that was believed to be related to the exacerbation of ulcerative colitis. He took levofloxacin and brought forward the appointment for the administration of infliximab. The vesicle has enlarged and ulcerated, and a few new vesicles had appeared. Fortunately, in May 2024, before the scheduled infliximab infusion, he was evaluated in our infectious disease unit. The clinical presentation seemed to be compatible with lymphogranuloma venereum (LGV) because of proctitis and the right painful lymphadenopathies. He denied travel in the last 6 months and reported the same for his casual sexual partner. However, the presence of 4 ulcers, 2 inguinal and 2 on the glans, and penile edema raised the suspicion of mpox. The chemistry examination was remarkable for the C-reactive protein increase (36.8 mg/l, normal <5), mild anemia (11.2 g/dl, normal 12–16 g/dl), and elevated white blood cell count (14,490 cell/μl, normal 4000–11000) with a normal leukocyte formula. Urethral, anal, and ulcer swabs were collected. Analyses for sexually transmitted infections by polymerase chain reaction (PCR) showed negative results for *Chlamydia trachomatis*, *Treponema pallidum*, *Neisseria gonorrhoeae*, and herpes simplex virus. Skin lesions, urethral and rectal swabs tested positive for mpox virus by real-time non-variola *Orthopoxvirus* PCR (cycle threshold [Ct] = 20 on the swab of the inguinal ulcer, Ct = 24.04 on the rectal swab, Ct = 20 on the urethral swab), while the result was negative in the blood. Syphilis serology showed positive results with a rapid plasma reagin of 1:8. Unfortunately, tecovirimat and other antivirals were non-available, and the patient was managed in the outpatient setting. Doxycycline 100 mg twice daily was ordered for 4 weeks because of penicillin allergy. After a week, urethritis and proctitis improved, as did the ulcerative lesions, which healed all but one. Urethral and rectal swabs were negative for mpox, while the swab of inguinal ulcerative lesion persisted positive with a low viral load (ct = 30.69). The patient achieved full recovery within two weeks under close monitoring. This case underscores key aspects of mpox, focusing on its transmission, clinical presentation, and differential diagnosis. Transmission likely occurred through an asymptomatic carrier, and neither the patient nor his casual sexual partner had traveled in the previous six months, suggesting the endemicity of the virus in our country. However, we did not evaluate the occasional sexual partner, and we cannot exclude that he had symptoms so mild that they were not noticeable to his partner. The patient exhibited only four skin lesions, with bleeding proctitis, lymphadenopathies, and bleeding

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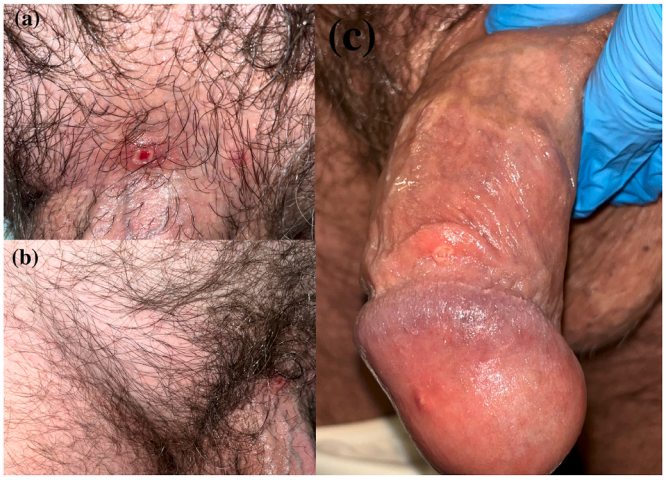

Fig. 1. (a) and (c) ulcerative lesions on groin and penis; (b) right lymphadenopathies.

urethritis as the primary disorders. Differential diagnosis with LGV proved challenging, as previously reported [5] and failure to recognize the infection could have led to a fatal outcome following the administration of infliximab in the present case. Vesicles are not typical manifestations of LGV, which usually presents as a single asymptomatic self-resolving ulcer, accompanied by lymphadenopathies and proctitis. Additionally, the emergence of penile edema, a novel manifestation of current mpox, and disease progression during levofloxacin treatment heightened suspicion of mpox. Vesicles and ulcers are also typical of herpes simplex virus, but in the latter, the lesions are usually more numerous and grouped in clusters [6]. Complicating the differential diagnosis in this case was the patient's history of ulcerative colitis, which led the patient to overlook the proctitis, attributing it to their existing condition. Further management challenges for mpox include limited accessibility to tecovirimat, cidofovir, or brincidofovir in Italy. In conclusion, despite a reduction in mpox cases, vigilance must be maintained, particularly in cases resembling ours. The true burden of mpox infection may be underestimated due to asymptomatic or paucisymptomatic circulation and manifestations with few vesicular lesions. Therefore, screening efforts should prioritize high-risk groups such as MSM and PLWH. High suspicion for mpox should be maintained in all patients presenting with proctitis, irrespective of the presence or absence of vesicles, or in cases resembling LGV. Incorporating mpox virus DNA research into available sexually transmitted infection molecular panels is warranted. Furthermore, vaccination should be promoted in high-risk individuals. Although infections among fully vaccinated persons can occur, two doses of the JYNNEOS vaccine were demonstrated to be efficacy in preventing many mpox cases and reducing the severity of symptoms in infected persons [7–9].

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CRediT authorship contribution statement

Luca Pipitò: Writing – original draft, Investigation, Conceptualization. **Marcello Trizzino:** Investigation. **Donatella Ferraro:** Investigation. **Cinzia Calà:** Investigation. **Giovanni Giammanco:** Investigation. **Antonio Cascio:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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