

# Human monkeypox coinfection with syphilis in an immunocompromised patient

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## Abstract

Monkeypox is a viral zoonosis from the Poxviridae family that spreads at an unprecedented rate. It is transmitted through contact with skin lesions, respiratory droplets, body fluids, and sexual contact. The diverse presentation of the disease leads to misdiagnosis. Thus, clinicians should have a high index of suspicion, mainly with diseases with skin lesions. The most vulnerable group to developing this disease are individuals with risky sexual relationships, sexually transmitted infections, or human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). To date, only one case of coinfection with the monkeypox virus, syphilis, and HIV has been reported; however, no cases have been revealed in the Mexican territory.

Herein we describe an unusual case of syphilis-monkeypox coinfection in an immunocompromised patient; despite his coinfection, he had a favorable prognosis. Furthermore, we attach allusive pictures of the natural evolution of dermatological lesions.

## Introduction

With the COVID-19 pandemic still ongoing, monkeypox (MPX) is emerging from what we knew as its niche, Africa. This recent viral zoonosis has quickly spread worldwide; since July 2022, the World Health Organization has recognized it as a public health emergency of international concern.<sup>1</sup> Data from January 1, 2022, to September 14, 2022, reveals 59,606 confirmed cases and 19 deaths reported worldwide. Regarding Mexico, 788 cases have been confirmed, and no deaths have been reported.<sup>2</sup> On May 8, 2022, Mexico confirmed the first case of MPX in its territory.<sup>3</sup>

Monkeypox is a DNA virus from the genus Orthopoxvirus family of Poxviridae that causes MPX infection.<sup>4</sup> Person-to-person transmission occurs through contact with skin lesions, respiratory droplets, body fluids, and sexual contact.<sup>5</sup> Due to the mode of transmission, the development of this disease is more likely in individuals with a sexually transmitted infection or human immunodeficiency virus or acquired immunodeficiency syndrome (HIV/AIDS).<sup>6</sup>

Here we report a case of MPX simultaneous with syphilis in an immunocompromised Mexican man. Additionally, we add allusive images of the natural evolution of dermatological lesions.

## Case Report

The case of a 32-year-old man, a native and resident of

Mexico City is here detailed. He has a history of occasional alcoholism since the age of 18, marijuana addiction, and intravenous use and inhalation of methamphetamine on multiple occasions for two years. HIV infection was diagnosed in March 2018 under antiretroviral therapy (ART) with Biktarvy (bictegravir/emtricitabine/tenofovir alafenamide) 50/200/25 mg daily with a good viro-immunological response (July 07<sup>th</sup>, 2022: CD4<sup>+</sup> lymphocyte 634 cell/ $\mu$ L, HIV-RNA <40 cp/mL). The patient has a surgical history of left inguinal lymph node resection in 2018 with a diagnosis of Kaposi's sarcoma without receiving chemotherapy treatment.

The current condition began on August 13, 2022; he complained of fever (38.5°C), asthenia, adynamia, night diaphoresis, holocranial headache, myalgia, and arthralgia. He reports that the previous weekend he had unprotected sexual relations with men (MSM) with three different people without knowing their health status. Subsequently, three weeks later, generalized dermatoses in the scrotum composed of papules and pustules appeared; therefore, the patient decided to consult a primary care physician who, due to syphilis suspicion, managed him with benzathine penicillin without improvement. Days later, the patient decided to spread betamethasone cream to dermatological lesions, presenting a worsening of the lesions, progression with the appearance of new lesions, and dissemination in upper extremities, palms of the hands with characteristics of umbilicated papules, and papules with a necrotic center, for which he attended to a tertiary care hospital. The clinical course of the lesions is represented in Figures 1-3. On August 17, 2022, the monkeypox real-time-polymerase chain reaction (RT-PCR) test was taken on suspicion of MPX, and the laboratory test is represented in Table 1.

He presented fever and crusted lesions with irregular edges, mainly on the upper and lower limbs and the scrotum, papular-type lesions on the knees without erythema, and no palpable lymph nodes. Vital signs reported the following parameters: blood pressure 110/68 mmHg, pulse rate 70/min, respiratory rate 20/min, oxygen saturation 97% on ambient air. The patient was kept in isolation and under airborne precautions. On August 20, 2022, MPX infection was confirmed by RT-PCR assays for orthopox and monkeypox viruses of samples taken from skin lesions and remained in isolation at home for two weeks. Syphilis infection was also confirmed by the venereal disease research laboratory test 1:16 positive, therefore, the conventional treatment continued.

The evolution was towards skin lesions with necrotic crust on the upper and lower extremities, genitals, knees, back, and feet. He did not present further complications and showed clinical improvement.

## Discussion

This case illustrates an MPX coinfection with syphilis in an immunocompromised patient. Syphilis lesions made a timely diagnosis of MPX difficult. The clinical presentation of our patient who started with syphilis lesions was confusing when establishing an accurate diagnosis. Both diseases are sexually transmitted, and there is a risk of acquiring both in risky practices. In London, Girometti *et al.* showed that, in 54 confirmed cases of MPX, 24% presented lesions consistent with primary syphilis, and 24% were living with HIV.<sup>7</sup> The cases are usually self-limited, and a large part of patients only need isolation at home, a course we exemplified.<sup>8</sup> The coexistence of MPX and poorly controlled HIV infection is related to severity. De Sousa *et al.* present the case of a patient with newly diagnosed HIV infection and MPX with exu-

berant perianal lesions.<sup>9</sup> Unlike our patient, who had adequate adherence to his antiretrovirals, a good viro-immunological response. There were no complications that require hospitalization.

Our case exemplifies the natural history of the disease. The incubation period for the disease is 4-21 days, typically with 1-5 days of fever, chills, headaches, fatigue, myalgia, sore throat, and a rash that lasts 2-4 weeks. The rash first appears as macules (1-2 days), then develops into papules (1-2 days), followed by vesicles (1-2 days), and finally pea-sized pustules with umbilication or blisters (5-7 days) (1-2 mm in diameter), before the formation of scabs with eventual fall. The lesions are frequently located in the mouth, face, hands, feet, genitals, and eyes.<sup>10</sup>

The approach to this disease must include a wide range of differential diagnoses that simulate its presentation, such as syphilis, disseminated gonorrhea, herpes simplex, lymphogranuloma venereum, molluscum contagiosum, disseminated cryptococcosis, hepatitis, and exanthematous diseases.<sup>11</sup>

Concurrent HIV with MPX disease usually has a good evolution in people with undetectable viral load and high CD4<sup>+</sup> count on ART.<sup>6</sup> Recently, in the Czech Republic, the case of a patient with HIV and simultaneous syphilis in MPX infection was published. However, the presentation was different since he had tonsillar and perianal lesions.<sup>12</sup> On the other hand, contact tracing represents a challenge for the health system because many patients have sexual relations with multiple anonymous people, as is the case of our patient, which limits stopping the spread of the disease.

**Table 1.** Laboratory test.

Lab test	Results	Reference range
Hemoglobin, 10 <sup>6</sup> / $\mu$ L	12.4	12.2-18.1
Platelets, 10 <sup>3</sup> / $\mu$ L	255	142-424
Leukocytes, 10 <sup>3</sup> / $\mu$ L	6.0	4.6-10.2
Lymphocytes, 10 <sup>3</sup> / $\mu$ L	2	0.60-3.40
Neutrophils, 10 <sup>3</sup> / $\mu$ L	3.34	2.00-6.9
ESR, mm/hr	36	0-22
Glucose, mg/dL	92	70-109
Urea, mg/dL	49	15-38
BUN, mg/dL	23	7.8-18
Creatinine, mg/dL	0.81	0.60-1.30
Torch profile		
Cytomegalovirus IgG, AU/mL	188.1	$\geq$ 6.0
Cytomegalovirus IgM, index	0.68	$\geq$ 1.0
Rubella IgG, IU/mL	33.60	$\geq$ 10
Rubella IgM, index	0.15	$\geq$ 1.6
Lymphocyte subpopulation		
CD4, %	29	23.75-44.73
CD4, cell/ $\mu$ L	593.4	372-1305
CD8, %	38.9	14.03-37.53
CD8, cell/ $\mu$ L	795.5	217-1042
CD3, %	69.5	50.32-74.57
CD3, cell/ $\mu$ L	1420.5	762-2288
Ratio CD4/CD8	0.75	0.75-2.51
Ab HCV	13.69	$\geq$ 1.0
PCR HIV quantitative, copy/mL	<40	40-100 $\times$ 10 <sup>6</sup>
Ab herpes I (IgG)	4.8	Reactive $\geq$ 1.0
Ab herpes II (IgG)	79.78	Reactive $\geq$ 1.0
VDRL	Positive 1:16	Negative

ESR, erythrocyte sedimentation rate; BUN, blood urea nitrogen; IgM, immunoglobulin M; IgG, immunoglobulin G; Anti HCV, hepatitis C antibody; PCR HIV, polymerase chain reaction for human immunodeficiency virus; Ab, antibody; VDRL, venereal disease research laboratory.



**Figure 1.** Evolution of dermatological lesions on the back and thumb of the left hand. A) Day 1: papular lesions on the back of the left hand; B) Day 5: two umbilicated vesicle lesions on the back of the left hand; C-D) Day 10: umbilicated pustular lesions with central hematic crust on the back of the left hand; E) Day 5: topical steroid-damaged lesions dermatosis localized in left thumb with an erythematous base; F) Day 6: dermatological lesions on the left thumb; G) Day 8: dermatological lesions on the left thumb; H) Day 10: dermatological lesions on the left thumb.



**Figure 2.** Evolution of dermatological lesions on the left hand's forearm and palm. A-C) Day 6: umbilicated vesicle lesions on the left forearm; D) Day 10: umbilicated pustular lesion with central hematic crust on the left forearm; E) Day 3: a macular lesion with an erythematous base and nascent pustule in the palm of the left hand; F) Day 6: umbilicated vesicle lesion in the palm of the left hand; G-H) Day 10: an umbilicated pustular lesion with central hematic crust in the palm of the left hand.



**Figure 3.** Evolution of genital lesions and other locations. A-B) Day 5: topical steroid-damaged lesions dermatosis localized in scrotum and base of the penis; C) Day 10: a crusted lesion in the scrotum and base of the penis; D) umbilicated pustular lesion with hematic crust on the right forearm; E) Lesion with a scabby imprint on the right arm; F) Umbilicated pustular lesion to the malleolus of the right foot.

In the same way, the similarity of the lesions represents a challenge for the clinician.<sup>13</sup> Currently, there is no vaccine or specific treatment for MPX. Management aims to prevent complications or bacterial superinfection of skin lesions, isolation of confirmed cases, and support measures. Tecovirimat is a promising drug for MPX; however, it is still in experimental studies, and the Food and Drug Administration has not approved its use.<sup>14</sup>

Self-medication without a confirmed diagnosis can lead to a worsening of the presentation. In Madrid, a patient resorted to empirical treatment with steroids or antibiotics with no dosage limit and worsened dermatological lesions presentation.<sup>15</sup>

## Conclusions

The diverse presentation of MPX leads to misdiagnosis; thus, clinicians should have a high index of suspicion. Young people suspected of having MPX with a history of MSM or HIV/AIDS should undergo tests to rule out sexually transmitted infections. Clinical practice guidelines are required to unify the management of this disease.

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