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Travel Medicine and Infectious Disease 50 (2022) 102455

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: www.elsevier.com/locate/tmaid

Monkeypox, severe hepatitis A, and syphilis in an HIV returning traveler from Spain to Romania

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ARTICLE INFO

Keywords:
Men having sex with men (MSM)
HIV
Monkeypox
Hepatitis A
Syphilis

Dear Editor,

Outbreaks of monkeypox were described in non-endemic areas starting in May 2022, mainly in men who have sex with men (MSM). Since June 2022, a total of 36 cases of monkeypox (MPX) were reported in Romania [1].

We describe a case of a 30-year-old MSM living with HIV who was admitted to the hospital for an acute onset of fever (38.6° C), malaise, nausea, loss of appetite, and jaundice, recently after he returned from Spain (where he traveled for one week, between 9 and 16 of July, in Palma de Mallorca and Barcelona). He admitted having unprotected sexual contact with 3 different partners in the previous month and travel history in Spain 2 weeks before the onset of the symptoms. He was diagnosed with HIV infection and severe immunosuppression in 2015 (nadir CD4 cell count of 121 cells/μL) and was on ART with tenofovir/lamivudine and dolutegravir.

Medical history revealed that within a week after returning from Spain, he initially developed a slightly itchy generalized macular rash, with remission after 2 days of 16 mg methylprednisolone. A few days later he noticed the presence of vesiculopustular lesions in the anogenital area, with progressive dissemination to the trunk, face, ear flap, limbs, and oral mucosa (a total of 10 lesions).

Physical examination at admission revealed jaundice, moderate hepatomegaly, inguinal and axillar lymphadenopathy, vesiculopustular lesions in the anogenital and lumbar area, on the limbs, palms, soles, and a few painful ulcerated lesions on the palatine mucosa. (Fig. 1).

Laboratory findings showed increased liver enzymes and bilirubin levels, a slight increase in C reactive protein (Table 1), positive IgM anti HAV, and positive serology for acute syphilis. Monkeypox virus DNA was detected by PCR with lower cycle threshold (Ct) values in skin lesions (Ct 17.4) and slightly higher in nasopharyngeal swabs (Ct 24.1).

Serological markers were negative for HBV, HCV, CMV, and EBV. CD4 cell count was 936 cells/μL), and HIV viral load was detectable (2820 copies/mL) as the patient mentioned some adherence problems.

He was treated with intravenous glucose and arginine, but in the first days of admission the clinical status worsened, and the patient complained of fever, abdominal pain, lack of appetite, and sleep disturbances. Prothrombin time decreased to 41%, and there was a marked increase in the levels of liver enzymes and bilirubin. Treatment with dexamethasone 8 mg/day (for 5 days), vitamin K and fresh frozen plasma was added and ART was stopped for 1 week due to liver failure. The abdominal ultrasound showed no abnormalities.

The patient was discharged after 2 weeks, with improved clinical status, no signs of encephalopathy or hemorrhagic manifestations, but with the persistence of jaundice and sleep disturbances. All MPX skin lesions evolved to crusted forms. He received a prescription with benzathine benzylpenicillin 2.4 MU/weekly for 3 weeks for the treatment of

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https://doi.org/10.1016/j.tmaid.2022.102455
Received 31 August 2022; Accepted 5 September 2022
Available online 9 September 2022

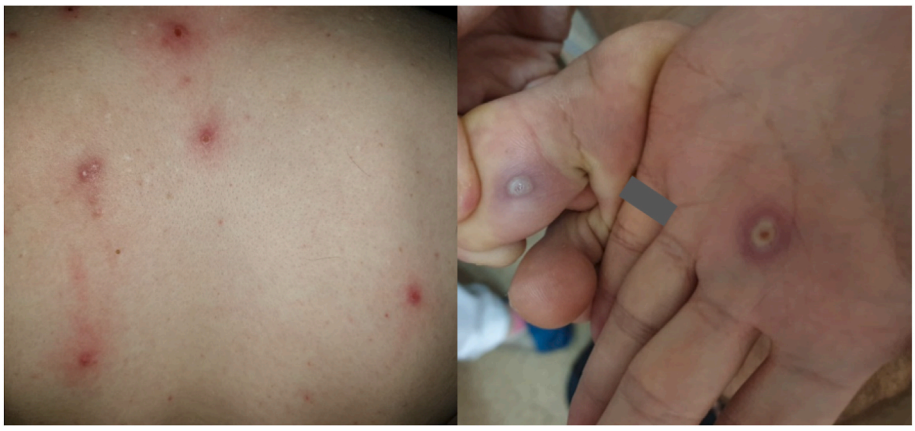

Fig. 1. Vesiculopustular lesions on the trunk (left) and the palms and soles (right).

Table 1
Evolution of the laboratory findings in a HIV infected patient with HAV and monkeypox.

Day of hospitalization/Lab screen	1	3	5	6	7	8	9	10	11
ALAT (U/L)	438	2038	3908	3750	3799	3072	2555	2004	1478
ASAT (U/L)	297	1572	2802	3851	1856	1068	601	–	211
Direct bilirubin (mg/dL)	4,2	7,70	9,20	10,97	10,79	12,20	13,35	13,71	12,22
Total bilirubin (mg/dL)	5,3	8,32	10,20	13,13	12,57	14,46	16,17	16,66	14,51
Prothrombin time (%)	–	78	56	56	41	42	47	53	55
C-reactive protein (mg/dL)	–	2,54	2,83	–	–	1,47	1,08	–	0,58

syphilis. Three weeks after discharge MPX virus was still detected in nasopharyngeal swabs (Ct 39).

In the first 6 months of the current year, we noticed an increase in the number of MSM diagnosed with acute Hepatitis A (HAV) and sexual fecal-oral route of transmission. In the same period, we started to diagnose the first cases of monkeypox in high-risk groups [2]. HAV is usually a mild disease and a severe/fulminant outcome is extremely rare. The incidence of HAV infections in developed countries is rare, being reported most often in older adults, due to a lack of acquired immunity during childhood [3,4]. Because adolescents and adults have a more robust immunological system, hepatic impairment may be more severe. In the developed world, HVA is transmitted more often by sexual route, particularly in MSM [4,5].

From the beginning of the year, 35 young MSM (median age 30 years) were diagnosed in our clinic with mild/moderate forms of HAV, with no significant differences in clinical outcomes between HIV-positive and negative patients.

However, this is, to our knowledge the first reported case of a patient living with HIV diagnosed simultaneously with monkeypox, hepatitis A and syphilis. We suspect that the patient acquired HAV and syphilis through sexual contact, before traveling to Spain, and MPX after his return, as he admitted continuing to have high-risk sexual behaviors and unprotected sex, with occasional partners.

We also suspect that monkeypox may also affect the liver by either direct (undescribed) or indirect mechanisms (e.g., immunological, not yet defined) and this may be the reason why this severe form was noticed in our patient. If this is the case, we will probably see more severe forms of hepatitis in other patients coinfected with MPX - HAV (or other hepatitis). Information on the increase in liver enzymes in patients with monkeypox infection is scarce, with few reports that mention mild-to-moderate increases in transaminases [6]. The treatment with corticosteroids remains controversial in acute hepatitis, but because of the immune mechanism involved in the destruction of hepatocytes, it may have a beneficial role in some cases.

The significance of this report is to highlight the importance of screening for sexually transmitted infections in key populations and to raise awareness of the risk of more severe and/or prolonged forms of hepatitis A in patients diagnosed simultaneously with monkeypox.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author's contributions

We consider that all authors equally contributed on this manuscript.

Declaration of competing interest

Nothing to declare.

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