Case Report

Coinfection of monkeypox virus and HIV-1 in a severely immunosuppressed patient: a catastrophic outcome

Coinfecção de vírus monkeypox e HIV-1 em paciente gravemente imunossuprimido: uma evolução catastrófica

Luana Vasconcelos Freitas[1]*
Gabriela Queiroz Fontes[1]
Ivana de Oliveira Cotrim[1]*
Wladimir Queiroz[1]
Giselle Burlamaqui Klautau[1]

[1] Instituto de Infectologia Emílio Ribas - São Paulo - SP - Brazil

Submitted: 31 October 2023
Accepted: 31 December 2023
Published: 27 February 2024

***Corresponding Author:**
Luana Vasconcelos Freitas
E-mail: luanavasconcelosfreitas@gmail.com

DOI: 10.5935/2764-734X.e20231232-en

ABSTRACT

Monkeypox (mpox) is a disease caused by the monkeypox virus (MPXV). The first human case was recorded in 1970 and it's endemic to Central and West Africa, with few outbreaks reported outside the continent. In May 2022, an increase in the number of cases of the disease was observed worldwide, with a higher prevalence among homosexual men and proven transmission through direct contact, including sexual exposure. In this context, the association of mpox with sexually transmitted infections, such as HIV infection, was evidenced. The present case portrays the coinfection of MPXV and HIV-1 in a severely immunosuppressed patient, emphasizing the importance of the interaction of both infections in the clinical prognosis.

Headings: Monkeypox virus. HIV-1. AIDS-Related Opportunistic Infections. Case report.

RESUMO

A monkeypox (MPOX) é uma doença causada pelo vírus monkeypox (MPXV), endêmico desde 1970 na África Central e Ocidental, com poucos surtos relatados fora desse continente. Em maio de 2022, observou-se mundialmente um aumento no número de casos da doença, com maior prevalência em homens que fazem sexo com homens e comprovada transmissão através de contato direto, incluindo exposição sexual. Nesse contexto, evidenciou-se a associação da MPOX com infecções sexualmente transmissíveis, tal como a infecção pelo HIV. O caso apresentado retrata a coinfecção de MPXV e HIV-1 em paciente gravemente imunossuprimido, ressaltando a importância da interação de ambas as infecções no prognóstico clínico.

Descritores: Vírus da varíola dos macacos; HIV-1; Infecções oportunistas relacionadas com a aids; Relato de caso.

INTRODUCTION

Monkeypox (mpox), also known as human monkeypox or monkey smallpox, is caused by the monkeypox virus (MPXV) of the *Orthopoxvirus* genus and is similar to the human smallpox virus, clinically and taxonomically.[1] It was first described in the Republic of Congo in 1970, and since then, it has mainly affected socially vulnerable populations, spreading to central and western Africa, where it has become endemic.[2] Since 2003, when the first outbreak outside this region was reported, it has received the attention of health authorities because of the potential risk of spread to other continents.

In May 2022, numerous cases of mpox were reported outside the endemic region,[3] with a significant change in the epidemiological profile of the disease, which is now associated with homosexual men with recent high-risk sexual activity.[4,5] Thus, the way in which the disease is transmitted through sexual contact has been well described[6]; consequently, it has been associated with other sexually transmitted infections, with up to 50% of confirmed cases of mpox being coinfected with the human immunodeficiency virus (HIV-1).[6,7]

We present a case report of a patient treated at a referral hospital for infectious diseases in São Paulo-SP, the Brazilian city with the highest number of confirmed cases of mpox.[8] The patient's unfavorable clinical outcome in a context of advanced immunodeficiency drew our attention because of the refractoriness to the proposed treatments, the prolonged time of disease activity, and a possible correlation with immune reconstitution syndrome.

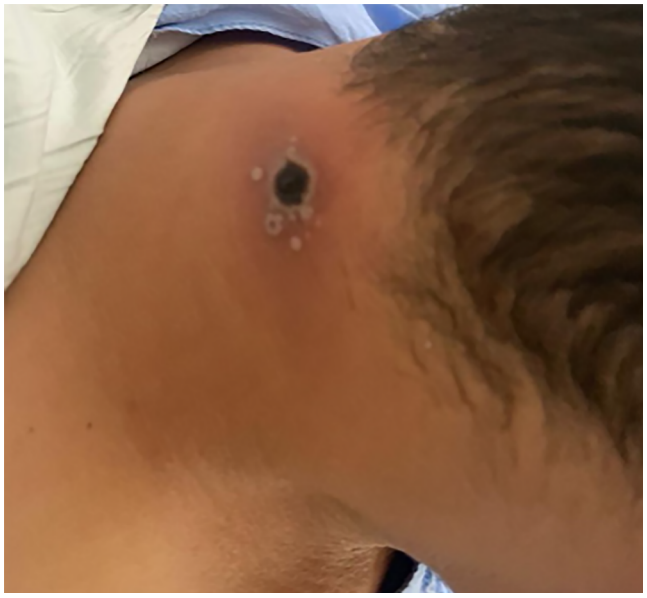

Figure 1. Initial mpox lesion in the posterior cervical region of the patient.

CASE REPORT

A 26-year-old man presented in July 2022 with high fever (40 ºC), myalgia, and headache. After 1 week, there was an eruption of painful umbilical papules on the nape of the neck (Figure 1) and wrists, with progression to the upper limbs and anal region and the rapid appearance of vesicles and disseminated pustules. The patient went to the emergency room 15 days after the beginning of the prodromes, complaining of severe perianal pain; in this first consultation, samples of the lesional crusts were collected for the testing of MPXV via the polymerase chain reaction technique, which showed positive. The patient reported prior sexual activity with women and men, but denied recent exposure. He also had no previous history of travel. He had a history of AIDS diagnosed in 2016 and made irregular use of the antiretroviral regimen (lamivudine, tenofovir, and efavirenz). The tests showed severe immunosuppression ($CD4^+$ TL of 4 cells/mm^3 and HIV-1 viral load of 1,428,516 copies/mL). He also reported a history of multiple previous opportunistic infections, such as disseminated histoplasmosis, neurotuberculosis, and neurosyphilis, as well as motor sequelae and epilepsy secondary to neurotoxoplasmosis, controlled with valproic acid. However, he was discharged with guidance and prescription of symptomatic drugs.

Four weeks after the onset of the condition, the patient returned for care because of worsening and increased dissemination of the lesions, worsening of pain with proctitis and cellulitis in the perianal region (Figure 2A), and tongue involvement (Figure 3). This time, the patient was hospitalized, and broad-spectrum antibiotic therapy was initiated, but the cutaneous involvement worsened rapidly and progressively, with new daily eruptions and the appearance of central necrosis. There was also an increase in the extent of the intergluteal necrosis (Figure 2B), in addition to significant hardened penile edema causing extrinsic obstruction of the urethra, with the consequent need for an indwelling urinary catheter (Figure 4). There was a clinical suspicion of Fournier's syndrome; however, it was decided against the surgical manipulation of the lesions due to a lack of knowledge and fear of the behavior of mpox with this type of intervention, considering that there have been no reports or recommendations in the literature in this regard. Broad-spectrum antibiotic therapy, a combination of meropenem and vancomycin at the recommended doses, to control secondary bacterial infection was maintained for a long period, but there were no signs of clinical improvement even after >30 days of treatment. Pain control was also quite difficult in the patient, despite the use of high-dose opioids. Regarding HIV virological control, rescue was performed with high-potency antiretroviral therapy (ART) — lamivudine, 300 mg; tenofovir, 300 mg; dolutegravir, 50 mg; and darunavir, 600 mg (twice a day) with ritonavir booster, 100 mg. The patient presented a negative viral load after 1 month of ART, with a new $CD4^+$ TL count of 30 cells/mm^3.

The antiviral drug tecovirimat was made available by the Brazilian health authorities for the treatment of mpox at the end of August 2022,[9] and its first dose (600 mg every 12 h) could only be administered approximately 1.5 months after the onset of symptoms. The next day, the patient had a tonic–clonic seizure episode, probably because of the metabolic pathways shared between the

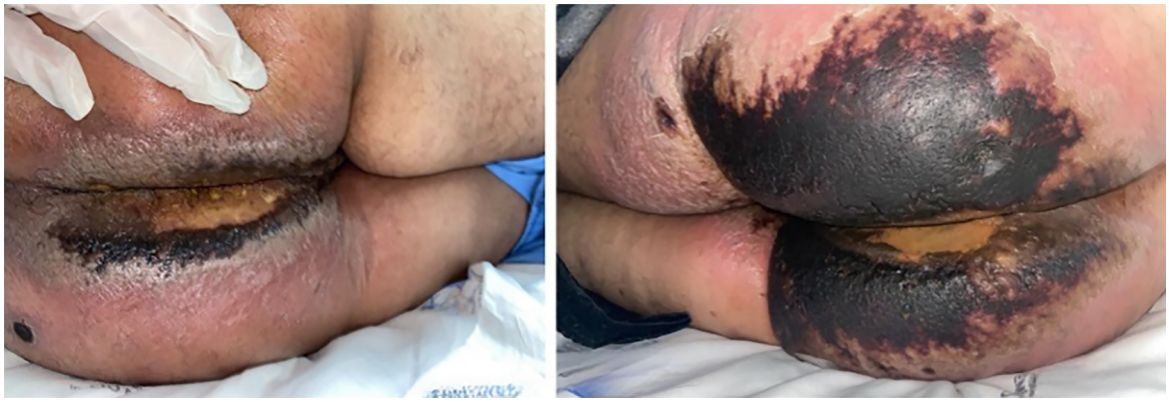

Figure 2. Evolution of mpox-associated perianal lesion in the first week of hospitalization(A) and after 4 weeks of hospitalization (B).

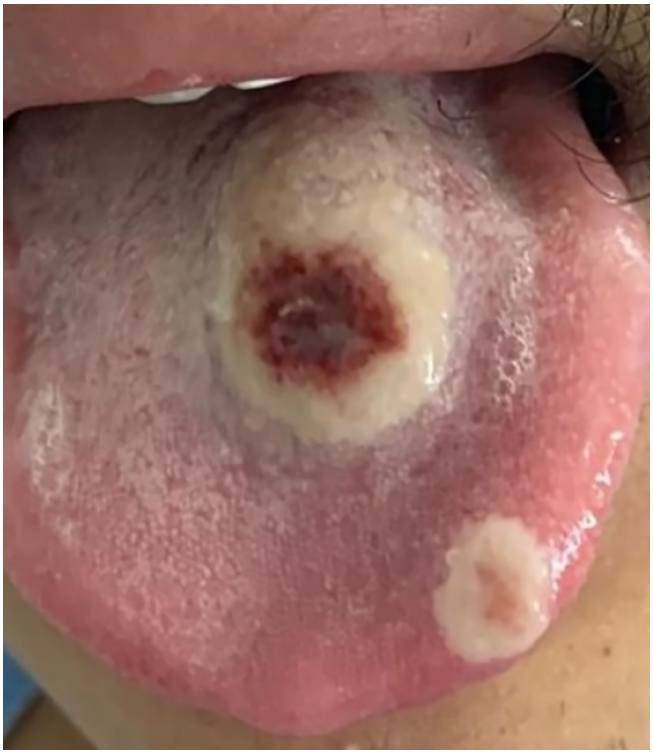

Figure 3. Mpox lesion on the tongue.

various medications he was using. The treatment of mpox, however, was prioritized and maintained, and dosage adjustments were made to the other medications and the anticonvulsant. The first 14 days of specific therapy did not show any evidence of remission or stabilization of the condition, while new daily lesions appeared on the skin, including at manipulation sites such as punctures for peripheral venous access and/or placement of adhesive dressings (Figure 5). Subsequently, tecovirimat cycle was repeated, but there was also no effective response.

At the beginning of the second month of hospitalization, the patient developed bronchospasm and progressive need for oxygen therapy. Chest computed tomography scans performed in this phase showed sparse nodular opacities in both lungs (Figure 6A). Subsequently, bronchoscopy was performed to elucidate the diagnosis of this pulmonary condition, considering the numerous diagnostic possibilities in the context of a person living with HIV/AIDS (PLWHA). Endoscopic inspection raised the suspicion of MPXV involvement in the respiratory mucosa (Figure 6B), which was later corroborated by the histopathological findings of endobronchial biopsies. During bronchoscopy, the patient had a cardiac arrest promptly reversed with cardiopulmonary resuscitation maneuvers, thus he was transferred under mechanical ventilation to the hospital's intensive care unit (ICU).

In October 2022, after about 3 months of the onset of the condition, 2 months of hospitalization, and almost 30 days in the ICU, the patient died. At the time of his death, he had multiple organic dysfunction - respiratory failure, kidney injury, bloodstream infection, and septic shock. Amid the aggravating factors and despite the treatments, new mpox lesions appeared even on the last day of his life.

DISCUSSION

The case presented assumes coinfection by two viral infections (HIV and MPXV) as a determining factor in the severity of the clinical presentation, evolution, and prognosis of the patient, possibly due to the immunological interaction resulting from the pathophysiology of the two diseases.[10,11] HIV-1-infected individuals without adequate virological control have a deficient T-cell response, both

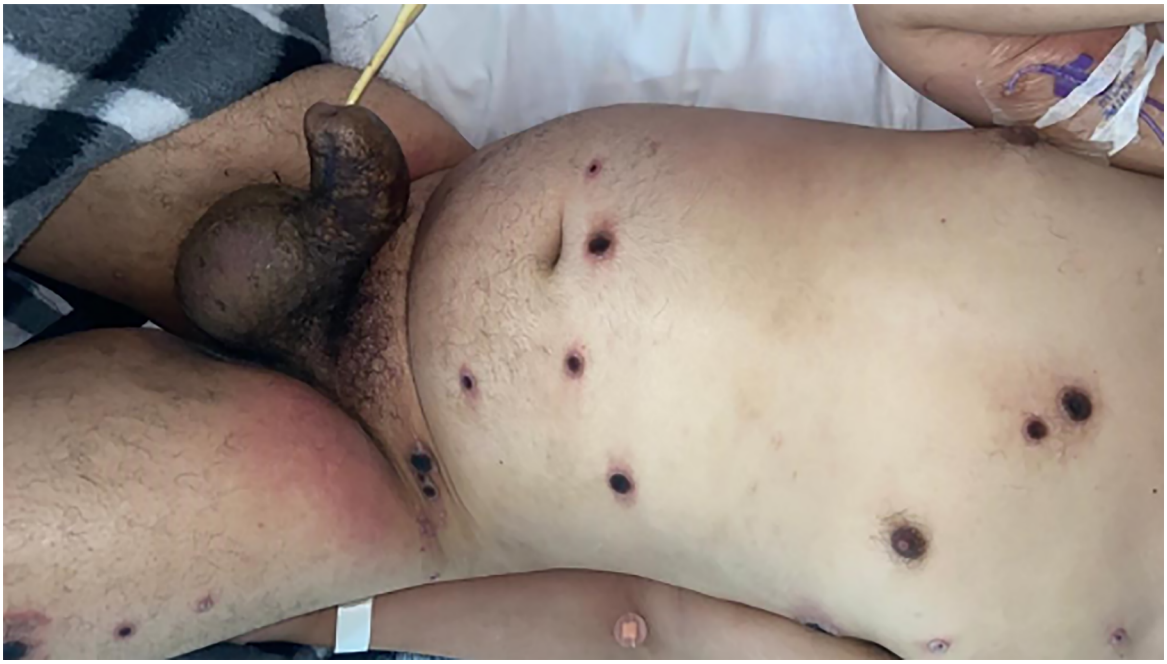

Figure 4. Mpox lesions disseminated throughout the body, associated with anasarca (second week of hospitalization).

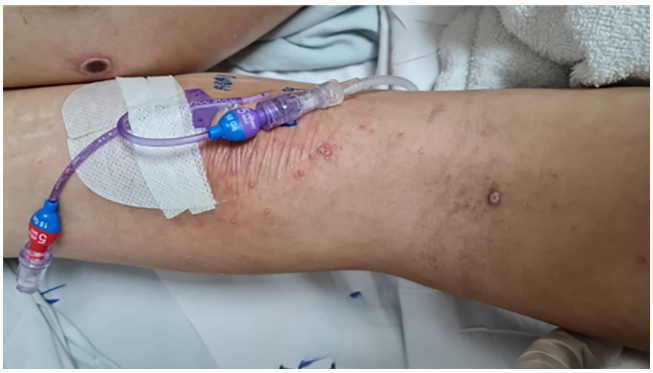

Figure 5. Pseudo-Koebner phenomenon: new mpox lesions appear after manipulation and invasion of the skin (venous access).

from a cellular and humoral perspective.[11] MPXV has the ability to evade the antiviral response by blocking the activation of TCD4+ and TCD8+ lymphocytes after their contact with infected antigenic cells, thus modulating the release of cytokines responsible for inhibiting viral replication.[12,13] The organization of immune response in coinfected patients is not well established, but other models of viral infection control, such as coinfection with hepatitis B, show that HIV-1 replication interferes with the immunological efficacy to combat these pathogens.[11]

Regarding the clinical presentation, some characteristics were observed in this case that had been little described in the literature, such as the appearance of isomorphic lesions at sites of invasion and manipulation of the skin, for example, after the insertion of venous accesses and the application of dressings, a phenomenon known as pseudo-Koebner's was observed.[14,15] Koebner's phenomenon is a dermatological sign described in psoriasis, involving the appearance of typical skin lesions in areas previously injured by mechanical, chemical, or biological agents; when it appears in a similar way in other diseases (including dermatoses caused by orthopoxviruses), it characterizes the pseudo-Koebner phenomenon.[14,15] This finding also justified the choice of the attending medical team to maintain a conservative approach in Fournier's syndrome (also little described as related to mpox), due to the risk of the surgical approach leaving extensive bloody areas and further aggravating the dissemination of the infectious condition.

At the time of this case, little was known in terms of scientific knowledge about the morbidity and lethality of mpox in PLWHA, particularly regarding the direct or indirect implications of the degree of immunosuppression and viral replication. Considering more recent scientific evidence, in patients diagnosed with mpox in a clinical context of $CD4^+$ TL count of <200 cells/μL, the progression to severe forms of the disease (including necrotic lesions, pulmonary involvement, secondary infection and sepsis) is more common than those whose count is >300 cells/μL.[16] All of the deaths in a retrospective worldwide series (which totaled 7% of the cases followed) occurred in patients classified in the first group with a count <200 cells/μL.[17] These data corroborate the definition of mpox as an opportunistic disease in PLWHA.

The severity of the present case is also directly related to the time of reintroduction of ART and the worsening

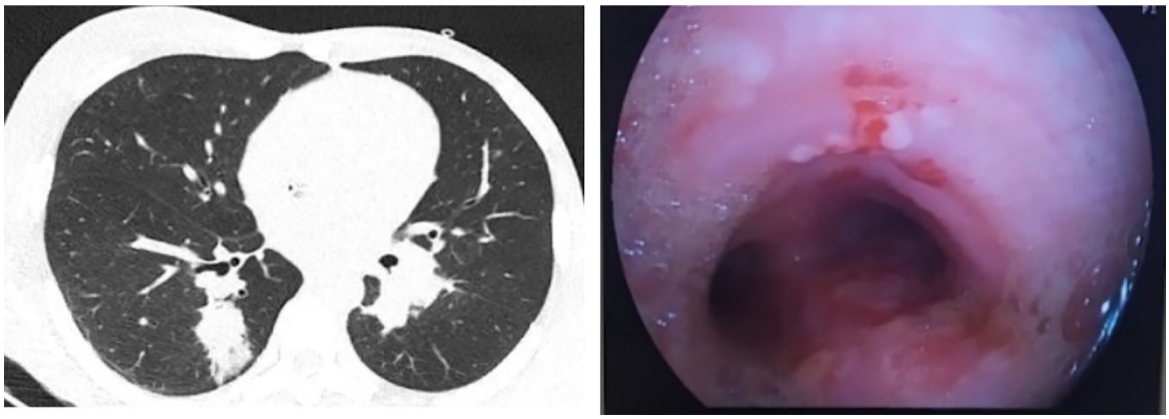

Figure 6. (A) Computed tomography scan of the chest showing nodular opacities in both lungs. (B) Endobronchial endoscopic imaging suspicious (confirmed by biopsy) of viral infection.

of symptoms after approximately 4 weeks, raising the suspicion that immune reconstitution syndrome (SIRS) influenced the clinical course of mpox. About 25% of the cases described in the literature in the second half of 2022 had suspected SIRS associated with mpox, 57% of which progressed to death.[16]

In instances of coinfection involving HIV and severe immunosuppression, uncertainties persist regarding the efficacy of specific antiviral treatments. Nevertheless, available literature suggests that the presence of HIV does not appear to influence the therapeutic response to tecovirimat.[18] Although, in our case, the time between the onset of symptoms and the introduction of the antiviral was longer than recommended, most patients with severe disease and severe immunosuppression had an unfavorable outcome. In a later analysis, drug-resistant strains have been identified.[16]

CONCLUSION

Although mpox is no longer a public health emergency in 2023, it is important to understand its behavior in PLWHA, particularly after it has been defined as a possible opportunistic disease. The present report aimed to describe a tragic case of this coinfection, highlighting elements that may be significant for the unfavorable evolution of the disease. The pseudo-Koebner phenomenon, for example, challenged some classical paradigms of the surgical approach to skin and soft tissue infections. On the other hand, the immune reconstitution caused by antiretroviral therapy must have had an impact on the immune modulation of mpox, with paradoxical response behavior. Meanwhile, the unsatisfactory clinical response to the specific antiviral carries some confounding factors due to its delayed onset, which in turn reinforces the need for early and optimized clinical management. Finally, the development of strong prevention strategies for this population should be reinforced.

""This case report deserved an official declaration of acknowledgement and ethical approval by its institution of origin and was peer-reviewed before publication, whilst the authors declare no fundings nor any conflicts of interest concerning this paper. It is noteworthy that case reports provide a valuable learning resource for the scientific community but should not be used in isolation to guide diagnostic or treatment choices in practical care or health policies.

REFERENCES

1. Petersen E, Kantele A, Koopmans M, Asogun D, Yinka-Ogunleye A, Ihekweazu C, et al. Human monkeypox: Epidemiologic and clinical characteristics, diagnosis, and prevention. Infect Dis Clin North Am. 2019; 33(4):1027-43. DOI: 10.1016/j.idc.2019.03.001
2. Gong Q, Wang C, Chuai X, Chiu S. Monkeypox virus: a re-emergent threat to humans. Virol Sin. 2022; 37(4):477-82. DOI: 10.1016/j.virs.2022.07.006
3. Kumar N, Acharya A, Gendelman HE, Byrareddy SN. The 2022 outbreak and the pathobiology of the monkeypox virus. J Autoimmun. 2022; 131:102855. DOI: 10.1016/j.jaut.2022.102855
4. Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, et al. Monkeypox virus infection in humans across 16 countries—April–June 2022. N Engl J Med. 2022; 387(8):679-91. DOI: 10.1056/NEJMoa2207323
5. Vusirikala A, Charles H, Balasegaram S, Macdonald N, Kumar D, Barker-Burnside C, et al. Epidemiology of early monkeypox virus transmission in sexual networks of gay and bisexual men, England, 2022. Emerg Infect Dis. 2022; 28(10):2082-6. DOI: 10.3201/eid2810.220960

6. Philpott D, Hughes CM, Alroy KA, Kerins JL, Pavlick J, Asbel L, et al. Epidemiologic and clinical characteristics of monkeypox cases—United States, May 17–July 22, 2022. MMWR Morb Mortal Wkly Rep. 2022 Aug 12;71(32):1018-22. DOI: 10.15585/mmwr.mm7132e3
7. León-Figueroa DA, Barboza JJ, Garcia-Vasquez EA, Bonilla-Aldana DK, Diaz-Torres M, Saldaña-Cumpa HM, et al. Epidemiological stuation of monkeypox transmission by possible sexual contact: A systematic review. Trop Med Infect Dis. 2022; 7(10):267. DOI: 10.3390/tropicalmed7100267
8. Ministério da Saúde (BR). Boletim Epidemiológico Especial: MPOX [Internet]. Brasília (DF): Ministério da Saúde; 2023; [acesso em 2023 Dec 22]. Disponível em: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/variola-dos-macacos/boletim-epidemiologico-de-monkeypox-no-24-coe-1
9. Ministério da Saúde (BR). Anvisa aprova liberação de medicamento para monkeypox para uso pelo Ministério da Saúde [Internet]. Brasília (DF): Ministério da Saúde; 2022; [acesso em 2023 Dec 22]. Disponível em: https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2022/anvisa-aprova-liberacao-do-medicamento-para-monkeypox-para-uso-pelo-ministerio-da-saude
10. Kaler J, Hussain A, Flores G, Kheiri S, Desrosiers D. Monkeypox: A comprehensive review of transmission, pathogenesis, and manifestation. Cureus. 2022; 14(7):e26531. DOI: 10.7759/cureus.26531
11. Geldmacher C, Koup RA. Pathogen-specific T cell depletion and reactivation of opportunistic pathogens in HIV infection. Trends Immunol. 2012; 33(5):207-14. DOI: 10.1016/j.it.2012.01.011
12. Hammarlund E, Dasgupta A, Pinilla C, Norori P, Früh K, Slifka MK. Monkeypox virus evades antiviral CD4+ and CD8+ T cell responses by suppressing cognate T cell activation. Proc Natl Acad Sci U S A. 2008; 105(38):14567-72. DOI: 10.1073/pnas.0800589105
13. Lum FM, Torres-Ruesta A, Tay MZ, Lin RTP, Lye DC, Rénia L, et al. Monkeypox: disease epidemiology, host immunity and clinical interventions. Nat Rev Immunol. 2022; 22(10):597-613. DOI: 10.1038/s41577-022-00775-4
14. Rubin AI, Stiller MJ. A listing of skin conditions exhibiting the koebner and pseudo-koebner phenomena with eliciting stimuli. J Cutan Med Surg. 2002; 6(1):29-34. DOI: 10.1007/s10227-001-0029-6
15. Joshi A, Rathi SK. Koebner phenomenon and pseudo-Koebner phenomenon due to disposable surgical masks in the Covid Era. Indian J Dermatol. 2022; 67(2):197-9. DOI: 10.4103/ijd.ijd_496_21
16. Ortiz-Saavedra B, Montes-Madariaga ES, Cabanillas-Ramirez C, Alva N, Ricardo-Martínez A, León-Figueroa DA, et al. Epidemiologic situation of HIV and monkeypox coinfection: A systematic review. Vaccines (Basel). 2023; 11(2):246. DOI: 10.3390/vaccines11020246
17. Mitjà O, Alemany A, Marks M, Lezama Mora JI, Rodríguez-Aldama JC, et al. Mpox in people with advanced HIV infection: A global case series. Lancet. 2023; 401(10380):939-49. DOI: 10.1016/S0140-6736(23)00273-8
18. McLean J, Stoeckle K, Huang S, Berardi J, Gray B, Glesby MJ, et al. Tecovirimat treatment of people with HIV during the 2022 mpox outbreak: A retrospective cohort study. Ann Intern Med. 2023; 176(5):642-8. DOI: 10.7326/M22-3132