Elsevier has created a Monkeypox Information Center in response to the declared public health emergency of international concern, with free information in English on the monkeypox virus. The Monkeypox Information Center is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its monkeypox related research that is available on the Monkeypox Information Center - including this research content - immediately available in publicly funded repositories, with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the Monkeypox Information Center remains active.

Travel Medicine and Infectious Disease 51 (2023) 102510

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

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

First reports of monkeypox and varicella-zoster virus coinfection in the global human monkeypox outbreak in 2022

Monkeypox (MPX) is a zoonotic virus closely related to smallpox responsible for the sudden increase in the number of MPX cases in humans in non-endemic countries during 2022. Most cases of disease in the current multi-country outbreak have been associated with sexual risk behaviors among men who have sex with men, with a higher prevalence of lesions in the anogenital region and oral mucosa due to skin-to-skin contact during unprotected sexual intercourse. Furthermore, it has been found that two out of every five individuals with MPX are living with HIV, and that the prevalence of concurrent sexually transmitted infections (STIs), such as syphilis, gonorrhea, and herpes simplex virus infection, is approximately 20% [1]. However, reports of coinfection with other viruses have been extremely rare.

Here, we described the first cases of MPX and varicella-zoster virus (VZV) coinfection in the current global human MPX outbreak. All cases were diagnosed between August 22 and November 11, 2022, in Sergipe state, Northeast Brazil. Samples were obtained from skin lesions and were all positive for MPX and VZV using real-time polymerase chain reaction (RT-PCR). Molecular diagnosis was described in detail previously [2] and processing of clinical samples was performed using a 5-plex assay (Kit Molecular 5Plex OPV/MPXV/VZV/MOCV/RP, Bio-Manguinhos/Fiocruz, Brazil). Positive samples had cycle threshold (Ct) values less than 37.

During the study period, 25 patients were diagnosed with MPX, of which five (20%) were also coinfected with VZV. Four patients were heterosexual men and the age ranged from 13 to 44 years. The most common systemic symptoms were fever and headache. All patients had skin lesions, mainly on the limbs and trunk, which ranged from papules to umbilicated pustules. None of the patients had lesions in the oral cavity or genital region and reported any known contact with a confirmed case, people experiencing similar symptoms, or recent travel abroad. The patients were in good clinical condition and did not require hospitalization. Serology tests for HIV and other STIs (syphilis and herpes simplex virus) were negative. Although three patients reported having been immunized against smallpox as a child, the other patients were unable to provide this information. None of the patients had a history of shingles vaccination. The clinical and epidemiological characteristics of the patients are detailed in Table 1.

To the best of our knowledge, this is the first study to report cases of MPX and VZV coinfection during the current outbreak. VZV is a common and ubiquitous human neutrotropic alphaherpesvirus that causes two distinct diseases, varicella (chickenpox) as a primary infection and shingles (herpes zoster) as a result of VZV reactivation. Most cases of varicella occur among children and adolescents, while age is considered a major risk factor for herpes zoster, whose incidence increases significantly in people over 50 years of age [3]. In African countries, where MPX is endemic and vaccine coverage against VZV is low, the co-occurrence of these two diseases has been common, particularly among children and adolescents [4,5]. In Brazil, the varicella vaccine has been made available free of charge by the National Immunization Program since 2013 [6], but herpes zoster vaccine is only offered in private clinics at a high cost. Therefore, the co-occurrence of MPX and VZV infections in Brazil should not be overlooked.

The mechanisms underlying the co-occurrence of MPX and VZV are unknown. However, VZV cutaneous lesions could serve as an entry point for MPX after direct contact with infected individuals, or MPX infection could reactivate latent VZV. Given the clinical characteristics and epidemiological context, it is possible to speculate that the positive samples for VZV DNA in this study are the result of virus reactivation even though there is no typical shingles manifestation. Although herpes zoster is an opportunistic infection that increases the risk of complications and hospitalization, the patients in this study were immunocompetent and had a limited clinical course. It has been suggested that MPX and VZV coinfection could modulate the severity of the overall infection [5]. Further studies need to estimate the rates of MPX and VZV coinfection during the current outbreak, elucidate the pathophysiological mechanisms, and better understand the clinical repercussions in immunocompetent and immunocompromised patients.

Authors contributions

All authors contributed equally to this manuscript.

Financial source

CD thanks CNPq and FAPERJ for research fellowships. These sponsors had no role in the study design, execution, analysis, interpretation of data, or decision to present the results.

Declaration of competing interest

The authors declare they have no conflicts of interest.

https://doi.org/10.1016/j.tmaid.2022.102510
Received 18 November 2022; Accepted 22 November 2022
Available online 28 November 2022

Table 1
Clinical and epidemiological characteristics of patients with monkeypox and varicella-zoster virus coinfection.

Variables	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	Male	Male	Male	Female	Male
Sexual orientation	Heterosexual	Heterosexual	Heterosexual	Heterosexual	Heterosexual
Age	44 years	20 years	21 years	13 years	46 years
MPX Diagnosis					
Method	RT-PCR	RT-PCR	RT-PCR	RT-PCR	RT-PCR
Sample	Skin swab	Skin swab	Skin swab	Skin swab	Skin swab
Days between the onset of lesions and testing	4	8	5	4	1
Ct values	29.8	34.4	33.5	35.0	36.0
Systemic symptoms					
Lymphadenopathy	Yes	No	No	No	No
Fever	Yes	No	Yes	Yes	Yes
Asthenia	No	No	No	No	No
Headache	Yes	Yes	No	Yes	No
Myalgia	No	No	No	No	Yes
Sore throat	No	No	No	No	No
Cutaneous lesions	Yes	Yes	Yes	Yes	Yes
Location					
Hands/feet	Yes	Yes	Yes	No	No
Arms/legs	Yes	Yes	Yes	No	No
Trunk	No	No	Yes	Yes	Yes
Face	No	No	No	No	No
Genital	No	No	No	No	No
Anal/perianal	No	No	No	No	No
Oropharynx/oral mucosa/lips	No	No	No	No	No
Hospitalization	No	No	No	No	No
Prior vaccination against varicella	NR	NR	Yes	Yes	Yes
Prior vaccination against shingles	No	No	No	No	No
Known contact with a confirmed case	No	No	No	No	No
Travel abroad	No	No	No	No	No
Sexual exposure before onset of symptoms	No	No	No	No	No
Concomitant sexually transmitted infection					
Syphilis and herpes simplex virus infection	No	No	No	No	No
HIV	No	No	No	No	No
Concomitant varicella zoster virus infection	Yes	Yes	Yes	Yes	Yes
Ct values	20.6	22.3	17.6	14.0	21.0

Ct, cycle threshold. NR, not reported.

References

[1] Martins-Filho PR, Tanajura DM, Vecina-Neto G. Multi-country monkeypox outbreak: a quantitative evidence synthesis on clinical characteristics, potential transmission routes, and risk factors. Eur J Intern Med 2022. https://doi.org/10.1016/j.ejim.2022.09.013.

[2] Martins-Filho PR, de Souza MF, Oliveira Góis MA, Bezerra GVB, Gonçalves CCA, Dos Santos Nascimento ÉR, et al. Unusual epidemiological presentation of the first reports of monkeypox in a low-income region of Brazil. Trav Med Infect Dis 2022;50:102466. https://doi.org/10.1016/j.tmaid.2022.102466.

[3] Bardach AE, Palermo C, Alconada T, Sandoval M, Balan DJ, Nieto Guevara J, et al. Herpes zoster epidemiology in Latin America: a systematic review and meta-analysis. PLoS One 2021;16:e0255877. https://doi.org/10.1371/journal.pone.0255877.

[4] Hoff NA, Morier DS, Kisalu NK, Johnston SC, Doshi RH, Hensley LE, et al. Varicella coinfection in patients with active monkeypox in the Democratic Republic of the Congo. EcoHealth 2017;14:564–74. https://doi.org/10.1007/s10393-017-1266-5.

[5] Hughes CM, Liu L, Davidson WB, Radford KW, Wilkins K, Monroe B, et al. A tale of two viruses: coinfections of monkeypox and varicella zoster virus in the Democratic Republic of Congo. Am J Trop Med Hyg 2020;104:604–11. https://doi.org/10.4269/ajtmh.20-0589.

[6] Andrade AL, da Silva Vieira MA, Minamisava R, Toscano CM, de Lima Souza MB, Fiaccadori F, et al. Single-dose varicella vaccine effectiveness in Brazil: a case-control study. Vaccine 2018;36:479–83. https://doi.org/10.1016/j.vaccine.2017.12.011.

Paulo Ricardo Martins-Filho*
Investigative Pathology Laboratory, Federal University of Sergipe, Aracaju, SE, Brazil

Fernanda Cardoso Menezes Dorea, Ludmila Oliveira Carvalho Sena, Gabriela Vasconcelos Brito Bezerra, Daniela Cabral Pizzi Teixeira
Central Laboratory of Public Health (LACEN/SE), Government of Sergipe State, Aracaju, SE, Brazil

Clarissa R. Damaso
Carlos Chagas Filho Institute of Biophysics, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil

Vitória de Jesus Menezes, Mércia Feitosa de Souza
State Health Secretariat, Government of Sergipe State, Aracaju, SE, Brazil

Marco Aurélio Oliveira Góis
State Health Secretariat, Government of Sergipe State, Aracaju, SE, Brazil
Department of Medicine, Federal University of Sergipe, Aracaju, SE, Brazil

Cliomar Alves dos Santos
Central Laboratory of Public Health (LACEN/SE), Government of Sergipe State, Aracaju, SE, Brazil

* Corresponding author. Universidade Federal de Sergipe, Hospital Universitário, Laboratório de Patologia Investigativa, Rua Cláudio Batista, s/n. Sanatório, Aracaju, Sergipe, CEP, Brazil, 49060-100.
E-mail address: prmartinsfh@gmail.com (P.R. Martins-Filho).