Preprint

https://doi.org/10.5327/DST-2177-8264-1471

DST - J bras Doenças Sex Transm 2025;37:e1471

Relato de Caso

LESÕES DE MPOX EM VULVA DE MULHER CIS HETEROSEXUAL COM ACHADOS DE BIOLOGIA MOLECULAR E MICROSCOPIA ELETRÔNICA: RELATO DE CASO

VULVAR MPOX LESIONS IN A HETEROSEXUAL CISGENDER WOMAN WITH MOLECULAR BIOLOGY AND ELECTRON MICROSCOPY FINDINGS: CASE REPORT

Título curto –

Mpox Lesion on the Vulva: Molecular Analysis and Electron Microscopy

Mauro Romero Leal Passos[1] https://orcid.org/0000-0002-6183-7985, Wilma Nancy Campos Arze[2] https://orcid.org/0000-0002-2620-0620, Izabel Christina Nunes de Palmer Paixão[3] https://orcid.org/0000-0001-7513-2567, Claudio Cesar Cirne dos Santos Pessanha[4] https://orcid.org/0000-0001-8376-1830, Caroline de Souza Barros[5] https://orcid.org/0000-0002-4678-3093, Kíssila Rabelo[6] 0000-0001-7579-7788, Jorge José de Carvalho[7] https://orcid.org/0000-0002-8058-8400, Renata de Queiroz Varella[8] Carolina Varella Leal Passos[9] https://orcid.org/0000-0003-3124-1774, Paula Varella Leal Passos[10] https://orcid.org/0000-0002-3806-6289, Christina Thereza Machado Bittar[11] https://orcid.org/0000-0003-2839-9677,

Autores:

Mauro Romero Leal Passos, MD. PhD. Chefe do Setor de Doenças Sexualmente Transmissíveis do Departamento de Microbiologia e Parasitologia, Instituto Biomédico, Universidade Federal Fluminense, Niteroi, RJ, Brasil. E-mail: mauroromero@id.uff.br – maurodst@gmail.com.

Wilma Nancy Campos Arze, MD. PhD. Universidade Federal de Integração Latino-Americana UNILA, Foz do Iguaçu, PR, Brasil. E-mails: wilma.arze@gmail.com;

Izabel Christina Nunes de Palmer Paixão. PhD. Instituto de Biologia da Universidade Federal Fluminense, Niterói, RJ, Brasil. E-mail: izabelpaixao@id.uff.br

Claudio Cesar Cirne dos Santos Pessanha. PhD, Universidade Federal Fluminense, Niterói, RJ, Brasil. E-mail: claudiocirne@id.uff.br

Caroline de Souza Barros PhD Universidade Federal Fluminense – Niterói (RJ), Brasil. E-mail: carolsb.uff@gmail.com

Kíssila Rabelo. PhD. Laboratório de Ultraestrutura e Biologia Tecidual (LUBT), Departamento de Histologia e Embriologia, Universidade Estadual do Rio de Janeiro, UERJ. RJ, Brasil. E-mail: kissila@gmail.com

Jorge José de Carvalho, PhD. Laboratório de Ultraestrutura e Biologia Tecidual (LUBT), Departamento de Histologia e Embriologia, Universidade Estadual do Rio de Janeiro, UERJ. RJ, Brasil E-mail: jjcarv@gmail.com

Renata de Queiroz Varella, MD. M.Sc. Secretaria de Saúde de Piraí, RJ, Brasil. E-mail: renataqvarella@gmail.com

Carolina Varella Leal Passos. MD, Universidade de Vassouras, Vassouras, RJ, Brasil. E-mail: carolinavarellalp@gmail.com

Paula Varella Leal Passos. MD. Universidade de Vassouras, Vassouras, RJ, Brasil. E-mail: paulavarellalp@gmail.com

Christina Thereza Machado Bittar, MD. M.Sc. E-mail: chbittar@gmail.com

Corresponding Author Information

Mauro Romero Leal Passos, Department: Sector of STIs (Sexually Transmitted Infections), Department of Microbiology and Parasitology, Biomedical Institute of the Fluminense Federal University (Universidade Federal Fluminense). Address: Rua Mario Santos Braga, s/n, Campus do Valonguinho, Centro, Niterói, RJ, Brazil., Zip Code (CEP): 24020-140. E-mail: mauroromero@id.uff.br – maurodst@gmail.com. Telephone: +55 21 99888-2897.

RESUMO

Introdução: A mpox, uma zoonose viral emergente, causou um surto global em 2022 apresentando padrões de transmissão interpessoal distintos dos observados em surtos anteriores. Embora inicialmente o foco tinha sido a transmissão entre homens que fazem sexo com homens, a ocorrência e características clinicas da mpox em mulheres são poucos compreendidas**.** **Objetivo:** Relatar caso de lesões em vulva em de mulher cis heterossexual com diagnsotico de mpox. **Métodos:** Relatar o caso de uma mulher cisgênero e heterossexual com lesões vulvares confirmadas como mpox atendida no Setor de Doenças Sexualmente Transmissíveis (DST) da Universidade Federal Fluminense (UFF). **Resultados:** Relata-se o caso de uma mulher cisgênero e heterossexual de 29 anos com lesões vulvares confirmadas como mpox. A paciente relatou histórico de frequência a locais com aglomeração no período anterior ao surgimento das lesões a confirmação diagnostica foi por biologia molecular (RT-PCR) e microscopia eletrônica. **Conclusão:** Este relato destaca a importância de considerar a mpox no diagnóstico diferencial de lesões genitais em mulheres e reforça a necessidade de uma abordagem abrangente na vigilância e compreensão da epidemiologia da doença em diversas populações.

Palavras-chave: Mpox, Monkeypox, Mulheres, Úlcera genital, Diagnóstico Molecular, Microscopia Eletrônica, DST

ABSTRACT

Introduction: Mpox, an emerging viral zoonosis, caused a global outbreak in 2022, exhibiting patterns of interpersonal transmission distinct from those observed in previous outbreaks. While the initial focus was on transmission among men who have sex with men, the occurrence and clinical characteristics of mpox in women are poorly understood. **Objective**: To report a case of vulvar lesions in a heterosexual cisgender woman diagnosed with mpox. **Methods**: We report the case of a 29-year-old cisgender, heterosexual woman with vulvar lesions confirmed as mpox, who was treated at the Sexually Transmitted Diseases (STD) Sector of the Federal Fluminense University (UFF). **Results:** We report the case of a 29-year-old cisgender, heterosexual woman with vulvar lesions confirmed as mpox. The patient reported a history of attending crowded places in the period before the appearance of the lesions. Diagnostic confirmation was achieved by molecular biology (RT-PCR) and electron microscopy. **Conclusion:** This report highlights the importance of considering mpox in the

differential diagnosis of genital lesions in women and reinforces the need for a comprehensive approach to the surveillance and understanding of the disease's epidemiology across diverse populations.

Keywords: Mpox, Monkeypox, Women, Vulvar Lesions, Molecular Diagnosis, Electron Microscopy, Transmission.

INTRODUCTION

Mpox, formerly called monkeypox, emerged in 2022 as a global public health concern.[1] Initially, mpox was considered a zoonosis endemic to regions of Central and West Africa, caused by a double-stranded DNA (dsDNA) orthopoxvirus that codes for 181 proteins[2], belonging to the *Poxviridae* family, with sporadic transmissions to humans. However, the global outbreak in 2022-2023 demonstrated a capacity for more efficient interpersonal spread, though not exclusively, among men who have sex with men (MSM) in non-endemic populations [3,4].

Although initial attention focused on transmission in male populations, specifically MSM, leading to an early association of the disease with this population, the transmission to other groups, including heterosexual women, its occurrence, and clinical characteristics in women remain less understood, representing a significant gap in epidemiological and clinical knowledge. [5,6] In Brazil, the female incidence is around 8% of total cases. Recent studies reveal that the female group presents a clinical profile and transmission pattern that demands specific attention for epidemiological surveillance, diagnosis, and clinical management. [7]

In women, vulvar lesions tend to be painful and can be confused with other sexually transmitted diseases, such as genital herpes and syphilis, making clinical diagnosis difficult without laboratory support.[8] This has been documented, underscoring the importance of a comprehensive approach to surveillance and diagnosis.[9] Mpox in women represents a crucial and underreported aspect of the disease's epidemiology.

It is necessary to explore the characteristics of mpox, addressing risk factors, routes of transmission, and the clinical presentation, which can vary but generally

includes fever, lymphadenopathy, headache, myalgia, and a characteristic rash that evolves through different stages: macules, papules, vesicles, pustules, and crusts.[10] The clinical manifestations of mpox include fever, headache, lymphadenopathy, myalgias, and a characteristic skin rash, which progresses through different stages and frequently affects the genital region, especially in women, where the lesions may mimic other sexually transmitted diseases.[10,11]

In addition to sexual contact, other routes of transmission, such as exposure to contaminated fomites and close contact in community settings, are suggested by recent case reports and series, highlighting the complexity of prevention and the challenge for epidemiological control of the disease in different groups.[9,12] The presence of painful genital lesions in women, associated with systemic symptoms and relevant social impact, emphasizes the necessity of specific protocols for diagnosis, treatment, and follow-up for this population.

The gold standard for diagnosis is the detection of viral DNA by real-time polymerase chain reaction (RT-PCR), which offers high sensitivity and specificity and is essential for disease monitoring.[13] However, in atypical clinical contexts or when rapid confirmation is necessary, electron microscopy (EM) allows for the direct identification of viral particles in the clinical sample, demonstrating typical MPXV morphological characteristics—oval, icosahedral particles, with lipid envelopes, measuring between 200–400 nm, and a biconcave core.[14,15]

OBJECTIVE

To report the case of a woman diagnosed with mpox, highlighting the clinical characteristics and the importance of early identification to interrupt the chain of transmission. This article follows the CARE Guidelines for clinical case reports.[16] Although genital lesions are a frequent symptom of mpox, especially in men who have sex with men, this report emphasizes the occurrence in a cisgender woman, expanding the understanding of the disease's clinical presentation and drawing attention to the need for surveillance in different populations within healthcare services.[17]

METHODS

We describe the case of a woman attended and followed up at the outpatient clinic of the Sector of Sexually Transmitted Diseases, affiliated with the Department of Microbiology and Parasitology of the Biomedical Institute, Valonguinho Campus, of the Fluminense Federal University (Universidade Federal Fluminense), in Niterói (RJ), Brazil. The patient was diagnosed with mpox at the beginning of the local disease outbreak, and this report is part of the first documented clinical records in this region. The approach involved detailed collection of clinical data, confirmatory laboratory tests, and clinical follow-up throughout the evolution of the condition.

CASE REPORT

The patient, a 29-year-old white, cisgender, heterosexual female (sex at birth female), residing in São Gonçalo (RJ), sought medical attention on August 22, 2022. She had incomplete high school education, was in a fixed, occasionally non-exclusive relationship for five years, started sexual activity at age 14, used condoms inconsistently, and had a history of treatment for Human Papillomavirus (HPV) infection. In the month preceding the appearance of the lesions, she reported frequenting various crowded places, such as motels and parties.

She was referred by a private physician with a suspicion of genital herpes that had been evolving for one week. She complained of fever, odynophagia, genital pain, and three days later, a small sore, a type of pustule, appeared after genital shaving.

More lesions subsequently appeared and worsened, affecting several areas of the vulva. Clinical Examination: Well-demarcated, umbilical ulcers along with pustular lesions extending to the perianal region (consented photos were taken). Clinical Examination Well-demarcated, umbilical ulcers along with pustular lesions extending to the perianal region (consented photos were taken). Material was collected from the genital ulcers for a Seegene Allplex PCR panel at a private laboratory, confirming the presence of HSV-1. RT-PCR for the detection of viral DNA was also performed on a lesion scraping by Lacen-RJ (State Central Public Health Laboratory), confirming MPXV infection. Electron microscopy was also performed on the lesion scraping at the Institute of Biology/UFF, and the findings were compatible with MPXV (a photo is available). Material was collected from

the patient's underwear for RT-PCR testing (private laboratory). The patient received appropriate guidance and the case concluded with resolution within one month. The sexual partner showed no signs of mpox or any other STI. Rapid tests for Hepatitis B and C, HIV, and syphilis were non-reactive in both individuals. These tests were repeated after 40 days, and they remained negative.

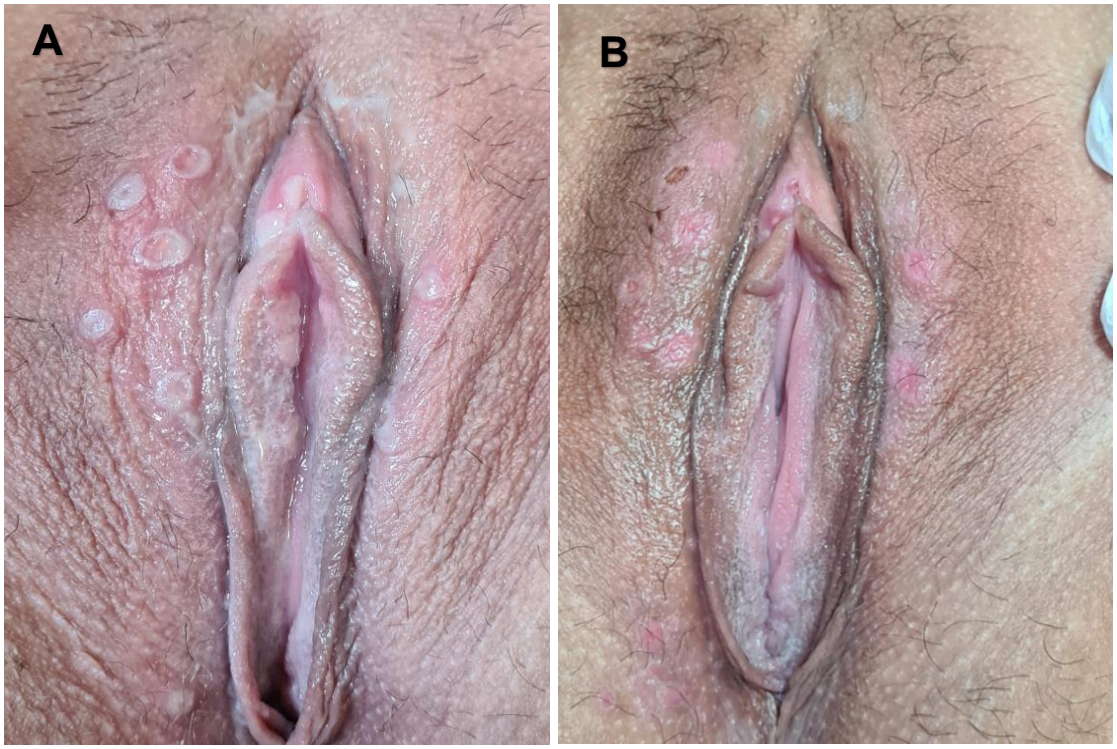


Figure 1: A) Umbilicated lesions, papules, pustules, and well-demarcated ulcers, with distribution across several areas of the vulva extending to the perianal region. B) Ulcers in resolution (after symptomatic treatment, control ten days later; patient still experiencing pain).

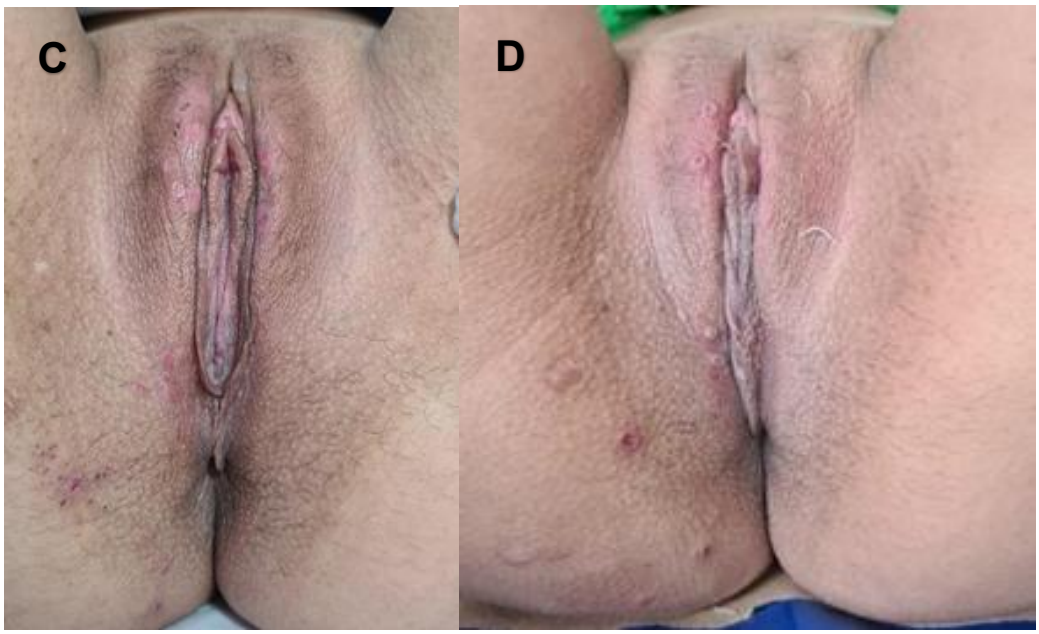
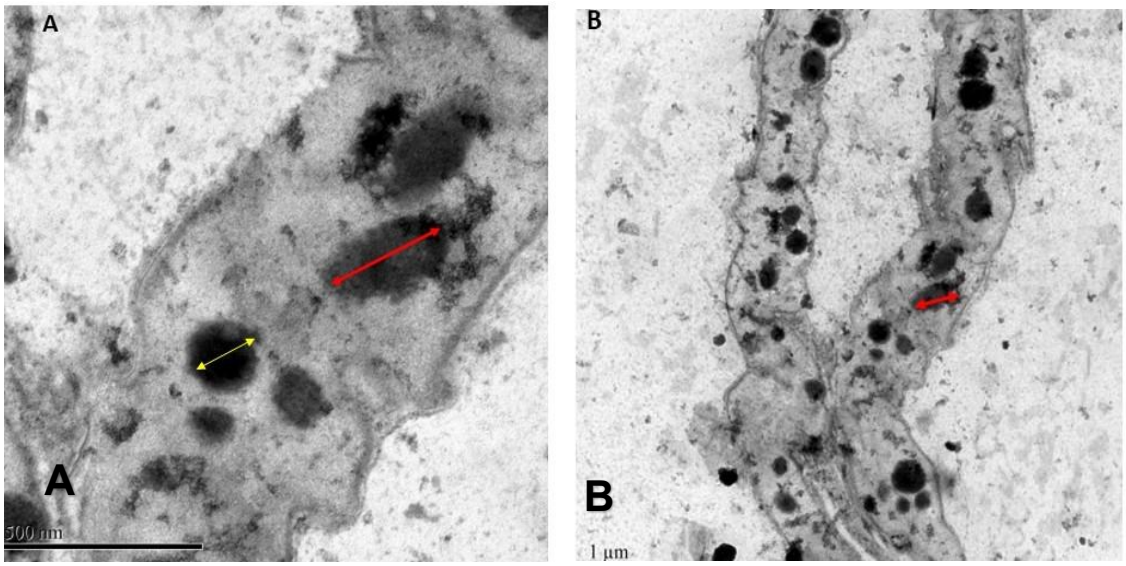


Figure 2: C-D, the images demonstrate the typical clinical evolution of mpox lesions on the skin, assessed 30 days after onset, showing the evolutionary characteristics of the skin lesions.



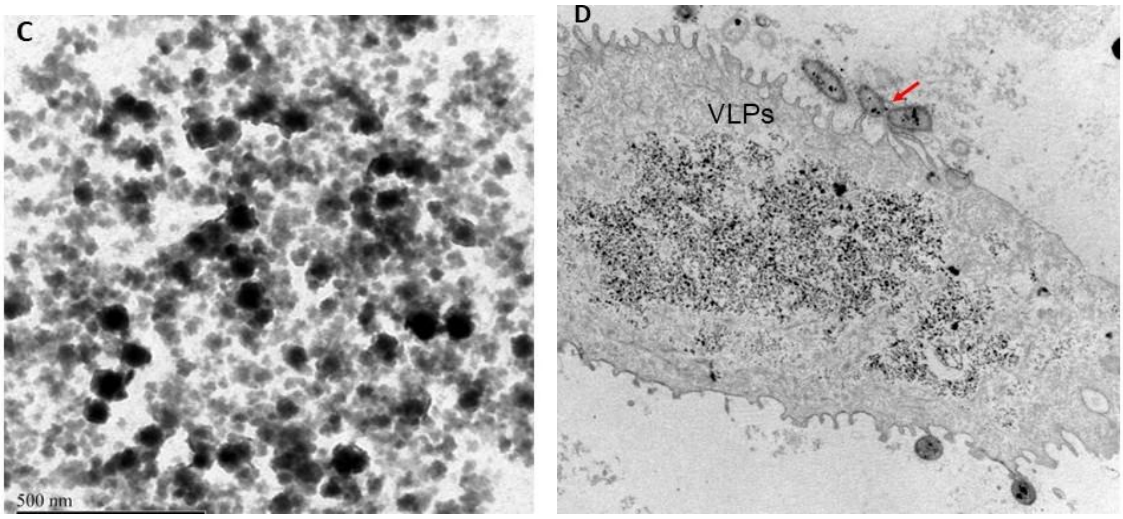


Figure **A-B)** Considering that MPXV is between 200-400nm and has a complex oval icosahedral shape, we can state that we have an image of an epithelial cell (A) or a strand of epithelial cells (B) with the presence of VLPs (Virus-like particles) consistent with the characteristics of MPXV (orange arrow), as well as VLPs that may correspond to MPXV in a transverse position or HIV, which is approximately 80-140nm (yellow arrow). **C)** Presence of a high quantity of leukocytes in the anal region. Since many of these cells are between 60-80nm, there is a high chance of this being a robust, chronic infiltrate, rich in lymphocytes and characteristic of viral infections. **D)** VLPs consistent with the characteristics of MPXV, close to an epithelial cell (orange arrow).

There is a high chance of it being a robust, already chronic infiltrate, rich in lymphocytes and characteristic of viral infections.

DISCUSSION

This case report describes the occurrence of mpox in a cisgender woman, highlighting the importance of considering this infection in the differential diagnosis of genital lesions, even in populations seemingly less affected by the initial outbreak. The initial clinical presentation, with fever, odynophagia (sore throat), and genital lesions that could mimic other STIs, such as genital herpes (confirmed by the detection of HSV-1), underscores the necessity of a comprehensive etiological investigation.

The patient's history of frequenting motels and crowded parties in the month before the lesions appeared suggests a possible non-exclusively sexual route of

transmission. Although intimate sexual contact was identified as the main route of transmission in the 2022 outbreak, [18] the possibility of transmission via contaminated fomites in shared environments, such as those mentioned by the patient, has been raised by various authors.[14,15] The absence of symptoms in the fixed sexual partner strengthens this hypothesis in this specific case.

The definitive diagnosis was established by the detection of MPXV DNA via RT-PCR and corroborated by the morphological findings compatible with the virus through electron microscopy. The use of both techniques demonstrates the robustness of the diagnosis in this case and the importance of different laboratory approaches in identifying mpox.

The use of electron microscopy proved valuable for confirming the viral infection, enabling the ultrastructural visualization of MPXV, showing oval icosahedral particles varying between 200–400 nm, an aspect considered pathognomonic of poxviruses.[14,15] This tool contributes to diagnostic confirmation in laboratory settings with greater complexity, serving as an important resource, especially in contexts of co-infection or atypical clinical forms.

The data indicate that, although the female group is less represented in the global outbreak, this may reflect prevalent transmission patterns but does not exclude the susceptibility and risk of infection in this population. In quantitative terms, the clinical and epidemiological manifestations in women demonstrate the need for a personalized approach, including protocols that consider the anatomophysiological and medico-psychosocial peculiarities of affected women. The location of the lesions in the vulvar region, as in this case, reinforces the importance of a detailed clinical evaluation in both sexes.

Strengths

The article's strengths include the robust laboratory diagnosis, utilizing both RT-PCR and EM (Electron Microscopy), which increases the accuracy and reliability of MPXV identification. The use of diverse laboratory methodologies demonstrates technical capability and contributes to the improvement of diagnostic protocols.

Another strong point is the novelty of the report within the Brazilian context, bringing a relevant contribution by expanding the clinical and epidemiological understanding and the need for a differential approach to genital lesions in women. This serves as an alert for the inclusion of mpox in the differential diagnosis and for the enhancement of surveillance protocols in healthcare services.

The case report presented here is among several cases from a Ph.D. thesis presented and approved at the Institute of Biology of the Fluminense Federal University (Universidade Federal Fluminense) [19].

Limitations:

The fact that this is an isolated case report of mpox in a cisgender woman limits the generalizability of the findings and does not allow for broad epidemiological inferences or more robust analyses of risk factors. Furthermore, the scarcity of similar reports in the literature makes it difficult to compare clinical manifestations, routes of transmission, and treatment response, highlighting the need for studies with a larger number of cases to strengthen the knowledge about mpox in women.

Conclusion

This case report of mpox in a cisgender woman with vulvar lesions, confirmed by molecular biology and electron microscopy, demonstrates a relevant clinical spectrum, with a higher frequency of genitourinary involvement, and contributes to the growing understanding of mpox epidemiology beyond the populations initially most affected, although it is less prevalent than in men.

The possible transmission via fomites, suggested by the patient's history and the absence of infection in her partner, reinforces the necessity of considering non-sexual routes of transmission. Electron microscopy stands out as an effective complementary tool in diagnosis, adding certainty and precision in atypical cases and for infection confirmation.

We emphasize the importance of including mpox in the differential diagnosis of genital lesions in women and of adopting an inclusive public health approach that considers gender diversity in epidemiological surveillance, prevention, and health education. This approach should consider not only sexual transmission but also contact with fomites and high-risk environments.

This study was approved by the Research Ethics Committee of UFF (CAAE number 56591822.9.0000.5243), as part of the genital ulcer project. The patient signed verbal and written informed consent (TCLE) to participate. Written consent was also obtained for the scientific use of the images.

Acknowledgements

We thank the patient for her collaboration and consent in the disclosure of this case. We also thank the team at the STI Sector-UFF and Lacen-RJ for their support in the laboratory diagnosis.

Funding

Own structures of the Fluminense Federal University (Universidade Federal Fluminense).

.

Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

MRLP: Patient assistance, Collection of biological materials, Photography, Text writing, Text revision, General supervision, Project conceptualization.

WNCA: Bibliographical research, Text writing, Text revision, Image processing..

ICNPP: Text revision, General supervision, Project conceptualization..

CCCS: Text writing, Literature review, Text revision.

CSB: Literature review, Text revision, Image processing.

KR: Electron microscopy analysis of clinical samples, Text revision..

JJC: Electron microscopy analysis of clinical samples, Text revision.

RQV: Patient care, Collection of biological materials, Text revision.

CVLP: Patient care, Bibliographical review, Text revision..

PVLP: Patient care, Bibliographical review, Text revision.

CTMB: Monitoring of molecular biology analysis of clinical samples, Text revision.

REFERENCES

1. Centers for Disease Control and Prevention. Monkeypox cases by age and gender, race/ethnicity, and symptoms. 2022 (acceso 12 abr 2024). https://www.cdc.gov/poxvirus/ monkeypox/response/2022/demographics.html

2. Karagoz A, et al. Monkeypox (mpox) virus: classification, origin, transmission, genome organization, antiviral drugs, and molecular diagnosis. Infect Saúde Pública. 2023;16(4):531-541.

3. World Health Organization (WHO). Mpox fact sheet. Geneva: WHO; 2024 Aug 25. Disponível em: https://www.who.int/news-room/fact-sheets/detail/mpox

4. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, Steffen R. The changing epidemiology of human monkeypox—a potential threat? A systematic review. PLoS Negl Trop Dis. 2022 Feb 3;16(2):e0010141. doi: 10.1371/journal.pntd.0010141.

5. Joshi MN, Vadher BK, Dudani AB. Mpox virus infection in women and outbreak sex disparities. Int J Infect Dis. 2024;124:123-128.

6. PAHO. Epidemiological Update of Monkeypox in women – 26 August 2022. Washington, DC: PAHO; 2022.

7. Souza ALP, Santos LG, Ferreira MFG, et al. Aspectos epidemiológicos da infecção pelo vírus monkeypox em Minas Gerais, Brasil, 2022. Rev Saude Publica. 2022;56:35.

8. Spicknall IH, Dang K, Owusu S, et al. Clinical presentation and differential diagnosis of monkeypox virus infection in the current outbreak. J Infect Dis. 2023;227(5):656-662.

9. Patel A, Bilinska J, Tam JCH, Da Silva Fontoura D, Mason CY, Daunt A, Snell LB, et all A. Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series. BMJ. 2022 Jul 28;378:e072410. doi: 10.1136/bmj-2022-072410. PMID: 35902115; PMCID: PMC9331915.

10. Petersen E, Abubakar I, Ihekweazu C, et al. Monkeypox—enhancing public health preparedness for an emerging lethal human zoonotic epidemic threat. Int J Infect Dis. 2022;125:26-34.

11. Thornhill JP, Barkati S, Walmsley S, et al. Monkeypox virus infection in humans across 16 countries — April–June 2022. N Engl J Med. 2022;387(8):679-691.

12. Cunha M, Oliveira M, Silva D. Transmission routes of monkeypox virus and public health implications. Braz J Infect Dis. 2023;27(3):101512.

13. Li Y, Olson VA, Laue T, Laker MT, Damon IK. Detection of monkeypox virus with real-time PCR assays. J Clin Virol. 2022;58(2):923-928.

14. Reed KD, Melski JW, Graham MB, et al. The detection of monkeypox in humans in the Western Hemisphere. N Engl J Med. 2004;350(4):342-350.

15. Karagoz A, et al. Monkeypox virus ultrastructural analysis and electron microscopy findings: implications for diagnosis. Viruses. 2023;15(9):2054.

16. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D, et al. The CARE guidelines: consensus-based clinical case reporting guideline development. Glob Adv Health Med. 2013;2(5):38-43. https://doi.org/10.7453/gahmj.2013.0088.

17.Agência Nacional de Vigilância Sanitária. Nota técnica GVIMS/GGTES/ANVISA no 03/2022. Orientações para prevenção e controle da

monkeypox nos serviços de saúde. Brasília: ANVISA; 2022 [cited on 2025 Jun 05].

18. Satapathy S, Shamim S, Soni S, et al. Multi-organ clinical manifestations of Mpox: an umbrella review of systematic reviews and meta-analysis. J Glob Health. 2024 Sep;14:02095.

19. Arze WNC, Tese de Doutorado (Orientador: Paixão ICNP; Coorientadores: Santos CCP, Passos MRL) Mpox em pacientes atendidos no Setor de Doenças Sexualmente Transmissíveis da Universidade Federal Fluminense no município de Niterói, RJ, Brasil: Universidade Federal Fluminense; 2024.