



Alteration in the clinical manifestations of monkeypox in the presence of HIV

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ABSTRACT

Introduction: The monkeypox virus is an orthopox virus belonging to the Poxviridae family, being a zoonotic infection, with prevalence in the male population, on reproductive age, mainly in men who have sex with men. The virus enters through direct contact with infected skin, body fluids or respiratory droplets. The clinic begins with general prodromal symptoms, followed by a phase of skin lesions in different areas of the body. **Objective:** To compare the development of monkeypox infection in immunocompromised individuals with respect to a normal course of the disease. **Materials and methods:** Review of bibliographic data from 33 scientific articles, using databases such as PUBMED and Google Scholar, with the keywords “Monkeypox”, “2022”, “Clinical manifestations” that included complete characteristics of the virus and published within a 5 year range. **Results:** There is evidence that demonstrates the existence of a coinfection of monkeypox with HIV, increasing the possibility of being a case of opportunism, resulting in an atypical picture in the evolution of the disease. It begins with rash in the genital area with pain and pustules; 3 days later general symptoms of an infectious process are added, ending with diffuse pruritus accompanied by pustules on the back and extremities. **Conclusions:** A relationship was determined between seropositive male patients with atypical lesions of the disease, affecting the symptomatologic evolution and a correct diagnosis.

Key words: monkeypox; human immunodeficiency virus; men who have sex with men; clinical manifestations.

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RESUMEN

Introducción: El virus de la viruela símica es un ortopoxvirus perteneciente a la familia Poxviridae, siendo una infección zoonótica, con prevalencia en la población masculina, en edad reproductiva, principalmente en hombres que tienen sexo con hombres. El virus ingresa a través del contacto directo con piel infectada, fluidos corporales o gotitas respiratorias. El cuadro clínico comienza con síntomas generales prodrómicos, seguidos de una fase de lesiones cutáneas en diferentes zonas del cuerpo. **Objetivo:** Comparar el desarrollo de la infección por viruela símica en individuos inmunocomprometidos respecto a un curso normal de la enfermedad. **Materiales y métodos:** Revisión de datos bibliográficos de 33 artículos científicos, usando bases de datos como PUBMED y Google Académico, con las palabras clave “Monkeypox”, “2022”, “Manifestaciones clínicas” que incluyeran características completas del virus y teniendo un rango de 5 años de antigüedad como límite. **Resultados:** Existe evidencia que demuestra la existencia de una coinfección del monkeypox junto con el VIH, aumentando la posibilidad de tratarse de un caso de oportunismo, dando como resultado un cuadro atípico en la evolución de la enfermedad. Éste comienza con una erupción en zona genital con dolor y pústulas, 3 días posteriores se agregan síntomas generales de un proceso infeccioso. Finaliza con prurito difuso acompañado de pústulas en dorso y extremidades. **Conclusiones:** Se determina una relación entre pacientes masculinos seropositivos, con lesiones atípicas de la enfermedad, afectando la evolución sintomatológica y un correcto diagnóstico.

Palabras clave: viruela símica; virus de la Inmunodeficiencia humana; hombres que tienen sexo con hombres; manifestaciones clínicas.

INTRODUCTION

Monkeypox virus (MPXV) is an emerging zoonotic poxvirus belonging to the Poxviridae family, it belongs to a group of DNA viruses. The virus has an oval or brick shape, wrapped in a lipoprotein membrane.^{1,2} In this outer membrane, it expresses surface proteins to adhere to, and penetrate host cells; it is a complex structure that serves as protection for the densely packed genetic material, which forms the nucleus and contains enzymes, transcription factors, and a double-stranded linear DNA genome. All this content is necessary for all poxviruses to be able to replicate inside the infected cells, in addition to using the machinery of the host.³

Epidemiology

The discovery of the virus can be traced back to 1958 in Denmark, in an animal facility that formed a non-fatal outbreak. 10 years after this event, the first report in humans was present in the Democratic Republic of the Congo in a 9-month-old child, with a history of not having been vaccinated against smallpox. Over the next 3 decades, cases of monkeypox were typecast in African countries; in 2003 numerous cases were reported in the United States of America, the first cases outside the African continent, and the

infectious agent was traced to small exotic mammals imported from Ghana. Successively between 2018 and 2021 the United Kingdom and Israel reported several cases, having an exponential growth.⁴⁻¹⁰ In 2022, cases were detected in 107 countries, but only in 7 of those countries most cases have usually occurred. This data from the OMS shows the importance and magnitude of the outbreak. By the year 2023 there are already 111 countries that have reported cases of monkeypox.

Transmission and pathogenesis

The most frequent mechanism of transmission of monkeypox is by direct contact, this can be by contact with infected materials, from animals to humans, the most frequently are rodents and primates mainly; the most common form of transmission is from human to human.⁶ In the latter, transmission has been observed with greater incidence in those who had previous sexual exposure with an infected person, where most patients identify as men who have sex with men (MSM).^{1,11-14}

There are two ways of acquiring the disease, one direct, typical of animals infected by bites or consumption of poorly processed foods; and the indirect by human-to-human contact, this being the most common.



The virus enters the body through contact with infected skin, body fluids, or respiratory droplets. Replication occurs rapidly at the inoculation site, which is commonly the airway epithelium, for further spread through regional lymph nodes.¹⁵ The incubation period is usually 7 to 14 days. After the initial viremia, the virus spreads to different areas of the body, such as the face, continuing with a cephalocaudal pattern, this is how it can cause localized lesions in the initial stage of the disease.¹⁶⁻¹⁷

Manifestations

Monkeypox is different from the other orthopoxviruses in that it produces disseminated skin lesions in the infected host, with signs and symptoms lasting from 2 to 5 weeks. The initial stage begins with prodromal symptoms, including fever, chills, headache, myalgia, asthenia, and lethargy.¹⁸⁻²²

The disease progresses and is characterized by developing in stages. The primary lesion appears on the third day, being of an enanthem character, which is located in the tongue and mouth; later, on the fifth day of the disease, macules, flat and without flanges, occur in the area of the face and extremities. Around the seventh day, papules develop, which progress to greasy lesions and vesicles, which will continue to form pustules. Finally, a healing period begins around the second week, indicating the terminal stage of the infection, which includes the formation of crusts and their respective desquamation, which may be accompanied by hyper or hypopigmentation. It should be emphasized that the degree of rashes and lesions depends on the viral load in the bloodstream during the viremia stage.

Complications related to monkeypox are encephalitis, pneumonia, bronchopneumonia, respiratory distress, keratitis, and scarring of the cornea that can end in permanent vision loss.^{6,8,22-25}

Diagnosis

There are multiple laboratory options to make the timely diagnosis of monkeypox, among which are the enzyme immunoassay, viral cultures, electron microscopy, histological sample, immunohistochemistry, virus isolation tests; and before all existing tests the polymerase chain reaction assay is used as a reference test due to its high specificity and sensitivity. It is important to mention that the differential diagnosis is severe chickenpox with lesions on hand palms

and foot soles, as well as the presence of lymphadenopathy in the submandibular, inguinal, and cervical areas.^{3,16,26-29}

Treatment and prevention

The Food and Drug Administration (FDA) approved the vaccine JYNNEOS in 2019 as a prevention of monkeypox for adults 18 years and older, who are at high risk of infection. Despite the absence of an FDA-approved treatment, there are drugs that serve as supportive measures for the treatment of monkeypox, which are only available through clinical studies, these are TPOXX (tecovirimat) approved by the FDA in 2018, under the Animal Rule and Tembeza (brincidofovir) approved by the FDA in 2021. Both approvals are based on efficacy data from animal studies.³⁰

Risk factors for the disease have been associated such as high-risk sexual activity such as men who have sex with other men, and carrying base immunodeficiency, among the most prominent is HIV positive.^{3,18,28-29}

METHODS

A review of bibliographic data of scientific articles was carried out, with peer review; using database search engines such as PUBMED and Google Scholar, with the keywords: "Monkeypox", "2022", and "Clinical manifestations". We chose 33 articles in English and Spanish, based on their relevance to the topic, as well as their originality and contribution to the targeted area of knowledge. The inclusion criteria for the selection of the articles were that they included the characteristics of the description of the virus, pathogenesis, clinical and diagnostic characteristics; including a 5-year age limit of publication and a specific focus on the features mentioned above.

The indexed articles are based on multicenter observational and prospective cohort studies of standardized data related to the life and sexual practices of patients confirmed with monkeypox.

RESULTS

From the literature reviewed, it was determined that 90% of the patients reported with monkeypox, were identified as men who have sex with sexually active men who have had unprotected sex. In addition to this, cases have been



detected where there is a coinfection of the monkeypox virus and HIV, this being very characteristic in the reports presented since it could speak of a case of opportunism on the part of the MPX, as well as the development of the symptomatology could also be involved. There is evidence that demonstrates the onset of atypical symptoms with a genital rash accompanied by pustules with white liquid content

and persistent pain in that area, 3 days later general non-specific symptoms typical of infection such as fever, fatigue, headaches, myalgias, and lymphadenopathy are added and 5 days after the presence of the first sign observed, diffuse pruritus begins with pustules on the back and extremities, corresponding to an atypical picture due to monkeypox infection (Figure 1; Table 1).

Timeline of typical evolution of monkeypox symptoms

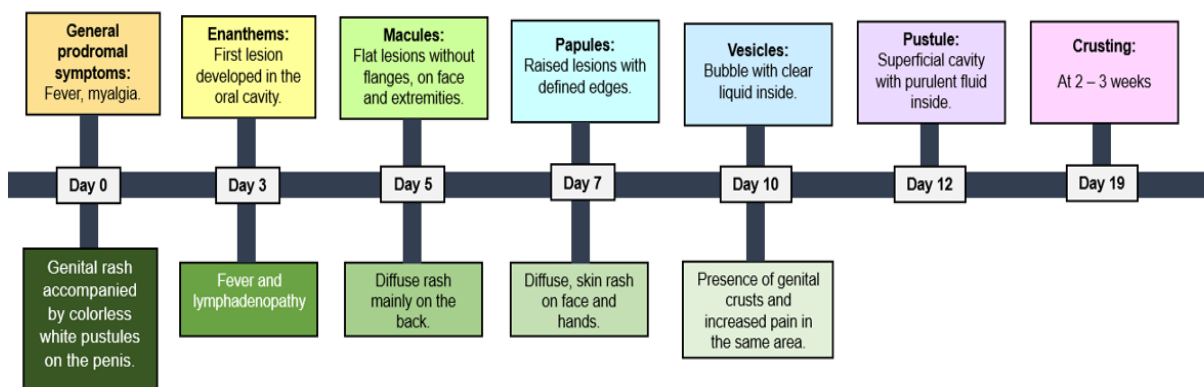


FIGURE 1. Comparative timeline of a typical and atypical evolution of monkeypox symptoms.

TABLE 1. Comparative table of manifestations between patients with monkeypox disease and HIV-positive patients with monkeypox disease without antiretroviral treatment

Typical evolution of monkeypox	Atypical evolution of monkeypox in HIV-positive patients without antiretroviral treatment
Symptoms	Symptoms
<ul style="list-style-type: none"> • General prodromal symptoms: Fever, myalgia, headache, backache, and lymphadenopathy. • First lesion are the enanthems developed in the oral cavity, especially on mucous membranes, common in patients with viral illnesses. • The second lesions are the macules, flat lesions discolored, without flanges, on face and extremities. Generally, do not include a change in the texture of the skin. • The third skin lesions are the papules, which are solid or cystic raised lesions with defined edges, less than 1 centimeter. • The vesicles are the fourth visible lesion, which are bubble with clear liquid inside. • At the end of the second week, superficial bulge with purulent fluid inside appear, which are the pustules. • Between the second and third week the crusting begins. 	<ul style="list-style-type: none"> • Genital rash accompanied by colorless white pustules on the penis. • Fever, headache, myalgia, chills, and lymphadenopathy. • Diffuse rash mainly on the back. • Diffuse, skin rash on face and hands. • Presence of genital crusts and increased pain in the same area.





According to the joint United Nations Programme on HIV/AIDS (UNAIDS) data, approximately 15.2 million people with HIV do not receive treatment. This group is considered the highest risk for presenting an atypical evolution and worse prognosis of monkeypox.³¹

DISCUSSION

The emerging infection of monkeypox has a great impact on the health system since it implies a high risk to the community; given that it has been identified together with smallpox as the most frequent poxvirus infection; with a significant percentage of 1 to 10% as fatal cases. It is relevant that currently, the existing reports describe a predominance of the male sex in infected patients, in particular men who have sex with men. It was determined that there is a relationship between seropositive male patients with atypical lesions, concerning compromise in their immune status, which affects the correct development of the disease since in a typical monkeypox infection, the expected symptomatology begins with nonspecific constitutional symptoms, followed by first enanthems lesion in the oral cavity, which evolve into macules, followed by papules, vesicles, pustules and finally scarring with a period of desquamation, indicating that the individual is no longer contagious.

It is essential to study the disease in the many possible contexts because the severity is varied, it depends as well on the state of immunity of people because those with HIV have a compromised immune system, which could quickly evolve into septic shock, leading to the death of the individual. Medical specialists in urology must have the ability to make a correct diagnosis of the present disease and know how to differentiate it from any other sexually transmitted diseases.

CONCLUSIONS

Evidence suggests that unexpected course of the disease compared to the predicted clinical picture of a typical monkeypox infection occurs in HIV patients without antiretroviral treatment (ART). A poor prognosis was detected in patients who do not have a previous diagnosis of acquired immunodeficiency (AIDS) and therefore do not have an ART treatment. For this reason, the centers for disease control and prevention (CDC) recommends starting ART treatment immediately upon receiving the newly diagnosed coinfection of HIV and monkeypox, regardless of viral load.³²

It was found that in patients who refused HIV antiretroviral therapy and infected with monkeypox resulted in higher number of hospital admissions, complications, and higher mortality.³³

The relevance of this topic is the timely detection of monkeypox, with a correct intervention of public health, as well as an effective clinical correlation in immunosuppressed patients, mainly seropositive.

It is necessary to take control and prevention measures towards this disease, including sex education as a follow-up protocol. In addition to continuous immunization of the population for the reduction of new cases and/or symptoms in severe cases.

CONFLICTS OF INTEREST

The authors declare no conflict of interests.

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