Official journal of the Spanish Society of Chemotherapy

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Mpox global outbreak: update in epidemiology, clinical spectrum and considerations in prevention and treatment

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Revista Española de Quimioterapia
doi:10.37201/req/s01.08.2023

ABSTRACT

Mpox is the most prevalent Orthopoxvirus infection in humans. Several clinical characteristics of mpox distinguish this disease from other rash illnesses. Complications are not uncommon. New therapeutics and vaccines are likely to change the course of the disease, especially in immunocompromised individuals. Clinicians must ensure that access to treatment and prevention measures are guaranteed especially in this particular population. This review exposes the epidemiology, clinical spectrum and updated considerations in treatment and prevention within the mpox global outbreak.

Keywords: Mpox, Monkeypox, Orthopoxvirus.

BACKGROUND

Mpox (formerly known as monkeypox) is a zoonotic viral disease caused by epitheliotropic viruses of *Orthopoxvirus*, from the family *Orthopoxviridae*. Since 2001, approximately 20 years after the cessation of universal vaccination against smallpox, the incidence of the disease has increased, becoming the most prevalent *Orthopoxvirus* infection in humans [1]. The disease in humans remained endemic in Central and West African countries, though sporadic outbreaks were reported out of these areas.

EPIDEMIOLOGY

Varied potential factors have contributed to mpox reemergence, such as waning vaccine-derived immunity, improved surveillance, ecologic shifts and human interactions with wildlife [2]. There are two distinct genetic clades of the mpox virus: the Central African clade (Congo Basin, clade I), and the West African clade (clade II). Clade II encompasses two subclasses: IIa and IIb. Clade IIb is responsible for the global outbreak of 2022. The disease caused by clade I is considered to be more severe and more easily transmitted. Cameroon is the only country where both clades of the virus have been found [3], and it is considered the geographic division of the virus. On May 2022, multiple EU Member States reported suspected or confirmed cases of mpox, with no epidemiological links to endemic areas. This is the first time that chains of person-to-person transmission of mpox have been reported throughout the world. Mpox spread rapidly and the World Health Organization (WHO) declared the mpox outbreak a Public Health Emergency of International Concern (PHEIC) on July 2022 until May 2023. In total, 111 countries worldwide have reported more than 87,500 cases, with 141 deaths. The 10 most affected countries globally are United States of America (n= 30,194), Brazil (n= 10,941), Spain (n= 7,551), France (n= 4,146), Colombia (n= 4,090), Mexico (n= 4,017), Peru (n= 3,800), The United Kingdom (n= 3,742), Germany (n= 3,691), and Canada (n= 1,484). Together, these countries account for 84.2% of the cases reported globally. Overall, 96.4% of cases with the available data are men, with a median age of 34 years (IQR 29-41) [4]. The ongoing outbreak is largely developing in men who have sex with men (MSM) networks; in Europe, 97% of cases have been documented in MSM. Generally, severity has been low, with few reported hospitalizations and deaths [4]. Viral transmission from person to person may occur by direct contact with the skin lesions of an infected host, with their body fluids, respiratory secretions, and contaminated fomites. Transmission by respiratory particles requires close and prolonged contact. Vertical transmission has also been described. A few infections have resulted from injury with sharp instruments, skin piercing and tattooing. Due to its routes of transmission sexual relations facilitate contagion, and it is close contact during sex the dominant form of transmission in the current outbreak. Some individuals can spread mpox virus to others 1-4 days before symptoms appear [3].

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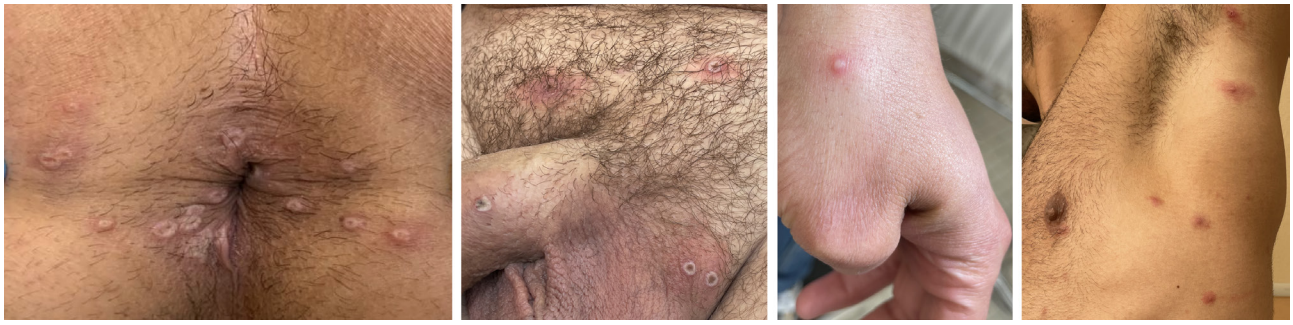

Figure 1 | **Patients with Mpox treated in Sandoval Center showing characteristic lesions.**

CLINICAL SPECTRUM

The clinical course of mpox has three stages. The first stage is the incubation period, which usually lasts 5-15 days. It is followed by an invasion period (between days 1-5), as the virus spreads through blood and the lymphatic system to internal organs and subsequently to the skin. It presents as fever, headache, lymphadenopathy, myalgia, and intense fatigue. Enlarged lymph nodes are firm, tender and sometimes painful, and are a distinct feature of mpox. The final stage and hallmark feature of mpox is a disseminated vesiculopustular skin rash, which begins 1-3 days after the effervescence of fever, but some studies show that this rash can appear before the onset of the fever [5]. The most affected areas are perioral, genital, and perianal regions, but also trunk, extremities and it can include palms and soles. The rash undergoes several phases, presenting first as enanthem, macules, papules, vesicles, pustules and finally crusts, over the course of 7-21 days (Figure 1).

Upon 2-4 weeks, successive outbreaks of skin lesions may appear, with lesions in different stages. The number of lesions vary from a few to several hundreds in immunocompromised patients. Complete removal of scabs can take up to 4 weeks since the onset of symptoms. Pitted scars and areas of hypo or hyperpigmentation may remain once all the scabs have fallen off. Anatomically, anogenital lesions are reflective of sexual practices [5]. Clinical distinction between rash illnesses is difficult. Given the similarities between smallpox, mpox and varicella, some clinical characteristics must be taken into account. The presence of large lymphadenopathy is distinctive of mpox. Varicella rarely has a prolonged febrile period, which is usually mild, and the rash progresses more quickly and rarely affects palms and soles. Additional rash illnesses that should be included in the differential diagnosis are secondary syphilis, measles, coxsackie, drug-associated eruptions, scabies, yaws, other herpetic infections and more rarely rickettsialpox [6]. Given the difficulty in clinical distinction between rash illnesses, diagnostic assays are an important component to the identification of *Orthopoxviruses*. The optimal samples for mpox diagnosis come from skin lesions: the fluid of vesicles and pustules, sometimes with the need of removing dry crusts to take a good sample (avoiding sharps instruments). If there are no skin lesions pharyngeal and rectal swabs might be a good option for the diagnosis. Polymerase chain reaction (PCR) is the laboratory test of choice due to its high accuracy (93.2-96.3%), sensitivity (90-100%), specificity (88.2-100%), positive predictive value (94.9-100%) and negative predictive value (87.9-100%) [7].

COMPLICATIONS

High prevalence of HIV and other sexually transmitted infections (STIs) have been reported in the mpox outbreak. People living with HIV have been particularly affected, representing approximately 40% of total mpox patients [8]. Disseminated and necrotizing forms of mpox have been described in individuals with HIV with inadequate immunovirological control, driving some authors to suggest that mpox could be included as an AIDS-defining condition [9]. Severe cases occur more frequently in children, pregnancy and in the immunocompromised. Complications (Figure 2) include pain management, secondary bacterial infections (including abscesses requiring surgical drainage), paraphimosis, phimosis due to scarring, pneumonia and respiratory distress, sepsis, encephalitis, multiple scars, keratitis with vision loss, abortion and myocarditis [10]. Severe outcomes and sequelae are more frequent among non-vaccinated patients. The case fatality rate in the current outbreak is <1%. Though uncommon, reinfections have been reported [11].

TREATMENT

Mpox is usually self-limited, with symptoms lasting 14-21 days. Supportive and symptomatic treatment should be performed. In complications due to secondary bacterial infections, antibiotics with activity against normal skin flora should be used. Several antivirals have been approved for the treatment of mpox. Tecovirimat is an oral or parenteral antiviral with *in vitro* activity against *Orthopoxviruses*. It inhibits the p37 protein involved in the formation and release of encapsulated virions. It may shorten the duration of illness and viral shedding.

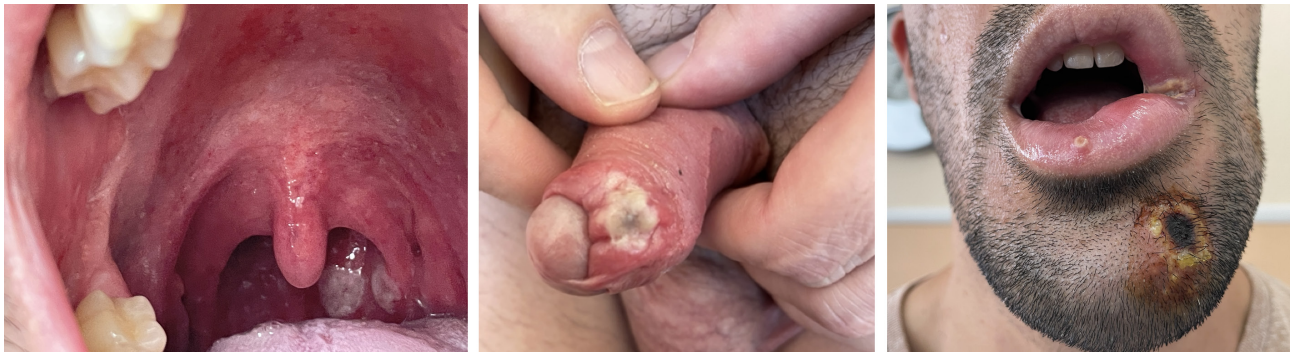

Figure 2 | **Pharyngeal lesions that avoid intake, genital ulcers with poor analgesic management and secondary skin bacterial infection as complications of mpox.**

It is the antiviral of choice. Tecovirimat is only approved for patients with severe illness (myocarditis, encephalitis, keratitis…) and/or patients with affected anatomical regions that can cause serious sequelae, and patients at high risk of severe disease according to clinicians' judgement [12]. All antivirals and even vaccinia immune globulin may be always considered under clinical trials.

PREVENTION

Small case series have reported mpox virus DNA detection in bodily fluids (semen) after healing of skin lesions, raising concern on the risk of onward transmission. Due to this consideration, WHO recommends patients to abstain from sexual intercourse until all skin lesions have crusted, the scabs have fallen off and a fresh layer of skin has formed underneath. The use of condom should be advised for 12 weeks after recovery to prevent potential transmission of mpox, though recent findings suggest that this period could be reduced [13]. Other preventive measures include: avoiding direct contact with skin lesions and respiratory secretions of infected patients, avoiding contact with objects, fabrics and surfaces that have been used by mpox patients, use of personal protective equipment (PPE) for health personnel, and isolation of patients until all skin scabs have fallen off.

VACCINATION

There is a vaccine available in Europe that is called Imvanex, commercialize in USA with the brand name Jynneos. It is an attenuated-live virus vaccine approved for the prevention of smallpox and mpox. It is administered intradermally as two doses of 0.1 ml separated 28 days in people aged 18 and over, and 0.5 ml doses subcutaneously in children, pregnant women and the immunocompromised. It is contraindicated in people allergic to chicken proteins, ciprofloxacin, gentamicin or benzonase. Indications in Spain as pre-exposure prophylaxis include people who maintain risk sexual practices (especially MSM) and people with occupational risk such as health professionals with no access to personal protective equipment (PPE). Regarding post-exposure prophylaxis, the vaccine is approved for close contacts of confirmed cases especially those with high risk of severe disease (immunosuppressed, pregnancy, children) and for health and laboratory personnel who have had close contact without PPE or incidences handling samples of patients with confirmed or suspected mpox cases [14]. Recently, a study has been published about the coverage of Jynneos vaccine in USA. The estimated adjusted vaccine effectiveness was 35.8% for partial vaccination (one dose) and up to 66% for patients that received two doses (full vaccination) [15].

CONCLUSIONS

Mpox has become a global concern. It is important to distinguish it from other rash illnesses and to maintain high suspicion. Infection may be associated with complications, especially STIs, superinfection and pain management. Other complications are more prevalent in immunosuppressed individuals. Clinicians must recommend preventive measures and vaccination. Investigation into new potential treatments is compulsory, along with the understanding of the long-term effects and the virus itself.

CONFLICT OF INTEREST

Authors declare no conflict of interest. All pictures were obtained with verbal and written consent from the patients treated.

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