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Review Article

Current understanding of multi-country human monkeypox outbreak: a narrative review

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ABSTRACT

Outbreaks of infectious diseases have occurred throughout history. They appear to be increasing in frequency, particularly because of the increasing emergence of viral diseases from animals. Monkeypox is a zoonotic orthopoxviral, similar to smallpox, although with lower mortality. Cases of human monkeypox are rarely seen outside of west and central Africa. The current outbreak is the first of its kind where the transmission is reported in Europe without known links to Africa. India reported the first case of monkeypox from the Southeast Asia region in the state of Kerala, on July 14, 2022. India till now (August 2022) has reported nine monkeypox cases and one death owing to the viral zoonosis infection. It causes flu-like symptoms such as fever, chills, and rash, usually mild, and most patients recover without therapy. As with most viral illnesses, the treatment's mainstay of clinical management for a typical monkeypox infection is supportive symptom management. Acting quickly and proactively, focusing on building surveillance, promptly identifying monkeypox infection, and implementing preventive measures will be vital for containing this pandemic.

Keywords: Monkey Pox, Pandemic, Infectious disease

INTRODUCTION

Outbreaks of infectious diseases have occurred throughout history. These events have powerfully shaped human civilization's economic, political, and social aspects, with their effects often lasting for centuries. These outbreaks have a major effect on modern medicine in the development of antimicrobial treatments, and immunization.[1,2] The shift from hunting to agricultural societies has favored the spread of infectious diseases in the human population. With time, trade between communities expanded, which in turn increased interactions between humans and animals and facilitated the transmission of zoonotic pathogens. Thereafter, increased population and urbanization, extended trade territories, and increased travel all over the globe like never before, raised the emergence and spread of infectious diseases leading to higher risks for outbreaks, epidemics, and even pandemics.[2,3] Since the Black Death Plague breakout in the 14th century, the Spanish Flu in 1918, and more recent outbreaks in the 21st century, including SARS, Ebola, Zika, and COVID-19 pandemics have had a severe impact on society.[2] Now, the outbreak of monkeypox in 2022, involving multiple countries in both endemic and nonendemic regions has generated significant international interest.

HISTORIC ASPECTS OF MONKEYPOX

Monkeypox virus was identified in 1958, during outbreaks of a pox-like disease, at a research facility in Denmark, where captive colonies of cynomolgus monkeys transported from Africa were kept. The first human case was discovered in 1970 in the Democratic Republic of the Congo during intensified smallpox surveillance.[4,5] Infections have occurred in squirrels, rats, mice, monkeys, prairie dogs, and humans. The disease in humans has remained endemic in Central African

countries and, outside Africa, a multistate outbreak of cases occurred in the United States of America in 2003, among people who had contact with imported animals.[6,7]

World health organization (WHO) claims that this current outbreak is the first instance of chains of transmission being documented in Europe without known epidemiological connections to West or Central Africa. Numerous other nations in central and western Africa have reported having an endemic monkeypox outbreak. This has been also reported in certain non-endemic countries e.g., USA, UK Belgium, France, Germany, and Italy.[8] The first case from the Southeast Asia region was reported in the state of Kerala, India, on July 14, 2022. In subsequent days, another 2 cases were detected in the same state. All three cases were males, who had traveled from the United Arab Emirates India till now has reported nine Monkeypox cases and one death owing to the viral zoonosis infection.[9,10]

VIROLOGY AND MODE OF TRANSMISSION

The *Poxviridae* is an ancient virus family having double-stranded deoxyribonucleic acid viruses which infect a range of animals including birds, reptiles, insects, and mammals. There are 2 subfamilies: *Chordopoxvirinae* and *Entomopoxvarinae*. Monkeypox belongs to the *Poxviridae* family, the *Chordopoxvirinae* subfamily, and the genus *Orthopoxvirus*. Although the poxviruses genome contains all requirement proteins to replicate, transcribe, assemble and exit, it needs infected individuals' ribosomes to translate mRNA.[11, 12]

Human-to-human transmission can occur through respiratory droplets, direct contact with body fluids or lesion material, and indirect contact with lesion material, such as through contaminated clothing or linens of an infected person. Animal-to-human transmission may occur by bite or scratch of infected animals like small mammals including rodents (rats, squirrels) and non-human primates (monkeys, apes), or through bush meat preparation.[6,8] After the viral entry from any route, the monkeypox virus replicates at the inoculation site and then spreads to local lymph nodes. Next, an initial viremia leads to viral spread and seeding of other organs.[6]

CLINICAL PRESENTATION

The incubation period of monkeypox is usually from 6 to 13 days but can range from 5 to 21 days. Symptoms can last for nearly 2-5 weeks.[8,11] Typical symptoms patients are presented with prodromal symptoms, such as fever, headaches, chills, malaise, and lymphadenopathy, followed by the development of a characteristic rash (Figure 1).[10]

Typically, within 1 to 5 days from the onset of fever, a rash evolves and resolves over a 2–4-week period. The rash usually starts in the mouth, and then spreads to the face and extremities, including the palms and soles (Table 1).

Table 1: Stages of rash.[5,11]

Days	Stages of rash
1-2	First, the rash appears as macules
1-2	Develops into papules
1-2	Followed by vesicles
5-7	ultimately pea-sized, hard pustules
7-14	crusting, scabbing, and eventually falling off. Patients are no longer considered infectious after all crusts fall off

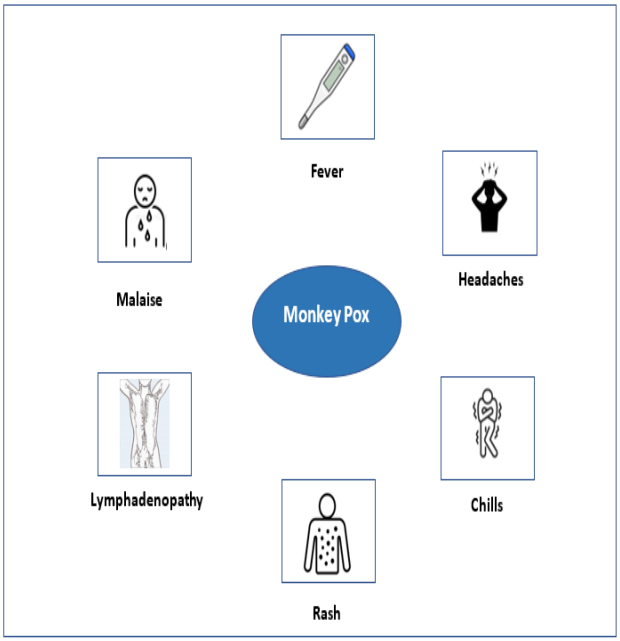

Figure 1: Signs and symptoms of monkeypox.[5,11]

The disease manifestation is very similar to chickenpox and therefore may be misdiagnosed, however, lymphadenopathy is more common in monkeypox infections. However, in the current 2022 outbreak, many patients have presented with atypical disease presentation, including no or few lesions, which are often localized in the genital or perinatal area, anal pain, and bleeding, present at different stages of development. Moreover, patients may present with only mild or absent prodromal symptoms which may begin after the onset of a localized rash.[4,11]

INVESTIGATIONS AND DIAGNOSIS

Diagnostic assays are essential to confirm MPV infection and need to be correlated with clinical and epidemiological information.[13] For the confirmation of monkeypox on the suspected clinical specimens, PCR for *Orthopoxvirus* genus [Cowpox, Buffalopox, Camelpox, Monkeypox] should be done, If the specimen shows positivity for the *Orthopoxvirus*, it should be further confirmed by monkeypox-specific conventional PCR or

real-time PCR for Monkeypox DNA. Additionally, virus isolation and the next generation sequencing of clinical samples (Miniseq and Nextseq) will help in the characterization of the positive clinical specimens.[13]

MANAGEMENT MODALITIES

Monkeypox disease usually has mild symptoms, and most patients recover without therapy. Currently, there are no specific treatments for monkeypox infection. As with most viral illnesses, the treatment's mainstay of clinical management for typical monkeypox infection is supportive symptom management.[6,11] Supportive care includes maintenance of adequate fluid balance as there is the possibility of increased fluid loss from the skin, decreased oral intake, and vomiting or diarrhea. Other measures such as hemodynamic support, supplemental oxygen, or other respiratory support and treatment of bacterial superinfections of skin lesions should be considered where indicated. Management of ocular infection/complications, specifically resulting in corneal scarring and/or loss of vision should be considered, whenever needed.[6,11]

The US food and drug administration (FDA) has not yet approved any specific therapies for monkeypox. However, there are antiviral agents such as cidofovir, brincidofovir, and tecovirimat that have activity against the monkeypox virus.[11] The infected patient should remain in an isolation room of the hospital or at home in a separate room with separate ventilation, wear a triple layer mask, and keep lesions covered as much as reasonably possible. Until all lesions have healed, and the scabs have completely peeled off, isolation must be maintained. For those who have been exposed, temperature and symptoms should be checked twice daily for 21 days, as that is the generally regarded top limit of the incubation period for monkeypox.[6,8]

VACCINE CANDIDATES

The only vaccination with FDA approval for the treatment of monkeypox is JYNNEOS. JYNNEOS is also permitted for use in the treatment of smallpox. JYNNEOS is a live virus vaccine that contains modified vaccinia Ankara-Bavarian Nordic (MVA-BN), a weakened, non-replicating orthopoxvirus. JYNNEOS may be safely used in significantly immunocompromised individuals who may not be indicated or recommended to receive certain live vaccines. JYNNEOS is approved for use in individuals 18 years of age and older who are determined to be at high risk for smallpox or monkeypox infection.[14]

CONCLUSION

Human monkeypox poses great challenges worldwide. The learnings we have from the recent pandemic will help us to spread awareness to the public. Acting quickly and proactively will be crucial for containing it.

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