REVIEW ARTICLE

Resurgence of Human Monkey Pox: A Review

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ABSTRACT

After being prevailing in Central and West Africa throughout the 1970s, sporadic cases of monkeypox sickness have surfaced in recent years. On the other hand, the monkey pox outbreak in the United States made headlines and garnered international attention in 2003. In 2022, the virus has caused a catastrophic pandemic, with over 50 nations being affected. There were 183 new cases of monkeypox recorded to WHO in April 2023, representing a 0.2% rise in overall cases, and 14 new deaths from the disease. Monkey pox shares the poxviridae family with the smallpox virus. One explanation for the rise of monkeypox in people is the discontinuation of smallpox immunizations. The zoonotic infectious illness is distinguished by a pustular rash resembling smallpox and systemic infection with severity ranging from mild to severe. Though the condition is self-limiting, the consequences it causes can be deadly. The illness has no particular therapy, however, it can be treated using antivirals that are effective against smallpox. Vaccines for smallpox have also been shown to be effective. The current article addresses the signs and symptoms of monkeypox sickness and the transmission pathways and treatment choices.

Keywords: Immunizations, Monkeypox virus, Vaccines.

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INTRODUCTION

While the globe is gradually adjusting to the COVID-19 pandemic, another threat has emerged: an alarming worldwide monkeypox epidemic. Since the first instances of monkeypox were detected in the UK, Spain, and Europe in early May 2022, the number of cases has been increasing. A zoonotic virus that can be transmitted to humans was first discovered in monkeys in 1958 by a Danish research team and was appropriately named "monkeypox." In 1970, human monkeypox was discovered in the Democratic Republic of the Congo when a toddler exhibited smallpox-like symptoms.

Sporadic epidemics of infection have occurred in Africa, mainly as a result of contact with animal reservoirs (particularly rodents). The secondary spread of such epidemics has been negligible outside of Africa.[1] After going undetected for 20 years, outbreaks were reported. In January 2022, monkeypox resurfaced. Over 50 nations across five WHO regions have reported over 3,000 illnesses and one death since January 2022. As the number of confirmed cases rose, the World Health Organisation proclaimed a "Public Health Emergency of International Concern."The smallpox virus and the monkeypox virus are both members of the Poxviridae family. Both

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viruses are genomic *Orthopoxvirus*es. Vaccination against the smallpox virus conferred cross-protection against the monkeypox virus. However, once the smallpox was eradicated, vaccination programmes were abandoned. This is one of the causes of monkeypox virus epidemics. The *Orthopoxvirus*, first detected in skin lesions on an imported macaque in 1958, was known to generate epidemics in captive monkeys. Several rodent and ape species have been shown to have *Orthopoxvirus* antibodies throughout Central and West Africa, but only twice have live monkeypox viruses (MPXV) been obtained from sylvatic animals, and it is still uncertain how widely the virus will likely propagate.[2]

Structure and Antigenicity of Monkeypox Virus

The *Orthopoxvirus* genus, of which monkeypox is a member, is included within the poxviridae family of viruses. The virus, which is brick-shaped and has dimensions between 200 and 250 nm, carries a linear, double-stranded DNA genome in a lipoprotein envelope.[3] Both chromosome ends include close hairpins and many open reading frames (ORF) longer than 180 nucleotides. Four additional open reading frames (ORFs) are present outside of the highly conserved core coding area and play a significant role in immunomodulation in determining host range and pathogenicity. The MPXV can replicate inside the cytoplasm because it can make the proteins required for transcription and replication.[4] Based on geographical, genetic, and phenotypic distinctions, the virus is classified into two clades: West African (WA) and Congo Basin (CB). Despite their similarities in epidemiology and clinical presentation, the CB clade poses a greater threat. The genomes of poxviruses contain proteins involved in replication, transcription, assembly, and egress, and they rely on host ribosomes for mRNA translation.[5] The Monkeypox virus replicates in lymphoid tissue, but it causes more lymphadenopathy. The virus enters the circulation after being found in mononuclear phagocytic cells and subsequently attacks skin cells. After infection, the spleen, bone marrow, and lymph nodes all play key roles in the initial stages of viral replication. Microvessels in the skin become a focal point for the accumulation of cell-associated viruses and infected macrophages. The infected macrophages would then enter the epidermis via these capillaries, infecting the adjacent basal layer cells. Necrosis, edema, and dermal obstruction followed shortly thereafter. After an immunological response was established, cytotoxic T cells appeared first. These cells quickly killed several infected cells before they could produce virions by engaging with antigens in the cell membranes. Virus multiplication was inhibited, and skin lesions were kept to a minimum when a cell-mediated immune response developed quickly. Monkeypox virus is transmitted orally, nasally, or topically. Lymph nodes in the area around the injection site get infected when the virus has replicated there. The virus infects other body systems after first entering the bloodstream (viremia). The incubation period following exposure lasts an average of 6 to 13 days but can last as long as 21 days.[6]

Sign and Symptoms

The early phase of the infection lasts 1 to 5 days and is characterized by fever, headache, myalgia, tiredness, respiratory discomfort, and lymphadenopathy, followed by the formation of lesions.[7,8] During this time, infected patients become infectious. Lesions first occur in the oropharynx and later on the skin. Serum antibodies can be discovered when lesions first occur. The characteristic sign of monkeypox is a widespread vesiculopustular rash.[9] Over the next 2 to 4 weeks, lesions progress from macular to papular to vesicular to pustular. Lesions grow and shrink at the same rate, typically between 2 and 10 mm. Lesions spend 5 to 7 days in the pustular phase before the development of crusts. Most instances clear up within three to four weeks after first showing symptoms, during which time crusts form and desquamate. The patient is no longer contagious once all crusts have gone off (Figure 1).[10]

Complications

Despite the rarity, MPX patients may suffer catastrophic and life-threatening complications. Lesions on the skin can get infected with bacteria, leading to cellulitis or an abscess. Exfoliation exposes portions of skin that may require surgical debridement and grafting due to fluid collection during the crusting phase. Other less common complications include retropharyngeal abscess, respiratory compromise, encephalitis, and death due to cervical lymphadenopathy. Children, the elderly, pregnant women, and individuals with impaired immune systems or other health conditions, such as those with HIV/AIDS or diabetes, are particularly vulnerable to the devastating effects of a viral outbreak.

Transmission

Transmission can occur from animal to human, between people, and from polluted surroundings to humans.[11] In animals, monkeypox viruses have been discovered in skin lesions as well as most or all fluids and excretions (e.g., urine,

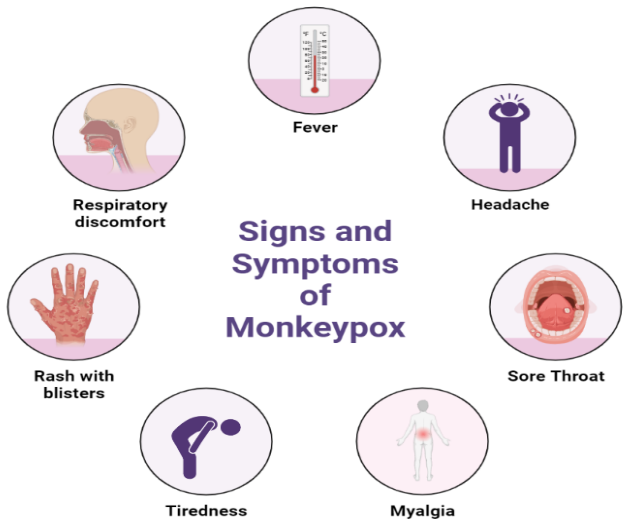

Figure 1: Sign and symptoms of monkeypox

faeces, and oral, nasal, and conjunctival exudates). Inhalation, direct injection into skin breaks, and ingestion of contaminated tissues are all possible modes of transmission (Figure 2).[12-14]

Diagnosis

A patient with a fever and rash may have monkeypox, particularly if lymphadenopathy is present. In most cases, lips and face are the first areas affected by the rash, followed by the rest of the body.[15] A visitor from an endemic area is observed for 21 days to see if they develop symptoms. Whenever symptoms occur, samples are taken and analyzed as quickly as feasible, depending on the severity of the illness. The asymptomatic traveler from an endemic region has symptoms and a rash. Isolation in PCR or viral culture for monkeypox DNA from a patient material can be used to confirm monkeypox infection. Roof lesions were collected in a simple tube with a scalpel or a plastic scraper, lesion fluid was collected with an intradermal syringe, and lesion base scrapings were retrieved in a simple tube with a sterile polyester swab and analyzed for diagnosis. Immediately following collection, specimens should be chilled (2–8°C) or frozen (-20°C). Nucleic acid amplification testing (NAAT) is used to confirm MPXV infection; this test uses real-time or conventional polymerase chain reaction (PCR) to seek specific viral DNA sequences. PCR can be used independently or in combination with sequencing. Although PCR or serology techniques for MPXV detection are being developed, they are not yet generally accessible. Serum tests for anti-*Orthopoxvirus* IgG and IgM (indicating prior exposure or vaccination) and electron microscopy visualization of *Orthopoxvirus* antigens are also sufficient diagnostic tests if the patient has not been exposed to another *Orthopoxvirus* of the same genus.[16]

Clinical Management and Treatment

Supportive care

Using a combination of topical and systemic therapy, the approaches discussed here aim to lessen the spread of infection, alleviate discomfort and pruritus, and hasten the recovery of damaged mucosa and skin. The methods used to treat cutaneous lesions include abscess incision and drainage, surgical debridement, skin grafts, povidone-iodine solution, moisturizing dressings, and topical medicines. In order to prevent corneal scarring from eye infections, topical antibiotics, antiviral medications, and corticosteroids have all been employed. It's not uncommon to have to treat a secondary bacterial infection with a combination of topical and oral medications. Local anesthetic gels and oral analgesics can be recommended for control of the pain.[17]

Prevention and treatment

Infections caused by the monkeypox virus do not have a particular therapy. Because of their shared genetic makeup, monkeypox and smallpox viruses can be treated and prevented with antiviral drugs and vaccines originally designed for smallpox.

Vaccines

The temperature of suspects who may have been exposed to viruses should be taken twice a day for 21 days. In order to prevent contracting smallpox or monkeypox after exposure, the Ankara vaccination should be administered. Any encounter to an infected person's blood, saliva, respiratory droplets, or scabs is deemed "high risk" and requires immediate post-exposure vaccination. According to the CDC, inoculation after 14 days of contact may reduce the severity of the condition, whereas

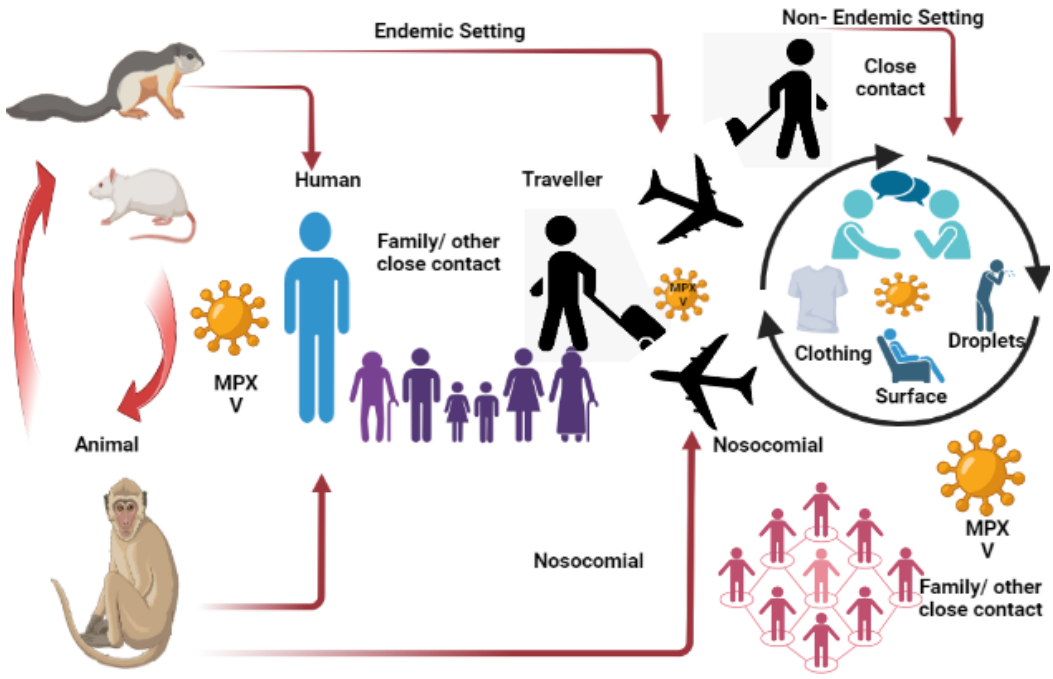

Figure 2: Mode of transmission

immunization after four days of exposure may prevent the onset of symptoms. Vaccine tweaking, unlike live vaccinia, which can cause severe reactions in those with allergies or impaired immune systems, Ankara is easily tolerated and increases antibody production. Bavarian Nordic A/S's JYNNEOS (Imvamune or Imvanex) vaccination against monkeypox has been approved for use in the USA, EU, and Canada. The JYNNEOS vaccine uses an attenuated form of the vaccinia virus that cannot reproduce. The ACAM2000 Vaccina Virus Vaccine is produced by Sanofi Pasteur Biologics Co. Previously, animal investigations have shown that the JYNNEOS vaccine or the ACAM2000 smallpox vaccine stimulates immunological responses and give good protection against monkey pox.[18,19]

Antivirals

Brincidofovir and tecovirimat, two oral medicines licensed for the treatment of smallpox, have shown effectiveness against monkeypox in animals. Tecovirimat is approved by the European Medicines Agency (EMA) to treat complications after vaccinia vaccination, including cowpox, smallpox, and modified vaccinia (MPX). In America, too, it has received FDA approval. Tecoviramat blocks the development of viral envelopes by attacking the protein p37, which is shared by all *Orthopoxvirus*es. It comes in fast-acting capsule form and should be taken twice daily for 14 days.[20] The US Food and Drug Administration sanctioned an IV formulation on May 19, 2022. Brincidofovir inhibits MPX virus replication by interfering with DNA polymerase-mediated synthesis. It is available as an oral tablet as well as a suspension and is administered to patients in two weekly dosages. Vaccinia, variola, monkeypox, and cowpox viruses are all vulnerable to the nucleotide analog cidofovir, which is authorized for the treatment of CMV retinitis in HIV-infected persons. It inhibits MPX virus replication by inhibiting DNA polymerase (McCollum). Another reason for studying antiviral techniques to treat poxvirus infections in humans is fear that genetic change may improve the aggressiveness of the variola virus and other poxviruses.[21] Isolation, a surgical mask, and maximum coverage of the lesions should be maintained until all crusts fall off of the lesions on their own and a new skin layer emerges.[22]

CONCLUSION

The genus *Orthopoxvirus*, of which the monkeypox virus is a member, is located in the family Poxviridae. However, while the virus was first discovered in macaques, its exact origin remains a mystery. After being confined to Africa until recently, reports of the monkeypox virus in the Western Hemisphere have sparked global alarm. The virus can spread from animals to humans and between humans. Social distance and contact tracing become essential to limit viral transmission inside humans. Though there have not been many fatalities linked with the condition, complications such as pneumonia, encephalitis, sepsis, loss of eyesight, and so on might be a source of concern. To avoid difficulties, supportive care is required. Smallpox vaccines and antivirals have proven effective against monkeypox virus.

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