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A REVIEW ON RECENT MONKEY POX OUTBREAK IN 2022

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ABSTRACT

Monkey pox, a zoonotic disease with clinical symptoms resembling smallpox, unexpectedly broke out and spread over the world after the outbreak of COVID-19, severely affecting several of the continents of the world. Monkey pox is currently a member of the genus otrhopox virus, which is a member of the sub family chorodoxvirinae. According to the available knowledge, small mammals and rodents have all been identified as potential sources of the monkey [ox virus]. The disease is characterized by a short febrile illness with lymphadenopathy followed by a rash which spreads centrifugally and passes through phases of macules, papules, vesicles, and pustules. Recovery occurs in most patients within 2–4 wk. Complications are more likely in children, pregnant women, and the immunocompromised. Specific diagnosis is by detection of viral DNA by PCR.Tecovirimat, brincidofovir, and cidofoviir are the medications used to treat monkey pox, immunoglobulin and new compounds are the vaccinations. This review will introduce a general overview of MPXV and describe the epidemiology, clinical features, evaluation, and treatment of monkey pox patients.

INTRODUCTION

Monkeypox, is caused by a rare zoonotic virus monkeypox virus, a species of the Poxviridae family, the Orthopoxvirus genus and the Chordopoxvirinae subfamily. In 1958, a Danish laboratory found the virus in monkeys, leading to the discovery of monkeypox. In Zaire (now the Democratic Republic of the Congo, DRC), a 9-month-old kid was found to have the first human case in 1970. Since then, monkeypox has spread to other African nations, primarily in Central and West Africa, have became endemic in the DRC. The first cases of monkeypox outside of Africa were identified in 2003.The emergence of epidemics outside of Africa emphasises the disease's global significance. Even in the 20th century, there have been more instances of monkey pox reported in more than 50 countries across five regions. [1] Current information reveals that the total Number of monkeypox cases recorded in the DRC has increased year after year, regardless of developments in the national Integrated Disease Surveillance and Response (IDSR) system. [2]

ETIOLOGY:

Monkeypox (MPX) virus is an enveloped double stranded DNA virus belonging to Orthopoxvirus genus of the Poxviridae family. The disease is transmitted from both animals to humans, and humans to humans[3]. The natural reservoirs are monkeys, squirrels, Gambian pouched rats, dormice, nonhuman primates, and other species. Humans are infected by bite/scratch, close contact, and by eating inadequately cooked meat of infected animals. Transmission between humans is by large respiratory droplets, direct contact, and through contaminated fomites. The role of

direct sexual transmission is uncertain, but intimate skin and mucosal contact during sex facilitates spread. Vertical transmission from mother to fetus or newborn leading to congenital MPX has also been reported.

EPIDEMIOLOGY:

Cases have been reported from 10 African countries since 1970. Nigeria was second worst affected with 181 cases followed by Republic of Congo (97 cases) and Central African Republic (67 cases). The increase in cases in Africa is attributed due to waning of immunity following cessation of smallpox vaccination and increased encroachment of sylvatic areas for human activities. The cases outside Africa were first reported from the USA in 2003, when 53 people (median age 26 y, range 4–53 y) were affected with the West African clade following contact with pet prairie dogs that, in turn, were infected from exotic animals from Ghana. In the period between 1st January 2022 and 22nd July 2022, 16,016 laboratory confirmed cases of monkeypox and 5 deaths have been reported to WHO from 75 countries/territories/areas in all six WHO regions [4]. The five countries that have reported the highest cumulative number of cases globally are Spain (n = 3125), the United States of America (n = 2316), Germany (n = 2268), the United Kingdom of Great Britain and Northern Ireland (n = 2137). The African region has reported only 301 lab-confirmed cases but all the 5 deaths. However, the African surveillance network reported 1400 cases with 63 deaths in 2022 [5]. Considering the increasing number of cases across the world, the WHO declared MPX as public health emergency of international concern (PHEIC) on 23 July 2022.

In India, as on 24 July 2022, 4 cases of MPX were reported; the first case was reported on 14 July 2022. All four were men. The first three were from Kerala with a history of foreign travel but the last case from Delhi had no history of foreign travel [6].

Re-emergence of monkeypox in endemic and nonendemic areas has been attributed to changing biologic nature of the virus, climate change, waning immunity following cessation of smallpox vaccination coupled with increased international travel following the lifting of COVID-19 restrictions and high-risk sexual activity

PATHOGENESIS

The clinical course of orthopoxviral virus in a vertebrate host is highly dependent on the virus's primary infection route. The virus then infects the mucosae of the oral and respiratory tracts, with the upper, middle, and lower airway epithelium being the primary targets for primary infection. The rapid relocation of VACV to draining lymph nodes within hours of inoculation indicates direct viral access to lymphatic vessels as a mechanism of dissemination. The viral infection was first observed in macaque monkeys, thus the name monkeypox.MPXV can also be transmitted through the placenta during pregnancy, resulting in foetal death. In some cases, potentially fatal complications such as encephalitis, secondary infection of the integument, bronchopneumonia, and sepsis can occur. The pathophysiology of systemic and sepsis human monkeypox virus infections with sepsis is mostly determined by neutrophils, as seen by the neutropenia and excessive inflammatory cytokine responses.[7] As previously mentioned, the monkeypox virus can be spread through contact with animals or people. The virus enters the host, grows at the point of entry, and then spreads through the lymphatic system. This results in primary viremia, a systemic infection. The virus will now begin to replicate in distant lymph nodes and lymphoid organs, which will cause infection of the epithelium and tertiary organs and the development of mucosal and skin lesions, leading to the clinical manifestation of this virus.

CLINICAL FEATURES:

In 54.29% of cases, fever was described as a sign or symptom, followed by inguinal lymphadenopathy (45.71%) and exanthema (40.00%). 22.86% and 25.71% of the participants, respectively, reported having asthenia, weariness, and headaches. In 17.14% of the patients, myalgia was present. In 31.43% of the patients, vaginal and anal lesions (ulcers and vesicles) both were reported. The least frequent symptom recorded was axillary lymphadenopathy (5.71% of the case series), while cervical lymphadenopathy was described in 11.43% of the sample. Diarrhea was reported in the English cluster

cases (5.71%).Smallpox-like symptoms are reflected in the signs and symptoms of MPV infection. The distinction is that lymphadenopathy is brought on by MPV infection rather than smallpox. Fever, chills, headache, muscle pains, backaches, and lethargy are the first symptoms of an MPV infection, which proceed to exhaustion. Monkeypox typically takes 7 to 14 days to incubate, but it can take up to 21 days. Following the onset of a fever, the infected person gets a rash on their face, which spreads to other body areas. The oropharynx is where lesions first form before spreading throughout the body. Around two weeks after exposure, serum antibodies are discovered. The prodromal phase is nonspecific and lasts generally for 0–5 d. It is characterized by fever, headache, lethargy, myalgia, and lymphadenopathy. The lymphadenopathy appears with onset of fever and may be unilateral/bilateral cervical, axillary, or inguinal. This is followed by the appearance of the rash which lasts for 2–4 wk. The lesions are polymorphic and painful till they become crusted. The number of lesions may vary from one to hundreds.

The stages in the development of the rash are:

The enanthems in the tongue and mouth appear first.

This is followed by macules starting from face spreading to arms, legs, palms, and soles (centrifugal distribution). This is unlike chickenpox where distribution is centripetal.

The rash goes through macular, papular, vesicular, and pustular phases. Classic lesion is vesicopustular. All lesions in the person are similar in nature, unlike chickenpox, where multiple phases can be found at the same time. However, pleomorphic rash may be seen in vaccinated patients.

The commonly involved sites in order of frequency are face (98%), palms and soles (95%), oral mucous membranes (70%), genitalia (28%), and conjunctiva (20%). Involvement of palms and soles is the hallmark of MPX.

By the 3rd day lesions progress to papules and by the 4th to 5th day, lesions become vesicles (raised and fluid filled), and by the 6th to 7th day, lesions become pustular, sharply raised, filled with opaque fluid, firm, and deep seated. These may umbilicate or become confluent.

By the end of the 2nd week, they dry up and crust over. The scabs remain for a week before falling off. The lesions heal with hyperpigmented atrophic scars, hypopigmented atrophic scars, patchy alopecia, hypertrophic skin scarring, and contracture/deformity of facial muscles following healing of ulcerated facial lesions.

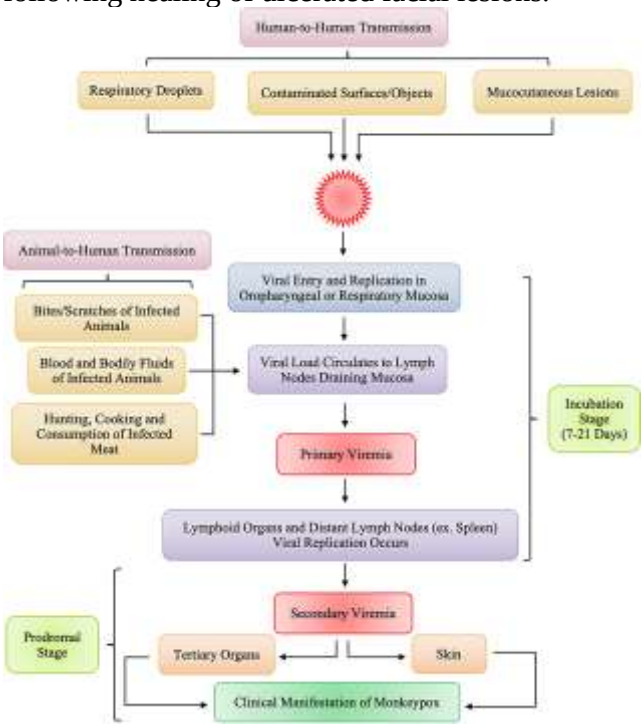

Figure 1: Pathogenesis of Monkey pox virus

The virus replicates at the initial infection site, resulting in a local inflammatory response. The virus then spreads to the regional lymph nodes and via the bloodstream (primary viremia) to lymphoid organs, which explains the signs and symptoms seen during the prodrome phase, including lymphadenopathies. The virus spreads again to the bloodstream (secondary viremia), leading to the end-organ involvement with the skin rash and other complications. Fever starts during the prodrome phase and resolves within 3 days of rash onset. Lymphadenopathy is a specific manifestation of monkeypox, differentiating it from smallpox and varicella. The skin lesions evolve from macules, to papules, to vesicles and pustules, and finally to crusts and scabs, each phase taking about 2 days on average. The skin lesions then resolve, often with

pitted scarring. Additional complications can occur from secondary bacterial infection or viral spread to other organs and could lead to death. The frequency of these complications is reported based on a description of cases from the 1981–1986 outbreak in the Democratic Republic of Congo and might not reflect the severity of other outbreaks caused by a different clade of the virus. Specific characteristics of the 2022 outbreak are highlighted

DIAGNOSIS

If a person exhibits the aforementioned symptoms and has a history of contact with or travel to monkeypox-endemic regions, monkeypox should be considered. The polymerase chain reaction (PCR) test can confirm a suspected case of monkeypox.[8] When cold chain is not readily available, it is vital to consider that viral DNA included in lesion material is stable for a certain amount of time if preserved in a somewhat dark, cool environment. Conventional tests including virus isolation from a clinical specimen, electron microscopy, and immunohistochemistry are still valid methods, but they need complex lab equipment and highly skilled technicians.

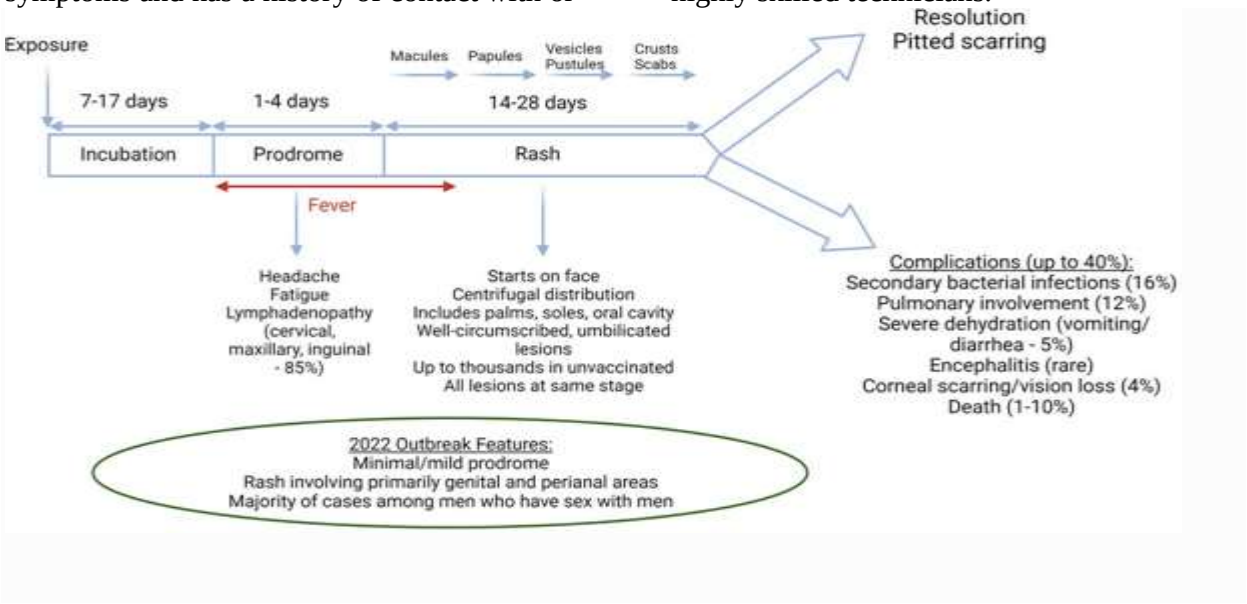

Figure2.Natural history and clinical manifestations of human monkey pox infection after initial exposure

Diagnostic Tests:

Test	Description	Sample used
PCR	It is based on NAAT; for the detection of monkey pc DNA, real time PCR is currently the gold standard	Lesion fluid
Viral culture	The virus is grown and isolated from a patient sample	Lesion fluid
Electron microscopy	An electron microscope is used to morphologically identify pox virus	Biopsy specimen, vesicular fluid
Immunohistochemistry	Tests are conducted for the presence of *Orthopoxvirus*-specific antigens	Biopsy specimen
Anti-Orthopoxvirus IgG a IgM tests	These tests can be used to assess recent or remote exposure of *Orthopoxvirus*	Blood specimen

TREATMENT:

I] ANTIVIRALS

Several antivirals have been shown to be effective in treating monkeypox infections like Tecovirimat, Brincidofovir, Cidofovir etc.

II]Vaccinia Immune Globulin (VIG)

The FDA has approved the hyperimmune globulin VIG for the treatment of certain vaccine-related side effects. These include vaccinia infections in people with skin disorders, aberrant infections brought on by the vaccinia virus, progressive vaccinia, severe widespread vaccinia, and eczema

vaccinatum (except in cases of isolated keratitis, e.g., ocular infections). The use of VIG for monkeypox or smallpox has not been evaluated in people, despite the fact that it is a possible therapy. Data on the efficiency of VIG against monkeypox and smallpox are mostly sparse. An IND application should be used to administer VIG treatments.[10]

IV] Novel agents under investigation

EV generation from MPXV and vaccinia virus is influenced by host Golgi-associated retrograde proteins. It has been discovered that tiny compounds like Retro-2 can reduce vaccinia virus infection by inhibiting the retrograde pathway. Two different tecovirimat-resistant viruses were strongly suppressed by PA104, indicating the potential benefit of using it in combination therapy with tecovirimat. The antiviral activity of the thymidine analogue N-methanocarbathymidine (N-MCT) against herpesviruses was originally described. In a mouse model of virus infection, N-MCT treatment administered intraperitoneally (100 mg/kg/day) decreased vaccinia virus titers in the liver, spleen, kidney, lung, and brain. Its effectiveness against human MPXV or orthopoxvirus infections calls for further research.

V] Cidofovir

Orthopoxvirus can be treated in an epidemic scenario using cidofovir, an antiviral that has been FDA-approved for the treatment of CMV retinitis in individuals with acquired immunodeficiency syndrome (AIDS).

PREVENTION:

Antibodies that are cross-reactive and protect against infection by other Orthopoxvirus species are produced by smallpox immunizations. During the smallpox eradication campaign, the first-generation live vaccinia virus vaccination was 85% successful in preventing monkeypox infection. This vaccination is contraindicated in expectant mothers, immunocompromised individuals, and those who have eczema and may result in significant adverse effects. Monkeypox can be prevented with either the smallpox (vaccinia) vaccination or the live, non-replicating smallpox and monkeypox vaccine. To prevent the beginning of the disease after exposure, the CDC advises that the vaccination be administered within 4 days after the date of exposure. Prophylactic vaccination administration as soon as feasible after exposure can prevent illness or considerably lessen it. When the smallpox vaccination is not advised, vaccinia immune globulin may be administered as a postexposure prophylactic drug option.

CONCLUSION:

The monkey pox outbreak has drawn the attention of scientists, epidemiologists, clinicians, and policymakers to the need to take prevention action and apply treatments for the monkey pox virus. We can control the monkey pox virus through vaccination, good hygiene habits, and self isolation (or quarantine) for patients and visitors.

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