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Review on Monkeypox

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ABSTRACT
The monkeypox virus is a rare viral disease capable of causing severe illness in humans and animals. A sooty mangabey and a rope squirrel were the only known wild outbreaks of monkeypox, which may be transmitted through saliva or respiratory excretions. Humans may contract monkeypox by inhaling droplets from their respiratory tracts, contacting bodily fluids, or contacting their environment contaminated by infected patients. Nosocomial transmission has also been described. Monkeypox has a 6 to the 13-day incubation period, and symptoms include lethargy, chills, fever, headaches, swelling of lymph nodes, asthenia, myalgia, and back pain. Viral culture, electron microscopy, immunohistochemistry, PCR, and the Tetracore Orthopox BioThreat Alert are used to determine the presence of monkeypox virus and the level of antibodies to the monkeypox virus. A specific clinically proven treatment is not available for monkeypox infection. Supportive care, symptomatic management, and antimicrobial therapy remain the main recommendations. Vaccination after exposure with the modified vaccinia Ankara vaccine may be recommended in some cases. LC16m8, another vaccine modified to prevent viral replication, protects nonhuman primates against severe monkeypox illness. Tecovirimat, a drug developed by World Health Organization (WHO) for treating smallpox, was found more dependable and tolerable in a clinical trial for Humans. However, its effectiveness in treating monkeypox in humans needs further investigation.
Keywords: Monkeypox, viral disease, Vaccine, Mpox.

I. INTRODUCTION

A monkeypox virus is an uncommon virus transmitted by animals and causes the disease. This virus is a member of the Poviridae family and belongs to subfamily Chordopoxvirinae, and Orthopoxvirus genus.[1] Several other members of this genus have been identified, including variola, vaccinia, ectromelia, and cowpox. [2]

The natural monkeypox host is unknown, but several mammalian species are susceptible. Wild virus outbreaks have been confirmed in two monkey species: the sooty mangabey in the Ivory Coast and the rope squirrel in the Democratic Republic of Congo (DRC).[3] A possible transmission mechanism is through saliva or respiratory excretions or contacting exudates or crusts. Another source of exposure may be viral shedding via feces.[4]

There are two major clades of human monkeypox virus (MPXV): the West African strain (WA) and the Congo Basin strain (CB). Several genes are lacking in the West African strains present in the Central African strains and are less virulent. Morbidity, mortality, and morbidity associated with the human-to-human transmission have been associated with human-to-human transmission.[5]

An electron microscope can measure the monkeypox virus at 200 - 250 nanometers in size. Poliovirus genomes are encapsulated in a lipoprotein envelope.[6] Data from historical studies indicate that the vaccinia virus (another orthopoxvirus) provides approximately 85% protection against monkeypox.[7]

HISTORY

It was named monkeypox after an outbreak of monkeypox was discovered in 1958 in captive monkeys imported from Africa for research in Copenhagen, Denmark. (von Magnus et al., 1959).[8] Basankusu Hospital in the DRC admitted a nine-month-old child on 1 September 1970, then Zaire, and diagnosed with the disease. It was discovered that the boy had smallpox, a disease in which Monkey pox-like virus was isolated. Individuals with infected skin develop disseminated rashes and fever after a two-week, asymptomatic incubation period.[9] The initial symptoms of monkeypox differ from those of smallpox, not only in terms of headache, fever, lymphadenopathy, myalgia, and fatigue. Face and extremities' skin develops within one to two days, followed by the mouth's skin. There may be a variety of lesions, depending on the severity of the rash.[10]

As the lesions progress, they progress from macular to papular to vesicular to pustular over two to four weeks. It usually occurs in pairs, ranges from 2 to 10 millimeters in size, and changes synchronously. Prior to the development of the crust, the lesions go through a pustular phase. As a result of the onset of symptoms, crusts form within seven to fourteen days and typically dissolve within three to four weeks. Upon removing all crusts, the patient is no longer considered infectious.[11]

Globally, more reported disease cases had been reported four decades after this report. Several African countries have recently reported more cases of the disease (more than 30 years after its discovery). Among them are the Central African Republic, Congo, Liberia, Cameroon, Congo, Sudan, Gabon, Sierra Leone, Nigeria, and others.[12]

EPIDEMIOLOGY

Children younger than ten are more likely to contract monkeypox in Africa than adults. 90% of people infected reside in villages of less than 1000 people, which makes it primarily a disease of rural populations. Males make up the majority of patients. Approximately 72% of people who contract African monkeypox acquire it from infected small mammals. In 28% of cases, the disease is transmitted from person to person. Among all susceptible contacts, the secondary attack rate ranges from 3.3% to 10%, significantly lower than the 25% to 40% rate associated with smallpox.[13]

Since 1978, monkeypox has not been transmitted to humans in West Africa. Central and northern DRC is considered to be endemic for monkeypox. Sudan reported 10 cases without death in 2005, while the DRC reported 11 cases with one death in 2003.[14]

Due to interethnic violence in northwestern DRC, refugees flooded into the Republic of the Congo (ROC) in 2009. As a result of the intensive community education program sponsored by UNICEF in refugee settlements, ten suspected monkeypox cases were identified. The program included modules on monkeypox recognition and prevention. A polymerase chain reaction assay was performed on 7 of these 10 cases, and two were positive.[15]

Nigeria has reported more than 500 suspected cases and 200 confirmed cases in the past year since the first case in over 40 years was reported in 2017. One case of this disease was reported in October 2018 by a Nigerian traveler to Israel.[16] An incident involving a Nigerian man travelling to Singapore occurred in May 2019.[17] The monkeypox virus was contracted by three members of a family in May 2021 during a trip to Nigeria.[18] There may be a human-to-human transmission based on the sequential development of symptoms within family members. An individual traveling from Nigeria to Texas reported one case in July 2021.[19] A person traveling from Nigeria to Maryland reported one case in November 2021.[20]

During the early months of May 2022, the United Kingdom was reported to have nine cases of monkeypox, with the first case having lately traveled to Nigeria. There were two confirmed transmissions within the patient's family to another adult and a toddler.[21] An adult male from Massachusetts who recently visited Canada was confirmed to have a monkeypox on May 18, 2022.[22]

Seventy-four thousand seven hundred monkeypox cases have been confirmed in more than 200 countries since October 19, 2022. All continents inhabited by humans have had cases of this disease.[23] As of October 19, 2022, there were 27,635 confirmed cases in the US.[24]

VIRUS TRANSMISSION MODES TO HUMANS

MPXV is still being determined on how it is transmitted from animals to humans.[25] Person to another person or through any animal are two possible routes. Infection can spread from one person to another by droplets from the respiratory tract, contact with fluids in the body, contamination of an infected patient's environment, or skin lesions. Viral entry occurs via skin breaks, respiratory tracts, or mucous membranes.[22] Infections spread more easily among hospital staff and family members who have prolonged contact with patients. Nosocomial transmission has been described.

In the flowchart above, we have shown direct contact with lesions on infected individuals' mucocutaneous surfaces as well as communication with contaminated objects. Monkeypox is also transmitted by the mucosa of the oropharynx or respiratory tract, much like smallpox. The monkeypox virus contaminates the respiratory and oropharyngeal mucosa following its entry into the body. As soon as the monkeypox virus enters a human, the mucosa becomes contaminated.

Lymph nodes in the local area are affected by primary viremia after replication. Secondary viremia can spread to distant lymph nodes and organs through circulation. A period of seven to fourteen days is typically associated with the incubation period, with a maximum period of 21 days. The incubation period of monkeypox is not contagious since there is no clinical manifestation during that time. The symptoms and clinical manifestations of monkeypox can identify a prodromal stage. Primary viremia occurs in lymphoid organs and leads to secondary viremia in tertiary organs and tissues, like the lungs, eyes, or gastrointestinal tract. The most infectious period of a person's life is during the prodromal state. This has several non-specific symptoms, including mucocutaneous lesions and lymphadenopathy.[26]

PATHOPHYSIOLOGY:

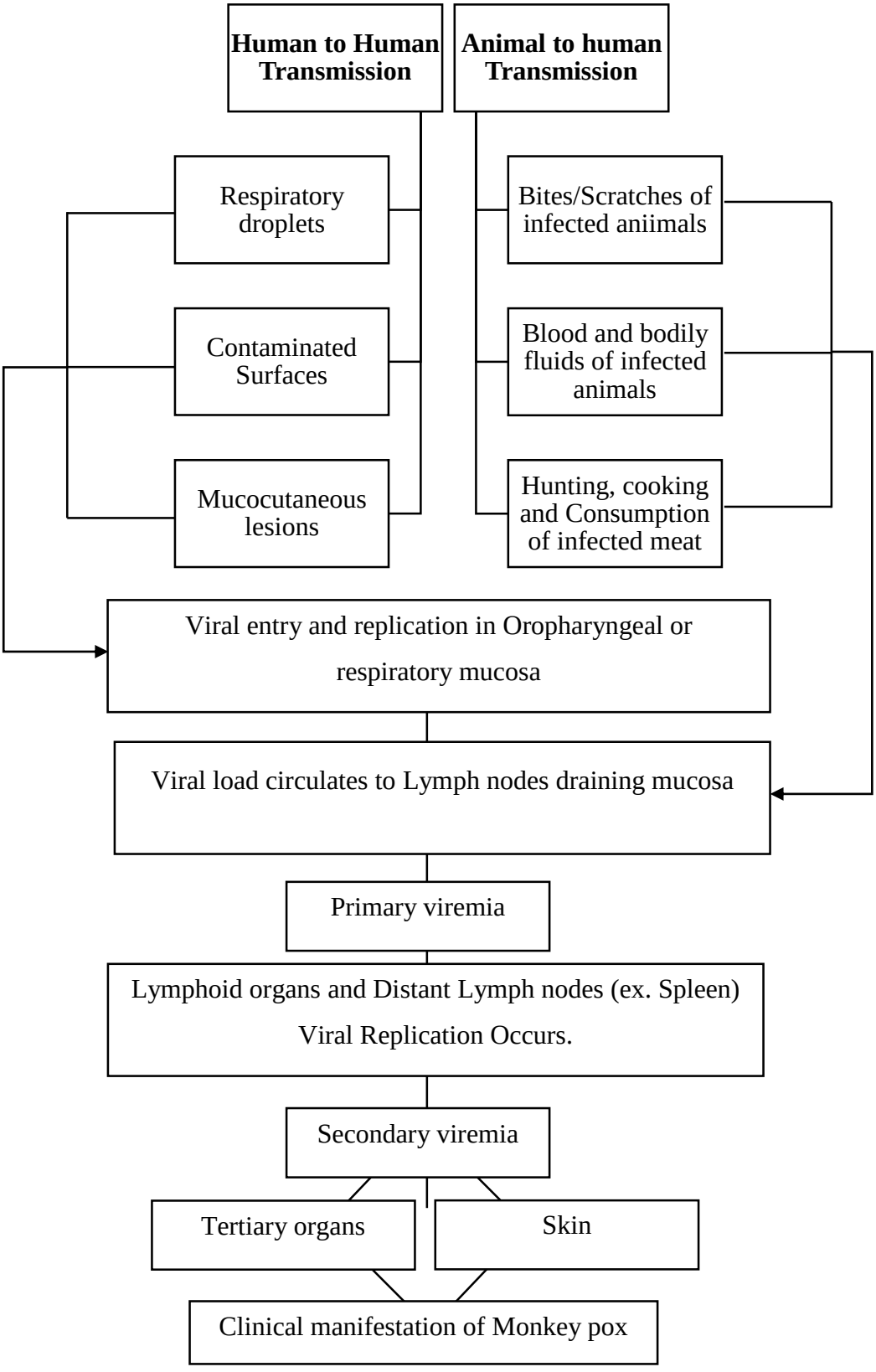

Fig1: An overview of monkey pox's pathogenesis.[11]

SYMPTOMS:

There is usually a 6 to 13-day incubation period for monkeypox, but it can be between 5 and 21 days.[27]

In the beginning, there is no specific symptom or sign, but symptoms such as lethargy, chills, fever, headaches, swelling of lymph nodes, asthenia, myalgia, and back pain can be present. Pharyngitis, conjunctivitis, and inflammation of the genital mucosa are associated with sore throats and shortness of breath. [24,25]

MPXV differs from smallpox in that its lesions look like crops, and it does not spread centrifugally. Every patient with human monkeypox develops lymphadenopathy, a clinical feature that distinguishes it from smallpox.[21,24]

An oropharyngeal lesion appears on the skin after it appears in the oropharynx. It is usually possible to detect serum antibodies by the time lesions appear.

COMPLICATIONS:

Among the complications, patients may suffer secondary bacterial infections, respiratory distress, sepsis, encephalitis, bronchopneumonia, permanent skin scarring, hyperpigmentation, conjunctivitis, and permanent corneal scars, as well as dehydration and death.[27]

DIFFERENTIAL DIAGNOSIS AND DIAGNOSTIC TESTS:

More than one disease or infection is associated with varicella, including disseminated herpes zoster or simplex, measles, secondary syphilis, chancroid, infectious mononucleosis, and molluscum contagiosum.

- Viral culture or viral isolation refers to the growing and characterization of a patient specimen with the aim of isolating a live virus.
- The use of electron microscopy allows visual classification of poxviruses other than Parapoxvirus through the use of negative staining.
- Testing for Orthopoxvirus antigens by immunohistochemistry.
- DNA signatures specific to monkeypox can be detected by PCR, including real-time PCR.
- The Orthopoxvirus IgG test is used to determine whether antibodies are present against Orthopoxvirus.
- The anti-Orthopoxvirus IgM test measures the level of antibodies to Orthopoxvirus.
- Testing for orthopoxvirus antigens in the Tetracore Orthopox BioThreat Alert.[26]

Polymerase chain reaction, electron microscopy, and virus isolation are the gold standard methods for confirming MPXV infection.[28]

As well as enzyme-linked immunosorbent assays (ELISAs), western blots (WBs), and immunohistochemistry (IHCs), monkeypox can also be detected using ELISA, WB, and IHC.

Several genes are involved in detecting monkeypox viruses, including those involved in envelope protein gene, the gatekeeper gene, DNA polymerase gene, complement binding protein, and the DNA-dependent RNA polymerase subunit 18.[29]

TREATMENT:

A specific clinically proven treatment is not available for monkeypox infection.[11] Supportive care, symptomatic management, and antimicrobial therapy remain the main recommendations for treating secondary bacterial infections.[25] Until the crust of the lesion falls off naturally and a new layer of skin is formed, all lesions should be covered as reasonably possible.[11]

Due to the 21-day incubation period for monkeypox, exposed individuals should monitor their temperature and symptoms twice daily for 21 days.

SUPPORTIVE MANAGEMENT: [26,27]

S.No	Symptoms/Signs	Management
1	Skin rash	• Simple antiseptics can be used to clean. • Fucidin/Mupironic Acid • If there are extensive lesions present, cover them with a dressing • Lesions should not be scratched or touched. • A systematic antibiotic may be considered in case of secondary infection
2	Corneal infection	• Antibiotics and antivirals are used in the treatment of ocular infections
3	The symptoms of dehydration may include poor appetite, nausea, vomiting, and diarrhea	• Encourage the use of oral fluids or ORS. • If necessary, intravenous fluids should be administered • A nutritious and adequate diet should be encouraged
4	Fever	• External cooling and antipyretic medications
5	Nausea and vomiting	• Antiemetics should be considered
6	Headache/ malaise	• Ensure adequate hydration and use of paracetamol
7	Bronchopneumonia	• CPAP, nebulizer treatments, and antibiotics for prophylaxis (oral or intravenous)
8	Sepsis	• Supplemental oxygen, antibiotics, corticosteroids, insulin are all used in conjunction with oral/intravenous antibiotics
9	Inflammation/Lymphadenopathy	• Medication to treat inflammation/pain administered orally or intravenously

VACCINATION:

Vaccination after exposure with the modified vaccinia Ankara vaccine may be recommended in some cases.[11, 24] When skin or mucous membranes are broken by respiratory droplets, body fluids or scabs from an infected patient, vaccinations should be administered immediately.To prevent or reduce the disease's severity, vaccinations should be given within four days of exposure.

It has been shown that LC16m8, another vaccine modified to prevent viral replication, protects nonhuman primates against severe monkeypox illness.[21]

Two vaccines are available to prevent monkeypox in the U.S. (JYNNEOS and ACAM2000). In monkeypox, a virus similar to smallpox is responsible for causing the infection. The JYNNEOS vaccine protects against monkeypox and smallpox and is available in two doses.

Vaccines for monkeypox and smallpox are available as part of ACAM2000. This product is not recommended for pregnant women, infants under 12 months of age, and individuals suffering from certain medical conditions, such as those with weakened immune systems, or from certain conditions or circumstances, such as heart disease or skin conditions. As far as monkeypox vaccinations are concerned, both should provide good protection.[14]

CDC recommends two doses of the JYNNEOS vaccine four weeks apart if exposed to an infected person. The effectiveness and durability of immunity after a single dose of vaccine are unknown, as it is expected to improve with two doses.[29]

ANTIVIRALS:

It was developed by the World Health Organization for the treatment of smallpox, and it was granted a license by the European Medicines Agency (EMA) to be used in the treatment of monkeypox in 2022 as a potential therapeutic for monkeypox, tecovirimat inhibits intracellular viral release. This drug has proven effective on infected animals by blocking the intracellular virus' release from the cell. Tecovirimat was found safe and tolerable in a human clinical trial reported by the CDC. The effectiveness of this treatment in treating MPX in humans needs to be further investigated. Likewise, cidofovir and brincidofovir (CMX001) have shown efficacy in animal and in vitro studies. Using an acyclic nucleoside phosphate, the first inhibits viral DNA polymerase, while using a cidofovir liquid conjugate, the second inhibits it.[22]

PREVENTION:

- According to the Center for Disease Control and Prevention, people should avoid close skin-to-skin contact with monkeypox-like rashes, avoid touching objects and materials used by monkeypox cases, wash their hands frequently after using the restroom, and use alcohol-containing hand sanitizers before eating.
- When caring for patients, wear the appropriate PPE.
- Rodents and primates must be avoided, and direct contact with blood and inadequately cooked meat must be limited to prevent MPXV spread.
- The general public needs extensive health education campaigns to help them understand how to avoid close contact with potentially infected animals and how to handle potential animal reservoirs properly.
- National health authorities should provide smallpox vaccinations to those who treat or are exposed to monkeypox patients or their samples. Monkeypox infection is prevented by 85% by smallpox vaccination. The Centers for Disease Control and Prevention (CDC) recommends vaccination within two weeks after significant, unprotected exposure to a diseased animal or a confirmed case of smallpox. [25-,28]

II. CONCLUSION:

In some areas of central Africa, monkeypox is endemic, particularly where people have direct access to remote forests. There are two possible routes to transmit from one individual to another or through an animal, and it can spread through droplets of body fluids or skin lesions. The presence of Lymphadenopathy distinguishes monkeypox from smallpox as a major clinical feature. It is also associated with bronchopneumonia, dehydration, respiratory distress, encephalitis, etc. Corneal scarring is the most concerning among all the complications, as it can result in vision loss. Several methods for detecting MPXV infection exist, but Gold standard methods are polymerase chain reaction, electron microscopy, and virus isolation. Specific clinically proven treatment is unavailable for this infection, but supportive care, symptomatic management, and antimicrobial therapy are the main options for treating secondary bacterial infections. Tecovirimat(antiviral) was found safe and tolerable in a human clinical trial reported by the CDC. The effectiveness of this treatment in humans needs to be further investigated.

Vaccination is the most effective way to prevent monkeypox infection and is recommended for anyone at risk of exposure. With the help of public health measures, the risk of contracting monkeypox can be minimized.

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