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A Review on Monkey pox Virus

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ABSTRACT

Monkeypox is a virus that is contagious between animals and humans and belongs to the Ortho poxvirus family of Poxviridae. In the 1970s, cases of monkeypox began to increase when smallpox vaccination was discontinued, attracting international attention. The virus got its name monkeypox because it was first identified in macaques. It is believed to be spread by a variety of rodents and small mammals, although the origin of the virus is unknown. Although monkeypox is sometimes transmitted from person to person, it can be spread by inhalation of droplets or contact with skin lesions of an infected person. Unfortunately, there is no definitive cure for monkeypox; however, supportive care can be provided to relieve symptoms. In severe cases, drugs such as tecovirimat can be given. However, there are no validated guidelines for the management of monkeypox symptoms. In this article, we have discussed various aspects of monkeypox, including virus structure, transmission, reproduction, clinical manifestations, vaccination, treatment, and current global distribution.

KEY WORDS: Monkeypox, Pandemic, Poxvirade, Vaccination

INTRODUCTION

The monkeypox virus was first isolated and identified in 1959 when monkeys sent from Singapore to a Danish research facility became ill. However, the first confirmed human case was in 1970, when the virus was isolated from a child with suspected smallpox in the Democratic Republic of the Congo. Concomitant immunity to mpox was previously achieved by vaccinia vaccination; however, the eradication of smallpox and the subsequent lack of vaccination efforts paved the way for smallpox to become clinically relevant. Additionally, since most smallpox cases occur in rural Africa, apparent underreporting may lead to an underestimation of the potential threat of this pathogen.[1-4].

Monkeypox virus belongs to the family Poxviridae, subfamily Chordo pox virinae, and genus orthopoxvirus. The genus encompasses many other poxviruses, including the smallpox, vaccinia, cowpox, and camelpox viruses, as well as more recently isolated poxviruses. These double-stranded DNA viruses are very similar

genetically and antigenically, which accounts for cross-immunity. Vaccination against smallpox generally provides some protection against monkeypox. [4]

EPIDEMOLOGY

Sporadic clusters and cases of human mpox have occurred outside of Africa. In 2003, Gambian giant rats imported from Ghana infected co-habitant prairie dogs sold as household pets in the Midwestern United States. This resulted in fifty-three human cases of mpox. In October 2018, one case occurred in a man who travelled from Nigeria to Israel. In May 2019, one case occurred in a man who travelled from Nigeria to Singapore. [5]

Precise prevalence and incidence are difficult to establish, given suspected shortcomings in disease reporting and confirmation. However, both metrics have increased since the discontinuation of routine smallpox vaccination. Demonstrated risk factors for mpox infection are living in heavily forested and rural areas of central and western Africa, handling and preparing bushmeat, caregiving to someone infected with the mpox virus, and not being vaccinated against smallpox. Male gender has also been correlated with infection risk. However, this may be confounded by the cultural norm that men frequently hunt and contact wild animals.[6]

ETIOLOGY

Mpox belongs to family: Poxviridae, subfamily: Chordopoxvirinae, genus: orthopoxvirus and species: mpox virus. In electron microscopy, the mpox virus is relatively large (200-250 nanometers). Smallpox viruses are brick-shaped and surrounded by a lipoprotein envelope that contains a linear double-stranded DNA genome.

In addition to relying on host ribosomes for mRNA translation, smallpox viruses contain all the necessary replication, transcription, assembly, and egress proteins in their genome. Smallpox is a zoonosis that spreads from animals to humans. Animal reservoirs for the disease are thought to include squirrels, rats, monkeys, primates, prairie dogs, hedgehogs, pigs, and mice found in areas of Africa where the vaccine was previously widespread. [7-9]

However, the current epidemic is mainly caused by human-to-human transmission through respiratory droplets, fomites, and direct contact with the lesions of an infected person. Recent analyzes have shown that viral loads are high in body fluids, including urine, saliva, semen, and feces, and in oropharyngeal and rectal swabs, suggesting that the main mode of transmission is sexual.[10]

PATHOPHYSIOLOGY

MPV can infect the human body through intradermal, mucosal, oral, and pharyngeal, and nasopharyngeal contact with susceptible individuals. After replicating at the inoculated site for an appropriate 6-13 days, they spread to regional lymph nodes and then enter the circulatory system (also called viremia).Blood-borne viruses infect host cells to spread to multiple sites, and viruses have immunomodulation abilities to avoid immune surveillance caused by horizontal gene transfer.

MPV has structural and functional similarities with other OPVs. An outer lipoprotein membrane with a geometric pattern of folds surrounds the egg-shaped or brick-like particle of the virus. The outer membrane surrounds and protects the dense nucleus and membrane bundles containing linear double-stranded DNA (197kb), transcription factors, and enzymes from external stress . Genes important for housekeeping are in the central region of and are highly conserved, while genes important for virus-host interaction (required for virulence) are found in the terminal region of and are less conserved among OPVs Although MPV is a DNA virus, its replication, assembly, and maturation occur in the cytoplasm of host cells (Figure 2). Additionally, most features of the VACV life cycle are likely to be common to the MPV, although the MPV life cycle is not well understood.[11-12]

In VACV & probably most MPV), there are two types of infectious virions: intracellular mature virus (IMV) and extracellular-enveloped virus (EEV) generated from infected host cells (32, 33). IMVs enter the host cell through activation of micropinocytosis, while EEVs through membranous fusion (34). When compared to EEVs, which are hypothesized to facilitate viral dissemination within an infected host, IMVs are the more common infective type and mediate host-to-host transmission. For the EEVs, they continuously released from infected cells and are believed to spread locally from tissue to tissue through bodily fluids (35). Although the fact that the aforementioned characteristics are for VACV, they likely apply to all OPVs. Conversely, different agents exist among OPV species. Most OPVs like the cowpox virus evade immune function through downregulation of MHC expression of antigen-presenting cells such as monocytes. While MPV demonstrated the ability to inhibit T-cell responses against other viruses through anti-CD3 stimulation.[13]

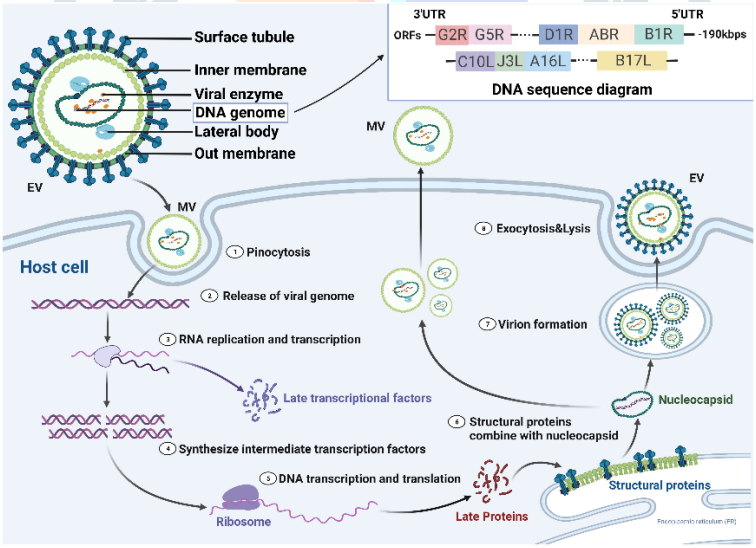

Fig.1 MPV life cycle in susceptible host cells.[14]

DIAGNOSIS

Due of the rarity of mpox, medical professionals may initially rule out other rash conditions like chickenpox or measles. However, enlarged lymph nodes often set mpox apart from other pox infections. Healthcare professional obtains a tissue sample from an open sore (lesion) in order to diagnose mpox. After that, it is sent to a lab for genetic fingerprinting, or polymerase chain reaction, or PCR testing. In order to test

for the mpox virus or antibodies produced by your immune system, you might also need to provide a blood sample.[15-16]

Alternatively, tests indicating the presence of Orthopoxvirus in a patient specimen, barring patient exposure to another of the same genus, can be sufficiently diagnostic, such as visualization on electron microscopy, immunohistochemical staining for orthopoxvirus antigens, serum studies for anti-orthopoxvirus IgM (indicating recent exposure) and IgG (indicating prior exposure or vaccination).[16]

MANAGEMENT

Treatment may be required for those with complications following vaccination with a replication-competent vaccinia vaccine. Vaccinia Immunoglobulin (VIG) is the preferred treatment for Vaccinia vaccine complications.

→ Early treatment in immunocompromised and other risk groups, e.g., children and pregnant patients. In pregnant patients, VIG may be preferred over Tecovirimat. In very young children, consider treatment for confirmed infection with serious or progressive infection. Consult an infectious diseases paediatrician for management of paediatric infections.

→ **Tecovirimat** for 14 days is the preferred treatment of monkeypox virus infection when treatment is deemed necessary. [17]

Dose: 200 mg capsules Adult 600 mg bd PO for 14 days; paediatric 13–25 kg: 200 mg bd, 25– 40 kg: 400 mg bd, >40 kg: 600 mg bd, with high fat meal

No dose adjustments for renal/hepatic failure.

Mechanism of action: Antiviral drug that inhibits the orthopoxvirus VP37 envelope wrapping protein. Prevents the formation of egress competent enveloped virions necessary for cell-to-cell and long-range dissemination of virus.

→ **Vaccinia immune globulin (VIG)** VIG is preferred for the treatment of complications associated with replication competent Vaccinia vaccination (ACAM2000™).

Dose of 6000 Units/kg intravenous. Consider higher doses where the patient does not respond to the initial dose. Multiple and repeated treatments may be required.

VIG provides passive immunity for individuals with complications to vaccinia virus vaccination. The exact mechanism of action is not known After intravenous administration of 6000 Units per kg to 31 healthy subjects in a double-blind study, the peak plasma concentration was achieved within 2 hours. The half-life of VIG was 30 days (range of 13 to 67 days)[18]

→ **Cidofovir**

Dose: 5 mg/kg body weight, intravenous

Induction treatment: Intravenous infusion at a constant rate over 1 hr administered once weekly for two consecutive weeks.

Maintenance treatment: Beginning two weeks after the completion of induction treatment, intravenous infusion at a constant rate over 1 hour administered once every two weeks.

Administration of Probenecid 2 g po 3 hours before Cidofovir, and 1 g 2– 8 hours post Cidofovir is recommended for most indications to increase blood levels. Probenecid may interact with several other medications. If probenecid cannot be administered the pharmacokinetics of Cidofovir may be less reliable.[19]

CONCLUSION

The primary habitat for monkeypox is the rainforests of central and western Africa. Unlike smallpox, the illness is a classic zoonosis since direct contact with an infected animal is the primary cause of most cases. Since the disease's symptoms in people can be quite similar to those of smallpox, chickenpox, or other vesiculopustular rash causes, prompt and reliable laboratory tests are essential to managing an epidemic. There is fear that MPXV might be utilised as a bioweapon due to the resemblance of African monkeypox patients to smallpox cases and the increasing lack of protection in the community after routine smallpox vaccination was discontinued.

Conflict of Interest: Nill

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