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Review Article

A REVIEW ON MONKEY POX DISEASE

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ABSTRACT

After the disastrous COVID-19 pandemic, now, monkey pox has spreaded its legs all over the world. Disease originated in Africa but its outbreak occurred in 89 countries since January 2022. As per the World Health Organization report, in between January 1, 2022, and August 10, 2022, 27,814 confirmed cases and 11 deaths occurred across 89 countries. Monkey pox is a viral infection which may occur in humans as well as in animals. Rope squirrel (*Funisciurus* spp.), Gambian pouched rat (*Cricetomys gambianus*), and Sooty mangabey monkey (*Cercocebus atys*) are suspected reservoir host for monkey pox. Its symptoms are similar to but milder than small pox. As orthopox viruses are morphologically identical to each other, Polymerase chain reaction is only test for detection of monkey pox-specific DNA signatures. There is no specific treatment for monkey pox infection but as monkey pox and small pox infections are hereditarily comparative so antiviral medications and antibodies created to safeguard against small pox are generally prescribed to prevent and treat monkey pox. One of the important measures for prevention from monkey pox is small pox vaccination to the individual and also to the healthy people in occupation who are at high risk of exposure except in immunocompromised individuals.

Keywords: Monkey pox, Viral infection, Polymerase chain reaction, Orthopoxvirus, Vaccines.

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INTRODUCTION

Human monkey pox is a zoonosis achieved by monkey pox disease, an orthopoxvirus and it is an immediate connection of variola infection (smallpox). In the genus Orthopox, there are 12 species and disease associated with this genus includes smallpox, cowpox, horse pox, camel pox, and monkey pox. Out of which, monkey pox becomes most infectious nowadays [1]. In the year of 1958, monkeypox virus (MPXV) was first found during an episode among monkeys at a Danish research center. In any case, it was not perceived as a human sickness until 1970, when a 9-month-old youngster became tainted in Democratic Republic of Congo, previously known as Zaïre [2,3]. The name monkey pox starts from the underlying disclosure of the infection in monkeys. It was first revealed in central Africa in 1970 and has generally impacted the absolute least fortunate and most underestimated networks in the world. In people, this illness has stayed endemic in Central African nations and beyond Africa. The multistate episode of cases announced in USA in 2003, among individuals who were in touch with imported animals (that time 800 little African warm blooded creatures were sent from Ghana to Texas) [4-6]. Symptoms, mode of transmission, suspected reservoir hosts, and treatment options of monkey pox are given in Fig. 1.

CURRENT STATUS OF MONKEY POX

Recently, the disease has increased in the cases in humans outside Africa in the month of May 2022. Its outbreak occurred in 89 countries since January 2022. As per the WHO report of August 2022, 27,814 confirmed cases and 11 deaths occurred in 89 countries which come under 6 WHO regions, from January 1, 2022, to August 7, 2022. The number of cumulative monkey pox confirmed cases and deaths from six WHO regions across 89 countries are given in Table 1. The instances that have been documented so far do not have any connections to endemic regions, but recent evidence indicates that cases have primarily, though not entirely, been found among men who have sex with men (MSM) who are seeking treatment in basic care and sexual health clinics [7].

India and Thailand come in South-east Asia region of the WHO, where total 13 confirmed cases and one death occur out of which India has reported nine confirmed cases and one death. As per the WHO report, first, monkey pox case was reported in India in Kerala on July 14, 2022. On July 24, 2022, Delhi received the first local transmission case report. The patient, a middle-aged male who had no recent history of travelling overseas, is thought to have spreading of the disease by contact with lesion exudates, saliva, or respiratory excretions [8].

STRUCTURE OF MPXV

It is a double-stranded DNA (dsDNA) virus with brick-like particles ranging in size from 220 nm to 450 nm in length and 140 nm to 260 nm in width. Their ultrastructure can be resolved with high resolution using electron microscopy (EM). The virion is made up of four main parts: The central core, the lateral bodies, the outer membrane, and the outer lipoprotein envelope. The viral dsDNA and core fibrils are found in the central core. The palisade layer, which is a tightly bound layer of rod-shaped structure, surrounds the central core. The outer membrane, which is surrounded by many surface tubules, encloses the central core, palisade layer, and lateral bodies (Fig. 2). At least 80 viral proteins are found in a mature virion [9].

TRANSMISSION OF MONKEY POX

It occurs in two ways that is transmission of monkeypox from animal to human or from human to human.

Transmission from animal to human (primary transmission)

The primary transmission starting from the bites/scratches from the wild infected animals.

This may be either incidental host or primary host as shown in Fig. 3. Many cases of primary transmission were reported with the hunting and consumption of those infected animals. MPXVs also found in the skin lesions and in almost all excretions such as urine, feces, oral, and nasal in animals. The most common routes of transmission include breathing and ingestion of infected tissues [11-13].

Transmission from human to human (secondary transmission)

In secondary transmission, humans can also become infected through aerosols during close contact or may be with direct contact with lesions.

Table 1: The number of cumulative confirmed cases and deaths due to monkey pox virus in six regions of the WHO reported from January 1, 2022, to August 7, 2022 [7]

World Health Organization regions	Confirmed cases	Deaths
Region of African	375	7
America region	10815	1
Region of Eastern Mediterranean	31	0
Region of Europe	16495	2
Region of South East Asia	13	1
Western pacific region	85	0
Total cases	27814	11

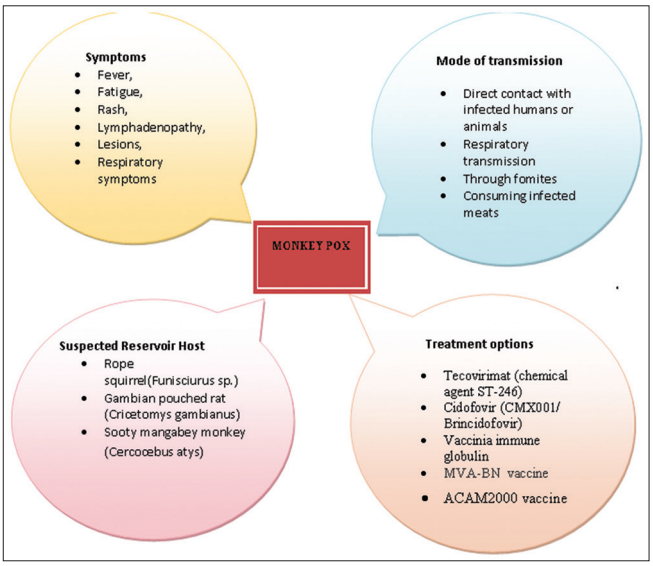

Fig. 1: Symptoms, mode of transmission, suspected reservoir hosts and treatment options of monkey pox

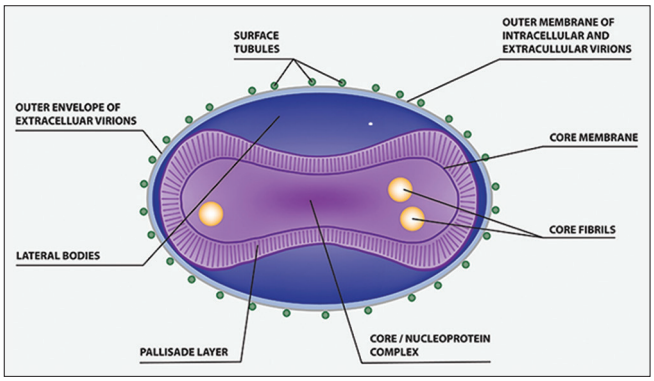

Fig. 2: Structure of monkey pox virus protein [10]

Human can get attacked through close contact with infected person/ objects or infected blood and body fluids as shown in Fig. 4. Recently, some cases were suspected through sexual communication mainly through MSM.

Few incidences in Africa linked with the handling and preparing for clinical cases and in the US some cases were reported among humans who had direct contact with infected animals [14-16].

SYMPTOMS OF MONKEY POX

The clinical symptoms are characterized by fever, rash, lymphadenopathy, fatigue, lesions, etc. Complications of monkey pox can include encephalitis, sight-threatening keratitis, pneumonitis, and secondary bacterial infections are all possible complications. Lymph nodes which have already swollen are firm, tender, and may be painful. Lymphadenopathy is not a sign of small pox, but it may be an evidence of infection with the MPXV, though more research is necessary to prove this hypothesis [17].

APPROACHES FOR MONKEYPOX DIAGNOSIS

There are two ways to diagnose monkey pox infection as shown in Fig. 5, first is primary diagnosis which involves morphological detection of orthopox virus by EM or by immunostaining, using immunohistochemistry (IHC) [18]. whereas confirmed diagnosis can be done by polymerase chain reaction (PCR) only. Some other tests are there like Anti-Orthopoxvirus IgG, Anti-Orthopoxvirus IgM, and Tetracore Orthopox BioThreat Alert, which can be used for detection of orthopox virus antibodies or antigens [19].

Primary diagnosis

It can be done by EM or by IHC.

EM

It detects viral particles in a biopsy specimen, vesicular fluid, viral culture, or scab material. As *orthopoxviruses* are morphologically identical from each other so skilled technician and high resolution microscope is needed for the task. Negative staining produces a visible image of a brick-shaped particle, enabling for the visual identification of a poxvirus.

IHC

IHC is the most common technique of immunostaining. In this antigens are identified in cells of a tissue section. It is the method of identifying antigens (proteins) in cells of a tissue section using the concept of antibody binding to a specific antigen in biological tissue. This test is used to detect the presence of orthopox virus specific antigen in biopsy specimens. It is performed to rule out the presence of other suspected agents. It is not specific test for detection of MPXV and should be carried out in a major laboratory by qualified technicians [20,21].

Confirmed diagnosis

It can be done by assay for genetic material, such as PCR.

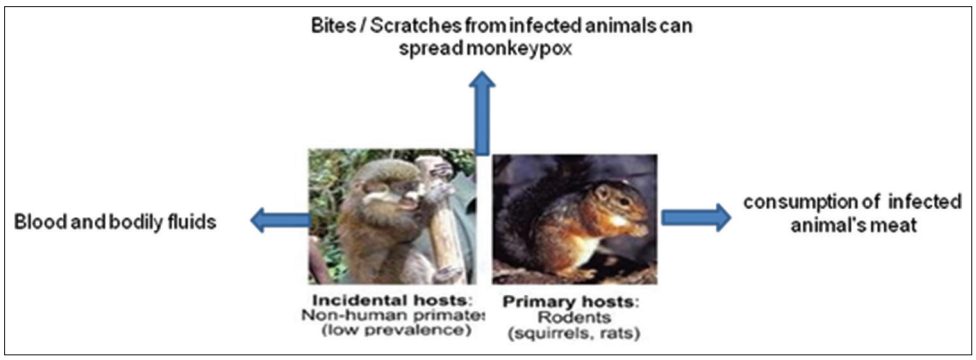

Fig. 3: Transmission of monkey pox from animal to human

PCR, including real-time PCR

This test is specific for detection of monkey pox-specific DNA signatures. This method can analyze dynamic cases utilizing lesion material of patient. Test utilizes viral DNA, which is steady assuming that sample is kept in dark and cool condition. As it is highly sensitive assay in which concerns should be given to avoid any contamination and require costly equipment and reagents so should be performed by skilled technicians [22].

Other tests

Anti-orthopoxvirus IgG

This test is used for detection of orthopox virus antibodies and can be utilized to detect previous occurrence of orthopox, including a microorganism or small pox vaccination. This test is not definite for monkey pox infection and its results will be altered by the previous small pox vaccination.

Anti-orthopoxvirus IgM

This test is used for detection of orthopox virus antibodies and can be used to detect recent exposure to orthopox, including a pathogen or small pox vaccination. This assay is not specific for MPXV.

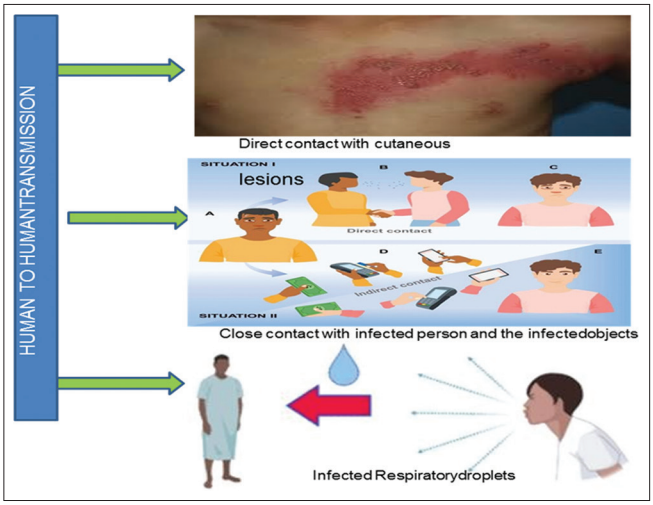

Fig.-4 Human to human transmission of monkey pox

Tetracore orthopox biothreat alert

This test is used for detection of orthopox virus antigens. It can quickly analyze a functioning case utilizing lesion material from patient. This test can be performed at optimum temperature with little skill. This examine is not explicit for monkey pox infection and less sensitive than PCR [23].

TREATMENT

There is no exact treatment for monkey pox infection but as monkey pox and small pox viruses are hereditarily similar so antiviral medications and preparations (vaccine) developed to protect against small pox are generally prescribed to prevent and treat monkey pox. Treatment of MPXV is supportive but may not be always advisable. In 2003, outbreak of monkeypox in the USA, the Centre for Disease Control recommended to euthanize all the suspected animals to prevent the zoonotic infection [24,25].

As per the WHO, treatment of monkeypox with an antiviral drug which was actually developed for the treatment of smallpox (Tecovirimat) got approved in January 2022 by the European Medicines Agency. Some treatment options developed uptill now for monkey pox treatment are as follows:

Tecovirimat (chemical agent ST-246)

It is an antiviral drug first reported in 2005, showed efficacy against orthopox virus infection when it was tested in several animal species. Having low molecular weight with the potency to act against multiple orthopox viruses such as smallpox, monkey pox, camel pox, cowpox, and mouse pox virus. This drug has undergone pre-clinical trials in animals and human volunteer shows good acceptance for up to 14 days oral route of administration. It acts in contradiction of the OrthopoxvirusV061 gene that encodes an important envelope protein (p37) which is required to produce extracellular virus. In cell culture ST246 inhibit formation of plaque and virus induced pathological changes [26-28].

Cidofovir (CMX001/Brincidofovir)

Brincidofovir (BCV) is an oral antiviral drug and lipid coupled prodrug of cidofovir (CDV). It has increased in the uptake of cellular material and can convert to active form easily with the help of intracellular enzymes as compared to cidofovir. This drug is bioavailable orally.

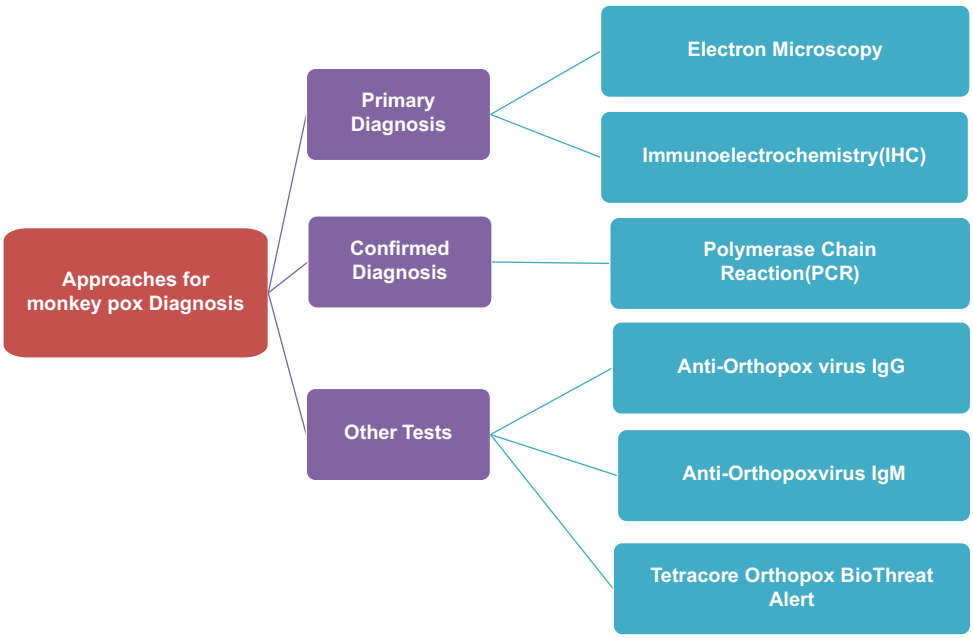

Fig.-5 Different approaches for monkey pox diagnosis

Brincidofovir incorporated in to viral DNA and causes inhibition of DNA polymerase enzyme. Brincidofovir, under the brand name Tembexa developed by Chimerix Inc. and approved by the FDA for the treatment of smallpox infection in June 2021. Tecovirimat in presence of CDV shows synergistic effect [29].

Vaccinia immuneglobulin

It is a hyper immune globulin prepared for few complications, for the vaccination of vaccinia virus. It is designated for the treatment of severe cases of unintentional inoculation with smallpox vaccine, eczema vaccine vaccinatum, and some other severe generalized and progressive vaccinia [30].

Modified Vaccinia Ankara (MVA)-BN vaccine

Bavarian Nordic JYNNEOS® smallpox (Monkeypox) vaccine is a type of live, attenuated vaccinia virus, MVA, which is not able to replicate in human body but showing effective immune response. The MVA is cultivated in Embryo of chicken, fibroblast cells, and a serum-free medium and cleansed and filtered. The two-dose MVA-BN (JYNNEOS®, USA, IMVANEX®, Europe; IMVAMUNE®, Canada) was approved by the U.S. FDA on September 24, 2019, and by the EMA in 2013 and is now indicated for preventing monkey pox and smallpox in adults suspected to be at higher risk to get infected [31].

ACAM2000 vaccine

This vaccine is recommended by the U.S. Food and Drug Administration to be used for people who are at high risk for small pox infection and it is made accessible for monkey pox disease under an Expanded Access Investigational New Drug application from 2019. It is a single dose vaccine and takes 4 weeks to reach immune protection at maximum. However, this vaccine has more side effects and adverse effects such as myopericarditis/pericarditis, so not recommended for people with very weak immune system and other issues [32].

PREVENTION AND CONTROL

One of the important measures for prevention from monkey pox is small pox vaccination to the individual and also to the healthy people in occupation who are at high risk of exposure. Vaccination can also be done in people who are exposed to monkey pox infected person or animal but not to be used in immunocompromised individuals [33].

Patients with assumed or confirmed case of monkeypox contamination should be retained in a separate distinct room. Door should be kept close. Patient should have a separate washroom. Patient's movement outside that room should be restricted and allowed only if medical needs arrive. Patients should use medical mask and appropriate gown to cover lesions if their transport outside the room is needed due to medical reasons. Patients with affirmed or suspected monkeypox infection must be segregated till the infection got ruled out. For patients with confirmed cases, isolation has to be maintained till all lesions have crusted, detached and fresh layer of strong skin has made underneath [34,35]. After confirmation of infection in patients, identification of close contact should be done both among health-care personnel and among social contacts. All contacts should be educated about the indications of monkeypox and will be instructed to monitor their temperature 21 days after exposure, 2 times in a day. Although they should not self-quarantined, it should decrease social interaction by wearing a facemask all the times [36].

All associates should be up-to-date about the symptoms of monkeypox and should educated to self-monitor their temperature twice every day for 21 days after exposure. Close contacts should not be quarantined, but should exercise extreme carefulness and reduce social interaction by wearing a facemask at all times.

Other measures for prevention and control are as follows

- Keep yourself away from contact with diseased animals (particularly sick/dead animals)
- Keep yourself away from contact with bedding and other resources adulterated with the virus
- Health-care staffs who enter the patient's room with PPE must include: Gown, gloves, eye protection (i.e., specs or a face shield), and NIOSH (National Institute for Occupational Safety and Health)-approved particulate respirator equipped with N95 filters or higher
- Food which contains animal meat should be properly cooked
- Wash your hands frequently as well as thoroughly with cleanser and water
- Avoid interaction with people who are suspected to be infected with the virus
- Washing machine and hot water (60°C) should be used to wash bed linens, towels etc.
- Do not share eating utensils with others and wash them properly with cleanser and hot water
- Contaminated exteriors and substances should be washed and disinfected with a hospital grade disinfectant or with diluted sodium hypochlorite solution (1:100).

Person attending to patient with monkey pox should be limited to only those who are essential for care and well-being of patient [37,38].

CONCLUSION

Conclusion-Monkey pox infection emerged as major threat since starting of 2022 and affected almost whole world. Future outbreaks of virus can be controlled by proper vaccination against this infection in addition to this apart from curbing this outbreak, efforts should be made to devise comprehensive measures to prevent and control future outbreaks of this zoonotic infection.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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