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An Inclusive Study on Monkeypox Virus

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ABSTRACT:

Monkeypox (MPX) is a rare zoonotic infectious disease caused by Monkeypox virus (MPXV). The first epidemics occurred mainly in central and western Africa, commonly known as "monkey pox". MPXV belongs to the genus Orthopoxvirus, family Poxviridae. The transmission cycle of the Monkeypox virus begins with the infection of the respiratory epithelium, after which it spreads lymphomatously to infect and replicate in the main systemic organs, indicating primary viremia. Monkeypox virus was aerosolized in monkeys and viremia was observed, after which the virus spread to the scattered lymph nodes, spleen, thymus, skin, oral mucosa, gastrointestinal tract, and reproductive system via lymphogens.

The initial mode of transmission is from animals to humans. Monkeypox is less contagious than smallpox and causes a less severe illness. Fever and other prodromal symptoms (eg, chills, lymphadenopathy, malaise, myalgia, or headache) may occur before the rash, but may also occur after the rash or may not be present at all. Most patients with the Monkeypox virus have mild symptoms and recover without any professional attention. Antiviral treatment is recommended for people who have symptoms and are at high risk of serious illness.

Key words: *monkey pox, viremia, orthppoxvirus*

INTRODUCTION

Monkeypox (MPX) is a rare infectious zoonotic disease caused by Monkeypox virus (MPXV). The first epidemics occurred mainly in central and western Africa, commonly known as "monkey pox". It is a double-stranded linear DNA virus belonging to the Poxviridae family, classified by the WHO as a disease with epidemic or pandemic potential. Its symptoms are similar to those of smallpox, but the disease is milder, presenting mainly as high fever, headache, lymphadenopathy, and systemic blisters and pustules, with a fatality rate of about 1 in 10 %.[1] Since the first cases of MPX were reported in Europe in early May 2022, more than 400 confirmed or suspected cases have emerged in at least 20 non-African countries.

MPXV belongs to the genus Orthopoxvirus, family Poxviridae. The virus particles are oval or brick-shaped and about 200 * 250 nm in size. Smallpox virus produces two infectious viral particles during replication: mature intracellular virus (MV) and extracellular enveloped virus (EV).[2] The family Poxviridae is divided into two subfamilies based on their definitive animal hosts: Entomopoxvirinae and Chordopoxvirinae. The subgroup Chordopoxvirinae infects vertebrates and is therefore organized into 18 genera, including Capripoxvirus, Cervidpoxvirus, Avipoxvirus, Molluscipoxvirus, Orthopoxvirus (OPV), Leporipoxvirus, Suipoxvirus, Yatapoxvirus and Parapoxvirus in isopoxvirus, Betapoxvirus, Del Gamentomopoxvirus, Del Gamentomopoxvirus. The Poxviridae subfamilies are classified into genera based on shared antigenic homology, serological activation of cross-tolerance, and phylogenetic grouping.[3]

Viruses continue to be responsible for a large number of emerging and re-emerging infections of medical importance, as well as a wide range of human and animal infectious diseases. Viruses pose a much greater threat to global public health than they did a century ago. Viruses cause the most feared and devastating human diseases, their ability to spread rapidly making them major contributors to the morbidity and mortality associated with infectious diseases worldwide. Nigeria recently began experiencing an outbreak of severe rash syndrome mimicking a form of varicella-zoster and smallpox, with monkeypox virus (MPXV) as the etiologic agent.[4]

HISTORY OF MONKEY POX

Monkeypox virus was first reported in 1959 during an outbreak of a smallpox-like disease among monkeys kept at a research institute in Copenhagen, Denmark. The first human case of MPXV in medical history was recognized on September 1, 1970, when a nine-month-old boy was admitted to Basankusu Hospital in the Democratic Republic of the Congo (then the Republic of Congo). The boy had a smallpox-like illness from which an MPXV

virus was isolated. 6 human cases of MPXV were described in Liberia, Nigeria and Sierra Leone between October 1970 and May 1971. The first index case of MPXV in Nigeria was recorded in 1971, and 10 cases of MPXV were reported between 1971 and 1978. Since then, several thousand human cases of monkeypox have been confirmed in 15 different countries, including 11 in African countries. Monkeypox has been imported into the United Kingdom, the United States, Israel and Singapore.[5]

EPIDEMIOLOGY

In 2003, an outbreak of MPX occurred in the United States. This is the first outbreak of MPX reported outside of Africa and has been linked to the transport of MPXV by marmots imported from Africa to the United States, resulting in a total of 47 people diagnosed in five states. In 2005, an MPX outbreak in Sudan reported a total of 10 confirmed and 9 suspected MPXV cases from September to December 2005. Between 2006 and 2007, a new human infection with MPX was detected in the DRC. Transmission of MPX has increased 20-fold since the 1980s, and people vaccinated against smallpox have a 21-fold lower risk of infection than unvaccinated people. Zoonotic transmission occurs in most cases. Since September 2017, MPX has broken out in Nigeria, with a total of 183 confirmed cases reported in 18 states as of November 2019. The outbreak was also the largest recorded in West Africa. French Later, imported cases of MPX were reported in Israel, the United Kingdom, Singapore, and other countries. Since May 2022, outbreaks of MPX have occurred in many countries of the world, which has raised a strong vigilance from scientists in many countries.[6]

PATHOPHYSIOLOGY

The transmission cycle of Monkeypox virus begins with infection of the respiratory epithelium by the virus, after which it spreads through the lymphomatous pathway to infect and replicate in major systemic organs, indicating primary viremia. During this stage, little or no virus is detected in the blood, since the virus is effectively cleared by the body's reticuloendothelial system. Primary viremia is followed by secondary viremia, which occurs when the virus is released from infected organs and lymphoid tissues into the blood and reaches the stratum corneum of the skin and mucosal epithelium to cause rash and mucosal lesions, respectively. It should also be noted that the severity of exanthema and enanthema depends mainly on the virion load in the blood during secondary viremia.

The mechanism underlying volume recovery is the movement of fluid from the intravascular to the extravascular compartment due to hypoalbuminemia and fluid loss in the gastrointestinal tract, as seen in systemic infections. This provides evidence that Monkeypox virus infection results in systemic involvement and that complications are not limited to mucosal and integrin surfaces as seen in the clinical presentation of the disease. Monkeypox virus was aerosolized in monkeys and viremia was observed, after which the virus spread to the scattered lymph nodes, spleen, thymus, skin, oral mucosa, gastrointestinal tract, and reproductive system via lymphogens.[7]

TRANSMISSION OF MONKEY POX

The initial mode of transmission is from animals to humans. Direct contact with infected animals or the possible ingestion of undercooked meat have been the main modes of transmission in past epidemics. Several animals have been implicated in the primary transmission of monkeypox infection. However, epidemiological investigations have established a close connection with rodents living in the woods. Human-to-human transmission has also been a driving factor in past outbreaks, such as the 1996-1997 outbreak in DRC, where 8-15% of contacts reported droplets respiratory, contact with mucocutaneous lesions, or fomites as secondary modes of transmission. . . Human-to-human transmission is driving the current MPXV epidemic, particularly through sexual contact, although other forms of close contact with infected patients also occur. There is also concern about the potential spread to pets and other animals, which could result in a zoonotic reservoir. Recent studies show that monkeypox viral DNA can be detected in skin lesions, as well as in saliva, urine, feces and semen. The viral culture of these fluids is not carried out; however, the spread of the virus in different fluids indicates that the virus may have other routes of infection that need to be explored.[8]

CLINICAL MANIFESTATIONS OF MONKEYPOX

The virus is transmitted by droplets and has an incubation period of 7 to 21 days (average 14). During this stage, the infected person is not able to transmit the infection to others. After this stage, viremia appears and clinical manifestations appear. At this point, the person can transmit the infection and spread the virus in the community. However, monkeypox is less contagious than smallpox and causes less severe disease. Fever and other prodromal symptoms (for example, chills, lymphadenopathy, malaise, myalgia, or headache) may occur before the rash, but may occur after the rash or may not be present at all.[9]

Monkeypox infection in pregnant women has rarely been reported, but may be associated with congenital infection, stillbirth, abortion, premature birth, or delivery of a healthy infant (91, 130–132). Although cases of monkeypox virus infection in pregnant women have been few, it is believed that this patient population is at greater risk of morbidity and mortality compared to non-pregnant adults. [10]

NEUROLOGIC COMPLICATIONS OF MONKEYPOX

Few neurological complications of monkeypox virus have been described. Headaches are a frequent manifestation in both categories 1 (Congo basin) and 2 (West Africa). Mood disorders, including depression and anxiety, and neuropathic pain are common. Skin lesions themselves can cause painful scarring and, depending on the site involved, can cause dysphagia, rectal pain with anal fissures, etc. It is not known if some of the pain can be dermatomal, similar to that seen in varicella-zoster, but the pain can be severe. Conjunctivitis occurred in about 20% of patients during a recent outbreak in the DRC, which can lead to decreased vision. This may also be a potential virological seeding site in the central nervous system. Monkeypox rarely causes encephalitis.[8]

DIAGNOSIS

The main diagnostic modalities for monkeypox virus (hMPXV) include PCR, viral culture and isolation, electron microscopy with negative fluorescence staining, immunohistochemistry for specific orthopoxvirus antigens, and IgM/IgG serologic tests. A lateral flow-based rapid screening test called the Tetracore Orthopox BioThreat Alert is available to prioritize sample testing for hMPXV. An even more sensitive point-of-care diagnostic tool based on gravity-driven continuous flow antigen capture ELISA was also developed. Known as the Antibody Immuno Column for Analytical Processes (ABICAP) immunofiltration tool, it can detect all zoonotic orthopoxviruses. An even more sensitive point-of-care diagnostic tool based on gravity-driven continuous flow antigen capture ELISA has also been developed. Known as the Antibody Immuno Column for Analytical Processes (ABICAP) immunofiltration tool, it can detect all zoonotic orthopoxviruses.[11]

Rapid, sensitive and accurate detection of MPXV can promote rapid control of monkeypox outbreaks. Current detection methods for human MPXV include nucleic acid-based detection (RT-qPCR, etc.), antibody-based detection (IgM/IgG serological test) and peptide-based rapid antigen test specific (RAT).[12]

Sample, material collection and storage temperature for MPXV diagnostic and differential purpose [13]

Type of Sample	Material Collections	Storage Temperature	Purpose of Collection
Serum	Serum separator tubes	Samples collected should be stored in the refrigerator (2-8°C) until they are sent to the laboratory and should be sent in the cold chain.	Serology should be considered for differential diagnosis and to aid in research.
Oropharyngeal swab	It should be taken with a dry swab or VTM (Dacron or polyester flocked swabs should be used)	The collected samples must be cooled (2-8°C) until they are sent to the laboratory and must be sent to the cold chain	Recommended for diagnosis, if possible, in addition to skin lesion material.
Skin lesion material, including: ➢ Swabs of Lesion exudate ➢ Lesion roofs ➢ Lesion crusts	It should be taken with a dry swab or VTM (Dacron or polyester flocked swabs should be used)	The collected samples must be cooled (2–8° C) until they are sent to the laboratory and should be sent in the cold chain.	Recommended for diagnosis.

TREATMENT OF MONKEYPOX

Most patients with the Monkeypox virus have mild symptoms and recover without any professional attention. However, some patients may require hospitalization and supportive care for nausea, vomiting, risk of dehydration or pain management. Antiviral treatment is recommended for people who, as stated before, are at high risk of serious illness.

There are several antiviral medications that can be used to treat monkeypox. Some of these drugs were developed to treat smallpox in animals, but are expected to have the same activity against monkeypox. Among all available antivirals, tecovirimat is the treatment of choice in most cases. Patients with severe disease can also benefit from dual therapy with tecovirime and cidofovir. Public health officials must be notified when these treatments are initiated.[14]

Tecovirimat

Tecovirimat is available in intravenous and oral form. This drug inhibits the VP37 protein present in the orthopoxvirus and therefore prevents the interaction of the virus with the host cell. This results in the inhibition of infectious viral particles and prevents infection of the host cell. The dose of tecovirimat depends on the patient's weight and renal function (IV); the duration of the treatment is 14 days.

The only contraindication to tecovirime, when administered IV, is severe renal insufficiency with a creatinine clearance of 30 ml/min. The oral form, on the other hand, presents no contraindications, regardless of the form of renal function. Tecovirimat has not been studied in pregnant or lactating women. It is not known whether tecovirimat is present in breast milk. If treatment is indicated in a pregnant or lactating patient infected with monkeypox virus, tecovirimat should be considered first-line treatment for these patients.[14]

Dosage of Tecovirimat - Adults; 600 mg twice a day for 14 days; children (13 kg or more), if 13 kg to less than 25 kg: 200 mg twice a day for 14 days, if 25 kg to less than 40 kg: 400 mg twice a day for 14 days, if 40 kg or more: 600 mg twice a day for 14 days.[15]

Cidofovir

This drug is effective against Monkeypox in animal studies. However, there are no significant clinical data on its effectiveness against monkeypox infection in humans. The mechanism of action of cidofovir involves the conversion of cidofovir to its active metabolite called cidofovir diphosphonate. This cidofovir diphosphate then causes selective inhibition of viral DNA synthesis, thereby suppressing viral replication. Severe acute renal failure leading to dialysis may occur after one or two doses of this drug. Renal function should be monitored with each dose of cidofovir. Patients to be treated with this medication also receive intravenous saline for rehydration and oral probenecid. Probenecid decreases the renal clearance of cidofovir by blocking renal tubular secretions, thus reducing the incidence of nephrotoxicity.

Patients are at risk of neutropenia with this medication, so the patient's neutrophil count should be monitored while receiving this medication. There is a risk of metabolic acidosis, as well as liver failure and pancreatitis. Cidofovir should be avoided in pregnant women because it can be teratogenic; however, if its use is warranted, systemic treatment should be avoided if possible, during the first trimester. It is not known whether cidofovir can pass into breast milk at this time. However, breastfeeding is not recommended due to possible serious side effects with this medication.[14]

The dose of Cidofovir - 5 mg/kg once a week for 2 weeks, followed by 5 mg/kg IV once every two weeks.[15]

Brincidofovir

This medication is similar to cidofovir, but probably has fewer side effects. This drug is a lipid conjugate that is converted to cidofovir intracellularly, which is then converted to cidofovir diphosphonate, an active metabolite of cidofovir. Cidofovir diphosphate causes selective inhibition of viral DNA, suppressing viral replication. Important side effects include hepatotoxicity. During the initiation of this drug, patients with liver dysfunction should closely monitor their liver function. If a patient develops liver failure during treatment, consider discontinuation of treatment if alanine transaminase (ALT) remains persistently elevated and 10 times the upper limit of normal. Pregnant women should avoid taking this medication because in utero exposure to brincidofovir can harm the fetus. It is not known whether brincidofovir can pass into breast milk; therefore, breastfeeding is not recommended while the patient is taking this medication.[14]

Brincidofovir Dosage - Adults weighing ≥ 48 kg: 200 mg once a week in two doses; adults and pediatric patients weighing ≥10 kg to less than 48 kg: 4 mg/kg oral suspension once weekly for two doses; Children weighing less than 10 kg, the dose is 6 mg/kg of oral suspension once a week for 2 doses.[15]

Trifluridine

This medication can be used to treat and prevent corneal and conjunctival damage in patients with monkeypox lesions affecting the eye. This medication comes in the form of topical antibiotic drops or ointments, which can be applied every four hours for seven to ten days. No dose adjustment is necessary for patients with hepatic and renal insufficiency. The mechanism of action of trifluridine involves interference with virus reproduction by inhibiting thymidylate synthetase, thereby reducing the viral load.[16]

PRESENT CIRCUMSTANCE OF MONKEYPOX IN INDIA

A suspected case of monkey pox has been reported in one of the hospitals designated to handle the disease in the country, the Union Health Ministry said on September 09, 2024, adding that further investigations are underway to confirm the diagnosis in a man who has a history of traveling in the country. one of the affected African countries. The Ministry of Health said that the patient suspected of having the viral disease was isolated and contact tracing was underway to identify the possible source of the infection.

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