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LEADING ARTICLE

Monkey Pox

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Abstract

Declaring a global emergency is a significant act. It is a rallying cry for countries to take the virus seriously, it raises awareness around the world and it can help poorer countries get the tools they need to control monkeypox (MPX). In principle, we have the tools to stop the virus. Monkeypox does not spread as easily as Covid and we already have a vaccine (developed for smallpox) that offers good protection. And while anyone can catch monkeypox, the outbreak is overwhelmingly concentrated in gay and bisexual men. This can make the outbreak easier to tackle, as efforts, including vaccines and public health information, can be targeted at those most at risk. But there are still countries where same-sex relationships are illegal and stigma and persecution can act as a barrier to help. Whether we can stop monkeypox is as much a societal and cultural challenge as it is about the virus. More than 16000 cases and 5 deaths have been reported in 75 countries since May 2022 persuading the World Health Organization (WHO) to declare the MPX outbreak as a public health emergency of international concern. As of 10 August, 2024, 162 MPX cases were found in Asia. Of these, 9 cases were reported from India. Since Bangladesh shares a larger common border with India, there is no reason for Bangladesh to feel relaxed reflecting the situation during the COVID-19 pandemic again; UAE also confirms its monkeypox cases among the population. The first case in India was a migrant from UAE. Keeping this in mind, Bangladesh also has a large number of a migrant in UAE making it more vulnerable. This is especially concerning as the knowledge level of monkeypox among the general population of Bangladesh is quite poor. On the 7th and 9th of June 2024, three suspected cases were found in Bangladesh which caught the eye of the public and health policy makers. The first case was suspected at the airport of a 32-year-old Turkish citizen while screening. He was then taken to the Infectious Diseases Hospital in Mohakhali, Dhaka. However, on 9th June the case was reported negative. And, the second time, two cases were seen, one was isolated in Chuadanga in a 60-year-old woman after local doctors detected symptoms of MPX. On the same day, a 42 years old man returning from India through Benapole Border Crossing was sent to Jashore Hospital after showing pox-like features.

Keywords: *Monkey pox.*

Introduction

In 1970, when smallpox was nearly eradicated, a previously unrecognized orthopoxvirus named monkey pox (MPOX) was identified in humans. The first known human case occurred in Democratic Republic of Congo (DRC) when a 9-year-old boy developed a smallpox like illness, which was eventually confirmed as human monkey pox by the World Health Organization. Similar cases occurring in 1970-1971 from the Ivory Coast, Liberia, Nigeria, and Sierra Leone were attributed to monkey pox infection.[1]

Monkey pox was limited to the rain forests of Central and Western Africa until 2003, when the first cases in the Western Hemisphere were reported. In late spring 2003, multiple persons were identified in the mid-western United States who had developed fever, rash, respiratory symptoms, and lymphadenopathy following exposure to ill pet prairie dogs infected with the monkey pox virus.[2]

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In the most recent outbreak, the United Kingdom reported 9 cases of monkey pox in early May 2022, with the first identified case having recently traveled to Nigeria. From this adult index case, there were 2 confirmed transmissions within the patient's family, to another adult and a toddler.[3] On May 18, 2022, the Massachusetts Department of Public Health announced a confirmed case of monkeypox in an adult male who had recently visited Canada.[4]

As of October 19, 2022, there were over 74,700 total confirmed monkey pox cases in more than 200 different nations. Cases were present on every inhabited continent.[5] In the US, there were 27,635 total confirmed cases as of October 19, 2022.[6] By March 7, 2023, there had been 30,235 reported MPOX cases in the US. Cases of monkeypox in the US peaked in early August 2022 with a 7-day moving average of 439. Owing to vaccination and avoidance in at-risk populations, the 7-day average of 48 cases have decreased as of October 19, 2022.[7]

An overwhelming number of cases in the current outbreak are among men who have sex with men. While sexual transmission has not been definitively confirmed, this mode of transmission seems likely, especially given that initial lesions are often reported at sites of sexual contact.[8]

Epidemiology

This condition is rare and only known to be indigenous to the rain forests of western and central Africa.[9] Surveillance reports from 1981-1986 documented 338 cases in the DRC. In the 1996-1997 outbreak in the DRC, the attack rate was 22 cases per 1000 population. The 2022 outbreak involved 51 locations as of June 29, 2022, and included 5,115 confirmed cases.[5]

Monkeypox is considered endemic in northern and central DRC. Sporadic occurrences of disease are reported in neighboring countries.[10] Poxvirus infections have no racial predilection, and the incidence is equal in males and females, except in the 2022 epidemic, where patients are overwhelmingly male who have sex with men. The median patient age was 38 years.[11]

A morbidity and mortality report from the US Centers for Disease Control and Prevention revealed that, in the 2022/2023 outbreak, there were 38 MPOX-related deaths (1.3 per 1000 cases). Men represented 94.7% of mortalities, with 86.8% of mortalities being Black persons. The overwhelming majority of those who succumbed were immune-compromised secondary to HIV infections. [7]

It has been hypothesized that cessation of smallpox vaccination may be a factor in the increasing incidence, but this theory fails to account for why the disease has not reemerged in countries where the disease was seen previously, such as West Africa.[12]

Etiology[13]

In the DRC in 1997, animals caught from the wild were tested for the monkeypox virus. The following animals were found to have neutralizing antibodies against the monkeypox virus, suggesting a role as natural reservoirs: domestic pig, Gambian rat, elephant shrew, Thomas's tree/rope squirrel, Kuhl's tree squirrel, and sun squirrel. Human-to-human transmission supplanted the prominence of animal-to-human transmission in the 1996-1997 outbreak in the DRC. Crowded living quarters, poor hygiene, discontinuation of the smallpox vaccination, and decreased herd immunity were implicated. Respiratory droplets and direct contact with mucocutaneous lesions or fomites have been postulated as routes of human-to-human transmission.

There are two distinct clades of the virus

- Clade one (I): Formerly known as the Central African (Congo Basin) clade.
- Clade two (II): Formerly known as the West African clade.

  Clade (II) consists of subclades IIa and IIb; Clade II is associated with milder disease, fewer deaths and limited human-to-human transmission compared with Clade I.

Pathophysiology[13-16]

The mpox virus is a member of the genus orthopox; other members include cowpox, vaccinia, and variola (smallpox) viruses. It is a zoonotic virus with primary transmission believed to occur through direct contact with infected animals or possibly by ingestion of their inadequately cooked flesh.

Incubation period is typically between 6 to 13 days (range 1 to 21 days). The extent to which asymptomatic or presymptomatic transmission may occur is unknown. Replication-competent viral shedding has been documented in the presymptomatic phase, and presymptomatic transmission has been documented. Asymptomatic infection has been described, but the extent to which asymptomatic infection may occur is unknown. Asymptomatic infections may play a role in sustaining circulation of the virus resulting in sporadic cases and clusters.

Inoculation may be from cutaneous or mucosal lesions on the animal, especially when the skin barrier is compromised secondary to bites, scratches, or other trauma. The infection was first seen in laboratory monkeys in 1958, thus, the name monkeypox, although rodents are believed to be the major reservoir in Africa.

Following viral entry, the virus replicates at the site of inoculation (e.g., skin or respiratory route). The virus can infect epithelial cells, dendritic cells, and macrophages in the respiratory tract, or keratinocytes, fibroblasts, Langerhans cells, dendritic cells, and macrophages in the skin. The virus binds to host cell surface glycosaminoglycans and undergoes endocytosis to enter the cell. Infected cells travel to nearby draining lymph nodes (primary viremia). The virus reaches distant lymph nodes and organs via the circulation. This phase of the infection is asymptomatic. During the prodromal stage, secondary viremia occurs from the lymphoid organs to the skin and other organs (e.g., eyes, lungs, gastrointestinal tract, gonads), and nonspecific symptoms develop from the immune system being triggered. Infection of skin and mucosa leads to appearance of pustules and ulcers.

Clinical Feature[17]

The most reliable clinical sign differentiating monkeypox from smallpox and chickenpox is enlarged lymph nodes, especially the submental, submandibular, cervical, and inguinal nodes (Fig.-1).

Fig.-1 *Lymphadenopathy in monkeypox. Large nodes in the mandibular, cervical, or inguinal region are commonly seen in monkeypox. The presence of significant lymphadenopathy helps differentiate monkeypox from smallpox and chickenpox*

In the exanthema stage, within a particular body region, lesions evolve synchronously over 14-21 days, similar to the development of lesions with smallpox. However, unlike smallpox, skin lesions may appear in crops. In contrast to smallpox, the lesions do not have a strong centrifugal distribution. Lesions progress from macules to papules to vesicles and pustules; umbilication, crusting, and desquamation follow (Fig.-2 & Fig. -3). Most lesions are 3-15 mm in diameter.

Fig.-2 *Umbilicated papule on the lower part of the leg. This smaller lesion still shows the typical umbilicated morphology*

Fig.-3 *Vesicular rash on the dorsal aspect of the hand. Vesicopustules are seen; some have a central umbilication*

Ocular monkeypox[17]

Ocular monkeypox is a potentially sight-threatening infection and requires urgent assessment and treatment. Signs and symptoms include vision changes, eye pain, itching, redness, swelling, and foreign body sensation. Clinicians should consider prompt initiation of treatment with systemic antiviral therapy, in addition to trifluridine ophthalmic drops in patients with ocular manifestations.

Diagnostic Criteria[18]

The diagnostic criteria are summarized below:

Confirmed case

Meets 1 or more of the following laboratory criteria:

- Isolation of the monkeypox virus in culture from a sample obtained from the patient
- Demonstration of the monkeypox virus on PCR in a specimen obtained from the patient
- Demonstration of the monkeypox virus by immunohistochemical methods in samples obtained from the patient in the absence of exposure to another orthopoxvirus

Probable case

This is contact that meets current epidemiologic criteria as per the CDC. It is the occurrence of fever and vesicular-pustular rash, with the onset of the first sign or symptom at most 21 days after the last exposure, meeting the epidemiologic exposure.

Suspected case

This is contact that meets current epidemiologic criteria per the CDC. It the occurrence of fever or unexplained rash and 2 or more other signs or symptoms, with the onset of the first sign or symptom at most 21 days after exposure, meeting the epidemiologic criteria. Symptoms are as follows:

- Chills and/or sweats
- Lymphadenopathy
- Sore throat
- Cough
- Shortness of breath
- Headache
- Backache

Laboratory Studies[19-21]

- On November 15, 2002, the US FDA recommends to detect monkeypox virus DNA in swabs from human monkeypox lesions in patients with suspected monkeypox cases.
- A viral culture should be obtained from an oropharyngeal or nasopharyngeal swab.
- A skin biopsy specimen of the vesiculo-pustular rash or a sample of the roof of an intact vesiculopustule should be analyzed.
- Tissue for PCR of DNA sequence-specific for the monkeypox virus may be obtained.
- Paired sera for acute and convalescent titers may be analyzed. Serum collected after more than 5 days for IgM detection or serum collected more than 8 days after rash onset for IgG detection was most efficient for the detection of the monkeypox virus infection.
- A Tzanck smear can help differentiate monkeypox from other non-viral disorders in the differential diagnosis.

Management[22,23]

The disease is usually self-limited; resolution occurs in 2-4 weeks. In the African cases, the mortality rate was 1-10%, and death was related to the patient's health status and other comorbidities. Most patients died of secondary infections. No fatalities were reported in the 2003 US outbreak.

Patients often feel poorly during the febrile stage of the illness; therefore, bed rest along with supportive care may be necessary. Hospitalization may be necessary in more severe cases; a negative pressure room is preferable. To avoid infection of health care workers and close contacts, airborne and contact precautions should be applied. Isolation must be continued until the last crust is shed.

Antiviral Agents

Tecovirimat (TPOXX)

Tecovirimat (TPOXX) is approved by the FDA and is indicated for treatment of human smallpox disease caused by variola virus. Also, the CDC holds an expanded access investigational new drug (EA-IND), also called compassionate use that allows for the use of stockpiled tecorvirimat to treat monkeypox (mpox) during an outbreak.

Cidofovir

Although cidofovir has proven activity against poxviruses in *in vitro* and animal studies, it is not known whether or not a patient with severe monkeypox infection will benefit from treatment. The CDC holds an EA-IND that allows for the use of stockpiled cidofovir for the treatment of orthopoxviruses (including monkeypox) in an outbreak. Cidofovir diphosphate selectively inhibits orthopoxvirus DNA polymerase-mediated viral DNA synthesis.

Brincidofovir

Brincidofovir (Tembexa) is indicated for treatment of smallpox caused by variola virus in adults and children, including neonates. Brincidofovir is a

prodrug of cidofovir diphosphate. Brincidofovir may have an improved safety profile over cidofovir The CDC is currently developing an EA-IND for to help facilitate use of brincidofovir as a treatment for monkeypox.

Vaccinia immune globulin (VIG)

Data are not available on the effectiveness of VIG in treatment of monkeypox complications. Use of VIG is administered under an EA-IND for treatment of orthopoxviruses (including monkeypox) in an outbreak. It is not known whether a patient with severe monkeypox infection will benefit from VIG treatment.

VIG can be considered for prophylactic use in a monkeypox-exposed person with severe immunodeficiency in T-cell function for which smallpox vaccination following monkeypox exposure is contraindicated.

Treatment of ocular monkeypox[24]

Patients with monkeypox can experience serious ocular complications. Cases of monkeypox are mostly self-limited; however, lesions that involve anatomically vulnerable sites can cause complications. Ocular monkeypox may occur when the virus is introduced into the eye, most typically from autoinoculation. Ocular infection can potentially cause conjunctivitis, blepharitis, keratitis, and vision loss.

Clinicians should consider prompt initiation of systemic antiviral therapy in addition to topical trifluridine in patients with ocular manifestations. The CDC emphasizes the importance of reducing the risk of ocular complications by practicing good hand hygiene and to instruct patients with ocular monkeypox to avoid touching their eyes and refrain from using contact lenses.

Guidelines Summary[8,25]

Clinical guidance on monkeypox and smallpox vaccination was updated in June 2022 by the US Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP).

ACIP recommends that individuals with occupations that may expose them to orthopoxvirus diseases receive pre-exposure prophylaxis with either Jynneos or ACAM2000. Examples of such occupations include healthcare workers as designated by public health authorities, clinical laboratory personnel directly involved with orthopoxvirus testing, and research laboratory personnel handling orthopoxvirus cultures.

If a person is exposed to monkeypox virus and has not received smallpox vaccination within the last 3 years, the CDC recommends administration of Jynneos within 4 days of exposure. Vaccination may mitigate symptoms without preventing the disease if received within 4-14 days of exposure.

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