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Review Article

Emergence of monkeypox virus: a public health threat

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ABSTRACT

The human monkeypox virus is a zoonotic infection that is closely related to smallpox virus. It more commonly exists in forested habitats of western and central Africa. In the recent outbreak of the monkeypox virus, the total number of positive cases escalated to 32,760 and 12 deaths were reported so far. With rodents being primary reservoirs, the virus spreads through animals, fomites, respiratory droplets and, direct contact. It typically presents as a vesiculo-pustular rash along with fever, headache, malaise and chills. Taking this clinical spectrum into consideration, differential diagnosis to rule out smallpox is very much significant. Though there are no licensed therapies for monkeypox, treatment regimens and vaccination for small pox can also be used for monkeypox. Effective prevention relies on avoiding contact and limiting respiratory exposure with the infected patients by following standard precautions. This review article gives an insight into epidemiology, clinical presentation, diagnosis, transmission, vaccination, and prevention of infection.

Keywords: Monkeypox virus, Smallpox virus, Outbreak, Vaccination

INTRODUCTION

Monkeypox is a rare zoonotic infection caused by monkeypox virus. It belongs to *Poxviridae* family, *Chordopoxvirinae* subfamily, and *Orthopoxvirus* genus. It is closely related to the variola (smallpox) virus and causes smallpox-like vesiculo-pustular rash in humans.[1] It was first identified in 1959 in Copenhagen in captive cynomolgus monkeys and was also recovered in outbreaks of illness in apes or monkeys in the USA, France and, Netherlands. Hence, it was named monkeypox. However, it's a misnomer because monkeys are not the only natural reservoirs of the disease.[3] Monkeypox virus was first discovered to cause infection in humans in 1970 in the Democratic Republic of Congo and 54 cases identified between 1970 and 1979 in forested habitats of Western and Central Africa.[2] This literature review mainly focuses on epidemiology, transmission, clinical features, diagnosis, vaccination and prevention strategies of monkeypox virus, keeping in view recent outbreak of infection.

VIROLOGY

Monkeypox virus has a double-stranded DNA genome with nearly 2,00,000 base pairs and on electron microscopy, the virus shows a brick-like shape measuring 200-400 nm. Two distinct Strains of the virus are isolated from Western and Central Africa, with the West African strain being less virulent.[3]

EPIDEMIOLOGY

Background

Monkeypox virus was first identified as a human pathogen in the Democratic Republic of Congo, in an infant who presented with smallpox-like eruptions.[2] Many outbreaks continue to occur in small villages, rural areas, and tropical forests with human-animal contact. In 2003, an outbreak in the United States was the first outbreak outside Africa. It was linked to contact with infected pet dogs.[5] Between

August 2017 and August 2018 monkeypox outbreaks occurred in the Democratic Republic of Congo, Central African Republic, Nigeria, where monkeypox has not been reported in the past 20 years.[4] Since September 2017, cases have been reported from Nigeria. Until April 2022 a total of 558 suspected cases have been reported from 32 states in the country.[7] Since May 2022, monkeypox has been reported in non-endemic and endemic countries. These cases are associated with travel to countries in North America and Europe, rather than West Africa.[6] The index case of the 2022 outbreak was confirmed on 7th May, in United Kingdom resident with a travel history to Nigeria. Monkeypox was confirmed through reverse transcriptase polymerase chain reaction on the isolates from the patient. The virus was genetically related to the West African clade.[7] Since January 2022, 91 member states of WHO reported monkeypox cases. The number of cases escalated, by August 11th, 2022 a total of 32,760 confirmed cases, including 12 deaths were reported. The most affected countries are the United States of America, Spain, Germany, The United Kingdom, France, Brazil, Canada, Netherlands, Portugal, and Italy.[8]

Transmission

The natural reservoir of the monkeypox virus is Rodents. It primarily transmits from animals to humans in the endemic regions via bites or scratches from infected animals, body fluids, cooking, and eating of infected animals. It secondarily transmits from humans to humans in the non-endemic regions via large respiratory droplets, fomites, and contact with lesions.[9]

There is more risk of transmission via sexual contact as lesions occur more commonly in the anogenital region. However, there is no evidence of transmission via seminal or vaginal fluids. There is also evidence of vertical transmission from mother to fetus.[10]

Clinical presentation

The incubation period of monkeypox is usually 5 to 15 days with a maximum duration of 9-21 days. Currently according to 2022 studies, the mean incubation period is 5-8 days.[11] The person is infectious from his prodromal state until the lesions scab off. People living in forest areas, bisexuals, persons having men to men sexual relationships, children <15 years of age, and those who have not been immunized to smallpox, people with HIV are considered to be high-risk individuals. The disease is self-limiting and typically presents with prodromal symptoms like fever, headache, chills, malaise and lymphadenopathy followed by a characteristic rash. The rash appears 1 to 4 days following fever. The rash progresses through macule-papule-vesicle-pustule-scab over 2 to 3 weeks. The lesions are deep-seated, firm or hard, and well-circumscribed, the lesions may also show umbilication.[5,12] The lesions are mostly seen on the trunk, hands, legs, sole, and foot. The size and stage of the lesions are the same unlike chickenpox.[13] In severe infection lesions coalesce, until a large section of skin is sloughed off. The rashes are painless but may present with pruritis during the healing phase. Presentation of monkeypox in the May 2022 outbreak is atypical even though the rash is the characteristic feature. The prodromal phase may be mild or even absent. Sometimes rash may be the first symptom even before the prodromal symptoms. The rashes are mostly seen in the anorectal region and on mucous membranes. The progression of the lesions in the same anatomical site is at different stages and sizes. Rectal symptoms include purulent or bloody stool, rectal pain and rectal bleeding. Recent studies reported case fatality ranging between 1-11%.[12]

Diagnosis

Diagnosis is based on the clinical presentation and history of travel to endemic countries. Laboratory diagnosis is made out by taking the sample from the pustular area for the detection of monkeypox viral DNA by reverse transcriptase polymerize chain reaction (PCR) and Electron microscopy. Diagnosis can also be made out by the detection of antigens by the immune-fluorescent assay and ELISA techniques.[14]

Prevention and control

To contain the person-to-person transmission, confirmed cases should be isolated. Health care workers should use personal protective equipment, N95 masks, double gloves, etc. Only the trained laboratory personnel should handle the samples collected from humans and animals. Transportation of specimens must be done in line with WHO guidelines. Prior smallpox vaccination is protective for frontline workers. To counter the animal to human transmission inappropriate handling of infected and dead animals should be avoided. Animals suspected to be exposed to the virus are segregated and kept under observation. Importation of rodents and non-primates must be hindered. Only cooked meat should be consumed.[15,16]

PRE-EXPOSURE PROPHYLAXIS

According to the June WHO guidelines, mass vaccination is not suggested. Only health workers and laboratory personnel dealing with Monkeypox virus infected-patients and/or their samples need vaccination. A 20-fold increase in monkeypox virus cases has been reported between 1980 and 2007 i.e., after the discontinuation of the smallpox vaccine.[17] Due to antigenic similarity between monkeypox virus and smallpox virus, the smallpox vaccine gives cross-protection against monkeypox virus.[18] According to U.S CDC, the vaccine should be administered 4 days before to exposure to the Monkeypox virus and within two weeks to reduce the severity of symptoms. The two FDA-approved smallpox vaccines (2nd generation) contain the replication-competent live vaccinia virus. They are Single dose ACAM2000 and Aventis Pasteur smallpox vaccine (APSV), but they can't be used in immunocompromised individuals. A single dose of ACAM2000 gives peak

protection in 28 days and may be associated with adverse effects like eczema vaccinatum, progressive vaccinia and increased risk of myopericarditis. Two dose modified vaccine Ankara virus Bavarian Nordic (MVA-BN) vaccine (3rd generation) under brand names JYNNEOS, IMVAMUNE and IMVANEX are the most recently approved vaccines that are safe for immunocompromised as they contain replication-deficient virus. JYNNEOS was approved by FDA in 2019 for ages above 18 years.[19]

POST-EXPOSURE MANAGEMENT

Confirmed cases must be isolated. There is no specific treatment, only symptomatic treatment and supportive therapy are given. Since smallpox and monkeypox both belong to family *orthoviridae*, TECOVIRIMAT which was treatment for smallpox also used for monkeypox.[20]

CONCLUSION

Monkeypox outbreak has been declared a global emergency by WHO on July 23rd, 2022. Since then, the number of cases escalated. Cases have been reported from endemic and non-endemic countries. Though monkeypox is a self-limiting disease, it increases the burden on health system amidst COVID-19 pandemic. Proper prevention measures and vaccination with smallpox vaccine can be proven effective in decreasing the burden of the disease. The countries should consider the seriousness of the situation and take necessary measures to counter outbreak.

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