Monkey Pox- A potential re-emerging threat

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Abstract

To better comprehend the variety of elements involved in disease transmission and distribution, the observed increase in the frequency of human disease requires further analysis and research. Large respiratory droplets are believed to be the main mechanism for human-to-human transmission, and these droplets usually require sustained close contact. Indirect contact with lesion material, such as through contaminated clothing or linens of an infected individual, as well as direct touch with body fluids or lesion material are other ways in which it can be spread. Although less severe clinically than smallpox, monkeypox (MPX) is a viral zoonotic disease. The best methods for preventing and controlling human monkeypox continue to be case isolation, contact tracing, avoiding contact with animals or objects thought to be harboring the etiologic agent, wearing personal protective equipment, and maintaining good hand hygiene habits. This is despite ongoing and unrelenting efforts to create an effective therapy.

Keywords: *Zoonotic disease, Animal efficacy ,Viral infection, Hygiene, Placebo*

Introduction

Monkeypox (MPX) is a viral zoonotic disease with symptoms similar to smallpox, although with less clinical severity. MPX was first discovered in 1958 in colonies of monkeys kept for research, hence the name 'monkeypox.'(1-3) The first human case of monkeypox was reported from Democratic Republic of the Congo (DRC) in 1970.Human monkeypox virus (MPXV) is a double-stranded DNA virus of the Orthopoxvirus genus of the family Poxviridae.(5-8) According to World Health Organization (WHO), in the present series of outbreaks being reported, this is the first time that chains of transmission are reported in Europe without known epidemiological links to West or Central Africa. Monkeypox has a clinical presentation very similar to that of ordinary forms of smallpox, including flulike symptoms, fever, malaise, back pain, headache, and characteristic rash. Given this clinical spectrum, differential diagnosis to rule out smallpox is very important. There are no licensed therapies for human monkeypox; however, the smallpox vaccine can protect against the disease.(9-10) This article will review the current state of knowledge about human monkeypox, with emphasis on epidemiologic characteristics, clinical features, diagnosis, treatment, and prevention.

Epidemiologic Characteristics

Human infection with monkeypox virus was first described in Central Africa in 1970 in a 9–month old child from Zaire (now the Democratic Republic of the Congo).(11-15) Since then, the MPXV has become the most pathogenic orthopoxvirus and is now endemic inthe most forested regions of Central Africa, mainly the Democratic Republic of the Congo, where it is considered a reportable disease as well as in some parts of West Africa.(15) According to World Health Organization (WHO), in the present series of outbreaks being reported, this is the first time that chains of transmission are reported in Europe without known epidemiological links to West or Central Africa. This has been also reported in certain non-endemic countries e.g. USA, UK Belgium, France, Germany, Italy, Netherlands, Portugal, Spain, Sweden, Australia, Canada, Austria, Canary Islands, Israel , Switzerland and India.

Clinical Features

Monkeypox begins with fever, headache, muscle aches, and exhaustion. The main difference between smallpox and monkeypox is that monkeypox causes swollen lymph nodes (lymphadenopathy) while smallpox does not.(17) Swelling of lymph nodes may be more generalized or localized to several areas. The illness begins with Fever,Headache ,Muscle aches, Backache ,Swollen lymph nodes Chills ,Exhaustion, Weakness . (18)

Within 1 to 3 days after the appearance of initial symptoms, the patient develops a rash, often beginning on the face then spreading to other parts of the body. Lesions typically begin to develop simultaneously and evolve together on any given part of the body. Lesions progress through the following stages before falling off: Macules Papules → Vesicles →Pustules → Scabs.(19)

Natural reservoir is yet unknown. However, certain rodents (including rope squirrels, tree squirrels, Gambian pouched rats, dormice) and non-human primates are known to be naturally susceptible to monkeypox virus. The incubation period (interval from infection to onset of symptoms) of monkeypox is usually from 6 to 13 days but can range from 5 to 21 days.

Human-to-human transmission is known to occur primarily through large respiratory droplets generally requiring a prolonged close contact. It can also be transmitted through direct contact with body fluids or lesion material, and indirect contact with lesion material, such as through contaminated clothing or linens of an infected person. (20,21)

Animal-to-human transmission: may occur by bite or scratch of infected animals like small mammals including rodents (rats, squirrels) and non-human primates (monkeys, apes) or through bush meat preparation. (22-24)

Diagnosis

The clinical picture of monkeypox is very similar to that of chickenpox and that of smallpox, definitive diagnosis

is key to keeping natural disease under control The pathogenesis and clinical picture of the human monkeypox largely resemble that of a discrete, ordinary smallpox, with an incubation period of 7 to 17 days, an initial febrile prodromal period of 1 to 4 days, and a rash period of 14-28 days. MPXV and smallpox share similar appearance, distribution, and progression of lesions.(25-27)The characteristic features include a prodrome of fever, headache, muscle aches, backache, and lymphadenopathy, later followed by generalized well-circumscribed rashes of typical centrifugal pattern that progress through macular, papular, vesicular, and pustular phases .(28,29) . A second febrile period occurs when the lesions become pustular, and is often associated with a deteriorating condition of the patient. (30)A more severe disease is associated with pronounced illness, high viremia, and death, as observed following direct human–to-human transmission, however, without sustained infection.(31).

Diagnostic Tests for Monkeypox or Orthopoxvirus

Test	Pros	Cons
Viral culture/isolation: Live virus is grown and characterized from a patient specimen	Can yield a pure, live culture of virus for definitive classification of the species. Orthopoxviruses produce distinctive “pocks” on chorioallantoic membranes; and other cell-based viral culture methods can be used. Patient	The assay takes several days to complete. Patient specimens may contain bacteria, hampering culture attempts. Further characterization must be done for viral identification. Must be performed at a major laboratory with skilled

	specimens from lesions are the most reliable for this method, as viremia is not present the entire duration of illness	technicians.
Electron microscopy: Negative staining produces a clear image of a brick-shaped particle, allowing for visual classification of a poxvirus, other than Parapoxvirus	Can be used to identify viral particles in a biopsy specimen, scab material, vesicular fluid, or viral culture. Can differentiate an Orthopoxvirus from Herpesviridae.	Orthopoxviruses are morphologically indistinguishable from each other. Must be performed at a major laboratory with skilled technicians and an electron microscope
Immunohistochemistry: Tests for the presence of Orthopoxvirus specific antigens	Can be used to identify antigens in biopsy specimens. This technique can be used to rule out or identify other suspect agents.	Not specific for monkeypox virus. Must be performed at a major laboratory with skilled technicians.
PCR, including real-time PCR: Tests for the presence of monkeypox-specific DNA signatures.	Can diagnose an active case using lesion material from a patient. The assay uses viral DNA, which is stable if a specimen is kept in dark, cool conditions. Designed to be specific for monkeypox virus.	Highly sensitive assays where concerns about contamination are warranted. These assays require expensive equipment and reagents. Must be performed at a major laboratory with skilled technicians.
Anti-Orthopoxvirus IgG: Tests for the presence of Orthopoxvirus antibodies.	Can be used to assess a previous exposure to an Orthopoxvirus, including a pathogen or smallpox vaccination.	Requires the collection of blood (serum) and a cold chain. This assay is not specific for monkeypox virus. Results will be affected by prior smallpox vaccination. The duration of response is variable.Must be performed at a major laboratory with skilled technicians.
Anti-Orthopoxvirus IgM: Tests for the presence of Orthopoxvirus antibodies.	Can be used to assess a recent exposure to an Orthopoxvirus, including a pathogen or smallpox vaccination. This assay could be used as a	Requires the collection of blood (serum) and a cold. chain. This assay is not specific for monkeypox virus. Must be performed at a major laboratory

	diagnostic for suspect Orthopoxvirus patients with prior smallpox vaccination.	with skilled technicians.
Tetracore Orthopox BioThreat Alert: Tests for the presence of Orthopoxvirus antigens	Can rapidly diagnose an active case using lesion material from a patient; a point-of-care diagnostic test. Can be performed at ambient temperature with little expertise	This assay is not specific for monkeypox virus. Needs to be tested in endemic settings. Less sensitive than PCR.

Abbreviations: IgG, immunoglobulin G; IgM, immunoglobulin M; PCR, polymerase chain reaction.

Treatment and Prevention

Initially, treatment of monkeypox infections was mainly syndromic, as there was no clinically approved and licensed antiviral agents for its specific treatment. While still at various stages of clinical trials, four compounds (NIOCH14, Cidofovir, CMX001, and ST246) may yield a good therapeutic effect.(32,33) Recently, the US Food and Drug Administration(FDA) approved in 2018 the first antipoxvirus drug intended to treat orthopoxviruses, such as smallpox and monkeypox.(34,35) This represents a long awaited addition to disease prevention strategies that have focused on selective antiviral chemotherapy. In addition, it is a move that could halt a lethal pandemic if the virus was to be released as a bioweapon or accidentally through a laboratory acquired infection. Tecovirimat or Arestyvir (previously ST246) was first reported in 2005 following screening of a chemically diverse library of more than 356 240 compounds,(36-38) and was reported to be a selective and potent inhibitor of the replication of multiple orthopoxviruses.(37) The antiviral agent, tecovirimat, also known as Tpox, has never been tested in humans with smallpox, as the disease was declared eradicated in 1980,65 two years after the last known and reported case of smallpox in 1978.
Tecovirimat, a virion egress inhibitor, was very effective at protecting nonhuman primates challenged with variola virus (the causative agent of smallpox)(39) and MPXV(40) as well as in two animal models deliberately infected with monkeypox and rabbitpox, in accordance with the US FDA Animal Efficacy Rule.68 It also caused no severe side effects when safety ested in a placebo controlled pharmacokinetic and safety trial involving 449 healthy adult human volunteers.(41) Therefore, tecovirimat is the only currently available antipoxvirus therapeutic agent, and it is stockpiled as part of the US Strategic National Stockpile for use as a defense to treat smallpox virus infections in the event of a possible bioterrorist attack.(42) Nevertheless, the smallpox vaccine, although with limited use due to cost and safety concerns of a live vaccinia virus vaccine, is cross protective against many orthopoxviruses, including MPXV .(43) Despite continuous and unrelenting efforts to develop an effective therapy, other public health measures, such as case isolation, contact tracing, avoiding contact with animals

or materials suspected of harboring the etiologic agent, use of personal protective equipment and good hand hygiene practices, remain the best measures for preventing and controlling human monkeypox.

Conclusion

Human monkeypox has the potential for spread via zoonotic reservoirs,Civil conflict and displacements cause concerns for movement of the virus into an area without monkeypox (44,45) or movement of individuals to more heavily forested areas more prone for interaction with wildlife and a range of zoonoses. The documented rise in incidence of human disease needs further evaluation and consideration with additional studies to better understand the range of factors involved in disease transmission and spread. There are still many unanswered questions about human disease, animal reservoirs, and the virus itself—advances in our understanding of this important zoonosis will help better guide prevention strategies and mitigate human disease.

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