Proceedings of the 3rd International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/22/20230983

Research progress of Monkeypox and its current prevention and treatment options

Xinmei Zheng

Nanjing University of Science and Technology, Nanjing, 210000, China

zhengxinmei@njust.edu.cn

Abstract. Monkeypox (MPX), a smallpox-like zoonotic infectious disease caused by the monkeypox virus (MPXV), was first detected in laboratory animals in 1958. Since the eradication of the smallpox virus in the 80s of the 20th century, MPXV has become one of the members of the pox virus family with the greatest public health impact, mainly in the central and western regions of Africa. However, since May 7, 2022, human cases of MPXV infection have been reported in several countries outside endemic areas in Africa. As of July 15, 2022, based on the latest data from the US Centers for Disease Control and Prevention, there have been at least 1,814 suspected or confirmed cases in the US, and a total of 12,556 confirmed cases have been reported in 68 countries around the world. The World Health Organization (WHO) has said that the spread of MPX epidemics in more than 70 countries is an "extraordinary" situation, listing it as a global emergency. This paper mainly reviews the physicochemical characteristics, gene characteristics, pathogenic mechanism, transmission mechanism, and clinical features of MPXV etiology. It also discusses and summarizes the current prevention and treatment options, in order to provide reference for the current exploration of monkeypox prevention and treatment.

Keywords: MPX virus, epidemiology, aetiology, pathogenicity, prevention and treatment.

1. Introduction

Starting from the reported monkeypox (MPX) cases in the UK on May 7, 2022, as of 5 p.m. EDT on June 14, 2022, a total of 1,879 confirmed cases of MPX have been reported by the US Centers for Disease Control and Prevention, involving more than 30 non-African countries, including the United Kingdom, Spain, Portugal, Germany, Italy, the United States, Canada, Australia, etc. [1]. It is the largest-ever MPX outbreak outside Africa. Most of the cases in this MPX outbreak do not have any travel history to the relevant endemic countries, which is a particular circumstance of great concern to the World Health Organization (WHO). Collecting and sequencing the genomes of MPX patients in countries such as France, Germany, Portugal, and the United States, the researchers found that each sequence obtained by sequencing was similar to that found in West Africa, suggesting that an outbreak of MPX outside Africa may be linked to a single case. The monkeypox virus (MPXV) genome sequences collected so far are most similar to those of the few MPX cases that emerged outside Africa in 2018 and 2019, and these few MPX cases had a travel history to West Africa. Based on this, it has been preliminarily speculated that patient zero of this MPX outbreak may have been infected through

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contact with animals or humans carrying the virus while visiting the African region, resulting in transmission [1].

This paper aims to sort out the physicochemical characteristics, gene characteristics, pathogenic mechanism, transmission mechanism, and clinical features of MPXV etiology. The author also studies MPX in terms of its current prevention and treatment options, so as to provide a theoretical summary for the current epidemic of MPX.

2. MPX aetiology

2.1. Physical and chemical properties and genetic signatures

MPXV can be destroyed at 56℃ within 30 minutes. It is not heat-resistant and can be quickly destroyed by organic solvents, including formaldehyde, methanol, sodium dodecyl sulfonate, phenol, chloroform, etc. However, it is resistant to drying and low temperatures and can be kept for a long period at 4℃ [2].

MPXV has the same morphological features as other orthopoxviruses, including a capsule, ovoid or brick-like granules, and linear double-stranded DNA (dsDNA). When viewed under an electron microscope, MPXV, one of the biggest and most intricate animal viruses, has a diameter length of roughly 200250nm and is made up of four primary components: the core, lateral body, outer membrane, and exolipoprotein envelope. The lipoprotein outer membrane of the virions is geometrically corrugated, and their biconcave cores contain enormous dsDNA genomes with lateral bodies on either side [3]. The MPXV genome is approximately 197kb, and the end of the genome contains 1 identical but opposite-oriented end repeating an inverted sequence. There are tight hairpin structures at both ends of the genome containing approximately 190 open reading frames in length [4].

2.2. Pathogenesis

The replication process of MPXV is done in the cytoplasm. The invasion of the host cell is mainly completed by three steps: adsorption, membrane fusion, and core invasion. The specific cell receptor of the pox virus has not been determined, but four viral proteins, D8, A27, A26, and H34, have been found in VACV, which is most similar to MPXV, to mediate the adsorption of mature viruses in cells on the cell surface. The E8, A29, A28, and H3 proteins in MPXV are orthologous proteins as D8, A27, A26, and H3 in vaccinia virus (VACV), and these proteins of MPXV have the same function as the corresponding proteins of VACV [5]. Due to the high degree of homology between genomes, they may have the same characteristics in the viral fusion step [6].

3. MPX propagation mechanism

At present, the transmission route of MPX is not fully clear. Generally, rodents and primates such as squirrels and Gambian rats are often considered to be the natural host of MPXV. One of the main ways of human infection with MPXV is by the bite of infected animals or having direct contact with their blood or body fluids. Besides, having improperly cooked infected animals or undercooked infected animals can also cause cross-species transmission of the virus [7,8].

There is currently no evidence proving that MPX can be spread widely from person to person. In other words, person-to-person transmission is restricted. The longest recorded chain of transmission is within 6 generations, which means that the last person who is infected in the chain of transmission is supposed to be 6 generations away from the original patient [9]. After 2022, there appear a large number of MPX cases in homosexual and bisexual groups, with a concentration on men who have sex with men in an age range between 20 and 50. Most of these cases lack immune protection against MPXV. Meanwhile, the sexual transmission route has also been focused on by researchers [10].

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4. MPX clinical features

The symptoms of MPX are similar to, but to a lesser extent, those of smallpox patients. The incubation period of MPX is mostly 7~14 days, and the longest can reach 21 days. Patients usually have experience of contacting with an animal or a person infected with MPXV, initially presenting with flu-like symptoms, followed by skin herpes, pustules, and scarring after crusting.

The MPXV infection process may be roughly split into two phases. The prodromal period, which lasts 0–2 days, is characterized by fever, exhaustion, severe headaches, lymphadenopathy, muscular pains, etc. When the patient is infectious, the rash generally starts to develop 1–5 days after the fever and lasts for 7–21 days. The rash is mainly concentrated on the face and extremities, with facial rash in 95% of patients, palms, and soles in 75% of patients, oral mucosa in 70%, genitals in 30%, and conjunctiva in 20%. The rash lasts for about 2–4 weeks, evolving from plaques to papules, blisters, pustules, crusts, and finally shedding, at which time the patient is no longer infectious [11]. As a self-limiting condition, the severity of MPX depends on the patient's health, the extent of their viral exposure, and the kind of their sequelae. Children are more likely to experience severe instances, and case mortality rates range from 1% to 10% [12-13].

5. MPX prevention and treatment options

5.1. MPX Vaccine research

5.1.1. Vaccines currently in use. According to WHO, orthopoxvirus has immune cross-reactivity and cross-protection and can be used as an adjunct vaccine. Studies have found that smallpox vaccination provides 85% protection and may reduce the severity of MPXV symptoms [14]. However, after 1981, smallpox vaccination was phased out globally, and people under 40 years old lacked adequate immunity to MPXV. To date, the modified attenuated non-replicating VACV (Ankara strain) vaccine is the only MPX vaccine approved by the US Food and Drug Administration, which is manufactured by the Danish biotechnology company Bavarian Nordics and requires a total of 2 doses of immunity 28 days apart. Compared to the smallpox vaccine ACAM2000 produced by Emergent BioSolutions in the United States, JYNNEOS is safer and protects animals from fatal orthopoxvirus diseases, including MPXV infection in non-human primates, rabbit pox virus infection, and VACA infection [15-16].

5.1.2. Vaccines currently under development. In the study of Schultz et al. [17], the protective efficacy of the smallpox vaccine against MPXV infection was evaluated by the African dormouse model, and the survival rate of African dormouse infection with MPXV infection after 4 weeks was 100% after vaccination of African dormice in the vaccine group and 0 after infection with MPXV in the placebo group.

The study of Hatch et al. [18] showed that a single immunization of the third-generation smallpox vaccine could not completely avoid serious fatal infection, while booster immunization could effectively protect cynomolgus monkeys. Therefore, it is possible to consider reducing the virus on the basis of the smallpox vaccine and developing an MPXV attenuated vaccine.

MPXV mRNA vaccine, as a new vaccine, plays an important role in the prevention of major infectious diseases. mRNA vaccine can induce humoral immunity and cellular immunity at the same time and protect the body through a variety of mechanisms. On May 24, 2022, mRNA vaccine developer Moderna announced that she would use her mRNA vaccine research and development platform to develop MPXV mRNA vaccines.

5.2. MPX treatment options

At present, there is no specific drug for MPX, and the treatment principle of MPX is mainly symptomatic supportive treatment while strengthening nursing and management of complications.

Symptomatic supportive care consists of rest, adequate fluids, and heat. Patients with fever symptoms can take antipyretics and analgesics such as acetaminophen to reduce fever. Patients with lesions can be disinfected with iodophor to avoid secondary skin infection. Intensive care mainly includes keeping the eyes, nose, mouth, and skin clean to avoid scratching rashes. Complications of MPX include secondary infections such as bronchopneumonia, sepsis, encephalitis, corneal infections, and vision loss, and antibiotics can be used to prevent secondary infections. In MPX outbreaks, the antivirals tercoviri [19], cidofovir [20], and brincidofovir [21] can be controlled.

6. Conclusion

In conclusion, MPX is a very harmful viral infectious disease. Compared with the past MPX epidemic, a new way of transmission appears at present, namely human-to-human transmission, including sexual transmission. Human-to-human transmission shows a rapid spread trend and is currently affecting not only African countries such as Central Africa and West Africa but also the rest of the world. MPX has become a global public health problem and it brings huge health threats and economic losses to society. In order to effectively reduce the risk of transmission of MPXV, it is important to enhance people's awareness of MPX prevention and strengthen MPXV surveillance and international cooperation. In order to eliminate the threat of the MPX epidemic to human health and life, it is necessary to further improve the level of immune protection of the population against MPXV, for instance, increasing the reserve of the smallpox vaccine and anti-MPXV drugs, vaccinating high-risk groups with MPX vaccine, and accelerating the development of safer and more effective MPX vaccines to provide practical and effective guarantees for the prevention and control of MPX epidemics.

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