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Review Article

Human Monkeypox: An Emerging and Re-emerging Infectious Viral Disease

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Abstract

The monkeypox is an emerging and re-emerging zoonosis that causes sporadic human infections in Central and West Africa's forested areas. Monkeypox virus, a member of the *Orthopoxvirus* family, is the etiological agent of disease. Monkeypox virus was discovered in the laboratory monkeys in 1958 at the State Serum Institute in Copenhagen, and the first human case of monkeypox virus was recorded in the Democratic Republic of the Congo in 1970. African rodents serve as the reservoir of the monkeypox virus. The respiratory, percutaneous, and permucosal exposures to infected monkeys, zoo animals, prairie dogs, and humans are the most common exposure routes of infection for human beings. The incubation period of the disease is 6 to 13 days, although it can take anywhere from 5 to 21 days. Most patients have a typical prodromal illness with fever, malaise, and lymphadenopathy for 2 days before the rash appears. The rashes mainly occur on the face, palms of the hands and soles of the feet. Maximum cases are observed in the persons who had direct contact with animals. If the characteristic skin lesions are present, and there is a history of exposure, monkeypox can be predicted. Laboratory culture, polymerase chain reaction (PCR), immunohistochemistry, and electron microscopy are the tools available for confirming the diagnosis. The prognosis of the disease in immunocompromised patients is poor. While working with nonhuman primates or other animals, care should be taken to treat and cover breaks in the skin as a routine preventive strategy. During interaction with monkeypox-affected animals, infection control techniques, such as proper hygiene, frequent hand washing, disinfection of surfaces and equipment, and the use of personal protective equipment (PPE) are critical.

Keywords: Control; Emerging; Monkey Pox; Monkeypox Virus; Prevention

Introduction

Emerging and re-emerging zoonoses of diverse etiologies are significant causes of morbidity and mortality in humans as well as animals [1-3]. In the last decades, several viral zoonoses, such as bird flu, contagious ecthyma, Ebola hemorrhagic fever, Hantavirus infection, Hendra virus disease, Nipah virus disease, Rift Valley fever, severe acute respiratory syndrome, swine flu, West Nile fever, etc., have emerged from different parts of the world and attracted

the attention of public health authorities [1-6]. Poxviruses include several zoonotic pathogens, such as cowpox virus, buffalopox pox virus, goatpox virus, monkeypox, and camelpox that affect both animals and humans in many regions of the world [1]. The poxviruses cause four diseases in nonhuman primates; monkeypox being the most common [7]. Monkeypox is a sylvatic zoonosis that causes sporadic human infections in forested areas of Central and West Africa [8].

Monkeypox is an emerging and re-emerging zoonotic infection of public health significance [9,10]. It is serologically linked to smallpox in humans; hence a smallpox vaccination can prevent monkeypox in humans [7]. Monkeypox was first observed in 1958, when two outbreaks of a pox-like disease occurred in research colonies of monkeys, hence the name 'monkeypox' was given [11].

Human monkeypox was first discovered in humans in the Democratic Republic of Congo in 1970. The majority of cases have been documented in rural areas of the Congo Basin and Western Africa since then, especially in the Democratic Republic of Congo. In the Democratic Republic of Congo, a large outbreak occurred in 1996-97. Monkeypox cases were confirmed in the Midwest of the United States of America in the spring of 2003, marking the disease's first recorded incidence outside of Africa [8].

The virus causes epithelial papular and vesicular lesions in both New and Old World monkeys and apes. The animal and the owner both are to be vaccinated for protection [7]. Monkeypox has the potential to spread from person to person and could be used in bioterrorism [10]. The primary goal of this mini-review is to delineate the emerging position of the monkeypox virus as a zoonotic pathogen of public health importance.

Etiology

Monkeypox is caused by the Monkeypox virus (MPXV), which is a member of the *Orthopoxvirus* family [1,12]. Variola (smallpox), vaccinia (used in the smallpox vaccine), camelpox, and cowpox virus are other *Orthopoxviruses* that cause diseases in humans [1,11,13]. There are two monkeypox clades, Congo Basin and West African, according to genomic sequencing, and differences in human pathogenicity and death have been documented in the two geographic locations [8]. The virus is enveloped, double-stranded DNA virus with a slightly pleomorphic core and lateral bodies, measuring 140-260 nm in diameter by 220-450 nm in length. It's resistant to phenolic disinfectants, and it's inactivated by polar lipophilic solvents like chloroform and low pH. At 60°C, complete inactivation of the similarly related vaccinia virus takes 2-3 hours, or minutes at 22°C after exposure to 20 nM caprylate [14,15].

Transmission

Monkeypox can be transmitted to humans by a bite from an infected animal or direct contact with the animal's lesions, blood, or bodily fluids [1,4,8,11,12]. Although it is less infectious than smallpox, the disease can spread from person to person. During direct and prolonged face-to-face contact, the virus is assumed to be transmitted via respiratory droplets. Monkeypox can also be transmitted by direct touch with an infected person's bodily fluids or virus-contaminated things, such as bedding or clothing [11]. The inoculation or transmission through the placenta (congenital monkeypox) is another method of transmission of disease [8]. Direct contact with the animals, particularly the rodents is considered the prime mode of disease transmission [11].

Epidemiology

Monkeypox virus was initially identified as the cause of a pox infection in captive monkeys in 1958 [11]. However, the first report of human monkeypox was made in a 9-year-old child in 1970 from the Democratic Republic of Congo [8,12]. Since then cases of human monkeypox have been reported from many African countries, such as Benin, Cameroon, Central African Republic, Cote d'Ivoire, the Democratic Republic of the Congo, Gabon, Liberia, Nigeria, Sierra Leone, and South Sudan [8,11]. A massive outbreak of monkeypox in humans was investigated in Nigeria in 2017 [8]. Monkeypox outbreak occurred in the Midwest of the United States in 2003, marking the first time the disease has been recorded outside of Africa. Pet prairie dogs, other small mammals in captivity, and people who have been exposed to sick prairie dogs have accounted for the majority of cases in the United States [8].

Natural host

Monkeypox has been detected in a variety of African animal species, including rope squirrels, tree squirrels, Gambian rats, striped mice, dormice, and primates. There are still questions about the virus's natural history, and more research is needed to determine the exact reservoir of the virus, and how it is maintained

in nature [8]. Squirrels of the genera *Funisciurus* and *Heliosciurus* have recently been recognized as hosts and reservoirs [16]. In the United States, the virus is considered to have spread from African animals to a variety of non-African species (such as prairie dogs) with whom they shared space [8]. Mice, rats, and rabbits have all been found to be infected by the virus in laboratory investigations [11].

Clinical symptoms

Monkeypox has a 7-14 day incubation period (time from infection to symptoms), although it can be 5-21 days [8]. The infection can be described in two stages: Fever, acute headache, lymphadenopathy, back pain, myalgia, and severe asthenia (lack of energy) characterize the invasion stage (0-5 days). The period during which the eruptions simultaneously is appearing on the face (in 95% of cases), on the palms of the hands and soles of the feet (in 75% of cases), and on the torso. The rash progresses from the macules to papules,vesicles and pustules, and then there is the formation of crusts. The monkeypox-affected children showed rashes on different parts of the body (Figure 1) [8]. Immunocompromised patients and patients with cellular immune response impairment can develop generalized exanthema and severe systemic illness with a lethal outcome. Humans have never been exposed to a hemorrhagic variant of monkeypox [17]. The case-fatality rate for human monkeypox is less than 10%. The majority of fatalities due to monkeypox occur in young patients [8]. In this context, Jezzek and co-investigators [17] reported that secondary bacterial infections of the skin were noticed in 19% of unvaccinated monkeypox patients.

Figure 1: Children showing monkeypox lesions on different parts of the body.
Source: CDC [11].

Monkeypox is a self-limiting rash that affects nonhuman primates. Fever and 1 to 4 mm cutaneous papules appear first, then develop into pustules and crust over. The center of a typical monkeypox lesion is red, necrotic, and depressed, with epidermal hyperplasia surrounding it. The face, limbs, palms, soles, and tail may all have these "pocks," but they are more common on the face, limbs, palms, soles, and tail [18]. Some animals have lesions only on their skin. Coughing, nasal discharge, dyspnea, anorexia, facial edema, oral ulcers, or lymphadenopathy may be noticed in severe cases. In spontaneous infections, disseminated infection with visceral lesions is uncommon. Only pneumonia is seen in monkeys who have been infected with an aerosol. The majority of naturally infected animals recover; nevertheless, fatalities do occur occasionally, especially in newborn monkeys. Infections might potentially be asymptomatic [19].

Diagnosis

The clinical manifestation of the disease is not very characteristic to make the diagnosis and therefore, laboratory techniques, such as virus isolation, electron microscopy, immunohistochemistry, and PCR are imperative to establish an unequivocal diagnosis on monkeypox [4,13]. Smallpox, chickenpox, measles, bacterial skin diseases, scabies, medicament allergies, syphilis, and rickettsial pox are among the most common differential diagnoses [8,13]. RT-PCR is used to routinely detect monkeypox virus DNA in clinical and veterinary specimens, as well as in monkeypox virus-infected cell cultures [20]. The enzyme-linked immunosorbent test (ELISA) is used to identify IgG and IgM antibodies, and immunohistochemistry is used to detect viral antigens [21,22]. Due to the accuracy and sensitivity, the polymerase chain reaction (PCR) method is considered the mainstay of laboratory diagnosis [8].

Treatment

Although there is no proven treatment for humans, animal research demonstrated that antiviral treatment with cidofovir or a similar acyclic nucleoside phosphonate analog is effective. Antiviral chemicals are more efficient in lowering mortality in animals than the therapeutic use of the smallpox vaccine [8,23]. The treatment in the majority of cases is supportive. Although many animals recover on their own and antiretroviral medications have been shown to be beneficial in experimental infections, the CDC recommends that all

animals with suspected monkeypox be killed to prevent the disease from spreading [11].

Prevention and control

A variety of precautions can be taken to avoid infection with the monkeypox virus: avoid coming in contact with animals that may be infected with the virus (including animals that are sick or that have been found dead in areas where monkeypox occurs), avoid touching any objects that have come into contact with a sick animal, such as bedding, isolate infected patients from those who might become infected, and after coming into contact with infected animals or humans, wash hands thoroughly [11]. In the event of a monkeypox epidemic in a monkey colony, the animals can be vaccinated using the virus itself as a preventive strategy [18]. JYNNEOS™ (also known as Imvamune or Imvanex) is an attenuated live virus vaccine approved by the U.S. Food and Drug Administration for the prevention of monkeypox [11].

Preventing the spread of monkeypox through animal trade, such as limiting or prohibiting the transportation of small African mammals and monkeys, prove successful in delaying the virus's spread outside of Africa. Smallpox vaccine should not be given to captive animals. Instead, diseased animals should be separated from the rest of the herd and placed in quarantine right away. Any animals that may have had contact with the infected animals should be isolated for 30 days and monitored for monkeypox signs. In the absence of a specific treatment or vaccine, the only approach to prevent infection is to raise public knowledge of the risk factors and educate people about the steps they may take to limit their virus exposure [8].

Conclusion

The monkeypox virus is an emerging infectious viral disease transmitted by animals to humans. The typical clinical presentation of the disease includes fever, rash, and swollen lymph nodes. Increased human-animal contact as a result of climate change and deforestation, bush meat eating, and poor health and research infrastructure, among other factors, may have established an immunological and ecological niche for monkeypox virus to re-emerge. Monkeypox is no longer restricted to endemic areas. As a result, monkeypox virus is a dangerous re-emerging disease with a worldwide reach. There is currently no effective or safe treatment for monkeypox virus infection. JYNNEOS, a novel smallpox vaccine, has been approved by the FDA for the prevention of both monkeypox and smallpox. It is emphasized to adopt the hand hygiene after handing the sick animals and infected biological materials to prevent the spread of infection. Further research on the reservoir, molecular epidemiology, and chemotherapy of monkeypox should be conducted.

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Contribution of Authors

All the authors contributed equally. They read the final version, and approved it for publication.

Conflict of Interest

The authors declare that they do not have any conflict of interest.

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