Review

Oral manifestations of monkeypox: Brief review

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Abstract

The current outbreak of monkeypox infection has caught the attention of people worldwide. Updated data showed a dramatic increase in the number of patients in many non-endemic countries. An emergence of monkeypox together with coronavirus disease 2019 (COVID-19) caused a tremendous burden on the healthcare system, globally.

The aim of this review was to briefly describe the current situation, transmission, clinical features, diagnosis, and prevention of the disease. Oral manifestations of monkeypox as well as those of similar viral diseases were elaborately delineated.

The outbreak of monkeypox in non-endemic regions has expanded to at least 47 countries with more than 4,100 new infections. The clinical features in non-endemic regions are atypical and different from those in central and western Africa. Milder symptoms with no death cases have been observed. The oral mucosa is often involved and oral lesions may initially be manifested before the rash spreads to the face and other parts of the body. The diagnosis of monkeypox is mainly based on clinical presentations and laboratory investigations. Prevention by avoiding close contacts with patients and sick animals and providing vaccination to those who have a primary contact with patients is essential.

Oral manifestations may occur prior to skin eruptions, suggesting that dentists and dental personnel should be well aware of the nature of the disease. Prevention and public awareness of the disease are crucial for mitigating further human-to-human transmission.

Keywords: infection, outbreak, monkeypox, oral manifestations

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Introduction

Monkeypox is a rare zoonotic disease caused by the monkeypox virus.[1,2] The monkeypox virus, as well as the smallpox virus, belongs to the Orthopoxvirus genus in the family Poxviridae. The first human case of monkeypox was recorded in 1970 in the Democratic Republic of the Congo. Since then, monkeypox has become an endemic disease in western and central Africa. Until recently, the outbreak of the disease has been reported in 47 non-endemic countries in Europe, North and South America, Asia, north Africa, and Australia.[3] As of June 24, 2022, more than 4,100 confirmed cases have been reported. Notably, 87% of all cases have occurred in European countries.[4] Although the main cause of the new outbreak remains unclear, it is believed that the cessation of smallpox vaccination, which provided some cross-protection against monkeypox, resulted in an increased human-to-human transmission.[2]

The objective of this review was to briefly report the updated information on the outbreak, transmission, clinical features, oral manifestations, diagnosis, and prevention of monkeypox. Oral manifestations of monkeypox and other viral infections, as well as the zoonotic nature of the disease and other related viral infectious diseases were delineated and discussed.

Methods

The PubMed database and Google Search engine were used to achieve updated and relevant data on monkeypox from 2004 to 2022. The key words were "monkeypox", "outbreak", "oral lesions", and "oral manifestations". Only relevant articles written in English were chosen. The most recent reports of the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC) and Public Health England were also thoroughly analyzed. Hand searches were performed on viral zoonotic diseases and oral manifestations of viral infectious diseases including herpes simplex virus (HSV), herpes zoster, chickenpox, measles, hand-foot-and-mouth disease, human papillomavirus (HPV), and coronavirus disease 2019 (COVID-19). The exclusion criteria were articles without reliable sources or poorly written articles.

Results

Twenty-six relevant articles/reports were taken for consideration and used for the review of the disease's transmission, clinical features, oral manifestations, diagnosis, and prevention. Additionally, 11 hand-searched articles were used for the discussion.

Transmission

In general, human-to-human transmission occurs through direct physical contact with ulcerated skin or mucosa, respiratory droplets or contact with contaminated materials such as linens, bedding, electronics, and clothing.[5,6] Pregnant women can pass the virus to fetuses via the placenta.[7] Airborne transmission of monkeypox virus remains a controversial issue. If it does occur, it may not be the main route of transmission.

Alarmingly, most cases in non-endemic regions are associated with men who have sex with men (MSM), aged between 20–50. For example, all cases reported in Italy were MSM who had multiple sexual partners or practiced unprotected sexual intercourse.[8] These data suggest a human-to-human transmission of monkeypox infection through sexual contact.[8,9] However, more data are required to define monkeypox as a sexually transmitted disease. This unexpected pattern of transmission is believed to occur by a coincidental introduction of monkeypox into MSM networks and then the disease has remained circulating there.[9] The latest press briefing from WHO reported that cases from Germany and Italy showed monkeypox DNA in some patients' semen. These findings raise a probability of sexually transmitted nature of the disease.[10]

Clinical features

Historically, monkeypox infection begins with a non-contagious incubation period, ranging between 7–14 days or 5–21 days.[1] During this period, patients remain asymptomatic. Notably, the symptoms of patients with monkeypox in the endemic regions are more severe and cause a certain number of fatalities, while lesions in patients in non-endemic regions are more localized and have a different distribution of rashes. So far, there is no death report in patients from the non-endemic regions.

Monkeypox begins with the prodrome: fever, chill, headache, back pain, myalgia, asthenia, and lymphadenopathy.[1] Infected patients may be contagious during the prodromal period.[11] It is of interest to note that the main difference between symptoms of smallpox and monkeypox is that monkeypox causes lymphadenopathy while smallpox does not. Involved lymph nodes in monkeypox include submandibular, cervical, axillary, and inguinal lymph nodes and may be bilateral or unilateral. Following the prodrome, lesions may first develop in the mouth and/or oropharynx prior to the skin.[7,11] The skin rash tends to be more concentrated on the face and extremities, including palms of the hands and soles of the feet.[12,13] The lesions progress through several stages: macule, papule, vesicle, pustule, and crust. Patients are considered contagious until all the lesions become crusted.[14] The lesions are often described as painful and later itchy. Scars with hyper/hypopigmentation could occur after scabs have fallen off. The illness typically lasts for 2–4 weeks.

The signs and symptoms of patients in the new outbreak, non-endemic areas are atypical and quite different from those in western and central Africa. These include genital, perianal and perioral/oral rash, fever, lymphadenopathy, and pain when swallowing.[6,8] The lesions on the anogenital area and oral mucosa may appear first before or without spreading to the other parts of the body, suggesting sexual contacts as the route of transmission.[3,15] Several patients developed pustules before having fever. Some patients who have only few localized skin lesions may not even have any pain symptoms. Interestingly, lesions at different stages may occur in the same individuals. Lesions in the anus and rectum can cause pain, bleeding, proctitis, and tenesmus.[3] These symptoms have never before been described in patients in the endemic region. In all, the symptoms of patients in the current outbreak regions are milder than those in the endemic region. Few hospitalizations have been reported and the main reasons for hospitalization were pain management and treatment of secondary infections.

Oral manifestations

Oral and oropharyngeal lesions of monkeypox can appear as the first lesions prior to skin rashes.[3,7,11] It is described that oral sore in patients with monkeypox is a common feature in combination with fever and swollen lymph nodes.[6,16] Notably, the CDC reported that 70% of individuals had lesions in the mouth and on the tongue.[17] These data suggest that saliva can harbor the virus and the transmission can occur through oral–skin and/or oral–anogenital contact.[18] Therefore, it is important for dentists and dental personnel to recognize and be aware of the oral lesions of monkeypox. The development of the oral lesions should be similar to that of the skin lesions, starting from macule, papule, vesicle, and pustule.[19] After breaking off the roofs of the vesicle or pustule, ulceration with pseudomembrane takes place. In a recent case in the US, a male patient as a returning traveler from Nigeria developed right cervical lymphadenopathy, numerous 2–4-mm pustules with central umbilication of the skin, particularly the face, neck and hands.[20] The oral lesions were described as a few round 2–3-mm erosions on the mucosa, suggesting that the initial vesicles or pustules have already broken off, and an intact pustule on the lower labial mucosa. Main symptoms and oral manifestations of monkeypox are shown in Table 1.[11,12,19,20]

Diagnosis

Monkeypox shares similar features of the mucocutaneous lesions with many diseases including chickenpox, measles, bacterial skin infections, scabies, syphilis, and medication-induced allergies.[12] Sometimes, it is difficult to distinguish between these diseases based only on the clinical presentation. Lymphadenopathy during the prodromal stage can be used to distinguish monkeypox from chickenpox or smallpox. If monkeypox is suspected, healthcare providers should collect a sample for further polymerase chain reaction (PCR), a technique that provides good specificity and sensitivity for the detection of monkeypox virus.[21] Samples should be taken from the roof or fluid from vesicles, pustules or dry crusts, stored in a dry, sterile tube without viral transport media, and kept cold. Biopsy is an optional means for obtaining the diagnosis.

Since the beginning of the COVID-19 pandemic, the biosample collected by a nasopharyngeal swab has been used as the gold standard for the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Recently, the saliva has emerged as a convenient and cost-effective biofluid for COVID-19 diagnostics and may eventually replace a nasopharyngeal swab.[22,23] The collection of the saliva is non-invasive, inexpensive and uses a simple technique without the need for special equipment. Since monkeypox infection often manifests in the oral cavity, the saliva in patients may harbor the virions of monkeypox and, therefore, could potentially be used as the biosample to detect the virus. Further investigation to validate the use of the saliva for monkeypox diagnostics will warrant great benefits for those patients.

Prevention

The measures to prevent monkeypox infection include: (1) avoiding contact with animals that could harbor the virus; (2) avoiding contact with any materials that have been in contact with sick animals; (3) isolating patients with monkeypox from others; (4) practicing good hand hygiene after contact with both infected animals or humans; and (5) using personal protective equipment (PPE) when treating patients.[7]

Table 1. Symptoms of monkeypox

Symptoms	Description	Distribution	Stages
Prodrome	duration: 5 days; fever, chill, intense headache, back pain, myalgia, intense asthenia, lymphadenopathy (bilateral/unilateral)	–	–
Skin lesions	begin within 1–3 days of appearance of fever	face, extremities, trunk, hand palms, foot soles, conjunctivae, corneas, genitalia, anorectum	macule, papule, vesicle, pustule, crust
Oral/oropharyngeal lesions	begin prior to skin eruption	lips, tongue, oral mucosa, oropharynx	macule, papule, vesicle, pustule, ulceration

Vaccination against smallpox provides 85% protection for monkeypox and prevents severe complications in infected patients.[24,25] Since the latest outbreak of monkeypox in the US, the U.S. Food and Drug Administration (FDA) has approved JYNNEOS™ (also known as Imvamune or Imvanex) for the prevention of monkeypox in individuals aged over 18.[26]

Discussion

It is of interest that a few viral infections in humans are zoonotic diseases, including monkeypox, acquired immunodeficiency syndrome (AIDS) and COVID-19. Monkeypox was first reported in 1959 as an outbreak of a pox-like disease in monkeys kept at a research institute in Copenhagen, Denmark.[27] The first human case was reported in 1970. Since then, human-to-human transmission has dramatically increased in central and western Africa. Recently, the disease has been imported to and spread out in several non-endemic countries. Acquired immunodeficiency syndrome is caused by 2 lentiviruses, namely human immunodeficiency virus type 1 (HIV-1) and human immunodeficiency virus type 2 (HIV-2). Previous data has shown that HIV-1 and HIV-2 are the result of multiple cross-species transmissions of simian immunodeficiency viruses, naturally infecting African primates.[28] Another possible zoonotic viral disease is COVID-19, caused by SARS-CoV-2. It is believed that SARS-CoV-2 emerged as a recombinant virus between the bat coronavirus and a coronavirus of unknown origin.[29] The resulting recombination of these coronaviruses enhances viral capability to cross the animal-to-human species barrier. Collectively, the zoonotic diseases such as monkeypox, AIDS and COVID-19 have shown the first animal-to-human transmission and subsequent human-to-human transmissions, and have been the cause of devastating morbidity and mortality throughout the world. The fundamental etiology of cross-species transmission of these diseases, however, remains unclear. The surveillance of any possible zoonotic diseases that may happen in the future and the etiology of animal-to-human and human-to-human transmissions are yet to be closely performed for the benefit of humankind.

Oral manifestations of monkeypox are described as vesicular or pustular lesions. After the rupture of the vesicle or pustule, the ulceration takes place. The lesions in patients with monkeypox may resemble those of viral infections that involve the oral cavity, including HSV infection, herpes zoster, chickenpox, measles, hand-foot-and-mouth disease, HPV infection, and COVID-19. Oral lesions in HSV infection are mainly vesiculobullous lesions.[30] The vesicles/bullae easily break up, developing into multiple painful, shallow ulcers on the lips and oral mucosa. Recurrent lesions are more localized and often involve the lip vermilion and keratinized oral mucosa. The varicella-zoster virus causes chickenpox as a primary form in children and herpes zoster as a secondary form in adults. Herpes zoster presents with multiple unilateral vesicular eruptions on the skin and oral mucosa in the areas innervated by the affected nerves.[31] A wide variety of oral lesions can be observed in patients with measles. These lesions include tiny, white plaque-like papules (Koplik's spots), ulcerations and necrotizing gingivostomatitis.[32] Hand-foot-and-mouth disease, mainly affecting children younger than 10 years, causes maculopapular or papulovesicular rashes on the hands and soles of the feet, as well as painful oral ulcerations.[33] Various HPV-associated diseases in the oral cavity, such as squamous papilloma, verruca vulgaris, condyloma acuminatum, Heck's disease, leukoplakia, lichen planus, and squamous cell carcinoma, do not produce oral vesicles or ulcerations but mainly keratinized verrucopapillary lesions.[34]

Currently, COVID-19 remains an overwhelming pandemic throughout the globe. Coincidentally, monkeypox has become spreading out in many non-endemic regions. The diseases cause a great burden on the global healthcare system. Since oral manifestations of monkeypox may mimic those of COVID-19, especially the vesiculobullous lesions and ulcerations (Table 2),[19,20,35,36] dental health professionals should be able to recognize and differentiate between the clinical features and oral manifestations of monkeypox and COVID-19, as well as oral viral infectious diseases mentioned above. In addition, oral manifestations following COVID-19 vaccination, particularly aphthous-like ulcers should also be included in the differential diagnosis.[37]

Conclusions

Monkeypox has become an emerging infectious disease that is increasingly spreading to many parts of the world. Healthcare providers should be aware of the nature of the disease. Oral lesions may present as initial lesions, suggesting that dentists and dental personnel are the first

Table 2. Table 2. Oral manifestations of monkeypox and COVID-19

Disease	Oral manifestations
Monkeypox	painful vesicular, pustular or ulcerated lesions occur on the lips, tongue, oral mucosa, and oropharynx
COVID-19	various types of lesions/symptoms include vesiculobullous lesions, candidiasis, ulcerations due to herpes simplex viral infection, non-specific ulcerations, transient lingual papillitis, glossitis, geographic tongue, petechiae, aphthous stomatitis, mucositis, pharyngitis, gingivitis, desquamative gingivitis, dysgeusia, xerostomia, oral pain, Kawasaki-like disease

COVID-19 – coronavirus disease 2019.

who may encounter monkeypox infection. It is important to note that recognizing and identifying oral lesions in patients with monkeypox leads not only to providing further investigation and appropriate care but also to preventing cross-infection among health personnel and patients.

Ethics approval and consent to participate

Not applicable.

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

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