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Case Report **OPEN ACCESS**

Monkeypox or hand-foot-and-mouth-disease: A case report

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ABSTRACT

Monkeypox is a rare disease originating in Africa and has recently gained the spotlight globally because of the increasing cases reported in Western Europe and North America. However, since July 2022, the World Health Organization has declared this disease a public health emergency of international concern as the cases were rising globally. We report a case of the severe form of rashes of hand-foot-and-mouth-disease to distinguish it from current outbreaks of the monkeypox virus. Hopefully, this case report will aid primary care physicians in their ability to recognize and distinguish between a severe hand-foot-and-mouth-disease rash and an infection with the monkeypox virus. So, effective management and treatment may aid patients in enhancing their quality of life.

Keywords: hand foot and mouth disease, monkeypox, fever, rash, zoonotic

INTRODUCTION

Monkeypox infection is a zoonotic illness that is caused by *Orthopoxvirus* which is a zoonotic illness. The current pandemic occurred in Europe for the first time, with the transmission networks found on May 6, 2022, by a person who had visited Nigeria, where the disease is common, and the person had symptoms consistent with monkeypox. On May 4, the individual returned to the United Kingdom (UK), bringing the outbreak to the country for the first time [1]. Between May 13 and May 21, 2022, the World Health Organization (WHO) received reports of 92 confirmed cases of monkeypox in 12 non-endemic countries which are Australia, Belgium, Canada, France, Germany, Italy, Netherlands, Portugal, Spain, Sweden, United Kingdom, and United States of America [1]. Most incidents are among young guys who identify as men who have sex with men (MSM). Scientists believe monkeypox spread at low levels in the UK or Europe for several years prior to its appearance in the MSM community. Some reports showed people who live in the same house with the affected person also have a risk [1]. It should be noted that, according to WHO, persons who have had personal contact with someone who has monkeypox are most at risk, and this danger is not restricted to MSM. Therefore, WHO is working with health authorities to prevent the disease from spreading further [1].

Human cases of monkeypox were first identified in the Democratic Republic of the Congo (DRC) in 1970, and it had spread to other parts of Africa (mainly West and Central), as well as cases outside of Africa due to infected prairie dogs [2]. The number of cases has increased at least ten times, and the median age of presentation has changed from young children (4 years old) in the 1970s to young adults (21 years old) from 2010 to 2019 [2]. Increment in cases was possibly due to the discontinuation of smallpox immunizations, which offered some cross-protection against monkeypox [2].

There is a various risks behaviour for monkeypox infection, including contact with infected animals, sharing a bed, sleeping in the same room or bed, residing in the same home, drinking from the same dish, daily contact with ill animals, and cleaning cages and bedding [2].

According to WHO, anyone who meets the criteria for a suspected case should be offered the testing. Suspected case is defined as any person, regardless of age, who has presented with an acute rash or one or more acute skin lesions since 1st January 2022, without apparent cause AND at least one of this following symptoms of sign; acute onset fever >38.5°C, lymphadenopathy, headache, myalgia, back pain, profound weakness, AND for which the clinical picture cannot fully be explained by the following frequent causes of acute rash or skin lesions: bacterial skin infections, disseminated gonococcus infection, primary or secondary syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, molluscum contagiosum, allergic reaction, measles, herpes simplex, varicella zoster, or herpes zoster.

Diagnostic tests are crucial for determining the presence of an orthopoxvirus infection. These tests work best when combined with clinical and epidemiological information, such as a patient's history of vaccinations of smallpox [3]. For the monkeypox virus or orthopoxvirus, there are numerous diagnostic procedures. These include Polymerase Chain Reaction (PCR) and real-time PCR, immunohistochemistry, electron microscopy, anti-orthopoxvirus Immunoglobulin G (IgG), anti-orthopoxvirus Immunoglobulin M (IgM), and Tetracore Orthopox BioThreat Alert [3]. In Malaysia, real-time PCR (RTPCR) technique is used to diagnose monkeypox. Serology and antigen detection test are not advised due to *their cross-reactions with other Orthopoxviruses.*

(a) (b)

Figure 1. The rash centrifugal distribution, fluid-filled blister and surrounded by an erythematous halo predominantly at extensor of (a) bilateral knees, and (b) hand (reprinted with permission of the patient)

In addition to monkeypox, there are differential diagnoses that must be distinguished based on the resemblance of the rash, and prodromal symptoms, such as chickenpox, measles, hand-foot-and-mouth-disease (HFMD), bacterial skin infections, scabies, syphilis, and medication-associated allergies. HFMD is caused by *Enteroviruses* family, primarily *Enteroviruses 71* (EV71), and *Coxsackievirus-A16* (CoxA16). It affects primarily children under the age of five [4]. The rashes presentations of HFMD are sometimes tricky to differentiate from monkeypox and other diseases. So, in this case report, we discussed a case of a 17-month-old, baby girl that presents with many skin rashes all over her body, severe on both sides of her knees, and oral ulcers.

CASE REPORT

A 17-month-old baby girl presented to the clinic with her mother complaining of multiple skin rashes all over her body, severe on the bilateral knee region and oral ulcers. The rashes started on the extremities and spread to the face, diaper area, palms, and soles. The rashes were described as a fluid-filled blister and surrounded by an erythematous halo. The most predominant area of the rashes and fluid-filled blister was at the bilateral knees and hands. The mother was worried about the appearance of the rash. It is painful, itchy, and causes her uncomfortable. However, she is still able to tolerate orally. She had episodes of high-grade fever two days prior the onset of rashes. However, there is no sign to suggest meningism. Her elder brother and sister also present with similar complaints but with a milder form. Otherwise, she had no history of recent travelling, and her immunization status was up to her age.

The patient's hemodynamic status was found to be stable during the physical examination. The skin showed various forms of rash, predominantly on the bilateral knees and hands, centrifugal distribution, fluid-filled blister and surrounded by an erythematous halo (**Figure 1**). However, no blood investigation and serology testing for monkeypox were taken. A week later, her condition improved. The fluid-filled rashes were flattening, crusted, and peeling off (**Figure 2**). Oral intake was also good, and she was active as usual, with no more itchiness.

(a) (b) (c)

Figure 2. The fluid filled rashes were flattening, crusted, and peeling-off on the soles, palms, and bilateral knees (a, b, c, and d). In the picture, the patient's mother put on calamine lotion. Written informed consent for publication of this image was obtained from the patient's mother. The patient gave written informed consent for the dissemination of pictures (reprinted with permission of the patient)

(d)

Figure 2 (continued). The fluid filled rashes were flattening, crusted, and peeling-off on the soles, palms, and bilateral knees (a, b, c, and d). In the picture, the patient's mother put on calamine lotion. Written informed consent for publication of this image was obtained from the patient's mother. The patient gave written informed consent for the dissemination of pictures (reprinted with permission of the patient)

Table 1. Key clinical characteristics of monkeypox, HFMD, and varicella

Characteristics	Monkeypox	HFMD	Varicella
Incubation period	7-17 days	3-6 days	10-21 days
Prodromal period	1-4 days	2-3 days	0-2 days
Rash period (from the appearance of lesion of lesions to desquamation)	14-28 days	5-10 days	10-21 days
Prodromal fever	Yes		Uncommon, mild fever if present
Fever	Yes, often between 38.5°C and 40.5°C	Yes	Yes, up to 38.5°C
Malaise	Yes		Yes
Headache	Yes		Yes
Lymphadenopathy	Yes	Rare	No
Lesions on palms or soles	Yes	Yes	Rare
Lesion distribution	Centrifugal	Hands, soles, buttock, and genitalia	Centripetal
Lesion appearance	Hard and deep, well-circumscribed, umbilicated	Small vesicles (2 to 8mm) on an erythematous base	Superficial, irregular borders, 'dew drop on a rose petal'
Lesion progression	Lesions are often in one stage of development on the body, slow progression with each stage lasting 1-2 days	Ulcers appearing on the oral mucosa, and emerging blisters on the hands, feet, and buttocks	Lesions are often in multiple stages of development on the body, fast progression

DISCUSSION

Monkeypox disease is an emerging zoonotic disease caused by the monkeypox virus. The Democratic Republic of Congo (DRC) is where the virus was initially discovered in 1970 [2, 5]. Transmission may occur in various ways, including contact with lesion exudate or crust material, respiratory excretions, or saliva. The clinical picture of monkeypox and smallpox are quite similar, but the lymph node enlargement that appears early, frequently at the onset of fever that distinguishes monkeypox and smallpox infection [5].

For monkeypox infection, prodromal features up to three to four days [3, 5, 6]. The incubation period is seven to 14 days [6]; Subsequently, the rashes start to develop on face and followed by deep, well-circumscribed macular, papular, vesicular, pustular, and ultimately crusty scab lesions developing centrifugally and presence of lymphadenopathy prior to or during the rashes [3, 6]. In this case, the clinical rash finding is like the monkeypox virus; however, the distinct different of monkeypox and HFMD is that in monkeypox virus, patient usually has lymphadenopathy. Patients are assumed to be contagious from the time the rash appears until it has desquamated four weeks later. Respiratory droplets, the placenta, close contact with skin abrasions, or fomites can all cause person-to-person transmission [6].

There have been several other cases of the monkey pox documented, including perinatal transmission, and pre-school age children [7, 8]. Similar to our case report, this one involved a small boy aged 4 years old, who contracted the illness from his father [8]. The child had a fever before developing a vesiculopapular rash that covered his face, trunk and entire body. However, after receiving supportive care, this boy passed away after his illness lasted for 12 days. Another case reports a 10-day old infant. A rash appeared nine days after the uneventful delivery in late April 2022. The rash was first vesicular, beginning on the palms and soles and later extending to the face and trunk, and over time it developed into a pustular rash [7]. Given that both his mother and father had the same rash and there was a high likelihood that he had monkeypox, a sample was sent, and monkeypox was identified. After four weeks of intensive care, she received good care and was successfully discharged.

The gold standard techniques to confirm monkeypox virus infection are virus isolation, electron microscopy and polymerase chain reaction (PCR) [6]. However, clinical

diagnoses are used in most remote cases. The primary care doctor must distinguish other illnesses such chickenpox, measles, HFMD, bacterial skin infections, scabies, syphilis, and medication-associated allergies from monkeypox due to the resemblance of the rash and prodromal symptoms.

Regarding HFMD, the most common serotype for HFMD were *Enterovirus 71* (EV71), and *Coxsackievirus-A16* (CoxA16). HFMD is a substantial public health concern for children throughout Asia, even though most cases are mild and self-limited. The bulk of outbreaks is documented in India, China, Cambodia, Vietnam, and Malaysia [9]. HFMD is spread through feces, saliva, or physical touch with a sick person or their belongings and mostly infects children under five years of age [4]. The most common presentation is mouth pain, a maculopapular rash, ulcers on the oral mucosa, and developing blisters on the hands, feet, and buttocks. However, HFMD can present in the severe form of rashes, including bullous change, discomfort, and pruritis that spreads beyond the hand, foot, and mouth same as this case. This severe form of rashes was caused by some enteroviruses, such as coxsackievirus-A6 (CoxA6) and coxsackievirus-A10 (CoxA10) [10]. This severe form of rash might be difficult to differentiate with the current monkeypox outbreak rash.

Although HFMD is common, this case report provided an opportunity to describe the difference of the severe form of HFMD and monkeypox infection. Regarding the clinical presentation of HFMD and monkeypox, several features have been identified that can differentiate these diseases. First, is respect to HFMD; the incubation period normally takes two to ten days to complete, on average taking three to five days. Typically, the rash is maculo-papular and occasionally vesicular. The vesicles may be surrounded by an inflammatory cuff. The rash distribution was on the mouth, hand, foot, and buttock [4, 9, 10]. The clinical diagnosis of the infection can be confirmed by one of the following: specific enterovirus nucleic acid sequences (CoxA16, EV71 or other) being detected; identification and isolation of enteroviruses like EV71, CoxA16, and other types that may cause HFMD; IgM antibody against disease-related virus present during the acute stage; When compared to the acute stage, the recovery phase's neutralizing antibody titer against the relevant enterovirus is at least four times higher [10]. The majority of HFMD cases are treatable as outpatients and symptomatically. To prevent cross-infection, patients should be isolated and pay attention to diet as well as skin health.

General measures for treatment of HFMD are isolation to prevent cross infection, symptomatic relief such as antipyretic for fever management, and encourage plenty of fluid intake to prevent dehydration [10]. There is no available specific anti-enterovirus medication. Monosodium phosphate vidarabine, ganciclovir, and acyclovir have no role in the treatment of HFMD. Whereas, for the monkeypox virus treatment; it does not currently have a particular treatment, patients are handled with supportive care and symptomatic therapy [5]. This case report intends to raise awareness among primary care practitioners; with current outbreak of monkeypox viruses, should always consider monkeypox as a differential diagnosis. This is important because it promotes early detection, diagnosis, and treatment, all of which lower morbidity and improve patients' quality of life.

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Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

REFERENCES

1. Kumar S, Subramaniam G, Karuppanan K. Human monkeypox outbreak in 2022. J Med Virol. 2023;95(1):e27894. https://doi.org/10.1002/jmv.27894
2. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, et al. The changing epidemiology of human monkeypox—A potential threat? A systematic review. PLoS Negl Trop Dis. 2022;16(2):e0010141. https://doi.org/10.1371/journal.pntd.0010141 PMid:35148313 PMCid:PMC8870502
3. McCollum AM, Damon IK. Human Monkeypox. Clin Infect Dis. 2014;58(2):260-7. https://doi.org/10.1093/cid/cit703 PMid:24158414
4. Yi Z, Pei S, Suo W, Wang X, Huang Z, Yi A, et al. Epidemiological characteristics, routine laboratory diagnosis, clinical signs and risk factors for hand, -foot -and -mouth disease: A systematic review and meta-analysis. PLoS One. 2022;17(4):e0267716. https://doi.org/10.1371/journal.pone.0267716 PMid:35482791 PMCid:PMC9049560
5. Sklenovská N, Van Ranst M. Emergence of Monkeypox as the Most Important Orthopoxvirus Infection in Humans. Front Public Health. 2018;6. https://doi.org/10.3389/fpubh.2018.00241 PMid:30234087 PMCid:PMC6131633
6. Beer EM, Rao VB. A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy. PLoS Negl Trop Dis. 2019;13(10):e0007791. https://doi.org/10.1371/journal.pntd.0007791 PMid:31618206 PMCid:PMC6816577
7. Ramnarayan P, Mitting R, Whittaker E, Marcolin M, O'Regan C, Sinha R, et al. Neonatal Monkeypox virus infection. N Engl J Med. 2022;387(17):1618-20. https://doi.org/10.1056/NEJMc2210828 PMid:36223535
8. Eltvedt AK, Christiansen M, Poulsen A. A case report of Monkeypox in a 4-year-old boy from the DR Congo: Challenges of diagnosis and management. Case Rep Pediatr. 2020;2020:8572596. https://doi.org/10.1155/2020/8572596 PMid:32328334 PMCid:PMC7171673
9. Li P, Huang Y, Zhu D, Yang S, Hu D. Risk Factors for Severe Hand-Foot-Mouth Disease in China: A Systematic Review and Meta-Analysis. Front Pediatr. 2021;9:716039. https://doi.org/10.3389/fped.2021.716039 PMid:34858899 PMCid:PMC8631475
10. Li X-W, Ni X, Qian S-Y, Wang Q, Jiang R-M, Xu W-B, et al. Chinese guidelines for the diagnosis and treatment of hand, foot and mouth disease (2018 edition). World Journal of Pediatrics. 2018;14(5):437-47. https://doi.org/10.1007/s12519-018-0189-8 PMid:30280313