

The first case of monkeypox in Hong Kong presenting as infectious mononucleosis-like syndrome

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Case Report

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Abstract

We report the first imported case of human monkeypox in Hong Kong, manifesting as infectious mononucleosis-like syndrome. Viral load in deep throat saliva was comparable to vesicle swabs collected from face, arm, and back of this patient, suggesting deep throat saliva as an alternative specimen for early diagnosis of monkeypox.

Introduction

Monkeypox is a zoonotic infection caused by monkeypox virus (MPXV). It was first described in human in 1970, with subsequent circulation in endemic areas such as central and west Africa (1). Since 2003, MPXV emerged outside Africa, and caused the first major outbreak in the United States of America (USA) linked to imported exotic animals (2). On 7 May 2022, a case of monkeypox in a traveller returning from Nigeria to the United Kingdom was reported, leading to the subsequent circulation of MPXV in predominantly sexually-active young males (3). This outbreak led to more than 50,000 cases in at least 90 non-endemic countries on multiple continents (4). The current human monkeypox outbreak was declared a Public Health Emergency of International Concern by the World Health Organization on 23 July 2022 (5). Here we reported the first case of imported human monkeypox in Hong Kong in September 2022, who presented with infectious mononucleosis-like syndrome, as the newly described manifestation in the literature.

Case Report

A 30-year-old Chinese male was admitted to Queen Mary Hospital with sore throat and dysphagia when he returned to Hong Kong on 5 September, 2022. He travelled to the USA from 3 August to 25 August, 2022, to Canada from 25 August to 2 September, 2022, and to the Philippines from 2 September to 5 September, 2022. One week prior to admission, he noticed two painless penile ulcers, with subsequent appearance of rash on the face, neck, trunk, and limbs, developing from papules, vesicles then to pustules (Supplementary Fig. 1). He enjoyed good past health. On admission, the patient was afebrile, with physical examination revealing bilateral inguinal lymphadenopathy and two painless ulcers at the inner prepuce of the penis. Laboratory testing on admission showed leucocytosis (white blood cells $10.99 \times 10^9/L$) and lymphocytosis (lymphocytes $4.51 \times 10^9/L$), with atypical lymphocytes up to 26.8%, and elevated alanine transaminase (ALT 61 IU/mL), with normal renal function test. Abdominal ultrasound revealed no hepatosplenomegaly. Serological tests were negative for blood-borne viruses including hepatitis B surface antigen, hepatitis C virus antibody, and HIV antigen / antibody. Further investigations for infectious mononucleosis including Epstein-Barr virus (EBV) viral capsid antigen IgM, cytomegalovirus (CMV) IgM, and Toxoplasma IgM/IgG were all negative. Electron microscopy of the vesicular fluid showed brick-shaped virions (Supplementary Fig. 2). Multiple specimens including deep throat saliva, throat swabs, vesicle swabs, rectal swab, urine, and blood were collected, with DNA extraction using EZ1 Virus Mini Kit version 2.0 (QIAGEN, Germany). These were subjected to MPXV real-time PCR using both commercial (TIB Molbiol, Germany) and in-house assays targeting the J2L/J2R and

TNF receptor gene of MPXV respectively. The diagnosis of monkeypox was confirmed by detection of MPXV DNA by PCR in all specimens, with deep throat saliva, throat swabs, and vesicle swabs showing lower cycle threshold value when compared with other clinical specimens (Table).

Further whole genome sequencing performed by nanopore sequencing showed that our strain belongs to Clade IIb; Lineage B.1.7 (Figure). It is most closely related to hMpXV/United_Kingdom/UKHSA-40/2022. Several unique nucleotide mutations were detected in our strain (compared to B.1.7 complete sequences deposited to GISAID as of 13 September 2022; numbering according to NCBI Reference Sequence: NC_063383.1), including C142797T (OPG164:S7L), C149137T (OPG174:D87N), G150706A, G186791A, C188491T, and deletion at nucleotide position 136513–136515 (OPG153:D372-).

Discussion

Classical monkeypox is characterized by prodromal symptoms of fever, headache, and myalgia together with regional lymphadenopathy and monomorphic rash. The rash develops through different stages ranging from macules, papules, vesicles, pustules with central umbilication to scabs within 14 to 21 days, distributing in a centrifugal pattern. Previous studies already reported that the clinical presentations of monkeypox in the current outbreak are atypical, with initial rash in the penile, perianal, and pharyngeal areas depending on the route of exposure, together with less extensive distribution of rash and mild systemic symptoms (6). Complications of human monkeypox include bronchopneumonia, myocarditis, encephalitis, and keratitis with permanent visual loss (7).

Leucocytosis and elevated alanine transaminase have been reported in monkeypox (8). However, our case appears to be the first one presenting as infectious mononucleosis-like syndrome in the literature. Common causes of infectious mononucleosis include primary infection of EBV, CMV, HIV, and *Toxoplasma gondii*, but these were excluded by serological tests in our case. Currently, it is uncertain whether human monkeypox can present as an infectious mononucleosis-like syndrome without rash, similar to zoster sine herpette. Therefore, monkeypox should be considered as one of the differential diagnoses in patients with infectious mononucleosis, especially for those with history of epidemiological exposure.

MPXV DNA could be detected in various specimens from patients as reported in the literature (7). Our study additionally demonstrated that the viral load in deep throat saliva was comparable to that in vesicle swabs collected from multiple sites. Therefore, deep throat saliva appears to be an alternative clinical specimen for early diagnosis of monkeypox.

Declarations

Biographical Sketch

Dr. Kelvin Hei-Yeung Chiu is Resident, Specialist in Clinical Microbiology and Infection, working in the Department of Microbiology, Queen Mary Hospital. His research interest is emerging infectious disease.

Informed consent

Informed consent has been obtained from the patient.

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Table

Table. Cycle threshold value of monkeypox virus PCR in clinical specimen obtained on admission

Specimen Type	Cycle threshold value using TIB MOLBIOL MPXV PCR	Cycle threshold value using In-house MPXV PCR
Deep throat saliva	21.13	17.95
Throat swab	22.01	18.79
Vesicle swab (right face)	19.68	16.55
Vesicle swab (left arm)	21.24	18.13
Vesicle swab (upper back)	22.88	19.66
Rectal swab	36.26	34.06
Plasma	33.65	29.68
Serum	34.23	31.45
Urine	ND	25.53

ND, not done.

Figures

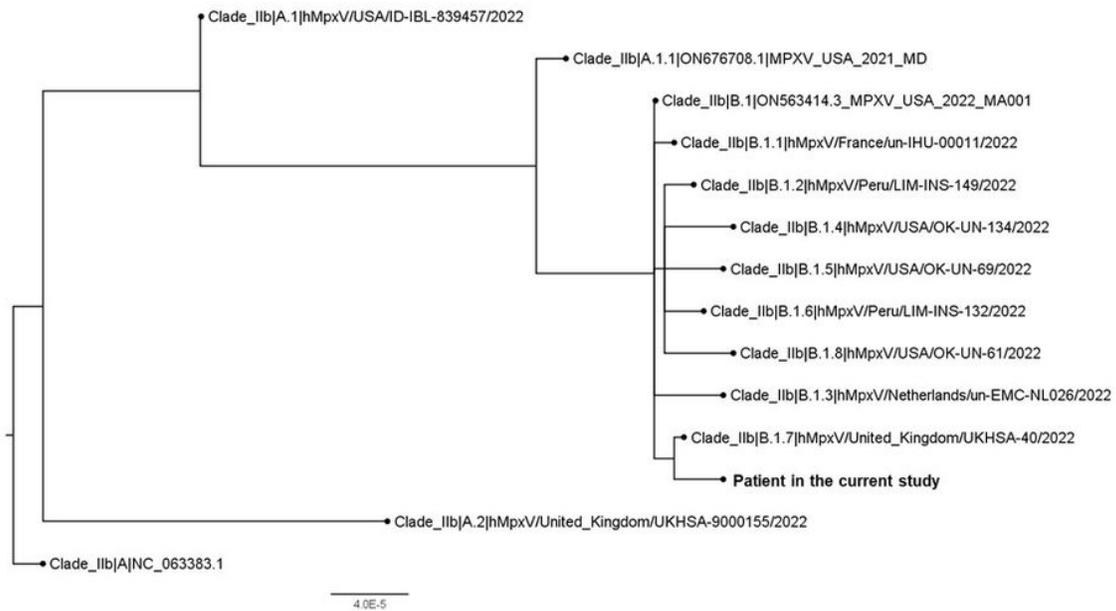


Figure 1

Whole genome phylogenetic analysis of the patients' strain. The tree was constructed by maximum likelihood method with IQTree2

Supplementary Files

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