A fatal case of monkeypox virus infection from Kerala India 2022

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Case Report

Keywords: Monkeypox, Fatal, Encephalitis, Traveler, UAE, India

Posted Date: September 15th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2030109/v2

Abstract

Monkeypox deaths have been rarely reported across the globe. A total of 19 fatalities have been reported globally from endemic and non-endemic countries in 2022. The current outbreak of Monkeypox had been largely limited to the community of men who have sex with men primarily with multiple bisexual or homosexual partners. The vast majority of the cases infected with Monkeypox had recovered and the complications like sepsis and encephalitis had been reported in the immunocompromised individuals. The mortality in Brazil and Mexico were primarily in the immunocompromised individuals, while in Spain the fatal cases were immunocompetent with no underlying conditions. To date, India had recorded 12 cases of Monkeypox infection from Kerala (n=5) and New Delhi (n=7). Here, we report the first fatal case of Monkeypox virus (MPXV) infection imported from UAE to Kerala, India in July 2022. A 22-year-old apparently immunocompetent male with no significant past medical history was admitted in an unconscious state to a private hospital in Kerala following a single episode of acute onset generalized tonic-clonic seizures. The clinical features, MRI findings, CSF picture, and EEG findings of this case suggest encephalitis. Only the case's oropharyngeal/nasopharyngeal swabs (OPS/NPS) were found to be positive for MPXV. The next generation sequencing on OPS/NPS specimen could retrieve 92.76% of the MPXV genome and belonged to A.2 lineage of clade IIb as observed in the other confirmed Monkeypox cases from India.

Introduction

The world has witnessed the emergence of Monkeypox virus (MPXV) from multiple countries in 2022.[1] Although it closely resembles the variola virus causing smallpox, the mortality rate of monkeypox (3-6%)[2] is far lower than smallpox (30%).[3] A total of 59,606 confirmed monkeypox cases have been reported with 19 deaths till September 14, 2022.[4] The deaths were from the endemic countries Nigeria (4), Ghana (4) and Central African Republic (2), and non endemic countries Spain (2), Brazil (2), Ecuador (1), Cuba (1), Belgium (1), USA (1) and India (1).[4] Till now, India has reported twelve confirmed cases of monkeypox from Kerala and New Delhi during July-September 2022.[5,6] Of these, nine cases have shown complete recovery without any sequalae, two cases still under isolation, and one case had succumbed to the disease.[6] All the confirmed five cases from Kerala were travelers from United Arab Emirates (UAE). Here, we report the first fatal case of Monkeypox virus infection imported from UAE to Kerala, India in July 2022.

Case Description

On July 27, 2022 a 22-year old apparently immunocompetent male with no significant past medical history was admitted in an unconscious state to a private hospital in Kerala following single episode of acute onset generalized tonic-clonic seizures. The clinical details regarding the case were extracted from the hospital and the history was obtained from the relatives. As the patient was in comatose stage, gaps in history provided by relatives could not be verified. The patient had developed fever, headache on July 15 while in UAE followed by development of painful right inguinal lymphadenopathy with pus discharge for which he had sought medical care on July 19. He was partially relieved of his symptoms and returned from UAE to Kerala, India on July 21, 2022. He played football on July 23, which led to worsening of pain in right inguinal area for which he consulted a surgeon on July 25 in Kerala and was diagnosed to have hidradenitis suppurutiva. He continued to have fatigue and low-grade fever which was not associated with persistent headache, alteration of sensorium, loss of appetite or weight. On July 26, 2022 evening he had a fever spike followed by generalized tonic clonic seizure.

On evaluation in emergency department of the hospital, his vitals were stable with no signs of meningeal irritation. The right inguinal lymphadenopathy with abscess formation and a single healed scrotal lesion were observed. Apart from that, there were no exanthemas. Suspecting encephalitis, the patient was shifted immediately to negative pressure single patient isolation intensive care unit.

At presentation, Glasgow coma scale score was 7 [Eye:01, Verbal:02; Motor:04]. The magnetic resonance imaging (MRI) of the brain revealed diffuse cerebral edema, altered signal intensity (FLAIR hyperintensity with mild restricted diffusion) in bilateral cerebral cortical and sub-cortical regions, bilateral caudate nucleus, putamen, posterior genu of corpus callosum. The electroencephalogram (EEG) was suggestive of generalized cerebral dysfunction. The MRI, EEG and cerebrospinal fluid (CSF) findings were suggestive of an acute-subacute meningoencephalitis (Table-1). Serological tests for HIV, Hepatitis B, Hepatitis C and syphilis were negative. At presentation, he had neutrophilic leucocytosis with normal hepatic function. Over the next 48 hours he developed coagulopathy and acute kidney injury [Table 1]. Myocarditis was ruled out by echocardiogram and cardiac biomarkers.

In view of presence of inguinal lymph nodes with abscess, along with the neuroimaging and CSF profile suggestive of meningoencephalitis, the patient was empirically started on anti-tubercular drugs, antibiotics to cover neurobrucellosis and acyclovir. On July 28, the patient developed features of worsening cerebral edema and was intubated and mechanically ventilated. Despite anti cerebral edema measures, he progressed to brainstem dysfunctionand succumbed on July 30, 2022. Just prior to death of the patient, his relatives obtained a test result from UAE, which showed that he had tested positive for MPXV at UAE on July 19. Right inguinal lymph node biopsy showed reactive change with foci of suppurative necrosis with no evidence of tuberculosis or fungal infection.

With this, the clinical specimens i.e., oropharyngeal swab (OPS)/nasopharyngeal swab (NPS), plasma and serum collected on July 30 was then referred to ICMR-National Institute of Virology for MPXV diagnosis. Only OPS/NPS of the case was found to be positive for MPXV (1.7×10^5 viral DNA copies/ml). The CSF specimen was unavailable to confirm encephalitis associated with MPXV. The next generation sequencing on OPS/NPS specimen could retrieve 92.76% of the MPXV genome and belonged to A.2 lineage of clade IIb as observed in the other confirmed Monkeypox cases from India.

The clinical features, MRI findings, CSF picture and EEG findings in this case were suggestive of encephalitis. MPXV encephalitis in immunocompetent is very rare. Encephalitis had been reported previously as the associated complication of Monkeypox infection, leading to fatality.[7,8] Encephalitis in this case could be either direct MPXV infection or due to autoimmune encephalitis like MOGAD [myelin oligodendrocyte glycoprotein antibody associated disease], which can be associated with viral infections.[9] The clinical and imaging features in this case are more in favor of direct MPXV encephalitis than MOGAD. However, the serum and CSF samples were not available to conclusively rule out MOGAD. All other usual causes of encephalitis had been ruled out by Film Array® Meningitis/Encephalitis panel (Biofire Diagnostics) and additional testing for Japanese encephalitis virus, West Nile virus and Nipah virus (Table-1). In this case, apart from a doubtful healed scrotal lesion and lymph node abscess, no other skin lesions were present.

Conclusion

This is the first fatal case of Monkeypox reported from India. This case highlights the importance of maintaining a high index of suspicion to diagnose MPXV in those presenting with atypical manifestations, exanthematous fever with epidemiological linkage from MPXV endemic or outbreak countries. The OPS/NPS specimen as well as possibly urine specimens should be considered as the critical specimens for MPXV diagnosis in cases with no active skin lesions. In conclusion, the overall findings of the case and the history confirm that the case to be infected with MPXV.

Declarations

Ethical approval

The study was approved by the Institutional Human Ethics Committee of ICMR-NIV, Pune, India under the project ‘Providing diagnostic support for referred samples of viral hemorrhagic fever and other unknown etiology and outbreak investigation’.

Consent statement

The informed consent was obtained from the patient's relative for the use of the clinical details in the study.

Author Contributions

PDY, MV, AR, FA, RRS contributed to study design, data analysis, interpretation and writing and critical review. PDY, MV, FA, RRS, AR, ABK, KP, AKP, LCG, NM, AS, DYP, AMS, ARP, ATK, KK contributed to data collection, interpretation, writing and critical review. PDY, RRS, AR, MV, PA contributed to the critical review and finalization of the paper.

Conflicts of Interest

Authors do not have a conflict of interest among themselves.

Financial support & sponsorship

The intramural grant was provided from ICMR-National Institute of Virology, Pune for conducting this study.

Acknowledgement

Authors extend gratitude to Smt. Veena George [Hon'ble Minister for Health and Family Welfare, Kerala], for her exemplary leadership and efficient coordination of the Monkeypox virus disease control activities, and "The Team Kerala Health," the district administration, press, media, and people for their efforts in streamlining the public health responses. We would also extend our gratitude towards Dr. Asha Thomas, Additional Chief Secretary Medical Education and Mrs. Tinku Biswal, Principal secretary for Health, Kerala. The authors also extend gratitude to Dr. Thomas Mathew, Director of Medical Education and Dr. Preetha PP, Director of Health Services for their immense support. Authors would like to thank the members of the district rapid response team of Thrissur for their role in case investigation. Authors also would like to thank family members of the deceased for co-operating with the investigation. Authors express their gratitude for the excellent technical and scientific support from all the staff of ICMR-NIV Kerala Unit, Alappuzha. Authors are also thankful for the staff of the Administration section, ICMR-NIV, Pune for their support during the outbreak response. We also acknowledge the excellent technical support from Mrs. Triparna Majumdar, Mrs. Savita Patil, Dr. Rajlaxmi Jain, Ms. Jyoti Yemul, Ms. Pranita Gawande, Ms. Pratiksha Vedpathak, Mrs. Shubhangi Sathe, Ms. Vaishnavi Kumari, Mr. Sunil Shelkhande, Ms. Nandini Shende, Mr. Raj Hawale, Mr. Ajay Kumar, Mr. Yash Joshi, Dr. Abhinendra Kumar from Maximum Containment Facility of ICMR-NIV Pune for the diagnosis and data management.

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Table

Table-1: Laboratory investigations of the Monkeypox death case from Kerala India

Parameters	Values detected	Interpretation
• **Hematological/Bio-chemical test**		
Haemoglobin (11.6-15.5 g/dL)	14.5	
TLC (4000-10000/µL)	18,210	Leucocytosis
Differential count [Neutrophils/Lymphocytes/Monocytes/ Eosinophil/Basophil]	84/12/2/1.5/0.1	Reactive lymphocytes, neutrophilic Leucocytosis with toxic changes
Platelet (150000-450000/µL)	2,43,000	
ESR (0-22 mm/hr)	42	Elevated
Blood Urea (8-21 mg/dL)	29	Elevated
Serum creatinine (0.6 to 1.2 mg/dL)	2.30	Elevated
Prothrombin Time (11-12.5 sec)	13.7	Elevated
D-Dimer (<500 ng/mL)	1240	Elevated
Ferritin (24 to 336 mg/L)	299.3	Elevated
C- Reactive Protein (<0.3 mg/dL)	12.9	Elevated
Procalcitonin (<20 ng/mL)	0.12	
Haptoglobin (36-195 mg/dL)	308	Elevated
LDH (150-333 IU/L)	584	Elevated
ANA (4.55 ± 0.53)	4.49	
INR (0.8-1.1)	1.06	Elevated
aPTT (21-35 sec)	36	Elevated
AST(24-40 U/L)	14	
ALT (44-80 U/L)	19	
ALP (50-130 U/L]	94.1	
Total bilirubin (0.1-1.2 mg/dL)	0.62	
Direct bilirubin (upto 0.5 mg/dL)	0.12	
Serum Albumin (6 to 8 g/dL)	4.3	Reduced
Serum Globulin (3.5 to 5.0 g/dL)	2.6	Reduced
Serum Sodium (142.67 ± 2.64mEq/L)	137	
Serum Potassium (4.47 ± 0.35 mEq/L)	4.2	
RBS (<200 m/dL)	113	
HbA1c (<5.7%)	5.8%	
• **Urine test**		
Urine routine and Microscopy	Albumin trace, few pus cells, presence of	Acute Kidney injury

	bacterial counts and amorphous urates	
• **Blood Culture**		
Blood Culture	No growth in 72 hours	
Microbial MINIBAL Culture and sensitivity	Gram stain- Pus Cell 10-15 Culture- No pathogen isolated	
• **Lymph node biopsy**		
Right inguinal lymph node biopsy	Reactive change with foci of suppurative necrosis with no evidence of tuberculosis or fungal infection	
• **Cerebrospinal Fluid test**		
CSF- cells- (0-5/cumm)	75	Polymorphnucleocytosis
Neutrophil	20%	
Lymphocytes	80%	
CSF protein (15-45 mg/dL)	84.3 mg/dl	Elevated
CSF Sugar (20-80 mg/dL)	58mg/dl (20-80)	
CSF ADA (0-0 IU/L)	13	Elevated
CSF LDH (0-0 IU/L)	39.0	Elevated
MTB (not detected)	Not detected	
CSF Culture and Sensitivity	Pus Cells 1-2, no growth in 72 hours	
Cytopathological examination	Paucicellular smear showing scattered lymphocytes only. No organism/malignant cells	
• **Other viral/bacterial/fungal pathogens tested**		
Escherichia coli K1	Not detected	
Haemophilus influenzae	Not detected	
Listeria monocytogenes	Not detected	
Neisseria meningitidis	Not detected	
Streptococcus agalactiae	Not detected	
Streptococcus pneumoniae	Not detected	
Cytomegalovirus (CMV)	Not detected	
Enterovirus (EV)	Not detected	
Herpes Simplex Virus 1 (HSV-1)	Not detected	
Herpes Simplex Virus 2 (HSV-2)	Not detected	
Human Herpesvirus 6 (HHV-6)	Not detected	
Human Parechovirus (HPeV)	Not detected	

Varicella Zoster Virus (VZV)	Not detected
Nipah virus	Not detected
Japanese Encephalitis	Not detected
West Nile Virus	Not detected
Hepatitis-B Virus	Not detected
Hepatitis-C Virus	Not detected
Human immunodeficiency virus-I & II	Not detected
Cryptococcus neoformans/gattii	Not detected
Syphilis	Not detected

TLC- Total Leucocytes count, AST- Aspartate aminotransferase, ALT- Alanine aminotransferase, ALP- Alkaline phosphatase, RBS-Random Blood Sugar, INR-International Normalized Ratio, aPTT-Activated Partial Thromboplastin Clotting Time, CSF-Cerebrospinal fluid, LDH-Lactate Dehydrogenase, ADA-Adenosine Deaminase, MTB-Mycobacterium Tuberculosis, ANA- Anti Nuclear Antibodies, HbA1c-Glycated hemoglobin