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Case Series

Human Monkeypox and Human Immunodeficiency Virus Co-infection: A Case Series in Makurdi, Benue State, Nigeria

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ABSTRACT

The Human monkeypox is a viral zoonosis which was first reported as a human disease in Zaire (present day Democratic Republic of Congo) in 1970. Outbreaks of the disease have occurred, though rarely, in some West African countries including Nigeria since then. However, in 2017 there was a large outbreak in Nigeria affecting many states. We wish to report the cases that were identified and managed successfully in Makurdi, Benue state because of their unique presentation as all but one of the patients had HIV coinfection which possibly was a risk factor for the monkeypox viral infection.

Keywords: *HIV, Monkeypox, Outbreak . .*

INTRODUCTION

The Human monkeypox is a zoonotic disease which is caused by the Monkey Pox Virus (MPXV), a member of the genus Orthopoxvirus (family Poxviridae, subfamily Chordopoxvirinae).[1] Human monkeypox is clinically almost identical to ordinary smallpox, and therefore, since the global eradication of smallpox in 1977, much attention has been paid to monkeypox as a smallpox-like disease and possible agent of bioterrorism.[1]

Monkeypox was first reported as a human disease in a 9 month old child from Zaire (the present Democratic Republic of Congo) in 1970 and most of the information in literature about human monkeypox came from the investigations of outbreaks in central and western Africa.[2]

The transmission of MPXV could either be animal-to-human, human-to-human. or from materials contaminated with the virus such as clothing or linens.[1,3] The virus enters the body through broken skin or the mucous membranes. Animal-to-human transmission may occur by animal bite or scratch, bush meat preparation, direct contact with body fluids or lesion material, or indirect contact with lesion material. Human-to-human transmission is thought to occur primarily through large respiratory droplets. The respiratory droplets generally cannot travel more than a few feet, so prolonged face-to-face contact is required. Other human-to-human methods of transmission include direct contact with body fluids or lesion material.[4]

The reservoir for MPXV is not known till date. However, there are data to suggest that monkeys are, similar to humans, incidental hosts, and that the reservoir is likely to be one or numerous species of rodents or squirrels that inhabit the secondary forest of central Africa.[4]

There is speculative evidence that HIV infection greatly enhances monkeypox infection and vice versa.[5]There have been some reports of Monkey-pox and HIV co-infection in some communities in Africa.[2,3]

Monkeypox was not recognized as a distinct disease until in1970, when the elimination of smallpox from the present Democratic Republic of Congo [DRC] revealed the continued occurrence of a smallpox-like illness in rural areas[2].

Subsequently, epidemiologic studies conducted from 1970–1979 detected a total of 47 cases of human monkeypox near the rain forests of sub-Saharan Africa, of which 38 occurred in the DRC and the remainder in Cameroon, the Central African Republic, Gabon, Cote d'Ivoire, Liberia, Nigeria, and Sierra Leone.[2, 3] All cases in the DRC occurred in areas bordering tropical rain forests and appeared to be associated with animal contact. Out of the 47 reported infections, 7 were fatal.

Following the emergence of monkeypox, the World Health Organization (WHO) conducted an active surveillance program in DRC from 1981 to 1986 which determined that monkeypox did not have the potential to occupy the niche vacated by smallpox[6]. Most of the cases then were from an animal source with secondary transmission from a human case occurring in a minority of the patients.[6]

In these outbreaks, children less than 15 years were the most affected and this might be linked to the cessation of smallpox vaccination and the fact that the immune systems in children are not yet fully developed.[6] The male-female ratio was equal.

In Nigeria, the first case of monkeypox was reported in 1971 in a 4-year-old boy from the South Eastern part of the country and another case was reported in 1978[7]. There has been no reported case of monkeypox in Nigeria since 1978 till the outbreak which started in September, 2017 when an 11year old boy and four other family members presented with clinical features of the disease at the Niger Delta Hospital, Bayelsa[8]. In this index case, there was a history of contact with a monkey.

There have been more cases of monkeypox reported subsequently and by January 2019 a total of 311 suspected cases and 7 deaths have been reported in 26 states. Of this, 132 were confirmed in 17 states (Benue, Bayelsa, Rivers, Cross River, Imo, Akwa-Ibom, Lagos, Delta, Edo, FCT, Abia, Oyo, Enugu, Ekiti, Nasarawa, Plateau,Anambra)[9]. Clustering of cases was revealed in Bayelsa, Rivers and Imo states but there was no evidence of epidemiological linkages across the states[10]. The genetic sequencing done suggested multiple sources of introduction of the MPXV into the human population. The male-female ratio for the confirmed cases was 2.5:1[10]. There are other disorders such as chickenpox and smallpox (currently eradicated) which have a similar presentation as monkeypox and efforts should be made by clinicians to know the various differences in their clinical presentations so as to make an appropriate diagnosis. The table below summarizes the different characteristics of these infections.

Table 1: Evaluation criteria for the differential diagnosis of patients with Monkeypox, smallpox, and chicken pox

Variable	Monkeypox	Smallpox	Chickenpox
Incubation Period (days)	7-17	7-17	12-14
Prodrome (days)	1-4	2-4	0-2
Symptoms (severity)			
Fever	Moderate	Severe	Mild or none
Malaise	Moderate	Moderate	Mild
Headache	Moderate	Severe	Mild
Lymphadenopathy	Moderate	None	None
Lesions			
Depth (diameter in mm)	Superficial/Deep (4-6)	Deep	Superficial
Distribution	Centrifugal	Centrifugal	Centripetal
Morphology	Homogenous	Homogenous	Heterogenous
Time to desquamation (days)	14-21	14-21	6-14
Palmar and Plantar involvement	Common	Common	Rare

It is therefore very pertinent to document the case series of 4 patients with monkeypox infection (out of which 3 were HIV positive) who lived in the same community in Benue state, Nigeria during the 2017/18 outbreak.

CASE REPORTS

It is interesting to note that there were lots of similarities among the cases. All the 3 patients who had the Human Monkey Pox and HIV co-infection were females. The only male patient, though free of HIV infection, had unprotected sexual intercourse with one of the female patients. The four patients lived in a town called Gboko located about 100Km from Makurdi, the capital of Benue

State in North-Central Nigeria. They all presented during the harmattan season (between November 2017 to January 2018) and had complete resolution of their lesions prior to discharge. The clinical diagnosis of HPXV for all the 4 patients was confirmed from swab samples taken from the skin lesions using Polymerase Chain Reaction at a Reference Laboratory in Dakar, Senegal.

CASE 1

A 20year old seamstress who developed high grade intermittent fever and multiple eruptions on her skin for a period of 2 weeks and was admitted at the Isolation Ward of the Benue State University Teaching Hospital, Makurdi. The lesions were distributed evenly on her face, trunk and extremities. She had developed the lesions a few days after intimate contact with her fiancé, a long-distance driver who had similar skin lesions, though he was afebrile. He resided in a distant town named Port-harcourt and visited her occasionally. She also had casual sexual intercourse a week prior to the onset of the lesions with a neighbor of hers who had similar lesions too. Physical Examination findings revealed numerous papules, large pustules and nodules on her scalp, face, trunk and extremities. The lesions covered about 80% of her total Body Surface Area (BSA) at presentation (Fig 1a). Most of the lesions on the face were coalesced. Notably, there were lesions on the palms of her hands and soles of her feet. She also had generalized lymphadenopathy and ruptured vesicles on her vulva suggestive of herpes genitalis. Investigations done revealed that she was HIV positive and was also pregnant. CD4 count was 64 cells/uL. She was subsequently placed on Highly Active Anti Retro-Viral Therapy (HAART) and acyclovir tablets for herpes genitalis. She was being managed conservatively for the MPXV infection and the lesions resolved after 42 days on admission prior to discharge. While on admission, she had an Intra-Uterine Fetal Death and fetal expulsion. She received several sessions of psychotherapy after discharge because of stigmatization from the public. Presently, she is adherent to the HAART and has resumed her routine duties. All attempts at contact tracing for the primary contact were unsuccessful.

CASE 2

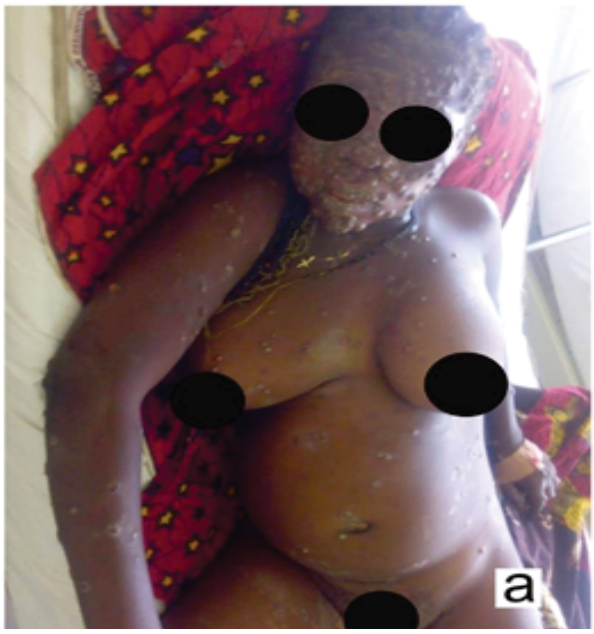
A 27year old Civil Servant undergoing the National Youth Corps Service who resided at the Youth Corpers' lodge located close to the home of the index case. He developed eruptions (papules and pustules) on the posterior aspect of his forearms, suprapubic area and inner thighs which started about 5 days after having unprotected sexual intercourse with the index case. The lesions covered <5% of his total BSA (Fig 1b). He had fever and malaise prior to the onset of the eruptions but was afebrile at presentation and throughout the course of the ailment. The skin lesions were discrete and few in number and he had only inguinal lymphadenopathy. Laboratory investigations done included a HIV screening which was negative. He was managed conservatively and had resolution of his lesions after 7 days on admission. He was counselled, prior to discharge to have a repeat HIV screening done in 6 months .

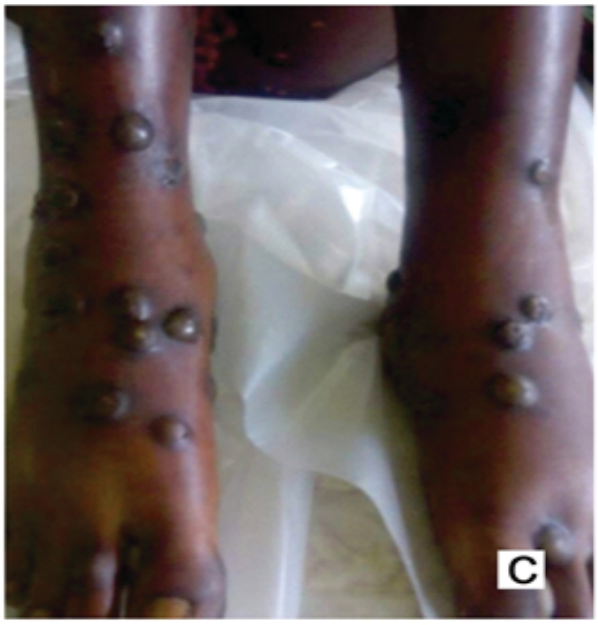
CASE 3

A 40 year old female trader who presented to our facility with numerous cutaneous eruptions (papules, pustules and nodules) limited to her lower extremities and covered about 20% of her Total Body Surface Area (Fig 1c). She had a low-grade fever, headaches and anorexia which commenced 3 days prior to the onset of the eruptions and continued till presentation. She travelled to Port-harcourt a week before the onset of the eruptions but denied any history of contact with anyone with similar eruptions. The forearms and legs had more lesions than the arms and thighs. She also had generalized lymphadenopathy. She was diagnosed of HIV infection 10 years ago and has not been compliant with HAART for 6 months. CD4 count done was 155 cells/uL. She was recommenced on HAART after due adherence counselling and was also managed conservatively. Most of the lesions (more than 90%) resolved after 10 days on admission with residual scars and post-inflammatory hyperpigmented macules and patches.

CASE 4

A 32year old female trader who presented to our facility with a history of fever for 2 weeks and cutaneous eruptions (papules, pustules and nodules) on the trunk and extremities for 1 week. Most of her lesions were on the dorsum of the hands (Fig 1d) There was no recent history of travel nor contact with anyone with similar lesions. She had presented earlier at a private hospital but was referred





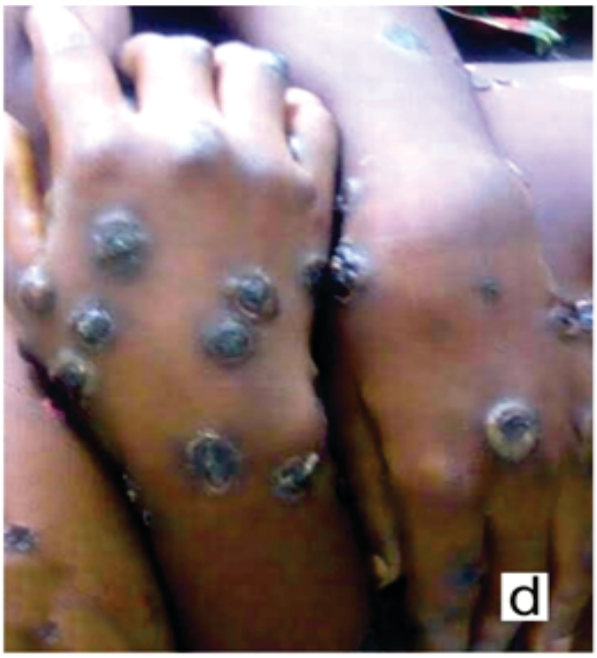


Figure 1a, 1b, 1c 1d: Images of the lesions in the 4 patients

to our facility due to worsening of her symptoms. She also had generalized lymphadenopathy. She was diagnosed of HIV infection 6 years ago and has been non-compliant with her medication for 2 years. Her CD4 count was 197 cells/uL. She was commenced on HAART after adherence counselling and was managed conservatively with resolution of most of her lesions after 10 days on admission. There were also residual scars and post-inflammatory hyperpigmented macules and patches.

DISCUSSION

We wish to highlight the salient features in these cases and compare their clinical features and outcomes with previously documented cases.

Demographics

In this case series, all the 4 patients were adults with an age range of 20 – 40 years. The male-female sex distribution was 1:3 which was similar to the national distribution during the period. In Benue state, there were no mortalities as all the patients were discharged after resolution of the eruptions. Although there were a total of 6 deaths out of the 89 confirmed cases in Nigeria and 4 out of the 6 patients that died had immunosuppressive diseases.[11]Interestingly all the patients lived in the same town and two of the patients had the disease after contact with individuals with similar eruptions. The clustering of the disease has been previously reported to occur in some communities[10]as it was in this situation and there is need for increased surveillance of the disease during outbreaks especially among people with immunosuppressive disorders.

Clinical Features

All the patients here had a prodromal phase before the eruption of the typical lesions as documented in previous studies.[12,13] Only 2 of the patients gave a history of contact with someone with similar lesions. This could be because they were unaware of the lesions in their casual contacts or may unwittingly have had rodent-human transmission. The lesions in all the HIV positive patients were widely distributed, with many coalesced lesions and consisted mostly of large pustules and nodules while they were sparse, discrete and consisted of pea-sized pustules and nodules in the HIV negative patient. The most florid lesions were in the index patient whose CD4 count was less than 100 cells/μL. It also took more time for the lesions to resolve among the patients who were HIV positive. This suggests that HIV infection and possibly any immunosuppressive disorder could give rise to more severe disease. Severity of monkeypox infection in persons with HIV infection has also been documented.[14]

DIAGNOSIS

The diagnosis of monkeypox infection could be made by cellculture, Polymerase Chain Reaction (PCR), Enzyme Linked Immunosorbent Assay (ELISA) or Western Blotting.[10] PCR being used for definitive diagnosis and all the patients admitted had swab samples taken from the pustular lesions for PCR at a Reference laboratory in Dakar, Senegal. The results of the samples sent for all the patients came out positive. Standard, contact and droplet precautions must be applied during specimen collection and all samples potentially infected with monkeypox virus should be handled in at least a Biosafety level 2 facility[10]. Currently, laboratory confirmation can be done in Nigeria at the National Reference Laboratory, Gaduwa, Abuja.[15]

CASE MANAGEMENT

At presentation, all the patients were reviewed at the triage and thereafter admitted to the Isolation ward of the hospital where they were managed till discharge. They were managed conservatively as indicated and had prophylactic antibiotic therapy to prevent super-imposed bacterial infection at the sites of the skin lesions. All the HIV positive patients were placed on Highly Active Anti-Retroviral Therapy. The index case was placed on oral acyclovir for genital herpes and also had fetal expulsion following an intra-uterine fetal death. The patients had complete resolution of their lesions with varying degrees of scar formation and post-inflammatory hyperpigmentation. All the patients had resolution of their lesions, with the last crusts being shed, within 7-10 days but the index case (who had the most severe lesions) had resolution of lesions in 42 days. It is recommended that the patients remain in isolation till the last crust is shed as direct contact with skin lesions and fomites can lead to the spread of infections.[16]

The patients were offered psychotherapy while on admission because of the cosmetic appearance from the disease and perceived fear that they would be stigmatized

by the community on discharge. The patients were also anxious and embarrassed due to the negative comments and remarks made by some of their friends, relatives and healthcare workers to them. Psychotherapy is highly recommended in patients with monkeypox disease to enable them cope with the psychological issues they are faced with.[15]

Infection Prevention and Control

Standard precautions were applied while managing the patients from presentation till discharge. This was to ensure that Health Care Workers, other patients in the facility and the people in the community do not get the infection. Health education on Monkeypox was done for the hospital staff to teach and update their knowledge on ways to prevent transmission of monkeypox infection.

Recommendations

There is also need to educate the public through print, electronic and social media about the disease stating emphatically that persons with healed lesions cannot transmit the disease so that they would not suffer stigmatization.

The health education should also include ways to prevent the infection such as avoiding contact with primates and for proper isolation of suspected cases. A lot of emphasis should be made on contact precautions while handling animals and thorough cooking of animals before ingestion.

There is also need to clarify some myths about monkeypox disease in some communities where it is believed that evil spirits are responsible for the infection and infected persons are stigmatized even months or years after resolution of their lesions.

Furthermore, access to basic health care should be provided for all and most especially persons with Immunosuppressive diseases such as HIV infection as they are prone to various opportunistic infections which may include monkeypox.

CONCLUSION

Human monkeypox infection can occur sporadically and persons with immunosuppressive diseases such as HIV infection are at risk. It is recommended that HIV screening should be done for any case of monkeypox and people living with HIV should be adherent to medication most especially in communities with monkeypox outbreaks.

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