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Case Report

Monkeypox and chickenpox co-infection in a person living with Human Immunodeficiency Virus

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Abstract

Introduction: The 2022 mpox global outbreak underscores the need for an improved understanding of mpox epidemiology, co-morbidities, and clinical management/outcome. We report a case of a 30-year-old Nigerian antiretroviral treatment-experienced person living with human immunodeficiency virus (PLHIV) who had PCR-confirmed mpox and chickenpox co-infection.

Case presentation: The patient presented with a generalized itchy rash of three weeks and antecedent low-grade fever. He had no recent travel, animal exposure, or same-sex relationship. Examination revealed generalized pustular and nodular eruptions without peripheral lymphadenopathy.

Results: CD_4 count was 78 cells/mm^3, wound swab microscopy revealed Gram-positive cocci in clusters and Gram-negative bacilli while culture yielded *Pseudomonas aeruginosa*. Despite supportive care and definitive antimicrobial therapy, his clinical condition deteriorated with sepsis-related multi-organ dysfunction and ultimately death.

Conclusions: Mpox and chickenpox co-infection may occur, with potentially fatal complications in the setting of advanced HIV disease. Increased surveillance for co-viral infections in PLHIV with febrile exanthema and aggressive management to improve outcome are recommended.

Key words: Mpox; chickenpox; co-infection; HIV; surveillance.

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Introduction

Human mpox is caused by the monkeypox virus (MPOXV), first identified in 1958 amongst monkeys [1]. It is a zoonosis endemic to the Central and West Africa rainforest. It belongs to the *Orthopoxvirus* genus and *Poxviridae* family [2]. Mpox re-emerged in Nigeria in 2017 about 40 years after the last reported case [3]. Between September 2017 and 01 January 2023, 988 confirmed cases with 15 deaths were reported in Nigeria [4]. The 2022 multi-country mpox outbreak in predominantly non-endemic countries and the declaration of mpox as a Public Health Emergency of International Concern (PHEIC), by the World Health Organization (WHO), buttresses the need for further research to inform mpox outbreak responses [2].

Chickenpox, the primary varicella infection is caused by the varicella-zoster virus (VZV), of the *Varicellovirus* genus *and Herpesviridae* family. Mpox and VZV co-infection has been reported in the mpox endemic Central African region [5–7]. Previous reports of human immunodeficiency virus (HIV) and mpox co-infection in Africa as well as the disproportionate representation of HIV and other sexually transmitted infections in mpox patients during the 2022 outbreak further justify the need to investigate co-infections among mpox cases [8]. We report a case of mpox and chickenpox co-infection in a severely immunosuppressed Nigerian man living with HIV to provide insight into the potential diagnostic dilemma and management challenges of the co-morbidities.

Case Presentation

On July 20, 2022, a 30-year-old male hair stylist presented to the Infectious Disease Unit of Federal Medical Centre (FMC), Owerri, Nigeria with a three-week history of generalized itchy rash that started on the face. There was a preceding history of low-grade fever three days prior to the onset of the rash. There was a history of anorexia and dyschezia but no other gastrointestinal symptoms. Haematuria and splitting of urine were noted but no dysuria or pyuria. He had no known drug allergies neither was there a history of insect bites. Travel history, animal exposure, sick contact, and family history were unremarkable. On

admission, axillary temperature was 37.3 °C, blood pressure was 155/73 mmHg, pulse rate was 142 beats⁄min, and respiratory rate was 28 cycles/minute. He had generalized well-circumscribed pustular and nodular eruptions on the head, trunk, limbs, genitals, palms, and soles with some exhibiting central umbilication (Figure 1). He had no oral lesions or lymphadenopathy.

He was diagnosed with HIV type-1 ten years ago and was on antiretroviral therapy (ART); Tenofovir/Lamivudine/Dolutegravir with poor adherence. Although a recent viral load was unavailable, his CD_4 count on admission was 78 cells/mm^3. Following a working diagnosis of human mpox (with chickenpox as a differential diagnosis), he was admitted and managed in the Isolation facility of the FMC Owerri. Skin lesion swab samples were collected for mpox virus (MPOXV) real-time polymerase chain reaction (RT-PCR) while blood samples were obtained for complete blood count (CBC), liver function test (LFT), malaria parasitaemia (MP), and renal function test (SEUCr). Serological testing for mpox and/or chickenpox was not deployed. A urine analysis likewise wound swab microscopy, culture, and sensitivity (MCS) were also done. Skin swab sample RT-PCR for both MPOXV and VZV performed at the National Reference Laboratory of the Nigeria Centre for Disease Control (NCDC) returned positive with cycle threshold values of 15.82 and 36.61 respectively. VZV RT-PCR testing is routinely performed on samples of suspected mpox cases by the NCDC due to previously observed trends. Other available laboratory results are summarized in Table 1.

He received intravenous fluids, oral acyclovir, analgesics (acetaminophen and/or opioids), antibiotics, oral multivitamins (vitamin C, vitamin A, vitamin E, zinc) antihistamine (cetirizine), and wound dressing. ART adherence counseling was offered. He received flucloxacillin and metronidazole as empirical antibiotic therapy which was switched to gentamycin and levofloxacin based on antibiogram. Despite these, the wound healed poorly discharging purulent exudate. There was a relapse of fever which became continuous in the fifth week. Unfortunately, in the sixth week of admission, he further deteriorated with sepsis-related multi-organ dysfunction and died on August 31, 2022.

Discussion

This was a case of laboratory-confirmed mpox and chickenpox coinfection occurring in the setting of advanced HIV disease (AHD) in an adult who subsequently died from sepsis-related multi-organ dysfunction. Adult PLHIV with $CD_4 < 200$ or WHO clinical stage 3/4 are said to have AHD [9]. Uncontrolled HIV infection has been shown to increase the risk for severe mpox with potentially worse outcomes [10,11].

Our patients' presentation was in keeping with severe mpox despite the absence of peripheral lymphadenopathy. Furthermore, the occurrence of pockets of laboratory-confirmed and suspected chickenpox cases in some parts of Nigeria heightened

Figure 1. A 30-year-old man living with HIV with mpox and chickenpox co-infection.

Patient had generalized papulopustular lesions with central umbilication with the most florid lesions on the face, scalp, lower and upper extremities. **A.** At presentation; **B.** Day 5 at hospitalization showing lesions on the scalp, trunk, and upper limbs; **C.** Lower limb involvement; **D.** Showing nodular lesion on the sole of the left foot.

Table 1. Table of investigations.

Investigation	Result	Reference values
LFT		
Total Bilirubin mg/dL	0.8	0-1
Conjugated Bilirubin mg/dL	0.2	< 0.4
AST IU/L	8	3-12
ALT IU/L	9	3-12
ALP IU/L	41	25-92
SEUCr		
Sodium mmol/L	128	135-150
Potassium mmol/L	3.7	3.5-5
Chloride mmol/L	94	96-108
Bicarbonate mmol/L	Not done	21-30
Urea mg/dL	18	15-40
Creatinine mg/dL	0.8	0.5-1.5
SEUCr follow-up		
Sodium mmol/L	137	135-150
Potassium mmol/L	4.3	3.5-5
Chloride mmol/L	100	96-108
Bicarbonate mmol/L	Not done	21-30
Urea mg/dL	20	15-40
Creatinine mg/dL	0.6	0.5-1.5
Urine analysis		
Appearance	Amber and Clear	N/A
PH	7.0	N/A
Glucose	Absent	N/A
Ascorbic acid	Absent	N/A
Ketones	Absent	N/A
Protein	Absent	N/A
Nitrite	Negative	N/A
Bilirubin	Absent	N/A
Urobilinogen	Normal	N/A
Blood	Absent	N/A
Microscopy		
WBC hpf	6-8	N/A
RBC	2-5	N/A
Epithelial cells	+++	N/A
Yeast cells	Nil	N/A
Casts	Nil	N/A
Crystals	Nil	N/A
Others	Nil	N/A
Wound swab MCS		
Gram stain	Gram positive cocci in clusters; Gram negative bacilli	
Culture	Moderate growth of pseudomonas aeruginosa after 48 hours incubation; Sensitive to: Gentamycin^{++}, levofloxacin^{+}, ofloxacin^{+}; Resistant to: Augmentin, Cefuroxime, Cefotaxime, Imipinem/Cilasta	
MP	*P.faliparum* trophozoite seen	
FBC		
Haemoglobin g/dL	10.8	12-18
WBC Total mm^3	10,000	3,000-10,800
Neutrophil %	56	40-75
Lymphocyte %	43	20-45
Monocyte %	0	2-9
Basophil %	0	0-1
Eosinophil %	1	1-5
Platelet count mm^3	431,000	
HBsAg	Non-reactive	N/A
Anti-HCV	Non-reactive	N/A
CD_4 count cells/mm^3	78	
FBG mg /dL	98	60-120

CBC: Complete blood count; LFT: liver function test; count; AST: Aspartate transaminase; ALP: Alkaline phosphatase; ALT: Alanine transaminase; MP: malaria parasitemia; SEUCr: renal function test; N/A: Not applicable; FBG: fasting blood glucose CD_4: Cluster of Differentiation Antigen 4; HCV: Hepatitis C Virus; HBsAg: Hepatitis B surface antigen.

the consideration of chickenpox as a differential diagnosis. Moreover, chickenpox has been reported to occur simultaneously with mpox in Africa [5–7]. The presence of a high rash burden with purulent craters coupled with the underlying severe immunosuppression increased his risk for a secondary bacterial skin infection which informed our action to institute empirical broad-spectrum antibiotics.

Despite the paucity of data exploring the clinical spectrum of mpox in PLHIV, our findings corroborate those of Ogoina *et al* who found PLHIV with mpox had a more protracted illness, larger lesions, and a higher rate of secondary bacterial infection compared to the HIV seronegative group [10]. An observational study from a global cohort of PLHIV in AHD have also shown persons with declining CD_4 count especially those $CD_4 < 100$ to commonly develop a myriad of complications from mpox including necrotizing skin lesions, secondary skin infection, sepsis, etc. [11].

A higher tendency to poor outcomes such as mortality among HIV/mpox co-infected patients was also reported by Ogoina *et al* [10]. Contrarily, no mortality was reported in a multi-national study involving non-endemic countries where 41% of the study participants were PLHIV [8]. This subset of PLHIV however had controlled infection (96% on ART, median CD_4 count of 680 (513-861) cells⁄mm^3, and viral load of < 50 copies/mL in 95% of them) [8]. It is possible that the co-existence of mpox and chickenpox in the background of severe immunosuppression contributed to the poor outcome seen in the index case. Incidentally, the literature is lacking on data highlighting the impact of mpox and chickenpox co-infection on clinical sequelae and outcomes in PLHIV hindering the comparison of the index case with any existing literature.

Although circumstances surrounding his poor adherence were not extensively elucidated, these actions possibly contributed to his development of AHD having been diagnosed with HIV 10 years ago as he was likely failing ART. Treatment failure is often encountered in ART-experienced cohorts where opportunistic infections are often implicated [12]. A systematic review further revealed that patients with AHD are at increased risk of mortality during the first six months following this diagnosis [13]. Nevertheless, we speculate that the interaction of multiple viral pathogens complicated by secondary bacterial skin infection may have worsened the clinical outcome of our patient since the predominantly circulating mpox clade reported in Nigeria is less virulent [14]. Malaria

parasitemia and mild anemia were additional co-morbidities in the patient.

The management of the index case was not met without challenges which were; financial, prolonged laboratory turnaround time, and psychosocial dysfunction. While MPOXV and VZV RT-PCR testing were available at no added cost to the patient, other components of his care were funded out-of-pocket. Out-of-pocket health expenditure remains a concerning cause of financial hardship in Nigeria, and this potentially has a disastrous impact on the in-hospital management of emerging infectious diseases. Albeit some time was lost trying to raise funds by the patient's family invariably delaying time to intervention. Delayed laboratory confirmatory diagnosis have previously been reported as a major challenge in our environment [15]. Despite establishing the presence of sepsis diagnostic constraints made us unable to confirm or exclude the presence of pneumonia, encephalitis, or other specific organ dysfunction which may have been present. We were also unable to conduct cellular laboratory interrogations, repeat MPOX and VZV RT-PCR assays as well as HIV viral load which could have helped to further characterize the dynamics of the triple infection with HIV, MPOXV, and VZV.

In the wake of mpox outbreaks internationally and reports of mpox and chickenpox coinfections in Africa, prompt routine laboratory evaluation for both mpox and VZV which often poses a clinical diagnostic dilemma is paramount [5,10]. As PLHIV were disproportionately affected by recent outbreaks of mpox globally, increased surveillance of mpox and other co-morbidities such as chickenpox among PLHIV in endemic regions such as sub-Saharan Africa is recommended [8,10,15–17] Importantly, where herd immunity for chickenpox is low, early diagnosis will further guide therapy in PLHIV where varicella vaccine use is not advocated in AHD. The opt-out approach to HIV screening should be considered for all suspect mpox cases while post-exposure prophylaxis for mpox may be considered in PLHIV in AHD [18]. Further prospective cohort studies to better understand the interactions between HIV, mpox, and VZV and their impact on clinical outcomes is recommended.

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Patient Consent Statement

Informed verbal consent was obtained for clinical photographs before the patient's demise. Ethical approval was obtained from the Health Research Ethics Committee of Federal Medical Centre, Owerri, Imo State, Nigeria.

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