Monkeypox Disease With Predominant Genital Symptoms: A Nigeran Case Report

Abstract

Mpox presents typically with macular papular body rashes with similar-looking sores in genital or oral areas. It may be missed, or wrongly managed as sexually transmitted infections (STI), especially in settings where symptom-based treatment practices are sufficient for care.

We describe a 40-year-old cisgender male, heterosexual Nigerian who developed some rash in the genital region associated with penile swelling. It was suspected to be syphilis and managed with presumptive antibiotics. Laboratory investigation (PCR) confirmed that it was a Mpox disease, and VDRLT was negative. Notably, in this case, the early symptoms were a paradigm case of Mpox disease presenting as an STI, which syndromically conformed more to an STI than the case definition for a suspected case of Mpox in our setting. Consequently, the expected early containment activities were delayed. This increased the potential of further disease spread. An Update of the standard case definition as well as a reclassification of the disease as a possible STI is recommended for enhanced surveillance, increased case detection, and reduction in the burden of unrecognized cases.

Key words: Mpox, STI, Case definition, Syphilis, surveillance.

Introduction

Human Mpox disease was a rare viral infectious disease often seen near tropical rainforests of Central and West Africa. The first human Mpox disease was reported in 1978 in the Democratic Republic of Congo (former Zaire) two years after the successful elimination of smallpox[1]. The

First Western outbreak was reported in the United States of America in 2003.[2] The disease is caused by the Mpox virus, a member of the Orthopoxvirus genus in the family Poxviridae.[1] The virus has two distinct clades: the Congo Basin and the West African clades [1]. The West African clad is known to be milder in morbidity and mortality.[3] Smallpox vaccination confers 80% immunity against Mpox. Two vaccines (MVA-BN and LC16) are approved for the prevention of Mpox for persons at risk, including exposed-close contact with cases of Mpox [4, 5]. Post-exposure Preventive Vaccination (PEPV) is advised for target groups like sexual partners, household contacts, HCWs, and individuals with other prolonged physical or high-risk contacts with the confirmed case [4].

Mpox can be fatal but is a much milder disease than smallpox. There is also no specific treatment recommended for Mpox by the World Health Organization, but some antivirals have been licensed for the treatment of Orthopoxviruses, such as tecovirimat [1, 6]. The case fatality in outbreaks is between 1% and 10%, and younger age groups are known to be the most affected.[1] Mpox disease is known to be transmitted from various wild animals but has limited human-to-human transmission [1, 7]. Clinical presentation of Mpox disease includes fever, headache, Back pain, myalgia, intense asthenia (lack of energy), and generalized macula-papular rash. Similar-looking sores in genital or oral areas may be missed or wrongly managed as common conditions of herpes or syphilis, especially in rural settings where symptom-based treatment care practices are predominantly sufficient for care [8, 9]. But the rash on the palm and soles of the feet with lymphadenopathy often distinguishes Mpox from other pox-like rashes [7].

In Nigeria, two cases of Mpox were first reported in 1971, and in 1978 another case was reported after which the disease became silent. In September 2017 Nigeria witnessed a resurgence in Mpox cases and has since then continued to have cases of Mpox in urban settings without epidemiological linkage [10],[11]. As of epidemiologic week 24 in 2022, Nigeria has

documented 622 cases and 8 deaths from 33 out of 36 states, including the Federal Capital Territory. Out of the total reported cases since 2017, 31 cases were confirmed from 112 suspected cases among 12 States by Epid week 23 of 2022 [10]. However, since the resurgence of Mpox in 2017 in Nigeria, the report of a co-presentation of Mpox and sexually transmitted infection has been mentioned by clinicians [12].

The first case of Mpox in Rivers State was diagnosed in October 2017 in Eleme Local Government Area (LGA). The patient was a male military officer who had returned from official duty offshore. The NCDC lists its standard case definition as "An acute illness with fever >38.3^{o}C, intense headache, lymphadenopathy, back pain, myalgia, and intense asthenia followed one to three days later by a progressively developing rash often beginning on the face (most dense) and then spreading elsewhere on the body, including soles of feet and palms of the hand; Probable case - A case that meets the clinical case definition is not laboratory-confirmed but has an epidemiological link to a confirmed case and Confirmed case - A clinically compatible case that is laboratory confirmed [13].

Surveillance is a core strategy for the containment of Mpox, [11] therefore, acceptable case definition must address the ease of finding cases of Mpox and greatly reduce missed opportunities in the identification of suspected Mpox cases in the event of an active search or at presentation in health facilities. The diagnosis of Mpox is by PCR. The differential diagnosis includes chickenpox, measles, bacterial skin infection, scabies, syphilis, medication-associated allergies, and common Sexually Transmitted Infections (STIs) presenting with cutaneous lesions (syphilis, Herpes, and Molluscum contagiosum).

Mpox usually presents as multiple deep-seated skin lesions that often start from the head after a prodromal phase, characterized by fever, malaise, headache, sometimes sore throat and cough, and swollen lymph nodes. Presentation as an STI is being reported in the changing dynamics of

disease epidemiology. It is now also postulated that the disease is sexually transmissible in extrapolation to the established transmission mode. The eventual transmission of a consequentially infectious rash during sexual contact can be plausibly conjectured.

Toll like receptor 2 and 4 (TLR2 and TLR4) play a considerable role in the host defense against microorganism [15] and elicit major contributions to the pathogenesis of MPXV, as the later inhibit TLRs-dependent innate responses. [16]

In combatting monkeypox infections, CD4 + T cells are complex and priming CD8 + T cells to differentiate into effector and memory T cells to promote B cells-dependent antibody responses. [17] CD11a is to normal lymphocyte development. [18]

Studies confirm that NK cells are infected with MPXV, are often associated with a Th1 response, NK-cell activation, IFN-γ production, and T-cell activation [19]. TGF-β1 suppresses the functions of Th1 and Th2, NK cells, and CD4+ effector cells, and promotes generation of Treg cells. While promotion of immune responses; TGF-β1 induces the generation of Th1 cells in combination with IL-6 [20].

IL-10 is an immune-regulatory cytokine having anti-tumor effect [21]. And observed in patients with serious MPV disease [22].

Containment of Mpox as in most infectious diseases, involves the identification and isolation of cases, with line-listing of contacts and follow-up, for the recognized incubation period (21 days). Decontamination of common surfaces and management of symptoms are also useful. Though newer drugs have been approved for treatment, Mpox is still largely managed symptomatically with antihistamines and analgesics. Mpox is listed as a priority disease for immediate notification on the Integrated Disease Surveillance and Response (IDSR) in Nigeria to enable rapid

containment. Yet, missed opportunities will obviously guarantee a reduction in case finding, worsen the iceberg phenomenon and increase the unrecognized burden of the disease.

The emergence of a cluster of cases of Mpox for the first time in history amongst patients in Sexually Transmitted Infections (STI) clinics in the western hemispheres[14] makes the case described in this report quite interesting and significant for public health attention. This is especially because investigation and differential diagnosis of STI presentations was hitherto not deliberately inclusive of Mpox[8] and did not take into cognizance the history and possibility of sexual transmission of Mpox disease. The case presented in this report highlights the necessity of surveillance for Mpox around STIs, high-risk patients for STIs, and STI clinics.

Case Report

A 40year old male (cisgender) Nigerian who works with an international organization as a networking officer. He covers all the States of the South-South and South-East regions of Nigeria, training and supervising other field workers in the organization across these States in Nigeria. He relates that after he returned from an official trip to Rivers State from a neighboring state, he developed a fever for four days. He was treated for malaria with sulphadoxine/pyrimethamine tablets prescribed by a Patent Medicine Vendor in his neighborhood on the fifth day (Day 5 of the appearance of the first symptom). The symptom persisted with a few rashes (described as painless, and papular) developing in the genital region on the third day of taking the antimalarial medicines (Day 7). This was also associated with penile swelling. He admitted to having casual non-protective sex about two weeks before the onset of symptoms. The patient is cisgender, married, and heterosexual with no history of anal *receptive* or anal *insertive* sex. There was no history of any chronic illness or known allergies. He also gave a history of living in self-contained appurtenances with his wife, three kids, and house help. They have a domestic (pet) dog that stays within the compound and has shown no sign of

ill health recently. He sought care in a private hospital the next day (Day 8) with a complaint of penile swelling and a few penile ulcers also described as painless and not associated with urinary symptoms, or discharge. He was subsequently referred to the State Teaching Hospital.

On examination upon arrival at the State Teaching Hospital on the same day (Day 8), the entire length of the phallus was found to be massively swollen and slightly tender with two deep-seated solitary ulcerative lesions on the glans penis and another at shaft, measuring about 0.5cm in diameter. The lesions were in similar stages and covered with cheesy exudates. The attending physician made a working diagnosis of Syphilis, and he was placed on presumptive antibiotics (Caps Ampicillin 500mg, Tabs Flagyl 400mg) as well as paracetamol, hematinic, and vitamin C tablets, and managed as an outpatient. Two days later (Day 10), symptoms worsened, and he returned to the hospital. Though the fever had subsided a bit, there were now several other deep-seated rashes on the trunk arms and face, with pustules, at various stages of development viz - papular, vesicular, and umbilicated pustular stages. No scabs were observed. The penile lesions were still wet, and the penis was swollen. The rashes on the body appeared to be centrifugal, being more in the face and extremities.

Further examination revealed the existence of a rubbery painless cervical lymphadenopathy (of about 1cm diameter). At this time, a clinical assessment of rash pleomorphism led to the suspicion of Mpox disease, but the patient left the hospital in denial. He was later compelled to contact the State response team the next day (Day 11), by the doctor working at his company Agency who insisted on standard care procedure and proper follow-up. His samples were collected on the same day and transported to the national reference laboratory for Mpox PCR diagnostic testing. The patient was categorized for home-based care management and was advised to proceed on strict self-isolation. He received counseling on health risks, possible outcomes, care responsibilities, prognosis, and the natural course of the disease. There was no

affirmative history of sexual activity after the development of rashes. As such, no other sexual contacts were listed. He was then advised to abstain from sex. Thermometers were distributed to all family high-risk contacts after risk assessment. They received guidance on symptoms to look out for and telephone contacts to report incidents and developments. They were taught how to conduct and report daily temperature measurements and the need to avoid large gatherings cautiously. The State provided thermometers and hand sanitizers for their comfort. While the syphilis screen (Venereal Disease Research Laboratory Test – VDRLT) turned out to be negative, the PCR results returned 48 hours later by email as a positive case of Mpox, and the patient was promptly communicated about the diagnosis on the telephone. He accepted the result and reassured the team of compliance with all public health protocols for the home management of Mpox while on self-isolation. Despite repeated counselling, he did not accept to reveal the details of the casual sex partners for contact tracing. The PHEOC was at the time already activated, on *Response mode*, because of other ongoing cases of the Mpox disease in the State. A three-person team from the Rivers State-PHEOC comprising of the incident manager, decontamination/Infection Prevention and Control (IPC) lead, and home care nurse visited the family twice. These visits are often structured, planned, and conducted with unmarked/unbranded official vehicles. At the initial visit, the team met with the family. It clinically assessed the patient and the progress of healing of the rash in addition to temperature assessment and skin inspection of the exposed contacts (patent medicine vendor and five family members). The patient identified his wife as the treatment supporter, and safe distance practices were re-emphasized. The management was also discussed with the treatment supporter, and she was taught how to dilute and use hypochlorite solutions, especially for wastes and cleaning of common surfaces. However, a few days later (Day 15), upon follow-up, we learned that the patient had traveled out of his residence to an offshore site for official duties. The patient was eventually reached with telephone calls while offshore. He reported doing very well and had no

new rashes, ulcers, or fever. He narrated that old lesions were drying off. There was no longer any pain or discomfort. He was pretty concerned that he might have facial scars and complications. The team further counseled him on the pathology and course of Mpox and reassured him of a good prognosis toward recovery. The case was followed up with daily calls until the patient reported that all the dried scabs had fallen off. Except for reports of hyperpigmentation in the skin, the rash left no scars as of Day 25. The six high-risk contacts exited surveillance at the end of 14 days of exposure to this case, as the follow-up period was uneventful. Derattization of the home was advised.

The result of investigations done for him on (Day 11) are as follows: VDRL/Khan test was not reactive; Full Blood Count: Hb 13g/dl (13 – 18); PCV 44% (40-54); WBC $4.2x10^5$g/l (4-11); Neutrophil 49% (40-75%); Lymphocytes 37% (20-40%); Monocytes 8% (2-10), Eosinophil 5% (1-6%); Basophil 1% (0-1%).

Patient perspective

An oral inquiry was made on the patient's perspective on Mpox and his fears. The patient said he thought the few macula rashes on his arms at the early stage of the disease were attributable to hypersensitivity from anti-malaria drugs he had earlier received. He relates that he was well treated without stigma by the PHEOC team and his family except when he had to visit the hospital, but worried about the eventual outcome. He said the counseling sessions helped him understand and master the science of Mpox disease, but he was happier when the disease scabs fell off without leaving scars on his skin.

Discussion on Mpox Case Report

This was a case of Mpox disease which presented with a genital ulcer and was initially managed as Syphilis which is a sexually transmitted infection (STI). Mpox is currently associated with STI presentations in other parts of the world, as observed in the United Kingdom, where a cluster

of Mpox cases was found among attendees at STI clinics.[14] The infection may have been due to contact with an infected sexual partner since he developed the rashes two weeks after unprotected casual sexual contact. The onset of symptoms is well within the incubation period of Mpox disease. He is cisgender and heterosexual unlike common presentations in the western part of the world where genital ulcers due to Mpox were noticed commonly among the populations of Men Who have Sex with Men (MSM).[15] However, this case was similar to a study done in Nigeria that linked Mpox to heterosexual casual sex partners.[12]

The lesions seen in Mpox disease differ in number and distribution and may be more severe in immunocompromised individuals. It is more commonly seen on the face, palms, and soles of the feet and in the genitals. In the recent European outbreak, there have been reported cases of painless anogenital lesions with no prodromal phase appearing a few days after sexual contact with an infected person.[16] However, in this patient, there was a prodromal phase where he had a fever and was treated for malaria four days before the onset of genital rashes; the rash did not begin in the face as elaborately prescribed in the national guidelines for case identification. Even the genital rashes were more in keeping syndromically, to the solitary genital ulcers for syphilitic disease.

Symptoms of Mpox could, therefore may, mimic some sexually transmitted infections like Herpes Simplex, Syphilis, Lymphogranuloma Venerium, Chancroid, Gonorrhea, Chlamydia, And Smallpox.[7],[17] In this patient, the phallus was found to be massively swollen and slightly tender with two deep-seated solitary ulcerative lesions on the glans penis and another at shaft of the penis. Single solitary lesions were hitherto not common presentations of Mpox disease and can be misdiagnosed for Syphilis, Lymphogranuloma Venerium, or even Chancroid[18]. In this case, it was misdiagnosed and managed as a case of secondary syphilis. Although our patient was HIV-negative and heterosexual, his presentation was similar to other cases reported in the

literature.[7,12,17] Some authors suggest that the initial development of Mpox lesions at the genital, perianal, and perioral or tonsillar regions, with a history of recent sexual contact, may be an indication of the initial site of inoculation.[18] Symptoms, in this case, resolved within three weeks of the onset of symptoms on conservative management without the patient requiring hospitalization, this is a reflection of the fact that Mpox disease is in most cases a self-limiting[19]. This case was also quickly contained due to the efficiency of the experienced Rivers PHEOC. No secondary transmission was recorded because of the deployment of notable IPC measures in an already activated EOC on *Response mode*. The elaborate public health interventions described in this case also show that management of Mpox disease in a manner as to prevent disease spread is quite laborious and resource demanding.[20] It requires skill, logistics and infrastructural capacity to enable preparedness using the PHEOC to achieve containment.

It is important to note that the patient initially rejected the diagnosis, possibly because of the fear of stigmatization, until his employers compelled him to report for treatment. Studies show that stigma does indeed affect health-seeking behaviour and cause a delay in presentation.[21] This can lead to the further spread of the diseases and increase the burden of unrecognized diseases in the community.

For this case, apart from a two-week history of undisclosed sexual contact, there was no history of contact with a suspected or confirmed Mpox case suggesting that there was no epidemiological linkage. But studies suggest the possibility of asymptomatic or pauci-symptomatic transmission of the disease.[18,22]. The patient was reluctant to provide the details of the casual sexual contact for contact tracing even though the State Public Health Law Cap 106 laws of Rivers State 1999, require the mandatory disclosure of all necessary health information to the health care provider that would be useful for the containment of infectious diseases. However, enforcement and prosecution are quite difficult in the circumstance when patients are

ill[23]; yet the right to care, confidentiality, consent and social acceptability are complex factors that influence disease patterns.[24] In the future, it beckons for other legal alternatives beyond counseling to ensure complete disclosure of information relevant to disease containment once public health safety is contextually considered supreme.

Limitation of Study

Travel contact could not be followed up as they were challenging to line lists without an available travel manifest or known identity of the commercial vehicle used in conveyance. The sexual contact could not be reached because of patient's refusal to disclose this information. Also, the animal contact (pet dog) could not be tested.

Conclusion and Recommendation

In conclusion, this was a case of Mpox disease presenting as an STI which was not a common presentation and in early stages did not meet the standard case definition for Mpox in our setting. As such, the patient was earlier managed as a case of syphilis until results proved otherwise. Consequently, the expected early containment activities were delayed. This increased potential of further disease spread and requiring more effort for effective containment. An Update of the standard case definition and a reclassification of the disease as a possible STI is highly recommended for enhanced surveillance, increased case detection and reduced burden of unrecognized disease. Similarly, reviewing the legal framework for enforcing patient disclosure of all information relevant for his care and public health safety is equally expedient.

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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