Male genital lesions in monkeypox virus infection: a case series

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Monkeypox virus (MPV) is a rare zoonotic infection caused by an orthopoxvirus. The sudden outbreak of more than 3000 MPV infection from 50 countries has led the WHO to declare the infection as an "evolving threat of moderate public health concern". Here, we describe a case series of two cases of the MPV with a similar onset of cutaneous lesions in the genital area but with different progression in 35 and 41-year-old males respectively. Both of our patients were reported heterosexual with a 10-day prior history of unprotected sexual activity with a sex worker. Case 1 was uncomplicated having rashes over the chest, back, arms, and legs along with the occurrence of fluid-filled painless vesicles which was managed with topical antibiotic cream and wound care using povidone-iodine dressing along with oral amoxicillin/clavulanic acid. On the contrary, case 2 had a progressive necrotic lesion, which spread from the root of the penis involving the foreskin despite supportive measures eventually requiring circumferential surgical debridement of the foreskin. Hence, given the current outbreak, we must consider the possibility of genital MPV in patients with suggestive lesions, anywhere on the body (including the genitals), added to an epidemiological link or history of intimate contact with individuals that may be at high risk for transmission.

Key Words: monkeypox virus, public health concern, cutaneous lesions, genital lesions

Introduction

Monkeypox virus (MPV) is a rare zoonotic infection caused by an orthopoxvirus that belongs to the poxviridae family and is often transmitted by bush animals. The global outbreak of the disease was declared by the World Health Organization (WHO) in May 2022 followed by a public health emergency of international concern in July 2022. The United Arab Emirates also declared its first case of monkeypox on 24th May 2022. It is a self-limiting disease with a fatality ratio of 3%-6%.[1] It is thought to be mainly spread through respiratory droplets and direct contact with skin lesions and scabs although transmission can also occur via fomites.[2] Skin lesions start as macules and progress into papules, vesicles, and pustules, which subsequently crust over and then desquamate.[2] High-risk groups include neonates, children, and those with immunodeficiency. Complications of infection include encephalitis, secondary skin infection, pneumonia, and ocular disease leading to loss of vision.[2]

Here, we describe a case series of two cases of MPV infection with a similar onset of cutaneous lesions in the genital area but with different progression.

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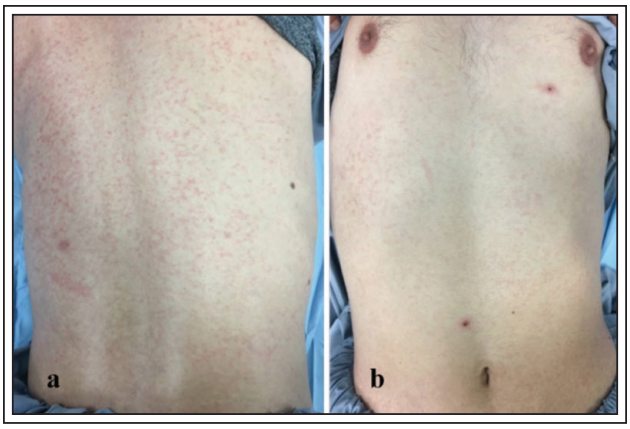

Figure 1. The occurrence of rash over the **(a)** back and **(b)** chest on presentation **(Case 1)**.

Case 1

A 35-year-old previously healthy male, presented with complaints of intermittent low-grade febrile episodes followed by the onset of rash initially in the genital region which gradually spread over the chest, back, arms, and legs along with the occurrence of fluid-filled painless vesicles. There was no associated urethral discharge, dysuria, or changes in the color, smell, and frequency of urine. The patient denied any contact with anyone known to have monkeypox infection, however, he reported having unprotected intercourse with a sex worker 10 days prior to the onset of the rash.

Upon examination at presentation, white ulcerated lesions of 1-2 cm were noted over the lateral aspect of the tongue and soft palate. Pleomorphic skin lesions including vesicles and papules were noted on the limbs and torso as well. External genitalia examination revealed necrotic ulcers with yellowish discharge at the scrotal root with less than 10 genital vesicles with non-tender palpable lymphadenopathy, Figures 1 and 2.

Thus, the patient was admitted with suspicion of MPV infection and sexually transmitted infection (STI) and was started with supportive treatment along with airborne and contact precautions while being given Azithromycin 1 g and 2 doses of Ceftriaxone 1 g once a day for 7 days. Samples collected from the genital lesions were found to be positive for Herpes Simplex and monkeypox DNA virus. The patient was then shifted to the isolation center and was continued on Tab Amoxicillin-clavulanate 875/125 mg twice a day for further 7 days for his genital lesions. Laboratory investigations included white blood cell (WBC) count, urea and electrolytes, procalcitonin, ferritin, glucose, liver, and renal function tests and were found to be normal. Wound culture from genital lesions was significant for *Klebsiella pneumonia* and *Pseudomonas aeruginosa* following which he was started on a 5-day course of Ciprofloxacin 500 mg OD by the infectious disease unit. There were no new lesions seen after day 3 of treatment and existing lesions crusted with eschar formation by day 11, followed by minimal scarring by days 14-15. By day 12, the genital lesions were in the healing phase with no active discharge and resolved by days 16-17, Figure 2c. The patient was discharged after 21 days of isolation from the presentation as per protocol.

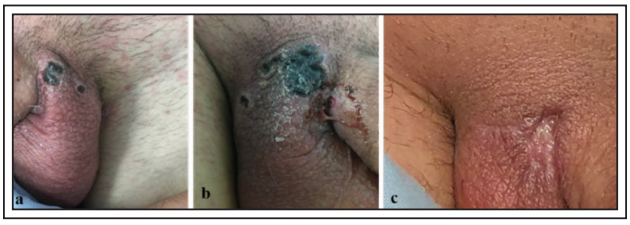

Figure 2. (a) Left and **(b)** Right side of the scrotum on presentation; **(c)** The patient on discharge **(Case 1)**.

Case 2

A 41-year-old male, known non insulin dependent diabetic on oral hypoglycemics along with a previous history of tuberculosis, presented with small vesicles in the penile area which started 4 days after unprotected intercourse with a sex worker. Over 10 days, these rashes spread to the torso, limbs, chest, and back respectively, Figure 3. In addition, he had developed

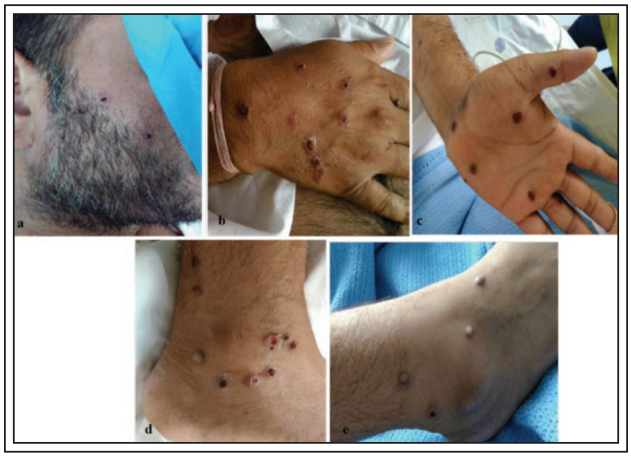

Figure 3. Day 8 of presentation **(a)** face; **(b)** right hand; **(c)** left palmar surface; **(d)** left leg; **(e)** right leg **(Case 2)**.

penoscrotal swelling with minimal greenish urethral discharge. The patient had dysuria but denied other lower urinary tract symptoms (LUTS). The patient was evaluated in a private clinic and given STI treatment, but due to the widespread nature of the rashes, was referred to our center for monkeypox evaluation.

The patient had no inguinal lymphadenopathy but had bilateral small non-tender cervical lymphadenopathy. The patient was initially referred to the urology department and Fournier's gangrene was ruled out as there was no fascial plane nor any soft tissue involvement, which was also confirmed by imaging. Later, he was admitted to the infectious disease unit for further management and started on Linezolid (Zyvox) 600 mg twice a day and Tazocin (piperacillin, tazobactam) 4.5 g thrice a day intravenously. The patient was vitally stable and his laboratory investigations were as follows: WBC (8.7), C-reactive protein (CRP) 82 mg/L, and Point-of-care test for glucose (POCT) 209 mg/dL. STI work ups including chlamydia, syphilis, herpes, and gonococci were negative including acid-fast bacilli (AFB) smear in urine samples, but throat and cutaneous lesions swabs for monkeypox DNA were tested positive. Hence, airborne and contact precautions were maintained. Meanwhile, cultures from genital lesions were positive initially for *Peptostreptococcus anaerobius* and *Candida parapsilosis*.

The genital lesions were kept on daily sterile dressing and antibiotics course was extended for another week, and anidulafungin was added to the regimen. One week later, a repeat culture from genital lesions showed scant candida growth, however, the genital lesions progressed with the occurrence of ulcers, bleeding, discharge at the base of the penis, and pus draining on pressing at the suprapubic area. There was no crepitus and the foreskin was intact, Figures 4a-c. The patient otherwise was hemodynamically stable with unremarkable laboratory parameters. The patient underwent circumferential debridement of the foreskin with complete degloving of the penis. The wound was irrigated and cultures were taken which showed carbapenemase-resistant *E. coli* sensitive to colistin only, Figures 4d-j. The patient was kept on a foley catheter and the daily inadine gauze dressing was done. See Figure 5 for the progression of lesions postoperatively.

The patient completed the below-mentioned regimen: tazocin (piperacillin, tazobactam) and linezolid (Zyvox) for 22 days, anidulafungin for 14 days, meropenem for 4 days, colomycin for 9 days, and tigecycline for 6 days. Antibiotics were escalated to colimycin and meropenem to which the patient showed a dramatic response. The patient was discharged after 5 weeks from the IDU and was instructed to follow up for his wound dressing and need for assessment for grafting but the patient lost to follow up. See Figure 5 for progression of lesions postoperatively.

Figure 4. (a) Peno-scrotal edema on presentation; **(b)** Day 2 **(c)** Day 4; **(d)** Day 7 of presentation; **(e)** Day 8 of genital lesion progression; **(f)** Day 12 of genital lesion progression; **(g)** Day 16 of genital lesion progression; **(h)** penile lesion; **(i)** Day 16 of genital lesion; **(j)** Day 17 (intraoperative inspection) **(Case 2)**.

Discussion

Monkeypox virus is a zoonotic disease that was first described in 1970 in the Democratic Republic of Congo.[3] In the mid of the year 2022, a sudden outbreak of more than 3000 MPV infections was

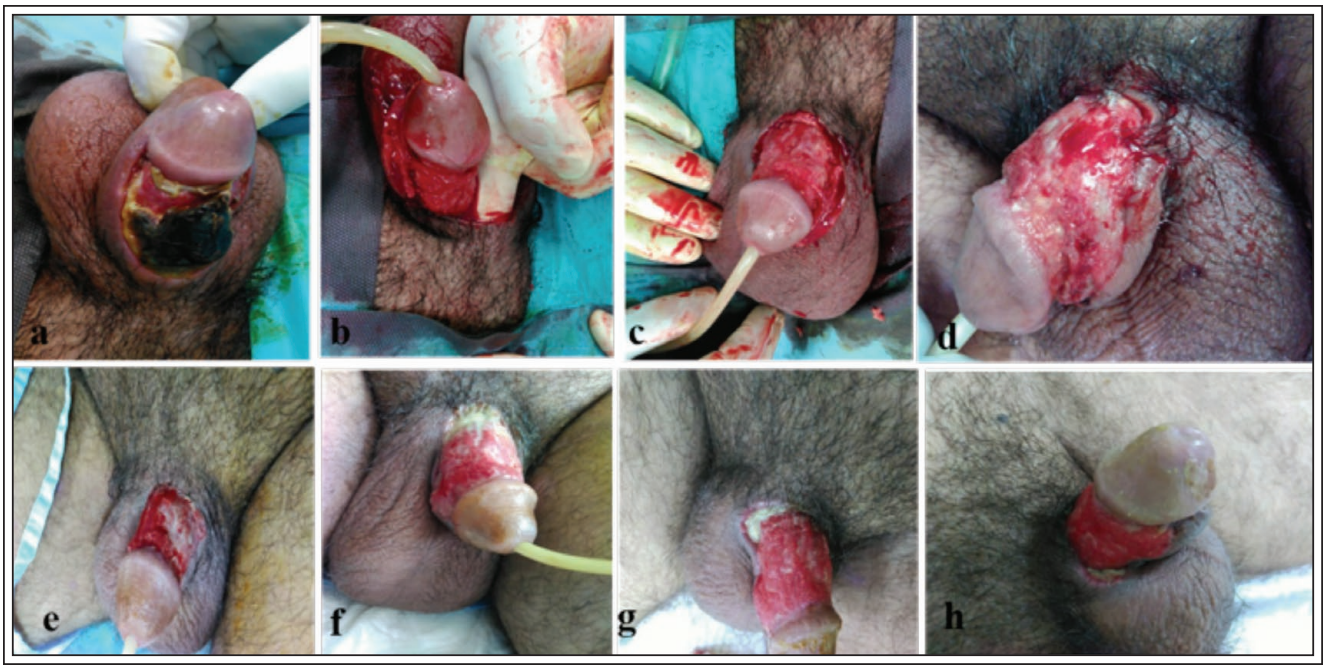

Figure 5. (a) Intraoperative status; **(b)** Day 17 (intraoperative exploration of wound); **(c)** Day 17 (circumferential debridement); **(d)** Day 18; **(e)** Day 19; **(f)** Day 21; **(g)** Day 27; **(h)** Day 28 postoperative status **(Case 2)**.

reported from more than 50 countries which led the WHO to declare the infection as an "evolving threat of moderate public health concern" on June 23, 2022.[4] The mean age for the presentation of MPV was found to be 36 years with 98% of participants being male in a recent systemic review headed by Darwin.[5]

The transmission of MPV infection occurs either by respiratory droplets or direct contact with skin lesions and contaminated fomites. An interesting case of MPV infection was documented in Korea in a patient having a painless ulcer on the penile shaft, and other cutaneous lesions over the body, with a negative sexual history but a close acquaintance being detected positive for MPV highlighting the concept of person-person transmission.[6] As per a cohort study conducted in Spain, the incubation period of MPV is currently understood to be about 7 to 10 days following exposure with a prodromal phase characterized by fever, malaise, sweats, lymphadenopathy, and headache, followed by skin eruption 2-4 days later.[2,7] The rash is known to begin as 2-5 mm macules which later progress to papules, vesicles, and pseudo-pustules. By 7 to 14 days of onset, these lesions dry, crust, and fall off. These lesions are known to evolve and progress simultaneously, affecting the face, palmoplantar surfaces, mucous membranes,and less commonly, genitals,[2,7] however in the current outbreak, the lesions were mainly located on the anogenital and perioral areas alone with few lesions on the trunk or acral areas of the body.[7] In line with the recent observations, the initial presentation of both our cases included painless, fluid-filled vesicles in the genital region with onset within 10 days of a prior history of unprotected heterosexual activity, with additional lesions presenting later on the torso, face, and limbs. Varying severities of genital lesions have been noticed worldwide ranging from painless penile ulcer,6 ulcerated penile ulcer,[8] secondary bacterial infection, and confluent lesions.[2] Similar to the case in Brazil,[8] our first case presented with a necrotic ulcer that started 8 days ago, accompanied by yellowish discharge at the scrotal root with bilateral tender inguinal lymphadenopathy. The second case, however, presented with pustules and crusted lesions starting 5 days ago, in addition to penoscrotal swelling, greenish penile discharge, and palpable cervical lymph nodes. Although not known previously, penile swelling and rectal pain were found to be among the common presentations and indications foradmission in a cohort study in Spain.[7]

It is to be noted that MPV is thought to be spread by close contact during sexual activity, predominantly in homosexual, bisexual, or other men having sex with men,[6] however, both our patients reported to be heterosexual with a 10-day prior history of unprotected sexual activity with a sex worker. Given the clinical

presentation and the history, we investigated both the patients for sexually transmitted diseases and varicella, wherein case 1 was found to be positive for herpes simplex and treated with antivirals. As per the Center for Disease Control and Prevention (CDC), in the absence of risk factors of MPV, other differentials should be considered including secondary syphilis, herpes, and varicella zoster.[9] Genital lesions may also direct toward chancroid, donovanosis, and other non-venereal genital ulcers.[10] Whereas in children, molluscum contagiosum (MC) and varicella zoster should be ruled out.[9] The transition to talking about children with STIs is awkward and confusing. Hence, more time is needed to discuss this and sexual abuse needs to be addressed.

CDC recommends three cutaneous samples for confirmation of MPV infection.[9] As per our protocol, we have also conducted 3 DNA- PCR tests which include two cutaneous samples and a nasopharyngeal swab wherein a patient is considered positive when MPV is detected in either one of the three samples. It should be noted that the samples from skin lesions were found to contain higher viral DNA when compared to the throat.[7] The use of nasopharyngeal swabs for viral detection was also noticed in a Korean case.[6] Furthermore, the detection of antibodies alone is found to be insufficient for diagnosis.[11]

Monkeypox classically presents with a non-specific systemic prodrome followed by a progressivevesicular rash. The clinical manifestations of MPV infection are divided into two periods: the prodromal period, which lasts 1-4 days and is characterized by non-specific symptoms (fever, headache, and fatigue), and the skin rash period which begins 1 to 3 days after the onset of fever. Lymphadenopathy can appear during the prodromal period and remains concomitant with the skin rash. The rash undergoes several stages of evolution from macules, papules, vesicles, and pustules following a centrifugal pattern, followed by the resolution over time with crusts and scabs, which drop off later during recovery. Lesions are often observed in the oral cavity and can cause difficulties in drinking and eating. Inflammation of the pharyngeal, conjunctival, and genital mucosa can also be observed.[8] The current outbreak is showing atypical features, such as only a few or even only one skin lesion; lesions that start in the genitals or perineal/perianal area and does not spread further; lesions that appear at asynchronous stages of development; the appearance of lesions before the onset of fever, malaise and other general symptoms belonging to the first period of the disease manifestation.[8] It has been reported that the presence of herald lesions at the point of sexual contact and the absence of prodromal symptoms are suggestive of sexual disease transmission[12] as was also observed in our cases. As per the literature review, most patients in this current outbreak present with painless anogenital lesions before a prodrome, with MPV genital lesions showing a propensity for secondary bacterial infections which were managed with antibiotics.[6]

There is no fixed guideline for the treatment of MPV. Patients are usually treated based on the severity of symptoms. Both our patients were managed in isolation wards and were treated with antibiotics (oral and intravenous) according to wound culture for secondary bacterial infections and supportive measures for pain control and wound care was given. Patient with uncomplicated lesions as in Case 1 was managed with topical antibiotic cream and wound care using povidone-iodine dressing along with oral Augmentin. On the contrary, case 2 had a progressive necrotic lesion, which spread from the root of the penis involving the foreskin despite supportive measures eventually requiring circumferential surgical debridement of the foreskin. Postoperatively, the wound was managed with gauze and betadine-soaked dressing showing adequate granulation tissue and healthy wound margins. A case report published by Sturgisa et al describes a case with concomitant sexually transmitted disease manifesting a more severe genital lesion and significant genital edema affecting urination with a history of sexual activity 8 months prior to presentation.[13] As per our protocol, MPV patients have to be isolated for 21 days or until all the lesions have healed; whichever is the longest. However, in the second case, due to extensive genital involvement, the patient was discharged after 31 days to be followed up with plastic surgery. In other reports, patients were discharged after 14 days, once lesions were noted in process of re-epithelialization.[8] Given the current outbreak, we must consider the possibility of MPV in patients with suggestive lesions, anywhere on the body (including the genitals), added to an epidemiological link or history of intimate contact with individuals that may be at high risk for transmission.[8]

Conclusion

During the current outbreak, the spread of the genital MPV infection is found to be linked with a prior history of sexual activity. Genital manifestation is common and can be confused with STIs. Hence, proper history is needed to rule out other STIs with MPV. Our case is unique as this is the case of uncontrolled diabetes with skin infection from MPV. Secondary infections are common in diabetes and need aggressive treatment either in the form of medications or surgical therapy. □

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