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Genitourinary Lesions Due to Monkeypox

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Abstract

Background: Since May 2022, 31 000 cases of monkeypox infection have been reported in nonendemic areas.

Objective: To describe a series of cases of monkeypox with genitourinary involvement.

Design, setting, and participants: This was a prospective observational study of men diagnosed with monkeypox disease with genitourinary involvement.

Results and limitations: A total of 14 patients were recruited. The median age was 42 yr. Of these patients, 43% sought a consultation for genitourinary symptomatology, and 71% had engaged in sex with other men. Eight patients (57%) were positive for human immunodeficiency virus, one diagnosed synchronously; the remainder had a median CD4 count of 463/\mu l. Six patients (43%) had a different sexually transmitted disease. Penile oedema was present in 43% of patients and two patients required surgical exploration.

Conclusions: Genitourinary involvement is frequent in monkeypox disease and is often the reason for the consultation visit.

Patients summary: In this report we looked at how monkeypox disease can affect the genitourinary area, causing swelling of the penis or skin lesions.

\section{1. Introduction}

Monkeypox is a zoonosis caused by monkeypox virus (MPXV), an orthopoxvirus. The disease is the most prevalent orthopoxvirus zoonosis since the eradication of smallpox in 1980\cite{1}. MPXV was first isolated from humans in 1970, and was previously isolated in 1958 from macaques used in research. Two different genetic clades of the virus can be distinguished, the Central African (Congo Basin) and the West African clade, with the latter usually giving rise to milder disease with more limited human-to-human transmission\cite{2,3}. MPXV is endemic in Central and West African areas\cite{4}. One of the most severe disease outbreaks was reported in 2017 in Nigeria, with more than 200 confirmed
cases and a reported mortality rate of between 3% and 12.5% [2,3,5].

Since May 2022, more than 40,000 cases have been reported in 87 countries not previously considered MPXV endemic areas [6]. In the current situation, transmission is mainly human-to-human. Transmission can occur through close contact with skin lesions, droplets, or fomites [7]. The virus has also been isolated from blood, urine, seminal fluid, and the nasopharynx [4,8]. The typical clinical picture includes fever, headache, palpable lymphadenopathy, and worsening general condition associated with a macular skin rash progressing to vesiculopustular lesions. The most recent series describes genital area involvement showing vesiculopustular lesions and associated penile oedema [4,9,10].

The aim of this study was to describe a series of cases of monkeypox with genitourinary involvement.

2. Patients and methods

This was a prospective observational descriptive study of male patients with confirmed MPXV infection and genital area involvement. All the patients with confirmed MPXV disease at our hospital and genitourinary symptoms between May and August 2022 were invited to participate in the study. Genital area involvement was defined as any skin lesions, skin changes, or oedema in the penile and scrotal areas.

All patients were diagnosed using polymerase chain reaction (PCR). For the PCR test, three swabs were taken from different skin lesions (vesicles/pustules were punctured and scabs were removed). When the patient did not present with lesions, a rectal swab was performed. Real-time PCR for qualitative detection of MPXV-specific DNA test was performed (FlexStar PCR, altona Diagnostics, Hamburg, Germany).

Screening for sexually transmitted diseases (STDs) was carried out systematically for human immunodeficiency virus (HIV), chlamydia, syphilis, Neisseria gonorrhoeae, Epstein-Barr virus, and cytomegalovirus.

Blood cultures were taken in cases with fever. STD screening was carried out systematically for human immunodeficiency virus (HIV), chlamydia, syphilis, Neisseria gonorrhoeae, Epstein-Barr virus, and cytomegalovirus. The typical clinical picture includes fever, headache, palpable lymphadenopathy, and worsening general condition associated with a macular skin rash progressing to vesiculopustular lesions. The most recent series describes genital area involvement showing vesiculopustular lesions and associated penile oedema [4,9,10].

The patients provided informed consent to publication of their case details. Data collection and management were conducted according to ethical practice and basic ethical principles.

3. Results

3.1. Patients

We present 14 cases of males with genitourinary involvement (Fig. 1) due to MPXV infection, with no history of travel to endemic areas. The sociodemographic and clinical characteristics are summarised in Table 1. The median age of the patients was 42 yr (range 20–56). All the patients (100%) were recruited from the same urban area.

3.2. Transmission

The median time between exposure (when known) and symptom onset was 13 days (range 3–30). Of the patients, 71% (n = 10) were men who had sex with other men and 14.2% (n = 2) had heterosexual intercourse. Two patients (14.5%) maintained that they had had no sexual intercourse in the weeks before symptom onset. 57% of the patients (n = 8) were HIV-positive; one patient was diagnosed at an STD screening clinic and the rest were HIV-positive patients on antiretroviral treatment with good control, with normal CD4 T-cell counts (median 663/μl). 43% of the patients (n = 6) presented synchronously with other STDs.

3.3. Clinical findings

In six patients (43%) the initial symptom was related to the genitourinary area. In the remaining patients, the median time from first symptoms to the onset of genitourinary symptoms was 5 days. All patients presented with cutaneous or mucosal involvement with vesicles and pustules, which evolved into scabs and were resolved in all cases. Genital oedema was present in 43% of cases (n = 6) and 57% (n = 8) had palpable lymphadenopathy in the groin area. All the patients had systemic symptoms such as malaise (n = 4, 28.5%), fever (n = 5, 35.7%), and different skin lesions such as papules, vesicles, pustules, and scabs (n = 14, 100%; Table 1).

3.4. Treatments used

Two patients (14.2%) required surgical intervention for abscess drainage (patient 2) and penile surgical exploration (patient 1). Treatment for uncomplicated cases was for symptom relief with antihistamines, analgesics, and non-steroidal anti-inflammatory drugs, with addition of amoxicillin/clavulanic acid when bacterial superinfection of the skin lesions was detected.

3.5. Atypical presentation

Patient 1 had an atypical presentation; he attended for consultation because of symptoms compatible with sepsis. He presented with fever (42 °C), hypotension (blood pressure 94/54 mm Hg), and tachycardia (140 beats/min) accompanied by headache and poor general condition; a test for SARS-CoV-2 infection was negative.

The patient presented with oedema of the penis with inflammatory changes on the surface, showing erythematous penile lesions, and the penis was warm on palpation. No rash, ulcers, or other skin lesions were observed at the time. Bilateral inguinal lymph nodes were palpable and a purulent discharge from the anus was observed.

Penile ultrasound and a computed tomography scan showed inflammatory changes in the skin and subcutaneous cellular tissue, proctitis without collections or abscesses, and prominent bilateral mesorectal and inguinal lymphadenopathies (Fig. 2A, C). The study was completed with pelvic magnetic resonance imaging, which revealed penile cellulitis, proctitis, and inflammatory pelvic lymphadenopathy (Fig. 2B).

Given the patient’s haemodynamic instability, an anuscoppy examination was performed under anaesthesia, which revealed intense anal inflammation, granuloma 3 cm from the sphincter (pathological anatomy of nonspecific proctitis); examination of the penis showed no abscesses or collections.

The patient had negative urine and blood cultures. Serology was positive for HIV-1 (viral load 7820 copies/ml and 265/mm³ CD4 T-lymphocytes) and Chlamydia trachomatis (serovar L1–L3).
Skin lesions appeared 21 days after this first episode, with fever and nonpainful papular lesions affecting the pubis, penis (glans penis and skin), all four extremities, and the oral and ocular mucosa. Lymphoedema persisted
on the penis with a 1.5-cm scabbed lesion in the dorsal region of the foreskin, while the surgical wound remained clean. A bladder catheter was used because of voiding difficulties. A PCR diagnosis of MPXV was made at this time. PCR determination of the virus was performed on a sample taken from the rectum, in which no amplification of the virus was observed, although the sample had to be deparaffinised to perform this technique. At 10 weeks after onset, all the patient’s skin lesions and penile oedema had resolved.

4. Discussion

We described 14 male patients with genitourinary involvement due to MPXV infection. The pattern usually described is centrifugal: lesions evolve simultaneously and there is greater involvement at the distal level (extremities and face) [5]. Genitourinary involvement has been described for some cases [8,11] and may suggest that the route of acquisition was via sexual contact [9]. Especially in case number 1, there was a high suspicion of sexual transmission owing to the granular lesion in the rectum; however, it was not possible to detect genetic fragments of the pathogen in the rectal biopsy.

In this series, 43% of patients (n = 6) presented for consultation because of a lesion in the genitourinary area as the initial symptom. Hence, urologists have a fundamental role in the differential diagnosis of MPXV disease [2], as it can be confused with other STDs such as secondary syphilis and lymphogranuloma venereum [11]. Skin lesions may take days or weeks to appear, and therefore the absence of skin lesions should not in itself exclude MPXV disease.

Urologists should know that MPXV infection may present as penile oedema and they should therefore maintain a high level of suspicion for such cases, making an early diagnosis of the infection and screening for other STDs. The urologist should also know that the normal incubation period is between 4.2 and 17.3 d (5th–95th percentile) and recommend isolation for case contacts is for 21 d [12]. The patient needs to know, given the epidemiological context, that he should seek medical attention for penile oedema and avoid contact with people because it could be caused by MPXV. Symptoms are usually self-limiting, but some patients may experience complications such as pneumonia, encephalitis, and keratitis.

Penile oedema occurred in 43% of the patients in our sample. This figure is higher than the 17.7% reported by Patel et al. [7], probably because our series included only patients with genitourinary involvement. Penile oedema has a variable evolution time and may persist for as long as 21 d, as in patient 1 (despite examination under anaesthesia), which is why we believe that a surgical approach should only be used in patients with purulent collections.

So far, only cutaneous sequelae due to MPXV infection have been reported [5]. However, we have found that penile lymphoedema can persist for weeks. Long-term studies are needed to rule out sequelae such as urethral strictures and infertility in the medium to long term.

In our series, 50% of patients were HIV-positive (on antiretroviral treatment) and just one (7%) was synchronously diagnosed with HIV. In previous series, the

Table 1 – Clinical and sociodemographic characteristics of the patients

| Case | Age (yr) | TES (d) | TSO-GU (d) | MSM | HIV Dx | Other STDs | Genitourinary symptoms | Other symptoms |
|------|---------|---------|------------|-----|--------|------------|-----------------------|--------------|
| 1    | 26      | 5       | 0          | Yes | Yes    | CD4 265)   | Chlamydia             | Penile oedema, perianal vesicle | Malaise, fever |
| 2    | 20      | 30      | 7          | Yes | No     | Gonococcus | Penile oedema          | Rectal itching and RD | Bilateral IA |
| 3    | 30      | 7       | 2          | Yes | No     | No         | Penile oedema          | VP lesions on pubis and GP | Right IA |
| 4    | 27      | 30      | 5          | No  | No     | Syphilis   | Inguinoscrotal abscess | Malaise, fever, asthenia | Bilateral IA |
| 5    | 40      | ?       | 7          | Yes | Yes    | CD4 589)   | No                    | Pustular lesions on DP | Arthralgia, asthenia |
| 6    | 30      | 14      | 0          | Yes | Yes    | CD4 811)   | ?                     | Pustular lesions on DP | Rectal itching and RD | Bilateral IA |
| 7    | 55      | 21      | 14         | Yes | No     | CD4 769)   | No                    | Scab lesions on the penis | Fever and malaise |
| 8    | 42      | 3       | 0          | Yes | No     | No         | No                    | Whorl lesion on the GP | Right IA |
| 9    | 56      | ?       | 0          | Yes | Yes    | CD4 663)   | No                    | Vesicles on the DP | Penile oedema |
| 10   | 55      | 21      | 0          | No  | No     | Herpes 2   | Penile oedema          | VP lesions on GP and foreskin 4–5 mm | Bilateral IA |
| 11   | 47      | 7–14    | 3          | Yes | Yes    | CD4 >500)  | Chlamydia trachomatis | VP lesion on the right scrotum, excessively raised | Malaise and arthralgia |
| 12   | 38      | 10      | 5          | ?   | ?      | ?          | VP lesions on the DP   | Low fever | Bilateral IA |
| 13   | 51      | 13      | 0          | Yes | Yes    | CD4 660)   | No                    | VP lesions on pubis and GP | Fever |
| 14   | 59      | 10      | 5          | Yes | Yes    | CD4 682)   | Mycoplasma genitalium | 2 scrotal lesions with purulent exudate | Right IA |

TES = time from exposure to symptoms; TSO-GU = time from symptom onset to genitourinary symptoms; MSM = men who have sex with men; HIV = human immunodeficiency virus; STD = sexually transmitted disease; Dx = diagnosis; CD4 = count of T cells positive for CD4 (in cells/µl); Al = inguinal adenopathy; RD = rectal discharge; DP = dorsum of the penis; GP = glans penis; VP = vesicopustular.
The number of HIV-positive patients has varied between 0% and 22.5–41% [4,5,8]. It has been postulated that HIV infections with severe immunosuppression could favour infection or aggravate symptoms [5]. In our series, patient 1 had the most severe monkeypox case, the only patient diagnosed synchronously with HIV and therefore without HIV treatment. The median CD4-positive cell count for our patients is similar to counts previously published (354–664 cells/µl) [5,7].

Following our experience, we recommend STD screening for all patients diagnosed with MPXV, as 29% of patients in previous reports had STDs [4]. In our series, other STDs coexisted in 43% of the patients. We suggest inclusion of MPXV in the differential diagnosis of STDs, as 1.33% of patients with other STDs had asymptomatic MPXV disease in a Belgian series [13].

Tecovirimat has been proposed for supportive care given its efficacy against this disease in animal models and phase 1 and 2 studies [14]. Its use is currently considered safe, with few adverse events, and it appears to reduce the duration of symptoms and hospitalisation time [8]. Among our cohort, a request for tecovirimat for patient 1 was submitted because of the torpid evolution, but the request was denied because the criteria for complications established by the authorising bodies were not met. Prior immunisation with smallpox vaccine may have a protective effect and reduce symptoms, so this is now indicated for prevention of MPXV disease in patients at high risk [15].

5. Conclusions

MPXV disease is currently being transmitted between humans. Penile oedema and involvement of the genitourinary tract are common, and in many cases is the main symptom prompting medical consultation. It is vital for urologists and surgeons to be aware of this disease for a correct differential diagnosis with regards other STDs, with which it can be confused or coincide.

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