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Case Report: Mpox – Not Just a Rash

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Abstract. Mpox (formally monkeypox) is an Orthopoxvirus associated with both zoonotic and person-to-person spread. Human mpox classically presents with rash and systemic symptoms. Although sporadic outbreaks of mpox have occurred worldwide, the 2022 outbreak is the first of pandemic significance. Thousands of geographically dispersed cases were reported beginning in May 2022. The clinical presentations and outcomes of mpox infection have varied greatly based on viral clade. Further guidance is needed for clinicians to diagnose and treat this emerging infection. We present five clinical vignettes of confirmed cases diagnosed in June and July 2022 in northern California to demonstrate the range of mpox disease, including myocarditis, pharyngitis, epididymitis, and proctitis. We note a significant overlap with HIV infection and a high rate of concurrent sexually transmitted infection. Given the heterogenous presentations of mpox disease, clinicians should maintain a high degree of suspicion in patients with oropharyngeal or genital lesions, proctitis, or new rash.

INTRODUCTION

Mpox (formally monkeypox) has emerged as the most significant Orthopoxvirus of public health consequence since the eradication of smallpox.[1] The 2022 mpox outbreak spread rapidly, resulting in more than 16,500 cases in 68 countries that have not historically reported the disease.[1] Distinct from prior outbreaks in sub-Saharan Africa, the current outbreak is occurring primarily in populations that identify as gay, bisexual, or other men who have sex with men, including people who are transgender. In addition, there is a high degree of concomitant diagnoses of other sexually transmitted infections, including HIV.[2] In this case series, we describe a range of presentations of mpox cases diagnosed during the current outbreak that have not been described routinely in existing literature.

CASES

Mpox with viral myocarditis. A 32-year-old man with history of treated syphilis reported headache, fatigue, and cervical/axillary lymphadenopathy 1 week after unprotected anal and oral intercourse with a male partner. Diffuse pruritic lesions appeared 4 days after his systemic symptoms. He presented to the emergency department after chest pressure developed on day 6 of illness. Laboratory testing was notable for leukocytosis of 11,650 cells/μL, a stable rapid plasma reagin titer of 1:2, and a high-sensitivity troponin level of 165 ng/L (reference range, < 22 ng/L). Swabs from truncal lesions were positive for Orthopoxvirus DNA. Electrocardiogram on admission and transthoracic echocardiogram were within normal limits, although his electrocardiogram developed nonspecific t-wave changes on hospital day 4 (Supplemental Figures 1 and 2). Viral myocarditis was suspected after extensive workup for other causes of myocarditis was negative. The patient had not received vaccines associated with myocarditis recently. He was started on tecovirimat for a planned 14-day course. All patients treated with tecovirimat were given a dose of 600 mg by mouth twice daily. The patient's troponin level normalized over 24 hours and chest pain resolved within 48 hours. Lesions improved after 4 days of treatment, and the patient was discharged on hospital day 10. Further details of this case are reported elsewhere.[3]

Mpox with pharyngitis and airway edema. A 42-year-old transgender woman living with well-controlled HIV on antiretroviral therapy (absolute CD4, 1,048 cells/μL; HIV-1 RNA undetectable) presented with headache, myalgias, and sore throat that developed 1 week after unprotected receptive anal and oral intercourse. Upon evaluation, she was noted to have tonsillar exudates and soft palate vesicles. A rapid *Streptococcus* A screen, oropharyngeal gonorrhea, and *Chlamydia* testing, and rapid mononucleosis testing were all negative. Four days later, she returned for evaluation of dysphonia and dysphagia. Examination revealed tonsillar swelling and muffled voice. Her white blood cell count was 9,530 cells/μL, C-reactive protein was 7.0 mg/dL (reference range, 0.0–1.0 mg/dL), and erythrocyte sedimentation rate was 28 mm/hour (reference range, < 16 mm/hour). Computed tomography of the neck revealed enlarged tonsils and severe airway narrowing. Dexamethasone 10 mg was administered intravenously, followed by methylprednisolone 125 mg intravenously, with improvement in airway edema. Six hours after admission, an umbilicated rash erupted on her thighs, buttocks, and trunk. Samples collected from the thigh, back, and oropharynx all were positive for Orthopoxvirus DNA. The patient was started on tecovirimat with resolution of dysphagia and improvement in skin lesions. On hospital day 3, she was discharged home in good condition, although she continued to develop new skin lesions for 3 more days.

Mpox with epididymitis and phimosis. Several patients with mpox had severe foreskin edema leading to phimosis and obstruction of urinary flow. We present a representative case of a patient with mpox complicated by phimosis.

A 36-year-old man living with HIV on antiretroviral therapy (absolute CD4, 498 cells/μL; HIV-1 RNA undetectable) presented with 1 week of painless penile lesions and unilateral scrotal pain. He reported headache, fevers, chills, and night sweats associated with the onset of the lesions. His symptoms developed 2 weeks after unprotected vaginal intercourse with

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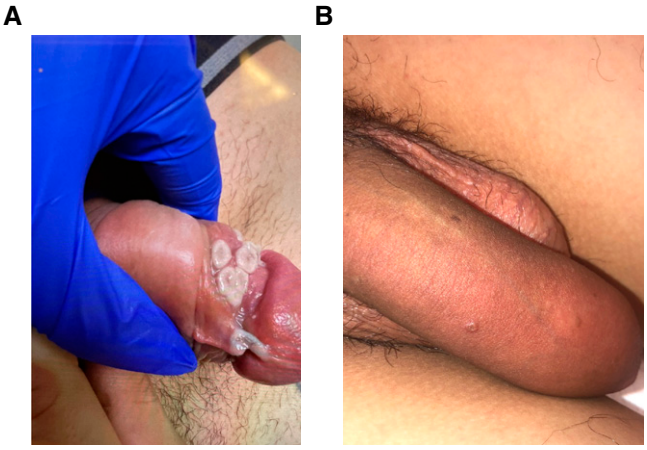

FIGURE 1. (**A**) Painless penile papules with broad umbilication prior to the development of phimosis. (**B**) Solitary umbilicated papule on foreskin with posthitis.

a cisgender woman. He described soliciting sex in exchange for money. On admission to the hospital, he was febrile to 39.3°C, with a heart rate of 96 beats/minute, and normal blood pressure and respiratory status. He had broad umbilicated papules on his genitals as well as 1- to 3-mm papules distributed throughout his body (Figure 1). His right scrotum, foreskin, and glans of his penis were edematous and tender, and within 24 hours of admission, his foreskin could not retract, leading to partially obstructed urinary flow. Laboratory values were notable for leukocytosis (20,950 cells/μL) and a lactate level of 3.0 mmol/L (reference range, 0.5–2.2 mmol/L). Urinalysis revealed microscopic hematuria but no leukocyte esterase or nitrites. Gonorrhea and *Chlamydia* testing from rectum, urine, and oropharynx were negative. Testicular ultrasound revealed acute right-sided epididymitis. Orthopoxvirus DNA was detected from swabs of penile lesions. He was started on a 14-day course of tecovirimat. Within 2 days of tecovirimat administration, the patient's penile edema and pain had decreased significantly, and within 4 days of treatment he was able to retract his foreskin.

Mpox with proctitis. The most frequent complication of mpox we have encountered is proctitis. Patients report rectal pain, mucoid or bloody anal discharge, and tenesmus. All patients with proctitis reported receptive unprotected anal intercourse as their suspected mpox exposure. Here we present a representative case of mpox complicated by proctitis.

A 22-year-old man developed fever, myalgias, malaise, cough, and sore throat 10 days after unprotected receptive anal intercourse with a male partner. Approximately 2 days after the onset of systemic symptoms, he developed perianal pain and pruritic perianal lesions associated with bloody mucoid anal discharge and tenesmus. Within 24 hours of the development of perianal lesions, he noted similar lesions on his abdomen, genitals, and forearms. Swabs from his skin lesions were positive for Orthopoxvirus DNA. Rectal, oropharyngeal, and urine testing for gonorrhea and *Chlamydia* was negative, although syphilis testing was consistent with active infection. The patient was prescribed a 14-day course of tecovirimat. He reported resolving symptoms after 4 days of treatment.

Mpox with detectable Orthopoxvirus DNA from intact skin. A 44-year-old man on pre-exposure prophylaxis for HIV presented with malaise, fever, headaches, and bright-red blood per rectum 16 days after an unprotected sexual encounter with multiple male and female partners. No cutaneous lesions were present during his initial evaluation. Intact skin on his penis and perianal region was swabbed and returned positive for Orthopoxvirus DNA. Two days after testing, sparse pruritic papules developed on his extremities, face, and trunk. No lesions developed in his genital or perianal region (Figure 2). He was given a 14-day course of tecovirimat. He reported crusting of all lesions by day 3 of tecovirimat treatment. Subtle cutaneous lesions are common among patients with mpox (Figure 3).

DISCUSSION

In this case series we describe a range of clinical presentations of mpox infection, including myocarditis, pharyngitis, and balanoposthitis, and a case of detectable virus on intact skin without visible lesions at the time of sample collection.

The diverse presentations in our case series raise important questions to guide further investigation. The presence of detectable virus on intact skin raises questions about risk of transmission prior to visible examination findings. Further investigation into the dynamics of viral shedding is essential to guide isolation recommendations. Swabbing additional sites over the course of disease could help characterize viral shedding patterns. Patients are advised to isolate until skin lesions have crusted over and are covered by healthy skin, but this does not account for the possibility that live virus could be shed for longer durations from other sites.[4]

Other sites, such as rectal and oropharyngeal sites, were positive for viral DNA in our cases. Some studies have addressed viral shedding from non-lesion anatomic sites. In a case series from Italy, seminal fluid had detectable DNA until day 9 in multiple cases.[5] In a separate report, rectal swabs had detectable DNA up to 7 days from symptom onset in multiple patients.[6] Most transmission has been attributed to close contact with skin lesions, although rectal

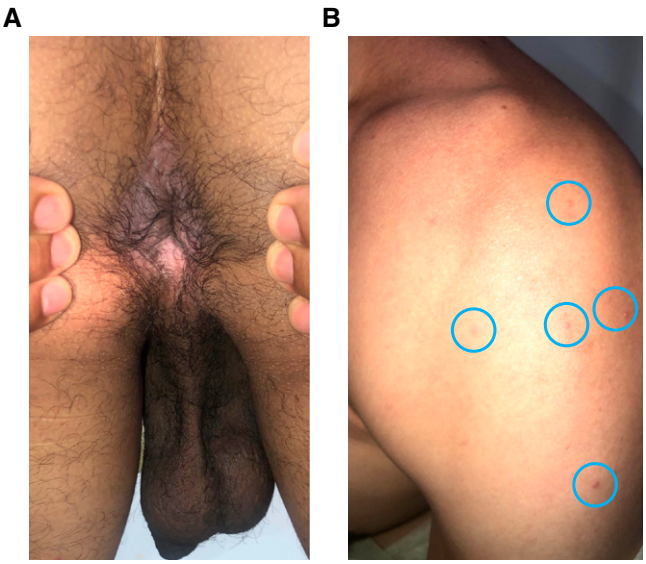

FIGURE 2. (**A**) Intact perianal region from which detectable Orthopox DNA was isolated prior to the development of cutaneous lesions. (**B**) Subtle lesions at the deltoid that developed approximately 48 hours after positive Orthopoxvirus DNA testing.

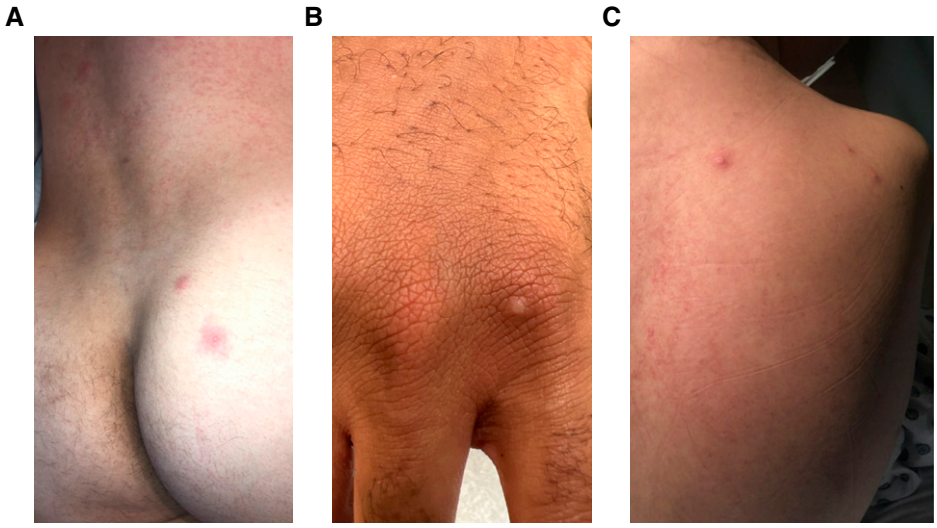

FIGURE 3. Images of lesions from confirmed mpox cases. (**A**) Diffuse pruritic erythematous papules. (**B**) Isolated, faintly umbilicated papule on knuckle, about 48 hours after onset of lesion. (**C**) Sparse, umbilicated papules on the back of a patient with severe pharyngitis.

and semen positivity raise questions about additional routes of transmission. Notably, unprotected receptive anal intercourse was reported in all cases of proctitis we encountered.

Furthermore, visceral involvement such as myocarditis remains poorly understood. We are not aware of reports describing myocarditis associated with mpox until this outbreak, although there have been cardiac complications associated with smallpox vaccines containing vaccinia virus.[2,7–9] Concern for myocarditis has also led to the CDC recommendation for some young adults to delay COVID-19 vaccine for 4 weeks after receiving the smallpox vaccine.[10] Clinicians should be vigilant in monitoring and reporting end-organ complications of mpox. Longitudinal analyses of mpox complications should be undertaken to inform clinical management and patient counseling more effectively.

Most cases identified at our institutions are treated with the antiviral medication tecovirimat. We found that most patients had an improvement in symptoms several days after initiation. Clinical data on the efficacy of tecovirimat in mpox cases is needed, particularly regarding transmissibility and symptom duration and severity.

The small sample of cases is a limitation of this report, as broader generalizations cannot be made reliably about the risk of certain clinical syndromes. However, clinicians should be aware of the range of presentations and complications of mpox and maintain a high degree of vigilance for atypical presentations of this novel public health emergency.

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REFERENCES

1. CDC, 2022. *2022 Mpox Outbreak Global Map*. Available at: https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html. Accessed December 14, 2022.
2. Thornhill JP et al., 2022. Monkeypox virus infection in humans across 16 countries: April–June 2022. *N Engl J Med 387:* 679–691.
3. Rodriguez-Nava G et al., 2022. Myocarditis attributable to monkeypox virus infection in 2 patients, United States, 2022. *Emerg Infect Dis 28:* 2508–2512.
4. CDC, 2022. *Isolation and Prevention Practices for People with Mpox*. Available at: https://www.cdc.gov/poxvirus/monkeypox/clinicians/isolation-procedures.html. Accessed December 14, 2022.
5. Antinori A et al., 2022. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. *Eurosurveillance 27:* 2200421.
6. Peiró-Mestres A et al., 2022. Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients, Barcelona, Spain, May to June 2022. *Eurosurveillance 27:* 2200503.
7. Saurina G, Shirazi S, Lane JM, Daniel B, DiEugenia L, 2003. Myocarditis after smallpox vaccination: a case report. *Clin Infect Dis 37:* 145–146.
8. Keinath K, Church T, Kurth B, Hulten E, 2018. Myocarditis secondary to smallpox vaccination. *BMJ Case Rep 2018:* 2017223523.
9. Morgan J et al., 2008. Myocarditis, pericarditis, and dilated cardiomyopathy after smallpox vaccination among civilians in the United States, January–October 2003. *Clin Infect Dis 46 (Suppl 3):* S242–S250.
10. CDC, 2022. *Smallpox/Monkeypox Vaccine (JYNNEOS™): What You Need to Know*. Available at: https://www.cdc.gov/vaccines/hcp/vis/vis-statements/smallpox-monkeypox.pdf. Accessed December 14, 2022.