Recognizing Minimal Cutaneous Involvement or Systemic Symptoms in Monkeypox

As of May 13, 2022, the World Health Organization reported a multicountry monkeypox outbreak, a viral disease rarely reported outside of continental Africa.1 Classically, patients develop cutaneous lesions following prodromal symptoms.2 However, in this current outbreak, patients not uncommonly develop few cutaneous lesions, often localized to the anogenital region, with minimal preceding systemic symptoms, as highlighted in this case.

**Report of a Case** A healthy man in his 20s presented to outpatient dermatology with 2 painless genital and a single facial lesion of approximately 10 days' duration. At onset, he noted mild malaise and sore throat without fever, headache, chills, or adenopathy. He reported 1 new asymptomatic sexual male partner 10 days before initial symptoms. Pertinent medications included emtricitabine/tenofovir daily for pre-exposure HIV prophylaxis.

Before dermatology evaluation, he was treated for presumed facial impetigo with mupirocin, 2%, ointment and condyloma with imiquimod, 5%, cream. Examination demonstrated 2 umbilicated and ulcerated, skin-colored papules on the genitals, as well as a honey-colored crusted papule on the face (Figure).

Polymerase chain reaction swab results were negative for herpes simplex virus and Varicella-Zoster virus. Results from the HIV and syphilis blood tests were negative. Subsequent polymerase chain reaction testing of each ulceration confirmed West African monkeypox virus.

**Discussion** Monkeypox is emerging as a potentially important pathogen, with more than 15,000 cases as of August 2022 reported in the US.3 In this current outbreak, community transmission has occurred mostly, but not exclusively, among men who have sex with men.1 Transmission happens via direct contact with open lesions, which may explain recent lesion localization to the anogenital region following sexual activity. However, there has been debate whether monkeypox represents a new sexually transmitted infection.4 Less frequently, transmission may develop via fomites or prolonged face-to-face contact with respiratory droplets. Use of contact and airborne precautions by health care clinicians is recommended in suspected cases (including N95 masks, gown, gloves, and eye protection).

Following monkeypox virus exposure, patients classically present with prodromal symptoms of fever, headache, malaise, and adenopathy within 5 to 21 days. Painful rash develops 1 to 3 days after fever in a centrifugal fashion, most often on the face (95%), followed by the hands/feet (75%), oral mucosa (70%), genitals (30%), and conjunctiva (20%).2 Lesions progress sequentially (macules, papules, vesicles, pustules, scabs) at the same developmental stage throughout the body.

Clinicians should be aware that patients during this outbreak have presented in an atypical manner (Box). Few or single cutaneous lesions may precede instead of follow mild systemic symptoms.1,5 Lesions may be asymptomatic, painful, or minimally pruritic. While clinical features may help provide clues to the differential diagnosis of isolated anogenital lesions, concomitant sexually transmitted infections have been reported and should be excluded via serologic, urine, or lesion swab testing in any suspected monkeypox case.5 Umbilicated lesions raise the possibility of molluscum contagiosum,
but molluscum completely lacks systemic symptoms and has a longer incubation period (IP) of 14 to 56 days. Painless ulcerations may mimic primary syphilis (IP, 10-90 days), lymphogranuloma venereum (IP, 3-30 days), or granuloma inguinale (IP, 4-28 days). Painful ulcerations are seen with chancroid (IP, 4-7 days) or herpetic infections (IP, 2-7 days). Disseminated gonococcus (IP, 1-14 days) may present as an ulceronecrotic papule. In addition, lymphogranuloma venereum, granuloma inguinale, and chancroid often demonstrate tender inguinal adenopathy. Patients with known exposure should be symptomatically monitored for 21 days, with notification of local health departments to help with contact tracing and outbreak prevention.

In patients with umbilicated or ulcerated lesions, particularly localized to the anogenital region, clinicians should perform a thorough social history and maintain a high index of suspicion for monkeypox, even in those with mild constitutional symptoms, who report a new sexual partner in the preceding 2 weeks. Increased public awareness of risk factors, the ability to recognize subtle skin findings, as well as the increased availability/dissemination of vaccines will be important in containing and preventing further outbreaks.

Rachel Eisenstadt, MD
Walter J. Liszewski, MD
Cuong V. Nguyen, MD

Author Affiliations: Department of Dermatology, Northwestern University Feinberg School of Medicine, Chicago, Illinois.

Corresponding Author: Cuong V. Nguyen, MD, Department of Dermatology, Northwestern University Feinberg School of Medicine, 676 N St Clair St, Ste 1600, Chicago, IL 60611-2941 (cuong.nguyen@northwestern.edu).

Published Online: October 6, 2022. doi:10.1001/jamadermatol.2022.4652

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank the patient for granting permission to publish this information.


