Mpox (Monkeypox) Clinical Pearls

Hannah Peterson, BS; Brandon L. Adler, MD; Maria T. Ochoa, MD

The 2022 mpox (monkeypox) virus outbreak represents the latest example of how infectious diseases with previously limited reach can spread in a globalized society. More than 86,000 cases have been reported worldwide, with more than 30,000 cases in the United States as of March 15, 2023.[1] Herein, we summarize the key features of mpox infection for the dermatologist.

Mpox Transmission

The mpox virus is a double-stranded DNA virus of the *Orthopoxvirus* genus and Poxviridae family.[2,3] There are 2 types of the mpox virus: clade I (formerly the Congo Basin clade) and clade II (formerly the West African clade). Clade I causes more severe disease (10% mortality rate), while clade II is associated with lower mortality (1%–3%) and has been split into subclades of IIa (exhibits zoonotic transmission) and IIb (exhibits human-to-human spread).[3,4] The current outbreak is caused by clade IIb, and patients typically have no travel history to classic endemic regions.[5,6]

In endemic countries, mpox transmission is zoonotic from small forest animals. In nonendemic countries, sporadic cases rarely have been reported, including a cluster in the United States in 2003 related to pet prairie dogs. In stark contrast, human-to-human transmission is occurring in the current epidemic mainly via intimate skin-to-skin contact and possibly via sexual fluids, meeting the criteria for a sexually transmitted infection. However, nonsexual transmission does still occur, though it is less common.[7] Many of the reported cases so far are in young to middle-aged men who have sex with men (MSM).[2,8] However, it is crucial to understand that mpox is not exclusive to the MSM population; the virus has been transmitted to heterosexual males, females, children, and even household pets of infected individuals.[2,9,10] Labeling mpox as exclusive to the MSM community is both inaccurate and inappropriately stigmatizing.

Cutaneous Presentation and Diagnosis of Mpox

Mpox has an incubation time of approximately 9 days (range, 7–21 days), after which affected persons develop macular lesions that evolve over 2 to 4 weeks into papules, vesicles, and deep-seated pustules before crusting over and resolving with possible residual scarring.[2,3,5,9,11,12] Palmoplantar involvement is a key feature.[11] Although in some cases there will be multiple lesions with centrifugal progression, the lesions also may be few in number, with some patients presenting with a single lesion in the anogenital region or on the face, hand, or foot (Figure).[6,9] Systemic symptoms such as prodromal fever, lymphadenopathy, and headache are common but not universal.[9,13] Potential complications include penile edema, proctitis, bacterial superinfection, tonsillitis, conjunctivitis, encephalitis, and pneumonia.[5,9,13]

A high index of suspicion is needed to diagnose mpox infection. The differential diagnosis includes smallpox; varicella-zoster virus (primary or reactivation); secondary syphilis; measles; herpes simplex virus; molluscum contagiosum; hand, foot, and mouth disease; and disseminated gonococcal infection.[2,3] For lesions confined to the genital area, sexually transmitted infections (eg, chancroid, lymphogranuloma venereum) as well as non–sexually related acute genital ulcers (Lipschütz ulcers) should be considered.[2]

Certain clinical features may help in distinguishing mpox from other diseases. Mpox exhibits synchronous progression and centrifugal distribution when multiple lesions are present; in contrast, the lesions of primary varicella (chickenpox) appear in multiple different stages, and those of localized herpes zoster (shingles) exhibit a dermatomal distribution. When these features are present, mpox causes a greater degree of lymphadenopathy and systemic symptoms than primary varicella.[3]

Clinical diagnosis of mpox is more than 90% sensitive but only 9% to 26% specific.[3] To confirm the diagnosis, a viral swab vigorously obtained from active skin lesions should be sent in viral transport media for mpox DNA-specific polymerase chain reaction testing, which is available from major laboratories.[2,3] Other supportive tests include serum studies for anti–mpox virus immunoglobulins and immunohistochemical staining for viral antigens on skin biopsy specimens.[2] When evaluating suspected and confirmed mpox cases, dermatologists should wear a gown, gloves, a fitted N95 mask, and eye protection to prevent infection.[5]

Treating Mpox

Symptomatic mpox infection can last for up to 2 to 5 weeks.[3] The patient is no longer infectious once the

Ms. Peterson is from the Loma Linda University School of Medicine, California. Drs. Adler and Ochoa are from the Department of Dermatology, Keck School of Medicine, University of Southern California, Los Angeles.

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Correspondence: Maria T. Ochoa, MD, 1520 San Pablo St, Health Sciences Campus, Los Angeles, CA 90033 (mariatoc@usc.edu).

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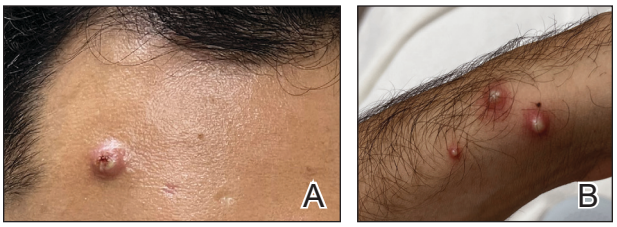

Clinical images from the 2022 mpox (monkeypox) outbreak. A, A pink papule with overlying pustules and crusting on the forehead. B, A cluster of large pustules, each with a rim of erythema, on the forearm. Images used with permission from Roneet Lev, MD (San Diego, California), and VisualDx.

lesions have crusted over.[3,11] The majority of cases require supportive care only.[2,3,5,14] However, mpox remains a potentially fatal disease, with 38 deaths to date in the current outbreak.[1] High-risk populations include children younger than 8 years, pregnant women, and individuals who are immunocompromised.[15] Tecovirimat, an antiviral medication approved by the US Food and Drug Administration (FDA) for smallpox, is available via the expanded access Investigational New Drug (EA-IND) protocol to treat severe mpox cases but is not widely available in the United States.[6,16-18] Brincidofovir, a prodrug of the antiviral cidofovir, possesses single-patient emergency use Investigational New Drug (e-IND) status for treatment of mpox but also is not widely available in the United States.[17] Intravenous vaccinia immune globulin is under consideration for high-risk individuals, but little is known regarding its efficacy against mpox.[5,16,17]

Two smallpox vaccines—JYNNEOS (Bavarian Nordic) and ACAM2000 (Emergent Bio Solutions)—are available for both preexposure and postexposure prophylaxis against mpox virus.[19] At this time, only JYNNEOS is FDA approved for the prevention of mpox; ACAM2000 can be used against mpox under the FDA's EA-IND protocol, which involves additional requirements, including informed consent from the patient.[20] ACAM2000 is a live, replication-competent vaccine that carries a warning of increased risk for side effects in patients with cardiac disease, pregnancy, immunocompromise, and a history or presence of eczema and other skin conditions.[3,21,22] JYNNEOS is a live but replication-deficient virus and therefore does not carry these warnings.[3,21,22]

Final Thoughts

Mpox is no longer an obscure illness occurring in limited geographic areas. Dermatologists must remain highly vigilant when evaluating any patient for new-onset vesicular or pustular eruptions to combat this ongoing public health threat. This issue of *Cutis*® also features a thorough mpox update on the clinical presentation, vaccine guidance, and management.[23]

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