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# Cutaneous manifestations and treatment of monkeypox cases in the United States

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To the Editor:

In the midst of the monkeypox (MKPX) outbreak in the U.S., dermatologists face the challenge of diagnosing and managing the cutaneous manifestations of the disease. Albeit in varying forms, cutaneous manifestations have been present in 100% of cases reported, per the CDC [1]. Delayed diagnosis of MKPX is possible due to other conditions with similarly appearing lesions.

In this narrative review of case reports, we describe the cutaneous manifestations and treatment of MKPX cases reported in the 2022 outbreak. Our search criteria included MKPX cases from the U.S. and Canada in which the clinical course was described from the time of patient presentation to resolution of symptoms. We searched Ovid Embase, Ovid Medline, PubMed, and Google Scholar databases for relevant cases in 2022, occurring before the time of search (September 1, 2022). We included all case reports and case series that discussed clinical findings, images, treatment methods, and outcomes.

Ten MKPX cases (100% male, 100% men who have sex with men (MSM), 50% HIV+) met search criteria ([Table 1](#)). In 4/10 cases, MKPX symptoms were mistakenly diagnosed and treated for herpes simplex virus (HSV), syphilis, or bacterial cellulitis. Successful treatment methods consisted of tecovirimat (5/10), supportive care (4/10), and antibiotic treatment (1/10).

The small sample size, in addition to the inclusion of case reports and series, may limit the generalizability of our findings. Of note, however, the demographic composition of our cohort is representative of the CDC's state-of-the-art epidemiological report (99% male, 41% HIV+, and 94% MSM), [1]. Mean time to diagnosis of MKPX from initial care visit was 2.8 days (SD, 2.52). The most commonly reported treatment option, tecovirimat, has yet to be fully studied in humans for use against MKPX. However, it has been approved based on its efficacy in animal models and prior successful use in the treatment of smallpox, which is classified in the orthopoxvirus genus, akin to MKPX [2]. Of note, tecovirimat was never the first line of treatment in the cases studied. Rather, among 5 cases, failure of first line of treatment for a mean of 4.8 days (SD, 3.54) resulted in prescription for tecovirimat. Thereafter, 5/5 patients on tecovirimat had resolution of symptoms in an average of 4.8 days (SD, 1.16). Dermatologists should be aware of tecovirimat as a treatment option, especially in immunocompromised patients for whom supportive care may not suffice. Although the Ankara vaccine was not successful in preventing one MKPX case described [3], studies show limited incidence of breakthrough infections (4%) with post-exposure Ankara administration [4]. Additionally, dermatologists should be aware of two live vaccines

(JYNNEOS and ACAM2000) approved for the prevention of MKPX.

Monkeypox was most commonly incorrectly diagnosed and treated as HSV and syphilis. Whereas MKPX and HSV both present as painful and pruritic vesicles, MKPX may be principally distinguished from HSV due to its hallmark umbilicated appearance (**Table 1**). Similarly, although MKPX may share features with secondary syphilis (diffuse rash including palmoplantar involvement), syphilis rarely presents as vesicular or umbilicated papules [5]. Diagnoses should be evaluated in the context of an individual's clinical history factors and confirmed using concurrent testing.

Given the prevalence of cutaneous MKPX manifestations, it is important for dermatologists to recognize this condition. Skin manifestations may appear before or even in the absence of febrile symptoms [6]. Although the paucity of reported cases in the literature limits our understanding of

MKPX, this review provides an initial roadmap with descriptions and visual reinforcements of the commonly appearing cutaneous signs of MPKX.






### Potential conflicts of interest



Dr. Steven Feldman has received research, speaking and/or consulting support from a variety of companies including Galderma, GSK/Stiefel, Almirall, Leo Pharma, Boehringer Ingelheim, Mylan, Celgene, Pfizer, Valeant, Abbvie, Samsung, Janssen, Lilly, Menlo, Merck, Novartis, Regeneron, Sanofi, Novan, Qurient, National Biological Corporation, Caremark, Advance Medical, Sun Pharma, Suncare Research, Informa, UpToDate and National Psoriasis Foundation. He is founder and majority owner of [www.DrScore.com](http://www.DrScore.com) and founder and part owner of Causa Research, a company dedicated to enhancing patients' adherence to treatment. The remaining authors have no conflicts to disclose.

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**Table 1.** Clinical descriptions and outcomes of monkeypox cases.

Study	Demographics of cases	Clinical Description	Time to MKPX Diagnosis from Initial Care Visit	Treatment	Outcome	Clinical Images
Escudero-Tornero et al. (2022) [6]	1, male HIV (-) homosexual	Whitish grey papulo-vesicular rash with central umbilication; perianal necrosis; afebrile	Same day	Supportive care	Resolution of vesicles after one week	
Lucar et al. (2022) [7]	2, male HIV+ homosexual	A) and B). Systemic febrile symptoms followed by oral ulcers and diffuse papules, including in the rectal area	6 days	Supportive Care, Opioids, Tecovirimat	A) Failure to resolve with supportive care (6 days) and opioid treatment (3 days); symptoms resolved on tecovirimat (7 days)	B) 
			3 days		B) Failure to resolve with supportive care (9 days) and opioid treatment (1 day); symptoms resolved on tecovirimat (4 days)	
Ortiz-Martínez et al. (2022) [8]	1, male HIV+ homosexual	Painless umbilicated penile lesions that spread diffusely; systemic febrile symptoms	6 days	Penicillin G, doxycycline, ceftriaxone, and amoxicillin-clavulanate 875/125 mg	Resistant to initial antibiotic (4 days) but improved after 4 days of treatment with amoxicillin-clavulanate	
Khan et al. (2022) [9]	1, male HIV (-) homosexual	2 to 8 mm, pink umbilicated papules diffusely spread throughout the body, sparing genital areas but including palms and soles	4 days	Supportive care	Self-resolution after 2 weeks	
Xia et al. (2022) [10]	1, male, HIV (-) homosexual	Systemic febrile symptoms and later, vesicular and pustular lesions beginning in palms and soles; sparing genital areas	Same day	Supportive care	Self-resolution after 3 weeks	

Matias et al. (2022) [3]	3, male 1 HIV (-) 2 HIV+ homosexual	A) Systemic febrile symptoms and painless penile ulcer followed by the appearance of diffusely painful, pruritic vesiculopustular lesions	3 days	HSV and syphilis empiric treatment followed by Tecovirimat	A) Failure of HSV and syphilis treatment (3 days); Resolution with tecovirimat (4 days)	A) 
		B) Systemic febrile symptoms, then pustules on forearms and hands, later spreading diffusely but sparing genital area	Same day	Ankara vaccine post-exposure; Tecovirimat	B) Failure of Ankara vaccine (2 days); resolution with tecovirimat (5 days)	
		C) Systemic febrile symptoms, maculopapular rash and vesicles in genital area; eyelid erythema	Same day	Antibacterial treatment, followed by Tecovirimat	C) Failure of antibacterial treatment (2 days); resolved with Tecovirimat (4 days)	
Sukhdeo et al. (2022) [5]	1, male HIV (-) homosexual	Fever, and day later: rectal pain but no genital lesions; pruritic papules and macules diffusely	6 days	Valacyclovir for presumed HSV followed by supportive care	Failure of Valacyclovir for presumed HSV treatment (6 days); Self-resolution with supportive care for 5 days	

HIV, human immunodeficiency virus; HSV, herpes simplex virus; NA, not applicable; MKPX, monkeypox.

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Matias et al. (2022), [3]; This open access article is available under the Creative Commons CC-BY-NC-ND license and permits non-commercial use of the work as published, without adaptation or alteration provided the work is fully attributed.

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