Pustular Eruption on the Face

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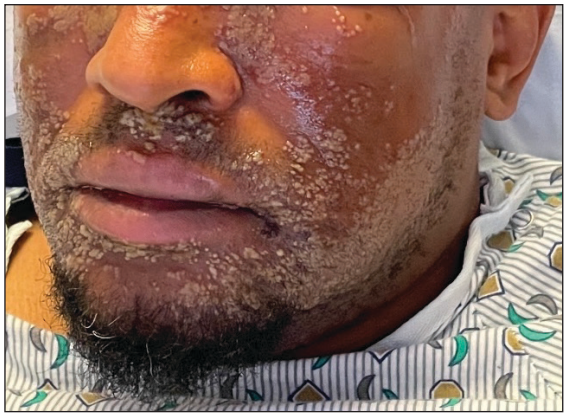

A 52-year-old man developed a sudden eruption of small pustules on background erythema and edema covering the forehead, nasal bridge, periorbital region, cheeks, and perioral region on day 3 of hospitalization in the intensive care unit for management of septic shock secondary to a complicated urinary tract infection. He had a medical history of benign prostatic hyperplasia, sarcoidosis, and atopic dermatitis. He initially presented to the emergency department with fever, chills, and dysuria of 2 days' duration. Because he received ceftriaxone, vancomycin, ciprofloxacin, and tamsulosin while hospitalized for the infection, the primary medical team suspected a drug reaction and empirically started applying hydrocortisone cream 2.5%. The rash continued to spread over the ensuing day, prompting a dermatology consultation to rule out a drug eruption and to help guide further management. The patient was in substantial distress and pain. Physical examination revealed numerous discrete and confluent monomorphic pustules on background erythema with faint collarettes of scale covering most of the face. Substantial periorbital and facial edema forced the eyes closed. There was no mucous membrane involvement. A review of systems was negative for dyspnea and dysphagia, and the rash was not present elsewhere on the body. Ophthalmologic evaluation revealed no ocular involvement or vision changes. Laboratory studies demonstrated neutrophilia (17.27×10^9 cells/L [reference range, $2.0–6.9\times10^9$ cells/L]). The eosinophil count, blood urea nitrogen/creatinine, and liver function tests were within reference range.

WHAT'S YOUR **DIAGNOSIS?**

a. acute generalized exanthematous pustulosis
b. allergic contact dermatitis
c. drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome
d. eczema herpeticum
e. *Orthopoxvirus* infection (mpox [monkeypox]/smallpox)

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The authors report no conflict of interest.
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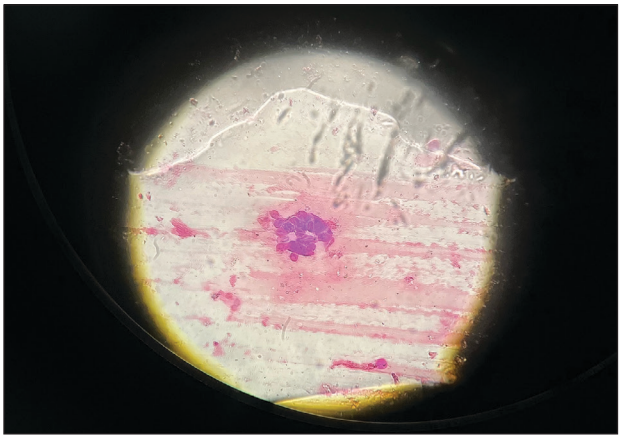
THE **DIAGNOSIS:** Eczema Herpeticum

The patient's condition with worsening facial edema and notable pain prompted a bedside Tzanck smear using a sample from the base of a deroofed forehead vesicle. In addition, a swab of a deroofed lesion was sent for herpes simplex virus and varicella-zoster virus (VZV) polymerase chain reaction (PCR) testing. The Tzanck smear demonstrated ballooning multinucleated syncytial giant cells and eosinophilic inclusion bodies (Figure), which are characteristic of certain herpesviruses including herpes simplex virus and VZV. He was started on intravenous acyclovir while PCR results were pending; the PCR test later confirmed positivity for herpes simplex virus type 1. Treatment was transitioned to oral valacyclovir once the lesions started crusting over. Notable healing and epithelialization of the lesions occurred during his hospital stay, and he was discharged home 5 days after starting treatment. He was counseled on autoinoculation, advised that he was considered infectious until all lesions had crusted over, and encouraged to employ frequent handwashing. Complete resolution of eczema herpeticum (EH) was noted at 3-week follow-up.



A Tzanck smear of a forehead vesicle revealed multinucleated giant cells and eosinophilic inclusion bodies (original magnification ×40).

Eczema herpeticum (also known as Kaposi varicelliform eruption) is a potentially life-threatening disseminated cutaneous infection caused by herpes simplex virus types 1 and 2 in patients with pre-existing skin disease.[1] It typically presents as a complication of atopic dermatitis (AD) but also has been identified as a rare complication in other conditions that disrupt the normal skin barrier, including mycosis fungoides, pemphigus foliaceus, pemphigus vulgaris, Darier disease, pityriasis rubra pilaris, contact dermatitis, and seborrheic dermatitis.[1-4]

The pathogenesis of EH is multifactorial. Disruption of the stratum corneum; impaired natural killer cell function; early-onset, untreated, or severe AD; disrupted skin microbiota with skewed colonization by *Staphylococcus aureus*; immunosuppressive AD therapies such as calcineurin inhibitors; eosinophilia; and helper T cell (T_H2) cytokine predominance all have been suggested to play a role in the development of EH.[5-8]

As seen in our patient, EH presents with a sudden eruption of painful or pruritic, grouped, monomorphic, dome-shaped vesicles with background swelling and erythema typically on the head, neck, and trunk. Vesicles then progress to punched-out erosions with overlying hemorrhagic crusting that can coalesce to form large denuded areas susceptible to superinfection with bacteria.[9] Other accompanying symptoms include high fever, chills, malaise, and lymphadenopathy. Associated inflammation, classically described as erythema, may be difficult to discern in patients with darker skin and appears as hyperpigmentation; therefore, identification of clusters of monomorphic vesicles in areas of pre-existing dermatitis is particularly important for clinical diagnosis in people with darker skin types.

Various tests are available to confirm diagnosis in ambiguous cases. Bedside Tzanck smears can be performed rapidly and are considered positive if characteristic multinucleated giant cells are noted; however, they do not differentiate between the various herpesviruses. Direct fluorescent antibody testing of scraped lesions and viral cultures of swabbed vesicular fluid are equally effective in distinguishing between herpes simplex virus type 1, herpes simplex virus type 2, and VZV; PCR confirms the diagnosis with high specificity and sensitivity.[10]

In our patient, the initial differential diagnosis included EH, acute generalized exanthematous pustulosis, allergic contact dermatitis, and *Orthopoxvirus* infection. The positive Tzanck smear reduced the likelihood of a nonviral etiology. Additionally, worsening of the rash despite discontinuation of medications and utilization of topical steroids argued against acute generalized exanthematous pustulosis and allergic contact dermatitis. The laboratory findings reduced the likelihood of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, and PCR findings ultimately ruled out *Orthopoxvirus* infections. Additional differential diagnoses for EH include dermatitis herpetiformis; primary VZV infection; hand, foot, and mouth disease; disseminated zoster infection; disseminated molluscum contagiosum; and eczema coxsackium.

Complications of EH include scarring; herpetic keratitis due to corneal infection, which if left untreated can progress to blindness; and rarely death due to multiorgan failure or septicemia.[11] The traditional smallpox vaccine (ACAM2000) is contraindicated in patients with AD and

EH, even when AD is in remission. These patients should avoid contact with recently vaccinated individuals.[12] An alternative vaccine—Jynneos (Bavarian Nordic)—is available for these patients and their family members.[13] Clinicians should be aware of this guideline, especially given the recent mpox (monkeypox) outbreaks.

Mild cases of EH are more common, may sometimes go unnoticed, and self-resolve in healthy patients. Severe cases may require systemic antiviral therapy. Acyclovir and its prodrug valacyclovir are standard treatments for EH. Alternatively, foscarnet or cidofovir can be used in the treatment of acyclovir-resistant thymidine kinase–deficient herpes simplex virus and other acyclovir-resistant cases.[14] Any secondary bacterial superinfections, usually due to staphylococcal or streptococcal bacteria, should be treated with antibiotics. A thorough ophthalmologic evaluation should be performed for patients with periocular involvement of EH. Empiric treatment should be started immediately, given a relative low toxicity of systemic antiviral therapy and high morbidity and mortality associated with untreated widespread EH.

It is important to maintain a high index of clinical suspicion for EH, especially in patients with pre-existing conditions such as AD who present with systemic symptoms and facial vesicles, pustules, or erosions to ensure prompt diagnosis and appropriate treatment.

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