A 62-year-old woman treated with several courses of corticosteroids for an undifferentiated rash came to the emergency department with progressively worsening cutaneous signs and symptoms and generalized weakness. She had scabies, and despite treatment continued to decompensate. Repeat skin biopsies revealed disseminated herpes simplex virus infection, and results of blood cultures were consistent with infection by methicillin-resistant Staphylococcus aureus. Despite antiviral and antimicrobial therapy, sepsis and multiorgan failure developed, and the patient died. This case illustrates the complications of the rare entity eczema herpeticum, which occurs most often in immunocompromised patients and is associated with a high mortality. Maintaining a high index of suspicion for this disease in decompensating patients with an unidentified rash is essential to avoid catastrophic outcomes. (American Journal of Critical Care. 2016;25:379-382)
highlights an important condition to consider in both critical care and primary care assessment of a patient with an undiagnosed rash.

A 62-year-old woman with a history of mild mental retardation, diabetes, hypertension, and hypothyroidism who was living in a group home came to the emergency department with a rash and generalized weakness. She had intermittently experienced a pruritic, generalized rash for approximately 1 year before she came to the hospital. Her caregivers at the group home had taken her to the primary care doctor for the workup of this rash throughout the year. The results of an outpatient skin biopsy were consistent with a drug eruption, thus prompting her primary care physician to have her stop taking hydrochlorothiazide and sitagliptin. Despite this step, the rash did not resolve.

The patient had an empiric trial of prednisone, which resulted in temporary resolution of the rash. However, whenever prednisone was discontinued, the rash would promptly reappear. The patient received repeated short courses of steroids (<7 days each) throughout the year. Despite the prednisone therapy, during the week before she came to the hospital, the rash started to evolve into white scaly plaques, and she had difficulty sleeping because of the marked pruritus. In the days before she came to the emergency department, the rash spread to her face and was accompanied by scleral injection and ophthalmalgia, prompting her primary care doctor to refer her to the hospital. She was promptly transferred to a tertiary care center because of the possibility of Stevens-Johnson syndrome.

On initial examination, the patient had normal vital signs. She had a diffuse erythematous, excoriated rash covering approximately 80% of her skin (Figure 1). Areas of denuded skin were concentrated over the anterior part of her chest and were draining serous fluid. Neither the Nikolsky sign nor mucosal involvement was present. Bilaterally her eyes had injected sclerae, crusting, and occasional yellowish discharge.

Collateral information from her group home and information from hospital social workers who evaluated her home environment indicated that other residents had similar rashes. Because of this information and the findings of the physical examination, a skin biopsy was performed, and empiric treatment with ivermectin and permethrin was started for suspected scabies. The biopsy results later confirmed the diagnosis of scabies. Additionally, the ophthalmology team identified bilateral ocular deep epithelialization and corneal abrasions, so ophthalmic erythromycin ointment was added to her treatment.

On hospital day 6, the patient became increasingly somnolent, hypoglycemic, tachycardic, and tachypneic. Her health care providers suspected septic shock with multiorgan injury, and she was transferred to the intensive care unit for intubation for airway protection, treatment with vasopressors and steroids for fluid-unresponsive shock, and empiric treatment with vancomycin, cefepime, and fluconazole. Chest computed tomography at that time revealed increases in bilateral pleural effusions and multifocal consolidation. Laboratory data revealed hyperlactatemia, acute kidney injury, and thrombocytopenia; continuous renal replacement therapy was started.

Because of the evolving skin changes, another skin biopsy was performed, which revealed viral inclusions and multinucleated cells consistent with a viral cytopathic effect (Figure 2). Because immunostaining for HSV-1/2 was positive for the virus, acyclovir was started for treatment of disseminated HSV infection. Despite therapeutic levels of vancomycin, subsequent blood cultures were positive for methicillin-resistant Staphylococcus aureus (Figure 1).
MRSA, so clindamycin was added to the treatment regimen. Vancomycin eye drops were also added because an ocular culture was positive for MRSA.

The patient further decompensated despite maximum multiorgan support. After a meeting with her group home coordinators on hospital day 11 to discuss her poor prognosis, the patient’s care was redirected to comfort measures. She was pronounced dead later that day.

An autopsy revealed extensive skin ulceration from disseminated HSV, persistent scabies, and an abscess on the anterior part of the chest wall. She had large bilateral pleural effusions, scattered septic emboli in both the lungs and the heart, and a serous pericardial effusion. No evidence of an HSV-induced cytopathic effect was detected in the visceral organs. The final cause of death was multiorgan failure due to a MRSA superinfection.

**Discussion**

This novel case of *S aureus* septic shock due to eczema herpeticum occurred secondary to scabies. The scabies triggered chronic atopic dermatitis, which, in combination with chronic doses of steroids, predisposed the patient to disseminated HSV infection, or eczema herpeticum. The resultant cutaneous lesions made her susceptible to secondary infection by skin pathogens, such as MRSA.

Scabies has diverse manifestations. It is classically described as a wavy line in the finger webs, wrists, elbows, axillae, buttocks, and genitalia. The lesions are often described as papules, nodules, and vesicles. Secondary manifestations include excoriations, eczematous eruptions, crusting, and infections. Care providers should maintain a particularly high index of suspicion in patients with a pruritic skin eruption that is worse at night and involves the trunk and extremities, although the eruption can have diverse signs and symptoms. Skin scrapings taken from acral areas, skin-colored ridges, vesicles, or nonexcoriated papules generally yield the greatest probability of visualizing the mite and therefore diagnosing scabies. A highly inflamed, excoriated area is unlikely to contain the mite that causes the scabies. Microscopic examination of skin scrapings can show no evidence of scabies because of a low mite burden or a sampling error. Treatment can be unsuccessful because of misdiagnosis, poor application of topical treatments, inadequate dosing, and drug resistance.

Eczema herpeticum, also known as Kaposi varicelliform eruption, is a rare skin complication of atopic dermatitis that often results from taking immunosuppressive agents to treat the primary skin condition. Eczema herpeticum, which is typically a challenging diagnostic dilemma for non-dermatologists, is characterized by cutaneous pain with new skin lesions. The rapid spread of these virally mediated lesions (usually from HSV-1) can rapidly lead to severe morbidity and mortality.

HSV is a ubiquitous human pathogen in adults; the primary infection most often occurs in childhood. Despite the prevalence of HSV infection and atopic dermatitis (approximately 17% of children worldwide), eczema herpeticum is surprisingly rare: it occurs in less than 3% of patients with atopic dermatitis. This low percentage is thought to be due to a complex interplay of environmental factors and host genetic characteristics, such as defects in the generation and expression of interferon-γ (IFN-γ), which result in uncontained viral reactivation.

The pathogenesis of eczema herpeticum is linked to the balance of CD4+ regulatory T cells and CD8+ effector T cells. CD8+ T cells are cytotoxic and inhibit HSV through the production of several cytokines such as IFN-γ and other chemical mediators, but, if unregulated, these effector T cells may also indiscriminately damage healthy tissue. In a normal immune system, a proper balance of CD4+ cells can suppress an excessive immune response to HSV by mitigating the cytotoxic effects of CD8+ T cells.

In our patient’s situation, the short courses of steroids may have initially suppressed CD4+ regulatory T cells. However, when the steroids were discontinued, the number and activity of CD4+ cells most likely increased, leading to excessively suppressed effector CD8+ T cells.
decreases in IFN-γ, and, ultimately, HSV reactivation. A similar phenomenon of HSV reactivation occurs in patients with genetic defects in synthesis and expression of IFN-α. The direct correlation between an increased presence of functional CD4+ regulatory T cells in lesion biopsies and the clinical disease activity of eczema herpeticum further support the pathogenic role of CD4+ cells in eczema herpeticum.7

Eczema herpeticum is mostly a clinical diagnosis. The infection is characterized by the acute appearance of vesicles mainly on the trunk and extremities, and particularly over eczematous skin. Increases in the titer of antibodies to HSV support the diagnosis of eczema herpeticum, and pathological evidence of viral inclusions and multinucleated cells on biopsy of the skin lesions, as well as immunostains for HSV-1/2, can confirm the diagnosis.7 Before the advent of antiviral therapies, mortality in patients with eczema herpeticum was 10% to 50%. Most deaths are due to viremia-induced multiorgan failure, including meningitis and encephalitis.8,9 The consequences of untreated disease highlight the importance of prompt initiation of systemic antiviral therapy for effective treatment.

The most commonly isolated organism from swabs of eczema herpeticum lesions is S aureus. In one study,9 this microorganism was found in the lesions of 8 of 24 patients (33%). However, the microbes isolated from the lesion are often nonpathogenic and rarely cause marked morbidity or mortality. Although secondary infections with skin pathogens, such as S aureus and Streptococcus pyogenes, can occur in eczema herpeticum, our case is the first reported case of death due to secondary MRSA infection and bacteremia. Physicians, nursing staff, and patient care providers should always consider eczema herpeticum in the differential diagnosis in any acutely decompensating patient with an unidentified rash, because the consequences of improper or delayed diagnosis can be devastating.

ACKNOWLEDGMENTS
We acknowledge Dr Sandy Liu, Pathology Department, University of Maryland Medical Center, who contributed to acquisition of microscopic images and their histological interpretation.

FINANCIAL DISCLOSURES
None reported.

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REFERENCES

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A Fatal Case of Eczema Herpeticum With Septic Shock Due to Methicillin-Resistant Staphylococcus aureus
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Am J Crit Care 2016;25 379-382 10.4037/ajcc2016495
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