Eczema herpeticum in Darier’s disease: a topical storm
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ABSTRACT
The occurrence of eczema herpeticum (EH) in patients with Darier’s disease (DD) is a rare occurrence. It is considered a dermatologic emergency due to its high mortality rate if misdiagnosed or left untreated. Here, we present a case of a 42-year-old woman with a longstanding history of DD who presented with EH secondary to herpes simplex 1. Since the incidence of EH is now increasing in adults, we take this as an opportunity to raise awareness among clinicians on the importance of a timely diagnosis of EH and initiating prompt treatment so as to prevent or minimize complications.

1. Introduction
Darier’s disease (DD) is a rare autosomal dominant keratinizing disorder, also known as keratosis follicularis, that occurs due to a mutation in the ATP2A2 gene on chromosome 12q23-24.1. This gene encodes for a sarco-/endoplasmic reticulum calcium ATPase pump (SERCA2) that has a role in the intracellular signaling of calcium, which regulates cell differentiation and initiating assembly at desmosomes. The mutation leads to loss of intracellular signaling of calcium, resulting in breakdown of desmosomes responsible for cell adhesion [1]. Patients with severe DD are predisposed to eczema herpeticum (EH) due to disturbances in cell-mediated immunity, absence of lymphokine production by peripheral lymphocytes, and immune system dysregulation [2]. Patients with this condition develop varying degrees of symmetrical thick, branny, brown, malodorous scale over the face, neck, and torso. Mild cases are treated with topical steroids and oral antibiotics, while severe cases generally respond to oral retinoids.

EH, initially described by Kaposi in 1887 and hence also known as Kaposi varicelliform eruption, is a disseminated herpes simplex infection of the skin that most commonly occurs in patients with atopic dermatitis. It can be confused with skin conditions including impetigo, atypical hand foot and mouth disease, and primary varicella infection. Misdiagnosis and delay of treatment have proven to be fatal [3].

2. Case description
A 42-year-old Caucasian female with a confirmed diagnosis of DD presented to the emergency department with a 3-day history of a progressive, painful, itchy rash (Figure 1). This event was much more sudden, severe, and painful when compared to her previous Darier’s eruptions. She denied any fevers but did endorse chills. There was no known exposure to any new medication, over the counter supplements, or any personal care products. No recent travel history or any sick contacts were reported.

Vital signs on this visit were within normal limits. Physical examination revealed the presence of erythematous vesiculopustules with central umbilication and crusted erosions involving the back, extending to the neck, anteriorly down the chest, and breasts bilaterally. Skin lesions were not warm but were tender to palpation (Figure 1).

Lab values such as Complete blood count (CBC) and chemistry were within normal limits. Blood cultures showed no growth after 5 days of incubation. Cultures of vesicles from the skin of thoracic spine and trunk were positive for herpes simplex virus. While in the emergency department (ED), the patient received one dose of IV morphine, IV acyclovir, and IV diphenhydramine. She was then admitted as a dermatologic emergency and treated with IV acyclovir and oral clindamycin. At her 10-day follow-up visit, all EH lesions had resolved with almost complete disappearance of lesions of EH. Discharge medications included 10-day oral courses of valacyclovir and clindamycin. At her 10-day follow-up visit, all EH lesions had resolved with only erythematous-like papules remaining.

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3. Discussion

DD is a rare keratinizing disorder. Reported prevalence ranges from 1 to 100,000 in the world with the incidence of the disease reported to be 4 new cases per million over 10 years [4]. Patients present at puberty with numerous yellowish-brown keratotic papules and plaques that preferentially involve seborrheic areas. However, there is great variability in the extent of involvement ranging from typical nail changes to generalized disease. It persists throughout life, running a chronic relapsing course with exacerbations reported by trauma, heat, sweating and UV exposure, lithium, and steroids. Herpes Simplex Virus (HSV) can compromise it as well.

The occurrence of EH with DD is a well-known finding [5–8] but a rare occurrence and is considered a dermatologic emergency. In its primary form, EH presents with monomorphic blisters or punched-out erosions which are red/black in color, in areas where the skin has been most affected by underlying skin disease. Lesions gradually spread and over time may become hemorrhagic with subsequent development into erosions that can be superinfected complicated by sepsis and death [9].

Although generally observed as a complication of atopic dermatitis, it has been recorded to occur secondary to several disorders which exhibit skin breakdown like DD, mycosis fungoides, pemphigus
vulgaris, ichthyosiform erythroderma, Hailey-Hailey disease, psoriasis, and severe thermal burns. Most cases are secondary to HSV1 or 2 but rarely can be caused by other viruses (cox-sackie, vaccinia, and varicella zoster virus (VSV)), and severity varies from mild to a fulminant but fatal disorder involving the visceral organs (eyes, brain, lung, and liver) [10]. Bacterial superinfection and bacteremia are usually the complications that cause mortality.

A retrospective review conducted by Wollenbarg et al. studied 100 patients with EH and found risk factors that could predispose to the development of EH. These included a high serum IgE and an early onset of atopic dermatitis. In addition, an HSV-specific cell-mediated immune defect could also result in the development of EH since T-cell-mediated immunity is important in the control of both primary and recurrent EH infections. Furthermore, a study done by Howell et al. identified deficient cathelicidin peptide in patients with atopic dermatitis. Cathelicidin is an inducible antimicrobial peptide which is an integral component of innate immune response with activity against...
various pathogens, hence further explaining the increased susceptibility to EH [11].

Prompt treatment with an antiviral (IV acyclovir) is needed and should not be delayed pending laboratory studies [10,12]. Viral swabs taken by scraping the base of a fresh blister with Tzanck smear showing epithelial multinucleated giant cells and viral culture of fresh vesicular fluid are the most reliable diagnostic tests, and patients with recurrence of HSV infection that would predispose them to EH should be offered prophylaxis with acyclovir or valacyclovir [4,12].

With this report, we hope to increase awareness of the condition among internists and to emphasize the need for correct and timely diagnosis and treatment so as to avoid fatal complications.

4. Conclusion

Atopic dermatitis is a common condition seen by internists, and we should, therefore, become familiar with early awareness of EH and prompt treatment with antiviral therapy as a means of preventing and minimizing complications [3].

One of the greatest challenges was recognizing that this episode was different from the patients' usual Darier flares in form of its distribution (back rather than chest or neck), primary presentation of pain rather than the regular itching, and the more vesicular form of lesions compared to the regular scaling and crusting as seen in the past.

DD is characterized by exacerbations and remissions, and patients with active DD should be cautioned against exposure to persons with HSV. They should also be warned against excessive exposure to the sun which can both aggravate DD and precipitate a flare of herpes simplex [13]. Eczema herpeticum like any HSV infection can recur, and therefore, after an episode of EH, patients often treated with daily suppressive oral antiviral therapy for at least 1–2 years following the event.

Disclosure statement

No potential conflict of interest was reported by the authors.

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