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Eczema Herpeticum

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Introduction

Eczema herpeticum (EH) is a disseminated cutaneous infection with herpes simplex virus that develops in a patient with atopic dermatitis.[1] EH typically presents as a sudden onset eruption of monomorphic vesicles and "punched-out" erosions with hemorrhagic crusts over eczematous areas. Patients may have systemic symptoms, such as fever, lymphadenopathy, or malaise.[2] Presentation ranges from mild and self-limiting in healthy adults to life-threatening in children, infants, and immunocompromised patients. Early treatment with antiviral therapy can shorten the duration of mild disease and prevent morbidity and mortality in severe cases.[3]

Etiology

Eczema herpeticum is due to cutaneous superinfection with herpes simplex virus (HSV), usually HSV-1, in patients with atopic dermatitis. Cases due to reactivation of HSV are more common than primary infection.[4] Patients with atopic dermatitis are prone to recurrent bacterial and viral skin infections due to impaired epidermal barrier function and immune dysregulation.[5] Disseminated cutaneous HSV infection can also occur in patients with other forms of dermatitis that impair the skin barrier and is known as Kaposi varicelliform eruption (KVE). KVE has been reported in patients with Darier disease, Hailey–Hailey disease, immunobullous diseases, burns, irritant contact dermatitis, mycosis fungoides, Sézary syndrome, ichthyoses, and pityriasis rubra pilaris.[6][7]

Risk factors associated with the development of EH are more severe atopic skin disease, decreased epidermal expression of filaggrin, and decreased production of cathelicidin and other antimicrobial peptides.[8] EH patients exhibit biomarkers associated with T-helper type 2 (Th2) cell responses, such as reduced interferon levels, elevated eosinophil count, and increased serum IgE levels.[5] EH patients are more likely to have food and environmental allergies, asthma, early onset of atopic dermatitis before age five, and history of *Staphylococcus aureus* and molluscum contagiosum infections.[5] The HLA-B7 allele has been found to be associated with an increased risk of EH.[9] Increased interleukin-10 (IL-10) and local IL-25 expression is found in EH patients and may play a role in the development of EH.[10] The Th2 shift of the immune system in EH patients is associated with decreased antimicrobial peptides in the epidermis and reduced defense against cutaneous HSV infection.

Epidemiology

Eczema herpeticum occurs in less than 3% of atopic dermatitis patients, affecting infants and children more than adults.[5] Atopic dermatitis is the most common chronic inflammatory skin disease in the world, affecting 10 to 20% of children in developed countries and 7 to 10% of adults in the United States.[11][12] Given the prevalence of HSV exposure, the comparative rarity of EH in atopic dermatitis patients suggests many host factors play an important role in the development of EH. A study of pediatric EH patients in Canada found that predictors of hospitalization included male sex, age less than one year, fever, and systemic symptoms at presentation.[13]

Another study in the United States found that the average age of hospitalized pediatric patients with EH was 3.26 +/- 0.1 years, and 41.8% of patients were female.[13] This study also reported higher prevalence, length of hospital stay, and cost of care occurring in Asian pediatric patients.[13] The epidemiology of EH in non-hospitalized and adult patients is not well defined.

History and Physical

Eczema herpeticum presents as a sudden onset eruption of monomorphic, dome-shaped, grouped, 2 to 3 mm vesicles on an erythematous base. Lesions are superimposed on areas of pre-existing atopic dermatitis, most commonly on the face, neck, and upper trunk. The lesions are pruritic, painful, and may spread to involve normal skin over seven to 10 days.[14] Within two weeks, the vesicles rupture and form characteristic "punched-out" erosions with the hemorrhagic crust. Small erosions may coalesce to form a larger erosion or ulceration with a scalloped border.

Numerous vesicles may appear in successive crops, and multiple morphologies may be present at the same time. Lesions that are secondarily impetiginized may have an overlying honey-colored crust. In patients with severe or poorly-controlled atopic dermatitis, the characteristic morphology may be difficult to recognize and can be misdiagnosed as an exacerbation of eczematous dermatitis.[15] Patients may have systemic symptoms, such as fever, malaise, and lymphadenopathy.[3] EH lesions generally heal without scarring within six weeks.[16]

Evaluation

The diagnosis of eczema herpeticum can be made clinically if characteristic morphology is present. Viral polymerase chain reaction (PCR) can be performed on vesicle fluid to confirm the diagnosis and determine the type of herpesvirus with high sensitivity and specificity.

If PCR is not available, a Tzank smear, direct fluorescent antibody (DFA) testing, and viral cultures can confirm HSV infection. Bacterial culture should be done if there is a concern for impetiginization. If the clinical presentation is atypical, a skin biopsy may be indicated. Laboratory tests may reveal lymphopenia and an increased erythrocyte sedimentation rate.[14]

Treatment / Management

Eczema herpeticum patients should be treated promptly with systemic acyclovir or valacyclovir to minimize the risk of complications and prevent progression to severe disease.

- **Mild cases** can be treated with oral acyclovir or valacyclovir for 7-21 days or until all lesions are crusted over.[17] The recommended dosage for oral acyclovir is 30-60 mg/kg/d divided into three doses per day in children and 400 mg 3 times per day in adults.[16][18] The dosage for oral valacyclovir is 20 mg/kg/d in children and 500 mg 3 times per day in adults.[4]
- **Severe cases** or **immunocompromised patients** should be hospitalized for intravenous acyclovir 5-10 mg/kg every 8 hours. Patients can be transitioned to oral acyclovir once there is clinical improvement, and the lesions start to crust over.[15] Supportive care with gentle emollients and cool compresses can provide symptomatic relief.
- **Critically ill** patients may need intravenous fluids, electrolyte repletion, wound care, pain control, and nutritional support. Patients should be counseled about the risk of autoinoculation, and frequent handwashing should be encouraged. EH lesions are considered infectious until crusted over.
- **Contact precautions** should be initiated for hospitalized patients, including patient isolation and the use of face masks and gowns for healthcare providers.[18] Patients should be monitored for the development of secondary bacterial infections and treated with systemic antibiotics according to culture and susceptibility results.[18]

Differential Diagnosis

The differential diagnosis for eczema herpeticum includes impetigo, hand-foot-and-mouth disease, eczema coxsackium, primary varicella infection, disseminated herpes zoster, disseminated molluscum contagiosum, acute generalized exanthematous pustulosis, dermatitis herpetiformis, cellulitis, and erysipelas. Misdiagnosis of EH can lead to delayed initiation of antiviral treatment and subsequent complications. Diagnostic clues that favor EH are painful lesions, monomorphic size of the lesions, and characteristic "punched-out" erosions in areas of pre-existing atopic dermatitis. Unlike herpes zoster, EH does not respect dermatomal boundaries.

Prognosis

Eczema herpeticum is a potentially life-threatening disease with mortality risk due to complications of systemic viremia, bacteremia, and fungal infection leading to multi-organ failure.[19] Prior to the use of acyclovir, mortality

rates in EH patients were reportedly 10% to 50% [20] Since the widespread implementation of systemic antiviral treatment, mortality rates have decreased significantly.

A 2011 study of 1331 hospitalized pediatric EH patients in the United States found no deaths and concluded that the mortality rate of hospitalized patients is low. The median length of hospital stay was three days, with 9.2% of patients requiring hospitalization longer than one week, and 3.8% required ICU admission.[21] A study in 2018 of 4655 hospitalized children with EH found a mortality rate of 0.1%, with 98.1% of patients classified as minor mortality risk. Only 4.5% of patients were classified as having major loss of function, while 33.1% had moderate, and the majority had a minor loss of function.[13]

Complications

Potential complications of EH include cutaneous superinfection with *Staphylococcus aureus (S. aureus)*, *Streptococcus pyogenes*, and molluscum contagiosum virus.[22][23] The study by Aronson et al. found *S. aureus* infection in 30.3% of hospitalized pediatric EH patients with 9.2% due to methicillin-resistant *S aureus and* 3.9% with bacteremia. 86.4% of patients were treated with oral or intravenous antibiotics.[21] Additional complications include meningoencephalitis and herpetic keratoconjunctivitis, which can result in scarring and blindness.[4] Disseminated systemic infections of HSV leading to bone marrow suppression, disseminated intravascular coagulation, and death has been reported.[15]

Deterrence and Patient Education

Patients with eczema herpeticum should be counseled that they are infectious until all lesions have crusted over and thus avoid close contact with others until then. Encourage patients to avoid scratching and wash hands frequently due to the risk of autoinoculation. Patients diagnosed with mild EH and treated as outpatients should be cautioned to seek emergency care if they develop systemic symptoms or worsening rash, as they may require hospitalization, intravenous acyclovir treatment, or antibiotic coverage.

Enhancing Healthcare Team Outcomes

Eczema herpeticum is considered a medical emergency and should be treated promptly with systemic antivirals, as misdiagnosis and delay in treatment can result in serious complications. An ophthalmologic evaluation is warranted in cases of EH involving the face and eyelids. A dermatology consult may be beneficial to confirm the diagnosis. Clinicians should be aware of the risk factors associated with EH, including severe or poorly controlled atopic dermatitis, food and environmental allergies, asthma, the onset of atopic dermatitis before age five, and history of *S. aureus* and molluscum contagiosum infections.

Patients with systemic symptoms or widespread involvement should be promptly referred to the Emergency Department. To improve patient outcomes and prevent morbidity and mortality, healthcare providers should have a high index of suspicion for EH in patients with a history of atopic dermatitis presenting with a sudden onset, vesicular, monomorphic rash in areas of pre-existing dermatitis.

Continuing Education / Review Questions

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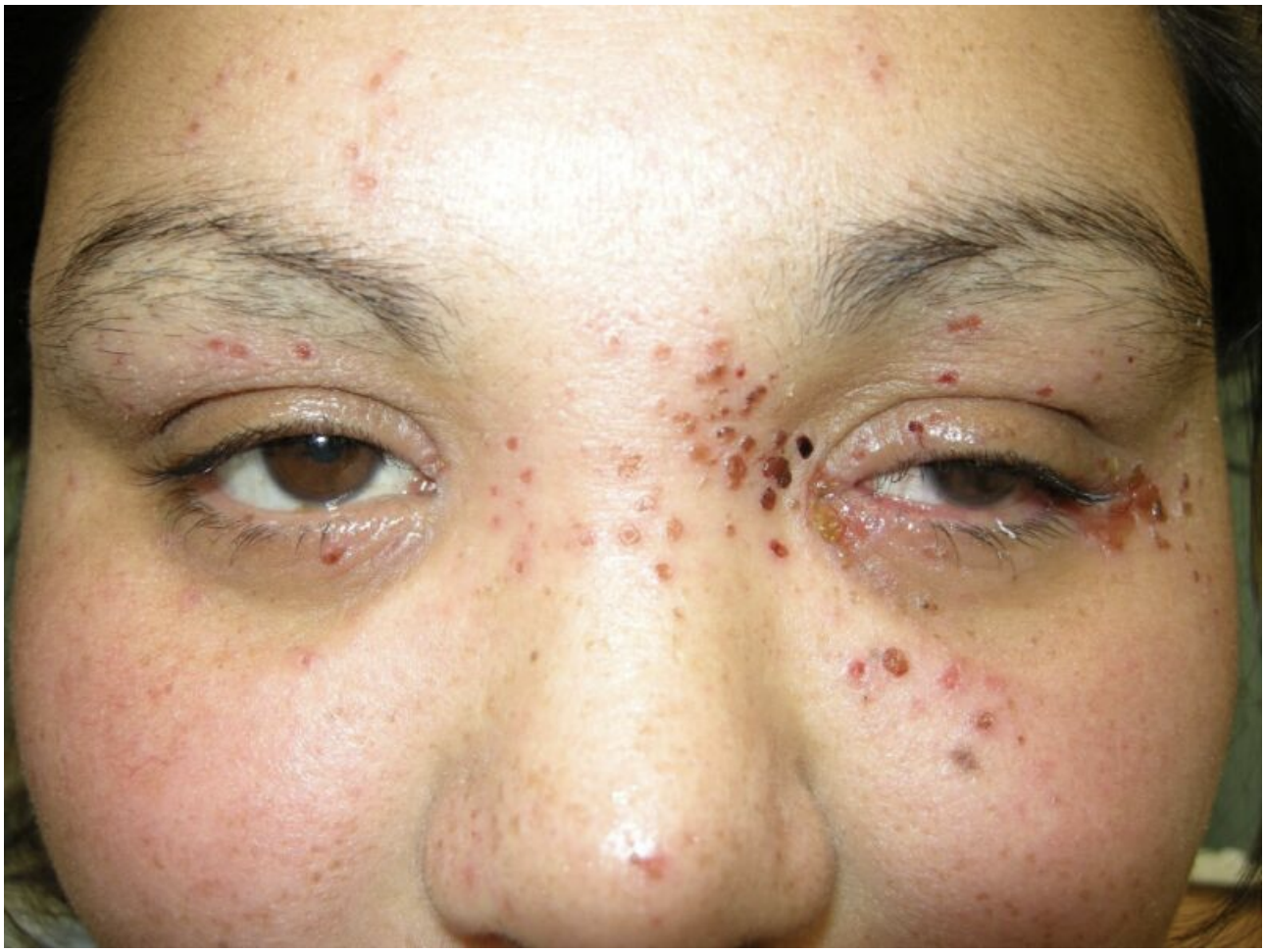
Figures



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