Autoeczematization: A Strange Id Reaction of the Skin

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PRACTICE **POINTS**

- Autoeczematization, or id reaction, is a disseminated reaction of the skin occurring at a site distant to a primary cutaneous infection or stimulus.
- T lymphocytes and keratinocytes are postulated to be involved in the pathogenesis of id reactions.
- Therapy includes treating the underlying pathology while providing topical corticosteroids for the autoeczematous lesions.

Autoeczematization, or id reaction, is a disseminated eczematous reaction that occurs due to a release of antigen(s) after exposure to a primary stimulus, with the eczema spreading to a site distant from the original one. This seemingly perplexing generalization most commonly is associated with stasis dermatitis or tinea pedis, though it may be caused by a wide variety of other disorders. We postulate that T cells are reactive to keratinocyte antigens that are produced during keratinocyte damage, which induce this autoeczematization. Studies with current technology are needed to facilitate further understanding of this phenomenon.

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Autoeczematization (AE), or id reaction, is a disseminated eczematous reaction that occurs days or weeks after exposure to a primary stimulus, resulting from a release of antigen(s). Whitfield[1] first described AE in 1921, when he postulated that the id reaction was due to sensitization of the skin after a primary stimulus. He called it "a form of auto-intoxication derived from changes in the patient's own tissues."[1] The exact prevalence of id reactions is unknown; one study showed that 17% of patients with dermatophyte infections developed an id reaction, typically tinea pedis linked with vesicles on the palms.[2] Tinea capitis is one of the most common causes of AE in children, which is frequently misdiagnosed as a drug reaction. Approximately 37% of patients diagnosed with stasis dermatitis develop an id reaction (Figure 1). A history of contact dermatitis is common in patients presenting with AE.[2-6]

Pathophysiology of Id Reactions

An abnormal immune response against autologous skin antigens may be responsible for the development of AE. Shelley[5] postulated that hair follicles play an important role in id reactions, as Sharquie et al[6] recently emphasized for many skin disorders. The pathogenesis of AE is uncertain, but circulating T lymphocytes play a role in this reaction. Normally, T cells are activated by a release of antigens after a primary exposure to a stimulus. However, overactivation of these T cells induces autoimmune reactions such as AE.[7] Activated T lymphocytes express HLA-DR and IL-2 receptor, markers elevated in the peripheral blood of patients undergoing id reactions. After treatment, the levels of activated T lymphocytes decline. An increase in the number of $CD25^+$ T cells and a decrease in the number of suppressor T cells in the blood may occur during an id reaction.[7-9] Keratinocytes produce proinflammatory cytokines, such as thymic stromal

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erythropoietin, IL-25, and IL-33, that activate T cells.[10-12] Therefore, the most likely pathogenesis of an id reaction is that T lymphocytes are activated at the primary reaction site due to proinflammatory cytokines released by keratinocytes. These activated T cells then travel systemically via hematogenous dissemination. The spread of activated T lymphocytes produces an eczematous reaction at secondary locations distant to the primary site.[9]

Clinical and Histopathological Features of Id Reactions

Clinically, AE is first evident as a vesicular dissemination that groups to form papules or nummular patches and usually is present on the legs, feet, arms, and/or trunk (Figure 2). The primary dermatitis is localized to the area that was the site of contact to the offending stimuli. This localized eczematous eruption begins with an acute or subacute onset. It has the appearance of small crusted vesicles with erythema (Figure 1). The first sign of AE is vesicles presenting near the primary site on flexural surfaces or on the hands and feet. A classic example is tinea pedis linked with vesicles on the palms and sides of the fingers, resembling dyshidrotic eczema. Sites of prior cutaneous trauma, such as dermatoses, scars, and burns, are common locations for early AE. In later stages, vesicles disseminate to the legs, arms, and trunk, where they group to form papules and nummular patches in a symmetrical pattern.[5,13-15] These lesions may be extremely pruritic. The pruritus may be so intense that it interrupts daily activities and disrupts the ability to fall or stay asleep.[16]

Histologically, biopsy specimens show psoriasiform spongiotic dermatitis with mononuclear cells contained in the vesicles. Interstitial edema and perivascular lymphohistiocytic infiltrates are evident. Eosinophils also may be present. This pattern is not unique to id reactions.[17-19] Although AE is a reaction pattern that may be due to a fungal or bacterial infection, the etiologic agent is not evident microscopically within the eczema itself.

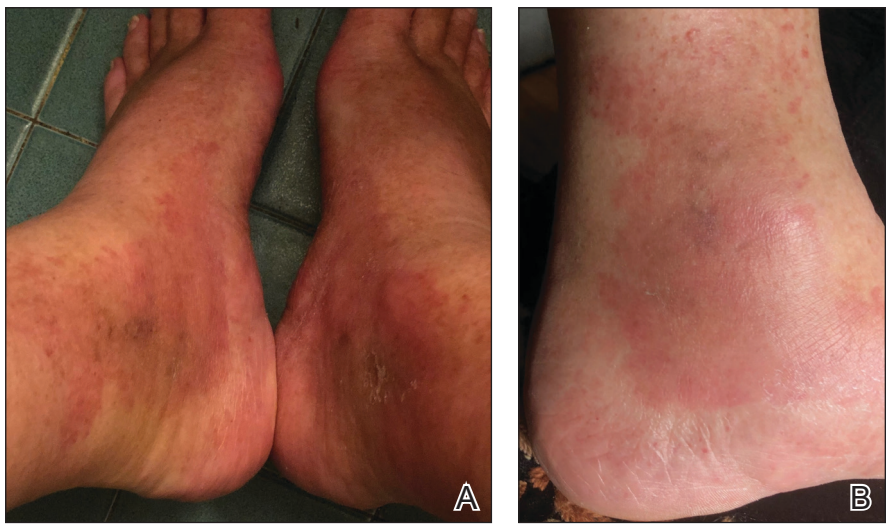

FIGURE 1. A and B, Stasis dermatitis with marked peripheral edema.

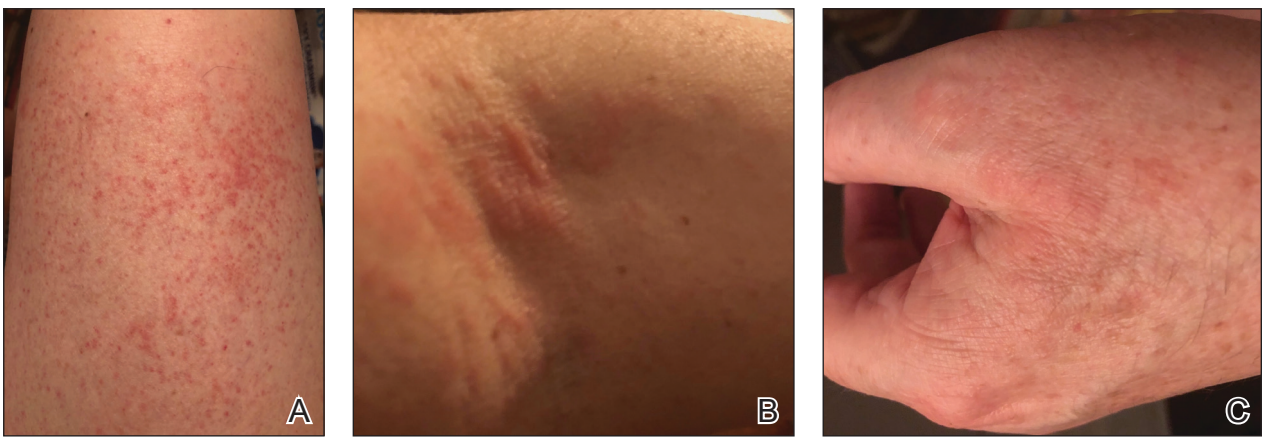

FIGURE 2. A, Id reaction on the leg and thigh. B, Id reaction on the antecubital fossa. C, Id reaction on the dorsal hand.

Etiology of Id Reactions

Id reactions most commonly occur from either stasis dermatitis or tinea pedis, although a wide variety of other causes should be considered. Evaluation of the primary site rather than the id reaction may identify an infectious or parasitic agent. Sometimes the AE reaction is specifically named: dermatophytid with dermatophytosis, bacterid with a bacterial infectious process, and tuberculid with tuberculosis. Similarly, there may be reactions to underlying candidiasis, sporotrichosis, histoplasmosis, and other fungal infections that can cause a cutaneous id reaction.[18,20-22] *Mycobacterium* species, *Pseudomonas*, *Staphylococcus*, and *Streptococcus* are bacterial causes of AE.[15,23-26] Viral infections that can cause an id reaction are herpes simplex virus and molluscum contagiosum.[27-29] Scabies, leishmaniasis, and pediculosis capitis are parasitic infections that may be etiologic.[14,30,31] In addition, noninfectious stimuli besides stasis dermatitis that can produce id reactions include medications, topical creams, tattoo ink, sutures, radiotherapy, and dyshidrotic eczema. The primary reaction to these agents is a localized dermatitis followed by the immunological response that induces a secondary reaction distant from the primary site.[17,18,32-38]

Differential Diagnoses

Differential diagnoses include other types of eczema and some vesicular eruptions. Irritant contact dermatitis is another dermatosis that presents as a widespread vesicular eruption due to repetitive exposure to toxic irritants. The rash is erythematous with pustules, blisters, and crusts. It is only found in areas directly exposed to irritants, as opposed to AE, which spreads to areas distant to the primary reaction site. Irritant contact dermatitis presents with more of a burning sensation, whereas AE is more pruritic.[39,40] Allergic contact dermatitis presents with erythematous vesicles and papules and sometimes with bullae. There is edema and crust formation, which often can spread past the point of contact in later stages. Similar to AE, there is intense pruritus. However, allergic contact dermatitis most commonly is caused by exposure to metals, cosmetics, and fragrances, whereas infectious agents and stasis dermatitis are the most common causes of AE.[40,41] It may be challenging to distinguish AE from other causes of widespread eczematous dissemination. Vesicular eruptions sometimes require distinction from AE, including herpetic infections, insect bite reactions, and drug eruptions.[18,42]

Treatment

The underlying condition should be treated to mitigate the inflammatory response causing the id reaction. If not skillfully orchestrated, the id reaction can reoccur. For infectious causes of AE, an antifungal, antibacterial, antiviral, or antiparasitic should be given. If stasis dermatitis is responsible for the id reaction, compression stockings and leg elevation are indicated. The id reaction itself is treated with systemic or topical corticosteroids and wet compresses if acute. The goal of these treatments is to reduce patient discomfort caused by the inflammation and pruritus.[18,43]

Conclusion

Id reactions are an unusual phenomenon that commonly occurs after fungal skin infections and stasis dermatitis. T lymphocytes and keratinocytes may play a key role in this reaction, with newer research further delineating the process and possibly providing enhanced treatment options. Therapy focuses on treating the underlying condition, supplemented with corticosteroids for the autoeczema.

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