DOI: http://dx.doi.org/10.3315/jdcr.2012.1124

Journal of Dermatological Case Reports

LETTER TO THE EDITOR

Application of dapsone 5% gel in a patient with dermatitis herpetiformis

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Dermatitis Herpetiformis (DH) is a rare, blistering skin disease described by Duhring in 1884.[1] DH is strongly associated with the HLA-DQ2 phenotype, a gateway in which dietary gluten reaches inflammatory cells and stimulates an autoimmune process. The etiopathogenesis involves IgA anti-endomysial antibodies directed against tissue transglutaminase (TG); the presumed skin autoantigen is epidermal TG. IgA/TG immune complexes form locally within the papillary dermis leading to neutrophil chemotaxis and degranulation (which forms neutrophilic abscesses), proteolytic cleavage disrupting the lamina lucida, and blister subepidermal blister formation.[2] Current standard-of-care for DH is oral dapsone and a gluten-free diet. We describe a teenage patient in whom resolution of lesions was achieved with adjuvant use of topical dapsone 5% gel (aczone), the first case in the literature.

A 14-year-old male had been suffering recurrent eruptions of blisters on his chest and arms for 16 months. He had been diagnosed with direct immunofluorescent proven DH based on granular IgA deposition in the upper papillary dermis. Though distinguishing LABD (linear IgA bullous dermatosis) from DH is often clinically impossible, the finding of IgA in a granular pattern at the dermoepidermal junction with accentuation in the dermal papillae was specific for DH in our patient. Upon an exacerbated eruption of blisters on the chest and shoulders, the patient presented to our clinic.

On physical examination he presented with multiple, well-defined, pink keratotic papules, plaques and diffuse, hypopigmented macules and patches on the chest and shoulders, equally distributed on the left and right side. Primary lesions were counted before treatment and numbered 33 on the left side and 34 on the right side of the chest, respectively.

The patient did not maintain a gluten-free diet and was receiving daily oral dapsone (25 mg). Twice daily application of topical dapsone (Aczone gel, 5%) was initiated on the right side of the patient's chest and Aquaphor ointment to the left. Two physicians were blinded to which side received the medication. The patient was asked to follow up in four weeks.

Over the following three days the patient's skin lesions did not improve on either side of the chest. The oral dosage of dapsone was modified to 25 mg and 50 mg on alternating days. The patient continued to apply the topical products unilaterally as originally prescribed. On a follow-up visit four weeks later, the blinded physicians observed improvement of the lesions on the right side of his chest in comparison to the left. Physical exam demonstrated two remaining ulcerated vesicles on the right chest and five on the left without signs of erosion. It was also noted that relative to the left side, the skin on the right side was significantly smoother. The patient was then allowed to expand usage of topical dapsone to all affected areas and had similar improvements.

There have been no reports on treating dermatitis herpetiformis using topical dapsone and the current standard-of-care remains oral dapsone. Most clinical remissions are related to dietary gluten restriction, however, the gluten-free diet is inconvenient and unacceptable to some patients. Oral dapsone (diaminodiphenylsulfone) is the current treatment and the most effective sulfone but many physicians would prefer a non-systemic treatment choice. Though patients intolerant to dapsone may consider therapy with sulfapyridines, there is significant risk for nephrolithiasis and some patients may not respond at any dose. Although this patient had received oral and topical dapsone simultaneously, he only applied topical dapsone 5% gel to the right side, the same side which demonstrated significant improvement of the lesions. The left side where aquaphor was applied did not show the same level of improvement at four-week follow-up.

High doses of oral dapsone simply increase toxicity while providing minimal benefit. The main side effects associated with oral dapsone may be classified as toxic/pharmacologic

or idiosyncratic/allergic; these range from hemolytic anemia, the most common complication within 2 weeks after starting therapy, to nephritis and renal failure, precluding the need for strict monitoring of renal function tests.[3] Hemolytic anemia occurs in virtually every patient on oral therapy and may even occur in breastfed infants since dapsone is secreted in breast milk. A notable complication, especially in patients with glucose-6-phophate dehydrogenase (G6PD) deficiency, is hemolysis and methemoglobinemia due to oxidative stress from the hydroxylamine metabolite.[4] Adverse effects of dapsone are generally dose-dependent and are more commonly observed in patients with comorbid conditions such as anemia and cardiopulmonary disease.[3] Other rare complications include agranulocytosis early on, as well as a systemic drug hypersensitivity syndrome, a serious complication that requires medication withdrawal and systemic corticosteroid administration.[5] Regular follow-up visits and routine laboratory monitoring of blood counts are needed for patients receiving treatment with oral dapsone, especially during the first 3 months.[5]

Dapsone is clinically useful in diseases containing neutrophilic infiltrates. Dapsone inhibits neutrophil myeloperoxidase, decreasing the damage from the neutrophil respiratory burst pathway mediated by this enzyme. The anti-inflammatory properties of topical dapsone benefit patients with acne and could also hinder the immunologic cascade and accompanying inflammatory process that occurs in DH. We attribute the efficacy of topical dapsone to a local inhibition of neutrophil chemotaxis to N-formyl-methionyl-leucyl-phenylalanine and interference of the CD11b/CD18-mediated neutrophil binding that induces chemoattractant signal transduction and inhibits leukotrienes. IgA adherence may also be inhibited though it remains to be proven.[5]

Concerning our review of the literature, we conclude that there is therapeutic explanation for the moderate therapeutic effects seen from use of topical dapsone in DH. Using topical dapsone alone or in combination with a lower dose of oral dapsone is preferable to high doses of oral dapsone. Additionally, facial disease may prove refractory to oral dapsone therapy; topical dapsone gel may provide a more tolerable alternative than breaking facial vesicles and applying a potent corticosteroid gel. In order to further study the utility of topical dapsone in DH, a more extensive trial of topical dapsone is warranted. In summary, aczone appears to be a promising therapeutic agent for patients with dermatitis herpetiformis who are refractory to oral therapy and noncompliant with a gluten-free diet.

References

1. Duhring LA. Landmark article, Aug 30, 1884: Dermatitis herpetiformis. By Louis A. Duhring. *JAMA*. 1983; 250: 212-216. PMID: 6345814.
2. Farrell RJ, Kelly CP. Celiac sprue. *N Engl J Med*. 2002. 346: 180-188. PMID: 11796853.
3. Caproni M, Antiga E, Melani L, Fabbri P, Italian Group for Cutaneous Immunopathology. Guidelines for the diagnosis and treatment of dermatitis herpetiformis. *J Eur Acad Dermatol Venereol*. 2009; 23: 633-638. PMID: 19470076.
4. Thiboutot DM, Willmer J, Sharata H, Halder R, Garrett S. Pharmacokinetics of dapsone gel, 5% for the treatment of acne vulgaris. *Clin Pharmacokinet*. 2007; 46: 697-712. PMID: 17655376.
5. Zhu YI, Stiller MJ. Dapsone and sulfones in dermatology: overview and update. *J Am Acad Dermatol*. 2001; 45: 420-434. PMID: 11511841.