Two Cases of Dermatitis Herpetiformis Successfully Treated with Tetracycline and Niacinamide

Dear Editor,

Dermatitis herpetiformis (DH) is a chronic, polymorphic, pruritic autoimmune blistering skin disease characterized by subepidermal blisters, neutrophilic microabscesses, and granular IgA deposition within the dermal papillae. DH is classified as a cutaneous manifestation of coeliac disease, a type of gluten-sensitive enteropathy (1). The treatment of DH includes dapsone and a gluten-free diet (GFD). Other therapies should be considered in patients who are unable to tolerate dapsone, including sulfapyridine and glucocorticoids. Herein we present two cases of DH with good responses to tetracycline and niacinamide combination therapy.

Case 1 was a 42-year-old man who was admitted to our hospital with a 3-year history of recurrent pruritic papules and bullous lesions involving the trunk and upper limbs. On examination, the patient showed disseminated erythematous papules on the upper limbs and back as well as vesicles. Nikolsky's sign for vesicles was negative (Figure 1, a-c). The results of routine blood examinations were within normal ranges. He did not have a history of chronic

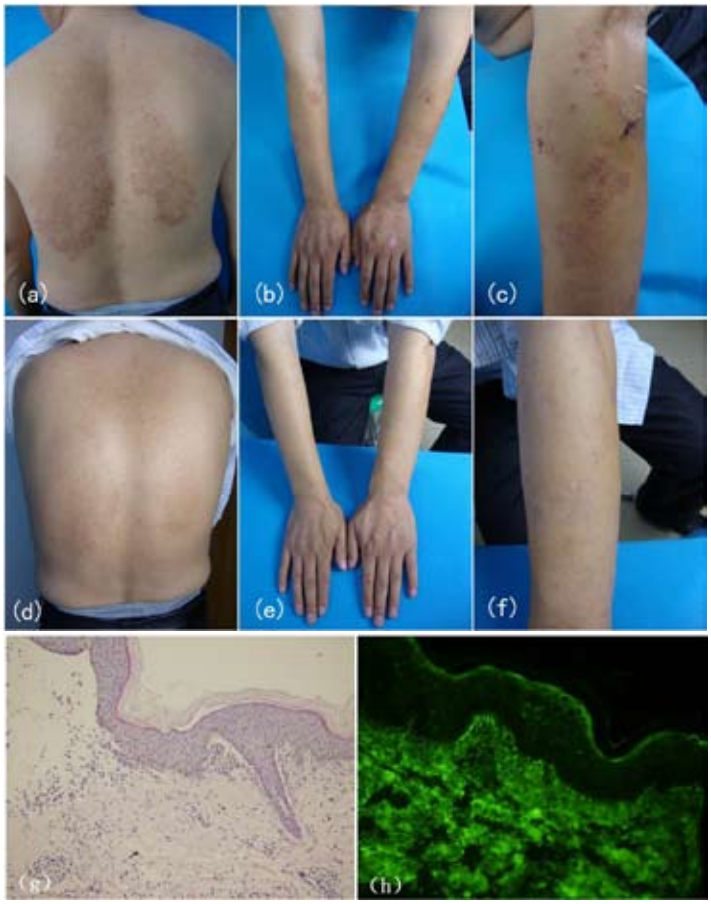

Figure 1. Clinical appearance before treatment (a, b, c) and after 2 weeks of treatment (d, e, f) in case 1. Subepidermal blisters and accumulation of neutrophils at the papillary dermis of the involved skin. (g) (hematoxylin and eosin, ×400). Direct immunofluorescence revealed fibrillar deposition of IgA on the dermal papillae (h).

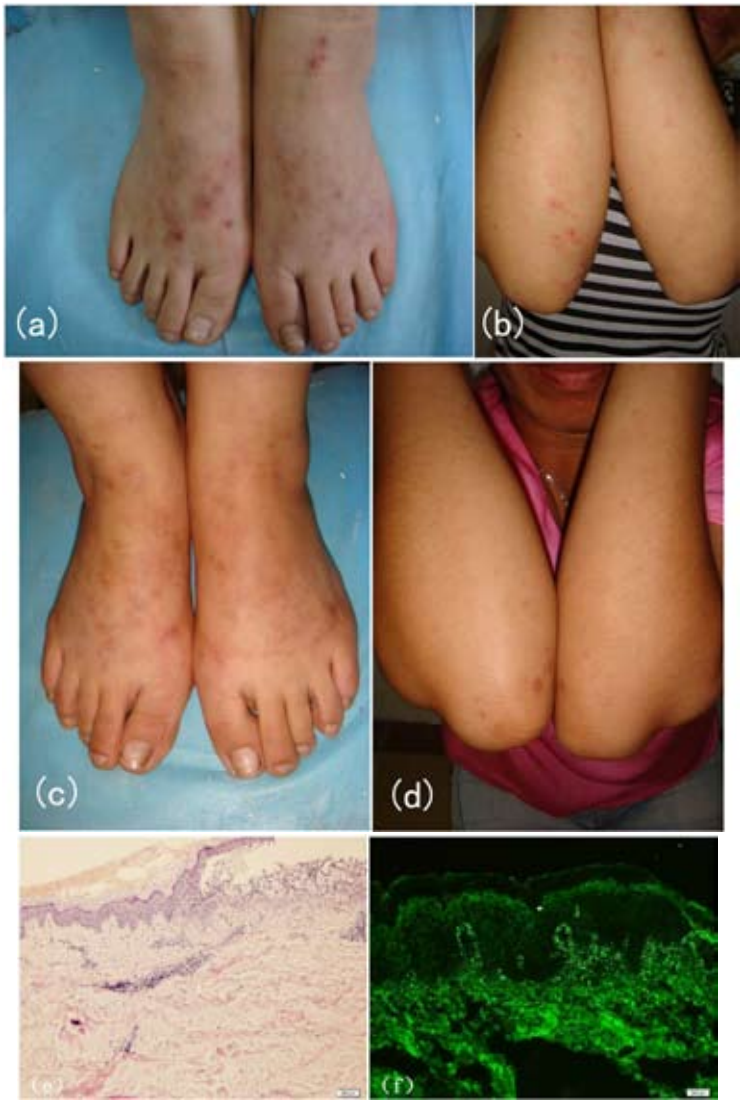

Figure 2. Clinical appearance before treatment (a, b) and after 1 month of treatment (c, d) in case 2. Subepidermal blisters and neutrophil infiltration at the upper dermis (e) (hematoxylin and eosin, ×400). Direct immunofluorescence revealed granular deposition of IgA on the dermal papillae (f).

diarrhea. The histologic examination showed subepidermal blisters and accumulation of neutrophils at the papillary dermis of the involved ski. Direct immunofluorescence revealed fibrillar deposition of IgA on the dermal papillae (Figure 1. g, h).

Case 2 was a 34-year-old woman who had a history of skin rash and pruritic lesions predominantly involving the arms and legs, which had been present for 10 months. She had been treated with prednisone (30 mg daily) with improvement; however, the lesions reappeared when the prednisone was discontinued. She had a history of constipation. On physical examination, the skin lesions manifested as erythematous papules, vesicles, and scabs on the limbs (Figure 2. a-c). She felt apparently pruritic. The histologic examination of the biopsy identified subepidermal blisters with a neutrophil infiltrate in the upper dermis. Direct immunofluorescence revealed granular deposition of IgA on the dermal papillae (Figure 2. e, f). The results of routine blood examinations were within normal ranges, with the exception of elevated IgE concentration (222.5 ku/L (normal range, 0-100 ku/L)).

The clinical manifestations and histologic and immunofluorescence examinations of the two cases confirmed the diagnosis of DH. The two patients were subsequently started on a strict GFD. At that time, dapsone was not available in the hospital. The patients were treated with oral tetracycline (500 mg four times daily) and nicotinamide (500 mg three times daily). The rash affecting case 1 resolved entirely in 2 weeks. The patient discontinued the medications after 6 months, and occasionally presented with a few

pruritic papules and vesicles, but the lesions resolved within 1 week. The lesions affecting case 2 completely healed within 1 month. The patient continued taking those medications and no recurrence of the skin lesions occurred during 2 years of follow-up.

Dapsone is considered first-line therapy for patients with DH (2). Recent findings have shown dapsone and lower dosages of sulfasalazine combination therapy in DH are effective and well-tolerated (3). Alternative monotherapeutic agents in mild autoimmune bullous diseases such as DH include a tetracycline group of antibiotics with niacinamide or its derivatives as well as sulfasalazine. Because dapsone is difficult to obtain in China except for patients with leprosy, we treated the patients with tetracycline and nicotinamide. To our knowledge, only a few cases of DH have been successfully treated with oral tetracycline and niacinamide (2,4). One of the patients was also prescribed heparin (4). Tetracycline has anti-inflammatory properties due to the inhibition of metalloproteinase activity and mast cell activation (5). Nicotinamide is a potent modulator of several pro-inflammatory cytokines. Nicotinamide can inhibit cytokine release (IL-1, IL-6, IL-8, and TNF-α) from immune cells, inhibit chemotaxis and degranulation of immune cells, inhibit lymphocyte blast transformation, and suppress T-cell activity (6). The non-antibiotic properties of tetracycline in combination with nicotinamide may participate in inhibition of antibody formation, modulation of pro-inflammatory cytokines, inflammatory cell accumulation, lymphocyte transformation, and T-cell activation.

In summary, we reported two typical cases of DH that were successfully treated with oral tetracycline and niacinamide, which completely healed the rash and relieved the symptoms within 1 month. The combination of tetracycline and nicotinamide can be recommended as a useful therapy for patients where dapsone is not available or for patients who do not tolerate dapsone.

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