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Wells Syndrome: Response to Dapsone Therapy

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Dear Editor:

Eosinophilic cellulitis, known as Wells syndrome (WS), is a rare recurrent inflammatory skin condition that was first described by Wells in 1971[1]. A number of therapies have been reported since then, including systemic and topical corticosteroids, cetirizine, interferon-α, griseofulvine, cyclosporine, and antimicrobial agents, with variable results. We report a case of WS that responded to treatment with dapsone.

A 67-year-old woman presented with a severely itching rash, consisting of urticaria-like, infiltrating, red-violet plaques on the upper and middle back, abdomen, thighs, and submammary region (Fig. 1A). She reported having recurrent lesions during winter for the last 3 years. She denied any associated symptoms, drug intake, or insect bites. Her medical history included chronic obstructive pulmonary disease. In the past, she had been investigated for urticaria, with negative skin prick tests and radioallergosorbent test.

Complete blood count analysis revealed 19.8% eosinophils (reference range, 0%～2%). Level of eosinophil cationic protein was elevated in peripheral blood (192 μg/L; reference, $<$4.4 μg/L). Levels of urea and electrolytes, antinuclear antibodies, anti-DNA, and C3 and C4 complement, as well as the results of liver function tests and chest radiography were normal. A skin biopsy (Fig. 2) revealed a deep perivascular infiltration of lymphocytes and innumerable eosinophils. Collections of eosinophils with eosinophilic granules (flame figures) among collagen bundles were noted. On the basis of the clinical and histological findings, a diagnosis of WS was established. As the patient had received several courses of prednisolone in the past without any improvement, dapsone was initiated at a dose of 100 mg daily. She responded to this treatment within 2 weeks (Fig. 1B). Subsequently, the dose of dapsone was tapered to 50 mg daily for the next 6

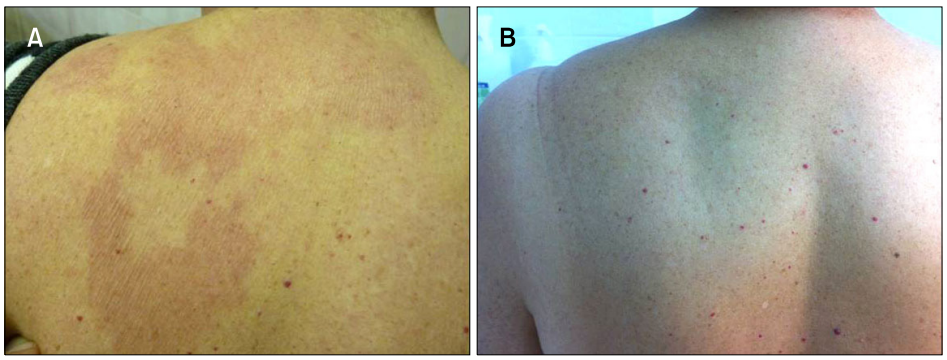

Fig. 1. (A) An indurated red-violet plaque on the upper back upon admission. (B) Clearance of eruption two weeks after the administration of dapsone 100 mg/day.

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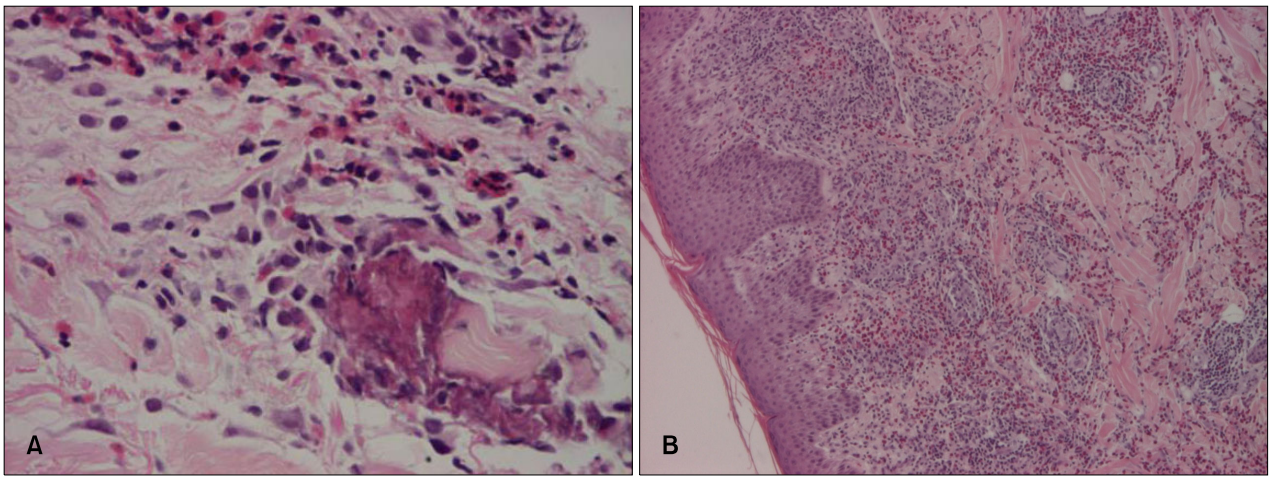

Fig. 2. (A) The presence of a "flame figure" is demonstrated in a diffuse infiltrate of eosinophils at the lower dermis (H&E, ×200). (B) Severe and diffuse dermal infiltrate of eosinophils and less in number lymphocytes and histiocytes (H&E, ×100).

months, with further clinical improvement and reduction of eosinophils (9%). The therapeutic regimen of dapsone was then modified to a dose of 50 mg administered thrice every week. At the last follow-up, 2 years after the initiation of treatment, she did not show the presence of lesions, eosinophils were within normal limits (2%), and the treatment was ceased. No adverse reactions were noted during this period. WS is primarily a disease in adults of any race and sex[2]. The etiology is unknown. However, there are several precipitating factors including insect bites; bacterial, viral, and parasitic infestations; and any type of drug. The disease usually presents with a mildly pruritic or tender cellulite-like eruption, with typical histological features characterized by edema, flame figures, and marked infiltration of eosinophils in the dermis. The management of WS is difficult and poses a therapeutic challenge.

The efficacy of dapsone in WS has been poorly reported in the literature[3,4].

The exact mode of action of dapsone in WS is still unclear. It has antimicrobial, anti-inflammatory, and immunomodulating properties. It is known for its anti neutrophilic action through an inhibitory effect on myeloperoxidase. Additionally, it has been shown to inhibit of eosinophil peroxidase, which is a cytotoxic granule protein of eosinophils that induces mast cell degranulation[5]. Mast cells produce interleukin (IL)-5, a key mediator in eosinophil activation. IL-5, originally discovered as an eosinophilic colony-stimulating factor, is a major regulator of eosinophil accumulation in tissues that can modulate eosinophil behavior at every stage, from maturation to survival. Considering that eosinophils are the primary IL-5RA-expressing cells, the above mentioned properties of dapsone might account for its beneficial effects in the therapy of WS.

Dapsone is effective and well tolerated in low doses by most patients. In addition, it is inexpensive and safer for long-term treatment compared with corticosteroids and other immunosuppressive agents. Our data suggest that dapsone at low doses can be used for long periods to control long-term WS.

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