

LETTER TO THE EDITOR

Long-term complete resolution of severe chronic idiopathic urticaria after dapsone treatment

Dear Editor,

Chronic urticaria is diagnosed when wheals are present on most days for more than 6 weeks. According to the guidelines from Europe and Japan, chronic urticaria is initially treated with non-sedating H1 antihistamines, and then up dosing and the addition of sedating H1 antihistamines or antileukotrienes are considered if patients are unresponsive to initial therapy.^{1,2} Only for refractory cases to these agents, second-line agents, including dapsone, may be added while they have low levels of evidence for efficacy.^{1,2} When we reviewed published work on PubMed, dapsone has been used with a good response rate for a certain subset of refractory cases in a small non-blinded trial and case series.^{3–5} Although anemia and liver dysfunction can occur with dapsone use, this agent has been well tolerated and only mild nausea was reported in these previous studies.^{3–5} Despite these favorable properties for treatment, long-term complete resolution of urticarial symptoms with dapsone has been rarely reported. We herein report a case of chronic idiopathic urticaria with long-term complete response to dapsone even after the discontinuation of treatment.

A 45-year-old Japanese woman presented with a 1-year history of persistent itchy wheals involving her trunk and extremities (Fig. 1). An individual wheal persisted for less than 24 h. No precipitating factors were identified. Skin biopsy showed perivascular neutrophilic infiltration and dermal edema (Fig. 2). Fibrinoid degeneration, leukocytoclasia and extravasation of erythrocytes were not evident. Because widespread wheals persistently developed despite 1-year combination therapy of H1 and H2 antihistamines (olopatadine 10 mg/day, bepotastine 20 mg/day and ranitidine 300 mg/day), we added dapsone 50 mg/day and then increased the dose to 75 mg/day. Wheals completely disappeared 2 months after the initiation of dapsone. Thus, we gradually reduced the dose over 7 months and finally discontinued dapsone. No adverse reaction was observed throughout the course of dapsone treatment. Antihistamines were also withdrawn afterwards. During the 1-year follow-up period without any medication, no relapse was noted.

Dapsone, one of the sulfones, is effective for dermatoses with abnormal neutrophil infiltration, such as dermatitis herpetiformis, pemphigus vulgaris, pyoderma gangrenosum and Sweet's syndrome.⁶ Dapsone exerts anti-inflammatory effects through inhibiting neutrophil chemotactic migration, protecting cells from neutrophil- and eosinophil-mediated injury, and reducing the release of prostaglandins and leukotrienes.⁶ Interestingly, in the present case, dapsone achieved long-term complete resolution of urticaria. A recent study demonstrated that 3 months of the combination therapy with dapsone 50 mg/day and desloratadine 10 mg/day

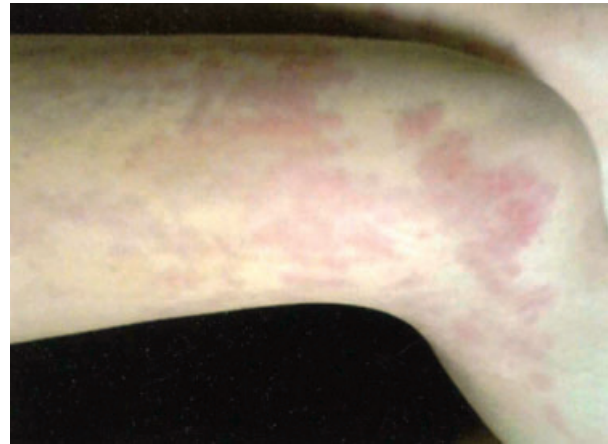


Figure 1. Wheals on the right leg.

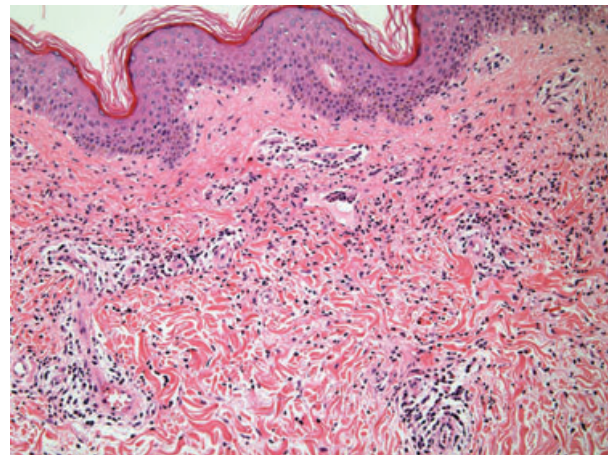


Figure 2. Skin biopsy shows perivascular neutrophilic infiltration and dermal edema (hematoxylin–eosin, original magnification $\times 200$).

achieved significantly greater reduction in urticaria activity as compared with desloratadine alone.⁴ In the same study, nine out of 38 patients treated with the combination therapy had complete remission while none achieved complete resolution in a group treated with desloratadine alone. Furthermore, five out of the nine complete responders did not experience relapses 3 months after dapsone withdrawal. Another study showed that nine out of 11

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patients treated with dapsone 25 mg/day and cetirizine 10 mg/day had a complete response within 3 months of treatment.³ Although these studies suggest the efficacy of dapsone in urticarial patients unresponsive to antihistamines, the effect of dapsone longer than 3 months after the withdrawal has not been well studied. Our patient experienced no recurrence during the 1-year follow-up period despite the complete discontinuation of treatment, including antihistamines. This result indicates that dapsone could have modified the disease course in this case.

In the present case, wheals were cleared 2 months after the initiation of dapsone. Engin *et al.*⁴ reported that only four out of 38 patients responded to dapsone at the first month, but finally 36 patients showed complete or partial response up to 3 months. Thus, at least 2–3 months of therapy is required to fully clarify the response to dapsone. Only a short-term use of dapsone may lead to a discouraging result.

Histopathologically, perivascular infiltrating cells were mainly composed of neutrophils in the present case. Dapsone appears to reduce a neutrophil adherence function mediated by integrins, and thus inhibits neutrophil migration to extravascular sites.⁷ We speculate that wheals disappeared because dapsone inhibited the perivascular recruitment of neutrophils. Importantly, Criado *et al.*⁵ reported that all of three urticaria patients with predominantly neutrophilic infiltrates showed complete response to dapsone during 30–90 days. Taken together, dapsone seems to be a good therapeutic option for chronic idiopathic urticaria especially

when histopathology shows neutrophil-rich infiltration. A proper clinical trial is required to obtain a higher evidence level.

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