

Prospective study of urticaria after diphencyprone therapy in patients with viral warts

Topical diphencyprone (DCP) therapy has been shown to be effective in the treatment of both viral warts and alopecia areata. Most side-effects of topical DCP therapy are mild, but severe reactions can sometimes require discontinuation of therapy. To investigate urticaria as a side-effect of topical DCP therapy, we made a prospective analysis of 83 patients treated with DCP for viral warts in Korea University Ansan Hospital from January 2005 to February 2006.

Information regarding age, gender, side-effects of topical DCP therapy, duration of treatment prior to urticaria, and duration of urticaria were evaluated. Follow-up in the case of urticaria was performed in our department or by the author using a telephone questionnaire. Patients were sensitized using a 1% solution of DCP in acetone applied to a 1-cm² area of skin on the inner upper arm. DCP was then applied to all the warts using a cotton bud and treated areas were dressed for 12 h to avoid passive transfer. Routine visits for examination and treatment were at intervals of 1–2 weeks and the concentration of DCP was tailored to each individual, according to response or side-effect.

We present a series of 10 patients who showed widespread urticaria induced mainly spontaneously after topical DCP therapy. Our series was comprised of eight men and two women, with a mean age of 24 years (range 9–51) and their symptoms persisted for a relatively long time (mean time 11 weeks, range 4–40) in spite of discontinuance of DCP and daily administration of oral antihistamine (Table 1). The mean time from sensitization with DPC to development of urticaria was 6.7 weeks (range 2–17) and 8 patients developed chronic urticaria with marked dermatographism (Fig. 1). During therapy, severe eczema/blister formation was observed, but vitiligo, persistent hypo/hyperpigmentation, and erythema multiforme-like reactions were not observed.

All our patients showed widespread urticaria which developed at distant sites as well as the sites of DCP application and did not start at the application site. We agree with



Figure 1 Severe dermatographism at a site distant to treatment site after 0.1% DCP therapy for periungual warts (patient 1)

the proposal of Francomano *et al.* that this phenomenon is not a contact urticaria.¹

To our knowledge, only five papers have been reported in the English literature on urticaria as a side-effect of topical DCP therapy for alopecia and viral warts.^{1–4} Although most papers have suggested that urticaria is a rare side-effect of topical DCP therapy, the data from our patients suggest that urticaria may be a long-lasting side-effect and not rare.

Although the pathophysiology of chronic urticaria remains unclear, some authors suggest that products of the activated immune system can lower the threshold of release of the cutaneous mast cells.⁵ Our hypothesis is that DCP therapy may activate immune system in patients treated with DCP and induce urticaria in the high prevalence. We could find no difference demographically and clinically between those patients who did and did not develop urticaria. Further investigations are needed to investigate immunologic or genetic differences between those patients.

Table 1 Demographics and clinical features of the patients who showed urticaria after topical DCP therapy

Patient	Sex/age	Duration of treatment prior to urticaria (weeks)	Duration of urticaria (weeks)
1	M/10	2	10
2	F/9	6	8
3	M/10	5	12
4	M/51	3	6
5	M/9	6	4
6	F/42	4	5
7	M/35	5	8
8	M/39	17	10
9	M/11	5	6
10	M/17	14	40

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Letter to the Editor: Vitiligo: auto-immunity and immune responses

Dear Sir,

I recently read the paper entitled: "Vitiligo: auto-immunity and immune responses" by Sehgal and Srivastava, published in the May 2006 edition of *International Journal of Dermatology*.¹

I was impressed by the title of paper and was hoping that it would neatly and methodically present to the readers our current status of knowledge regarding the pathogenesis of vitiligo.

Unfortunately, the paper comprises a long series of poorly connected statements highlighting recent research findings related to the immune pathogenesis of vitiligo, and to a lesser extent certain recent data about genes implicated in vitiligo. There is little in the way of logical progression of ideas and individual statements are poorly linked to each other, many appearing as random remarks. This is most apparent in the (important) section entitled "Lymphocyte studies." The authors supply the reader with a stream of research findings related to cutaneous lymphocyte infiltrates in vitiligo, but fail to convey the central role of cytotoxic T cell-mediated melanocyte destruction, which is now well-established.²

This was an opportunity for the authors to explain with some degree of lucidity how (in accordance with our current understanding of this patchily explored field) the various immunological findings/defects may contribute to the larger picture. That is, how the immune limb of the pathogenetic pathway might work in concert with the other limbs (genetic, neurogenic, biochemical, etc.) to effect melanocyte destruction.

There is, for example, increasing evidence that suggests the following paradigm:

- 1 Genetic polymorphism/mutation leads to structural/functional alterations in epidermal melanocytes, for example, alterations in rough endoplasmic reticulum and melanosomes, and impairment of calcium transport.³
- 2 Genetic mutations and HLA polymorphisms lead to dysregulated immune function that ultimately leads to overactivity of cytotoxic CD8+ T cells² and the elaboration of antimelanocyte antibodies.

- 2 Short KA, Higgins EM. Urticaria as a side-effect of diphenylcyclopropenone therapy for resistant viral warts. *Br J Dermatol* 2005; 152: 583–585.
- 3 Alam M, Gross EA, Savin R. Severe urticarial reaction to diphenylcyclopropenone therapy for alopecia areata. *J Am Acad Dermatol* 1999; 40: 110–112.
- 4 Skrebova N, Nameda Y, Takiwaki H, *et al*. Severe dermographism after topical therapy with diphenylcyclopropenone for alopecia universalis. *Contact Dermatitis* 2000; 42: 212–215.
- 5 Schocket AL. Chronic urticaria: pathophysiology and etiology, or the what and why. *Allergy Asthma Proc* 2006; 27: 90–95.

- 3 Genetic alterations lead to imbalances in the redox status of certain cells with the result of increasing potentially hazardous free radicals.⁴

Therefore, a plausibly weakened melanocyte is left at the mercy of various immunological and biochemical killing mechanisms.

Since a concordance of only 23% is seen in monozygotic twins,⁵ it should be borne in mind that there must be a strong environmental/nongenetic component to the causation of vitiligo. Indeed, in a certain avian model of vitiligo, a herpes-virus is implicated as the etiological agent.⁶

There is no doubt that the pathogenesis of vitiligo is a complex story, only partly unraveled. For the benefit of would-be researchers and those with a desire to learn and explore more, it is imperative that papers reviewing important data covering mechanistic and pathogenetic themes are clear and instructive.

Sincerely,

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- 2 Steitz J, Bruck J, Lenz J, *et al*. Peripheral CD8+ T cell tolerance against melanocytic self-antigens in the skin is regulated in two steps by CD4+ T cells and local inflammation: implications for the pathophysiology of vitiligo. *J Invest Dermatol* 2005; 124: 144–150.
- 3 Boissy RE, Liu YY, Medrano EE, *et al*. Structural aberration of the rough endoplasmic reticulum and melanosome compartmentalization in long-term cultures of melanocytes from vitiligo patients. *J Invest Dermatol* 1991; 97: 395–404.