

Vitiligo as an Adverse Reaction to Topical Diphenycprone

Dear Editor,

Diphenycprone (DCP) is a contact sensitiser used to treat dermatological conditions resulting from an altered immunological state, such as extensive alopecia areata. Adverse effects include local eczema with blistering, regional lymphadenopathy and contact urticaria. Rare adverse effects include an erythema multiforme-like reaction, hyperpigmentation, hypopigmentation and vitiligo. We report 4 patients with alopecia areata who developed the rare side-effect of vitiligo following DCP immunotherapy (Table 1).

The patients' ages ranged from 12 to 67 years old, with the mean duration of DCP therapy before the onset of vitiligo being 10.5 months. Most of the patients had previously failed intralesional triamcinolone therapy, except for patient 3 who had been started on SABDE (squaric acid dibutyl ester) and subsequently DCP because of her young age and extent of alopecia. The typical concentration of DCP used was variable, with vitiligo developing with concentrations as low as 0.0001% in patient 2. Vitiligo was preceded by contact dermatitis of the scalp in patient 2, but not in the other patients. Vitiligo involved sites distant from the location of DCP application in 2 out of 4 patients

(patient 2 and 3). DCP was discontinued in all patients except patient 1. Patient 1 was not keen to stop DCP as she felt that her alopecia areata was improving with the current treatment.

Patients 1, 2 and 4 had phototherapy as first-line treatment, with patient 1 receiving psoralen combined with ultraviolet A (PUVA), and patient 2 and 4 receiving narrow-band ultraviolet B (NBUVB) therapy (Table 2). Patient 3 was initially treated with systemic steroids due to the rapidly progressing and extensive vitiligo at both the sites of local DCP application and distant sites (periorbital area, neck, limbs and abdomen) (Fig. 1). She was switched to NBUVB after 2 months as her vitiligo did not improve with steroid therapy.

Patients 1 and 2 had good responses to phototherapy, with significant follicular repigmentation after 3 months of treatment. Patient 3 had good response for lesions on the face and neck, but repigmentation of acral sites was poor. Patient 4 had poor response to NBUVB even after 6 months of treatment, and phototherapy was discontinued. She was offered PUVA therapy but declined as she was not keen to trim her scalp hairs to allow topical psoralen application. For patients who responded well, a maintenance phase was

Table 1. Clinical Characteristics of Patients with Vitiligo following Diphenycprone Therapy

Patient	Age	Sex	Race	Duration of DCP therapy before onset of vitiligo	Last concentration of DCP used before developing vitiligo	Distant sites involved?	DCP stopped?
1	54	Female	Indian	9 months	0.05%, 2 coats	No	No
2	67	Male	Chinese	11 months	0.0001%, 1 coat	Yes - upper trunk, arms, legs	Yes
3	12	Female	Malay	10 months	0.01%, 2 coats	Yes - periorbital area, neck, abdomen, limbs	Yes
4	57	Female	Chinese	12 months	0.05%, 2 coats	No	Yes

Table 2. Patients' Response to Therapy for DCP-induced Vitiligo

Patient	Treatment received	Response	Time to initial repigmentation	Percentage of improvement (%)	Progress after phototherapy completed
1	Topical PUVA	Good follicular repigmentation	3 months	60-70	Improved
2	NBUVB	Good follicular repigmentation	3 months	50-60	Improved
3	Failed systemic steroids NBUVB	Good repigmentation at face and neck Poor repigmentation at acral sites and abdomen	2 months	40-50 (face and neck) 10-20 (acral sites, abdomen)	Stable (all sites)
4	NBUVB	Poor repigmentation	6 months	<5	Stable



Fig. 1. DCP-induced vitiligo occurring at a remote site (the neck).

instituted with the gradual tapering of the dosage and frequency of phototherapy.

Discussion

DCP-induced vitiligo is rare and may represent a Koebner phenomenon in predisposed individuals.¹ The initial depigmented patch usually arises on the site of DCP application. Electron microscopic studies have confirmed that the depigmentation is not post-inflammatory, supportive of the isomorphic phenomenon.² This is supported in our series as only 1 patient (patient 2) had contact dermatitis due to DCP application directly preceding the development of vitiligo. However, a chemical leucoderma has been noted to occur as a result of DCP-induced dermatitis.² Also, the concentration of DCP applied does not appear to affect whether the patient develops vitiligo. Patients have been known to develop vitiligo even with low DCP concentrations (e.g. following 0.0001% DCP in patient 2). Alopecia areata is known to be associated with vitiligo even in patients who do not undergo DCP therapy, and DCP may be an agent which unmasks vitiligo in these susceptible individuals.

Connubial vitiligo has been reported due to passive transfer of DCP to susceptible partners.³ Guttate hypo- and hyper-pigmentation ('dyschromia in confetti') can also occur.⁴ In some cases, vitiligo appears on body sites distant to the site of application; this has occurred in our second and third patient. The pathogenesis of this phenomenon is not known but it has been postulated that the contact

sensitiser may have induced vitiligo through a direct cytotoxic effect on the melanocytes following systemic absorption. Alternatively, the sensitiser may have "unmasked" latent vitiligo as a result of the Koebner phenomenon.⁵

Conclusion

Vitiligo is a rare but recognised side-effect of DCP contact immunotherapy; this may occur on sites of local application or remote areas. As vitiligo is disfiguring, particularly in dark-skinned individuals, a high index of suspicion is recommended. Treatment of this leucoderma includes discontinuation of DCP, application of topical steroids or phototherapy.⁶ In most cases, repigmentation may occur with treatment, but complete recovery is uncommon.

REFERENCES

1. Hatzis J, Gourgiotou K, Tosca A, Stratigos J. Vitiligo as a reaction to topical treatment with diphenylprone. *Dermatologica* 1988;177:146-8.
2. Duhra P, Foulds IS. Persistent vitiligo induced by diphenylprone. *Br J Dermatol* 1990;123:415-6.
3. MacDonald-Hull SP, Cotterill JAC, Norris JFB. Vitiligo following diphenylprone dermatitis. *Br J Dermatol* 1989;120:323.
4. Van der Steen P, Happle R. 'Dyschromia in confetti' as a side effect of topical immunotherapy with diphenylcyclopropenone. *Arch Dermatol* 1992;128:518-20.
5. Nasca MR, Micali G, Pulvirenti N, Licastro-Cicero R. Transient leucoderma appearing in an untreated area following contact immunotherapy for alopecia areata. *Eur J Dermatol* 1998;8:125-6.
6. Henderson CA, Ilchyshyn A. Vitiligo complicating diphenylprone sensitization therapy for alopecia universalis. *Br J Dermatol* 1995;133:496-7.

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