Photoallergic Dermatitis due to 8-Methoxypsoralen

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One adverse effect of PUVA therapy is the development of severe dermatitis. Only a few cases of photoallergy to psoralens during PUVA therapy have been reported. We describe herein a patient with photoallergic dermatitis induced by PUVA with 8-methoxypsoralen(8-MOP). A 38-year old woman with generalized vitiligo had acute pruritic exanthematous maculopapular lesions in the treated areas after PUVA therapy with 8-MOP. A patch test and photopatch test were performed with 8-MOP, 5-MOP, and 4,5,8-trimethylpsoralen(TMP). The patch test carried out with these psoralen derivatives were all negative, but the photopatch test showed a positive reaction to 8-MOP. The patient consequently had PUVA therapy with 5-MOP and she had no further experience of a photoallergic reaction.(Ann Dermatol 10:(3) 199~202, 1998).

Key Words : Photoallergic dermatitis, 8-methoxypsoralen

PUVA therapy has been widely used in the treatment of various skin disorders. One adverse effect of PUVA therapy is the development of severe dermatitis. Because of the well-known phototoxic capacity of psoralen, most of these dermatitis reactions have been considered to be phototoxic rather than photoallergic. Only a few cases have been reported of photoallergy to psoralens during PUVA therapy or from plants[1-8]. We describe herein a patient with photoallergic dermatitis induced by PUVA with 8-methoxypsoralen (8-MOP).

CASE REPORT

A 38-year-old woman with generalized vitiligo had received 7 years of PUVA therapy without any side effects. In our clinic, she was treated with oral 8-MOP 20 mg and an initial UVA dose of 4 J/cm^2. After her first treatment, intensely pruritic exanthematous maculopapular lesions developed in the treated areas (Fig. 1). This occurred 24 hours after PUVA therapy and rapidly disappeared with systemic and topical steroid treatment. She attended for a second session of PUVA therapy which provoked a similar eruption. A laboratory evaluation including complete blood cell count, platelet count, blood chemistry, urinalysis, antinuclear antibody, and ESR were within normal limits or negative. The patch test and photopatch test were done with 8-MOP, 5-MOP, and 4,5,8-trimethylpsoralen (TMP).

Psoralen derivatives were diluted in acetone or white petrolatum and applied to the back using Finn chambers. The light source used for the photopatch test was Sellas UVA (Dr. Sellmeier Co. Düsseldorf, Germany) and the irradiance at the skin surface was measured with UVA IL 442A radiometer (International Light Inc., Lawrenceville, MA, U.S.A.). The patches were removed after 48 hours and the reaction was evaluated. For the photopatch test, the test sites were immediately irradiated with UVA 5 J/cm^2. The skin reactions were evaluated at 24 and 48 hours following UVA exposure and were scored according to the International Contact Dermatitis Research Group (ICDRG) standards. The patch tests carried out with psoralen derivatives were all negative, but the photopatch test showed a positive reaction to 8-

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Table 1. Results of the patch and photopatch tests

Substances[a] (%)		UVA-shield	UVA-exposed[b]
8-MOP	3×10^{-1}[c]	-	++
	3×10^{-1}	-	++
	$3^{1}\times10^{-1}$	-	++
	1×10^{-2}	-	+
	1×10^{-3}	-	-
5-MOP	3×10^{-1}	-	-
	1×10^{-1}	-	-
	1×10^{-2}	-	-
	1×10^{-3}	-	-
TMP	3×10^{-1}	-	-
	1×10^{-1}	-	-
	1×10^{-2}	-	-
	1×10^{-3}	-	-

a, Psoralen derivatives were diluted in acetone.
b, 5 J/cm^2 UVA was exposed.
c, 8-MOP was diluted in white petrolatum.

MOP (Fig. 2, Table 1). No cross-reaction was observed with other psoralen derivatives tested. A diagnosis of photoallergic dermatitis due to 8-MOP was made. The patient consequently had PUVA therapy with 5-MOP and she had no further experiences of photoallergic reactions.

DISCUSSION

PUVA therapy with psoralen and long-wave ultraviolet radiation (UVA) has been widely used in the treatment of various skin disorders such as psoriasis, vitiligo and mycosis fungoides. PUVA therapy is associated with a variety of well-known side effects. The most frequent of these are pruritus, nausea, epigastric discomfort, fatigue and localized severe erythema or even blistering. Other uncommon side effects such as subungual hemorrhage, hypertrichosis of the face, nevus spilus-like hyperpigmentation, acneiform eruptions, drug reaction and urticaria have been reported[9-12]. One adverse effect of PUVA therapy is the development of severe dermatitis. Similar dermatitis reactions can be induced by contact with plants that contain psoralens following sun exposure as a phytophotodermatitis. Several authors have reported photoallergy to psoralen. Sidi and Bourgeois-Gavardin first reported 5 cases of allergic photocontact dermatitis to 8-MOP used for the treatment of vitiligo[1]. Photoallergy to 8-MOP was induced in 3 volunteers under experimental conditions, with positive photopatch test reactions using 0.1% 8-MOP[2]. A case was reported of allergic photocontact dermatitis due to 8-MOP, 5-MOP and imperatorin from

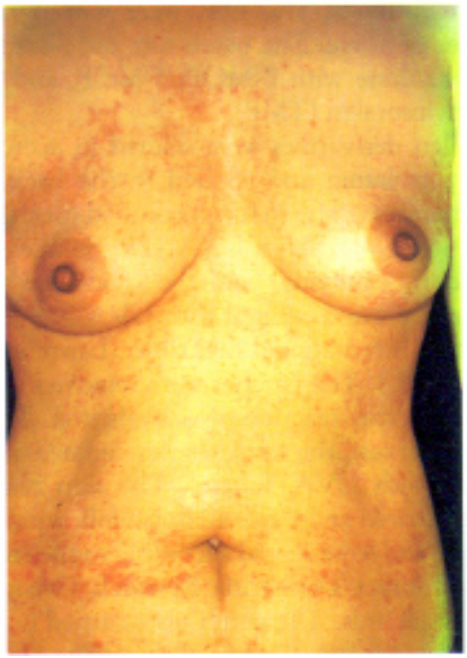

Fig. 1. Generalized eythematous maculopapular eruptions in PUVA-treated areas.

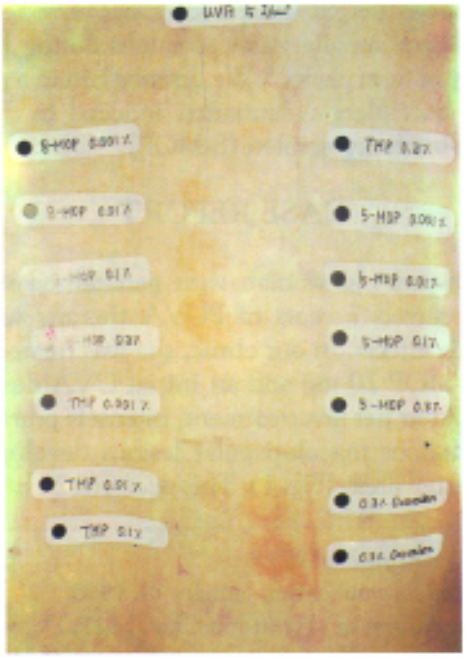

Fig. 2. Photopatch test mapping at 48 h after UVA exposure on the back.

plant sources and a concentration as low as 10^{-4}% for 8-MOP induced allergic reactions on photopatch testing[3]. A case was reported of photoallergic dermatitis from orally administered 8-MOP in a patient on PUVA for psoriasis, and in this case relatively small doses of UVA were sufficient to produce photoallergic reactions with topical and oral 8-MOP[4]. Three of 371 patients treated with 8-MOP developed an acute dermatitis in PUVA-treated areas and these dermatitis reactions were due to contact and/or photocontact allergy to psoralen[7].

Photoallergy is defined as an acquired altered photoreactivity dependent on an antigen-antibody or cell-mediated hypersensitivity state. Less time and less energy are required to evoke photoallergic reactions compared to phototoxicity[9]. Histologically, photoallergy looks very much like contact allergy with superficial and deep inflammatory lymphocytic infiltrates, edema, spongiosis and lack of necrotic keratinocytes (so-called sunburn cells)[2,9]. We diagnosed our patient as having a photoallergic dermatitis which could be separated from the well-known phototoxic properties of 8-MOP by the following criteria: a) the short time interval to the onset and peak of the reaction in less than 24 hours (phototoxic reaction to 8-MOP takes 24-48 hours for its development with a climax at 72 hours); b) clinical appearance of wide-spread lesions with pruritic tiny dense maculopapules.

The psoralens belong to a class of compounds known as the furocoumarins, which consist of a double ringed coumarin moiety to which a furan ring is attached. The derivative most widely used in photochemotherapy is 8-MOP, which is principally of plant origin but is available as a synthetic drug. TMP is a synthetic compound that is less phototoxic after administration and is primarily used for the treatment of vitiligo[13]. 5-MOP has been proved to be therapeutically effective taken orally and it is potentially less erythemogenic in photochemotherapy and does not induce intolerance reactions[14,15]. The photopatch test with psoralen derivatives showed a positive reaction only to 8-MOP, therefore 8-MOP could be verified as the agent responsible for the observed dermatitis. Cross reactions to 5-MOP and TMP were not observed and this is likely due to differences in chemical structure.

We should keep in mind that photoallergic dermatitis rarely occurs during PUVA therapy with 8-MOP. The occurrence of photoallergic dermatitis necessitates the termination of PUVA therapy with 8-MOP and alternative PUVA therapy with 5-MOP or TMP should be tried.

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