Chronic Photosensitive Dermatitis Due to Phenothiazines

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TORINUKI, W., KUMAI, N. and MIURA, T. *Chronic Photosensitive Dermatitis Due to Phenothiazines*. Tohoku J. exp. Med., 1982, **138** (2), 223-226 — A 74-year-old man had eczematous eruptions on sun-exposed areas. Photopatch tests were positive to chlorpromazine and promethazine, and the action spectrum for the photosensitivity was in the long-wave ultraviolet light (UV-A) range. It was concluded that the chronic photosensitive dermatitis was due to phenothiazines. — phenothiazines; photopatch test; photosensitivity

Chlorpromazine and other phenothiazines, such as promethazine, perphenazine, thioridazine and levomepromazine, have been widely used as tranquilizers, antipyretics, analgesics and/or antihistamines, and it is known that some of them may produce not only allergic contact dermatitis but also phototoxic and photoallergic reactions (Fisher 1967; Horio 1975; Horio et al. 1975). In the present case, photosensitive dermatitis was suspected because the eruptions were limited to sun-exposed areas and became aggravated in summer. Patch tests and photopatch tests with phenothiazines and halogenated salicylanilides that are typical photosensitizers were performed, and it was confirmed that phenothiazines caused the development of the eruptions. Whether these lesions resulted from a phototoxic or a photoallergic reaction of phenothiazine was also discussed.

REPORT OF A CASE

A 74-year old farmer had a 10-year history of recurrent pruritic eczematous eruptions on sun-exposed areas. The lesions first appeared on the forearms and hands, and then spread to the face, nape and V-shaped area of the neck. According to the patient, the skin conditions became worse in summer and better in winter. He had no known systemic illness. There was no family history of photosensitivity-related diseases. A physical examination revealed scaling and lichenified dermatitis on the scalp, face, V-shaped area of the neck, extensor aspect of the forearms and the dorsa of the hands (Fig. 1). There was fissuring and infiltration in many sites, particularly on the hand backs. From these findings, it was suspected that the case was photosensitive dermatosis. Blood cell counts, urinalysis, serum GOT and BUN were all within normal limits. Histologic examination of the eruption on the left forearm showed hyperkeratosis, irregular acanthosis and mild, perivascular mononuclear cell infiltration of the upper dermis (Fig. 2).

Fig. 1

Fig. 2

Fig. 1. Erythematous and eczematous eruptions on the neck and face.

Fig. 2. Histopathologic appearance of lesion from the left forearm, demonstrating hyperkeratosis and irregular acanthosis of epidermis, and perivascular lymphocytic infiltration of upper dermis.

PHOTOBIOLOGICAL EXAMINATIONS

The patient was hospitalized during the investigation and was carefully instructed not to be exposed to natural sunlight.

Light sources. The light sources used consisted of four black lights (Toshiba FL-20BLB) which emit rays between 300 to 420 nm, with a maximum at 360 nm (mainly UV-A) and four sunlamps (Toshiba FL-20SE) which emit rays between 280 to 370 nm, with a maximum at 310 nm (mainly UV-B). The energy intensity of the black lights and sunlamps were 3.9 mW/cm² at a target distance of 15 cm and 1.3 mW/cm² at a target distance of 20 cm, respectively (U.V. radiometer UVR-305/365; Eisai Co., Japan).

Patch and photopatch tests. Patch and photopatch tests were performed with 13 substances listed in Table 1. The substances to be tested were applied in duplicate on normal back skin and thoroughly protected from light to avoid "masked photopatch test" reactions. One row of the test sites was uncovered and irradiated with black light for 20 min at a distance of 15 cm, 24 hr after application. All the test sites were evaluated at 24 hr after irradiation. These tests were performed again at new skin sites on the back.

Histologic examination. A biopsy specimen taken with a 4-mm punch was obtained from a positive photopatch test site. The specimen was fixed in a 10% formaldehyde solution, sectioned and stained with hematoxylin-eosin.

TABLE 1. *Results of photopatch testing with black light*

Test agents	Concentration (%)	Reaction	
		First time	Second time
Tetrachlorosalicylanilide	1*	—	
Trichlorocarbanilide	1*	—	
Bitionol	1*	—	
Hexachlorophene	1*	—	
Irgasan CF ₃	1*	—	
Tribromosalicylanilide	1*	—	
Multifungin	1*	—	
p-Phenylenediamine	2*	—	
Diphenhydramine	1*	—	
Perphenazine	0.02†	+	—
Promethazine	0.5†	++	++
Chlorpromazine	0.05†	++	++
Dibucaine	0.3†	—	

* In white petrolatum.

† In physiologic saline solution.

Symbols: —, no response; +, faint mottled erythema; ++, definite erythema with slight edema;, not tested.

RESULTS

The results of the photopatch tests with black light are summarized in Table 1. The first test with perphenazine gave a faint erythematous reaction on the photopatch test site, but the second test was negative. With chlorpromazine and promethazine, however, definite erythema with slight edema developed. The tests with chlorpromazine and promethazine were performed again, and identical results were obtained. The positive photopatch test using black light showed that wavelengths longer than 320 nm (UV-A) were responsible for eliciting the photosensitive reaction. Immediate wheal formation was not observed on the photopatch test site with these three phenothiazines. The results of the patch and photopatch tests with halogenated salicylanilides were all negative. No reactions were observed in a normal subject with any of the same 13 substances and 20-min exposure to black light at a distance of 15 cm. The 20-min exposure of black light on non-applied skin showed no response in either the normal subject or this patient. The minimal erythema dose (MED) in UV-B range was determined on the back skin at 24 hr after exposure to the sunlamp for 0.3, 0.7, 1.0, 1.5 and 2.0 min, respectively. The patient revealed a faint mottled erythema at the site exposed to the light at a distance of 20 cm for 1.0 min, and a definite erythema for 1.5 and 2.0 min. Thereby, the MED of this patient was 1.0 min, the dose being within the normal range.

Histologically, perivascular collections of mononuclear cells were found at the positive promethazine photopatch test site. Epidermal spongiosis was not clearly observed and no sunburn cells were found.

DISCUSSION

Chlorpromazine and other phenothiazines are commonly used as routine therapeutic drugs for psychiatric diseases, and also as antihistamines and antipyretics. In the literature, Epstein et al. (1957) reported cutaneous photosensitivity caused by these drugs, and presently, phenothiazines are considered to produce not only allergic contact dermatitis (Levan 1957), but phototoxic and photoallergic reactions (Fisher 1967; Horio et al. 1975). Immediate allergic photosensitivity due to chlorpromazine was also reported by Horio (1975).

Attempts for differentiating phototoxic reactions from photoallergic ones have been reported (Harber and Baer 1972), but it may be difficult to distinguish them clinically. In general, a photoallergic reaction caused by drugs was considered to occur at a relatively low concentration of drugs and a low energy level of light compared to phototoxic reactions. A normal subject gave no response to the same concentration of phenothiazines and exposure to black light energy employed for the photopatch test in the present case. Lesions of our case were restricted to light-exposed areas and had been aggravated in summer suggesting probable correlation to sunlight. Histology of the eruption was compatible with chronic eczema. These data suggest that this patient was considered to have eczematous eruptions resulting from a phenothiazine photoallergy, though he did not remember whether or not he has ever received any kind of photosensitizing drugs including chlorpromazine.

It is known that, in photoallergic reactions, cross-reactions to structurally related agents often occur (Harber and Baer 1972). Simultaneous photosensitivity to chlorpromazine and promethazine in the case reported here seems to be due to a cross-reaction, since these two compounds are chemically related to each other (Ljunggren 1977). It was impossible to determine whether chlorpromazine or promethazine was the first photosensitizer, because medication before the occurrence of eruptions was unclear.

We would like to stress that a patient with a photosensitive skin disease should be examined for possible sensitivity to phenothiazines.

References

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