

TREATMENT OF PARAPSORIASIS EN PLAQUES, MYCOSIS FUNGOIDES, AND SÉZARY'S SYNDROME WITH TRIOXSALEN BATHS FOLLOWED BY ULTRAVIOLET LIGHT

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Abstract. Three patients with parapsoriasis en plaques (PEP), fifteen with mycosis fungoides (MF), and one with Sézary's syndrome (SS) were given a bath to which a small amount of trioxsalen solution had been added, and then exposed to ultraviolet (UV) radiation from a bank of dysprosium lamps. Within 2-6 months of this treatment the skin lesions healed completely or almost completely in all 3 patients with PEP, in all 7 with MF stage II and in 4 of 5 with MF stage III. Two patients with MF stages IV-V showed a fair degree of improvement. One with erythrodermic form of MF responded, but poorly. The patient with SS and the one with erythrodermic MF responded with severe phototoxic reactions.

Key words: Parapsoriasis; Mycosis fungoides; Sézary's syndrome; Photochemotherapy; Trioxsalen; PUVA

There is no known treatment which can produce a lasting cure for MF. Although in recent years three different approaches have been shown to have an excellent effect upon skin lesions in this state, a permanent cure is hardly to be expected. These three methods are megavolt electron-beam radiotherapy (8), topical painting with nitrogen mustard (7), and the PUVA therapy (oral 8-methoxypsoralen plus UV-A) (4). Sensitization of the skin by means of a bath before UV irradiation is presented here as an effective modification of the PUVA therapy.

MATERIAL AND METHODS

Patients

The series consisted of 7 men and 12 women aged 24-89 years (mean 68). The diagnoses and the response to treatment are reported in Table I. The diagnosis of MF and the staging of the disease rests on criteria established by the Scandinavian Mycosis Fungoides Study Group (5). All 3 patients with PEP showed histopathological features highly suggestive but not diagnostic of MF.

Previous and additional treatment

None of the patients received trioxsalen bath plus UV irradiation as the initial treatment.

While receiving photochemotherapy the patients were only allowed supplementary topical treatment with white soft paraffin and occasionally topical corticosteroids when irritative reactions were present. Exceptions were the patient with SS who was given cyclophosphamide throughout the treatment, 3 patients with solitary tumours treated with X-rays, and one patient with MF stage IV-V who received supplementation with the epipodophyllotoxin derivative VP-16-213 (Sandoz) during the maintenance therapy.

Trioxsalen baths and UV irradiation

Details of the regimen have recently been published (1, 3). After a 15 min bath the patient was immediately irradiated in a solarium comprising eight unfiltered dysprosium lamps (HQI-TS 400 W, Osram, Munich, W. Germany). The irradiance was found to be 12 mW/cm² in the UV-A (320-380 nm), 0.7 mW/cm² in the UV-B (280-320 nm), and 0.17 mW/cm² in the UV-C (<280 nm). Treatment was given on 5 days each week during the initial 6-8 weeks, and twice weekly during the following 2 months followed by maintenance therapy once weekly for an indefinite period of time. Six patients from remote districts were admitted to hospital once monthly for maintenance therapy on 5 successive days.

RESULTS

The treatment-observation period in September 1977 covered a range of 6-30 (mean 14) months. All 3 patients with PEP and 11 of 12 with MF stages II-III responded satisfactorily within 2-6 months, the skin becoming apparently normal or almost normal. Eight of these 11 patients have since returned with signs of recurrence, but the lesions have again cleared after a higher irradiation dose or a new series of treatment of 5 days per week. Regular treatment once weekly seems preferable to

Table 1. *Diagnosis and response to treatment*

Diagnosis	No. of patients	Response to treatment			
		Good	Fair	Slight	None
Parapsoriasis en plaques	3	3			
Mycosis fungoides II	7	7			
Mycosis fungoides III	5	4			1
Mycosis fungoides IV-V	2		2		
Mycosis fungoides erythroderma	1			1	
Sézary's syndrome	1				1

daily treatment for a whole week once monthly. Recurrences tend to appear in the third or fourth week after interruption of therapy.

Two patients with MF stages IV-V have improved but the lesions have not healed; the pruritus has disappeared completely but the infiltrations only partially.

Both patients with erythroderma, one of whom suffered from Sézary's syndrome, developed very severe phototoxic reactions. The woman with Sézary's syndrome was exceedingly sensitive to UV irradiation after the trioxsalen bath: as little as 2 sec of irradiation once daily on 3 successive days (approximately 0.02 J/cm² of UV-A) produced a severe erythematous, oedematous reaction with a prickly, stinging pain in combination with intolerable general malaise.

In seven instances the maintenance treatment has been discontinued; in three cases because of intolerance or non-response, in two cases because of apparent cure and in two instances the patients were too weak to stand the procedure.

Two patients died during the observation period, both with manifestation of MF involving organs other than the skin (2, 6).

Remarks on the response to treatment

Phototoxicity tests as recommended by the European Co-operative Clinical Trial of PUVA (10) have failed to provide reliable guidance in setting a suitable dose of UV irradiation. The best guide has therefore necessarily been clinical experience and informed guesswork. A suitable dose of irradiation produces some general erythema anytime between 5th to 21st day. The reaction is often accentuated in and around existing plaques. At the same time, it is usual for the patient to experience itching or prickling pain, which may be intolerable. Compared with patients with psoriasis, MF patients show a more pronounced phototoxic reaction (9), and UV irradiation can easily be overdosed. If this happens, the erythema will be intense and is often accompanied by oedema and sometimes even blistering. These reactions usually abate within a few days, provided the treatment is temporarily withdrawn. The symptoms can be relieved with topical corticosteroids. With increasing pigmentation of the skin the proneness to erythema subsides within 2-3 weeks.

Areas consisting of deeply infiltrated plaques or tumours tend to show more severe and more prolonged inflammatory reactions, often culminating in sloughing and ulceration before healing takes place.

The healing usually starts after 3 to 4 weeks. Patches of erythema and plaques show apparent clinical healing in most patients within 2 months, but tumours often respond slowly and may require several months, or even up to a year of treatment.

In 4 patients, blisters suddenly and unexpectedly occurred in normal-looking skin in the second month of treatment. In all of them the daily dose of irradiation had been kept constant at 1.5 J/cm² during the previous 2-3 weeks. Treatment was withheld for a short period while blisters rapidly healed, after which it was continued without side effects.

Table II. *UV irradiation schedule*

Time from start of treatment (months)	Irradiation dose at each visit J/cm ² (UV-A)	Mean cumulated irradiation dose J/cm ² (UV-A)
0	0.02-0.1-0.15	
0.5	0.05-0.4-1.0	2
1	0.05-0.8-2.0	9
2	0.1-1.0-2.5	15
6	0.4-1.5-2.5	36
12	0.4-1.5-2.5	58

If treatment is resumed after an interval of more than 2 months the patient reacquires proneness to severe phototoxic reactions. The UV dose must therefore again be kept low initially, but can be raised at a much quicker rate than during the previous period, whereupon healing takes place more quickly.

In certain patients, particularly those showing intense inflammatory response to treatment, marked pigmentation occurs at the site of the lesions. These sometimes disfiguring effects may persist for a very long period, but tend ultimately to merge after continued treatment.

Tumours and deep infiltrations have responded but have proved difficult to eradicate completely. Healing may be achieved by prolonged, intensive therapy. When a few additional tumours are present it may be practical to supplement trioxsalen baths and UV irradiation with local X-ray therapy.

Tumours sometimes heal with areas of fibrous scarring but often leave no noticeable sequelae apart from hyperpigmentation. In poikilodermatous skin the response seems to be equally satisfactory both clinically and histologically, but blotchy pigmentation, atrophy, and angiectasiae persist.

Certain areas of the skin are inaccessible to trioxsalen or UV irradiation and are thus difficult to treat. They include the scalp, face, palmar and plantar areas, and skin folds. The hair may have to be cropped short and treated like the face by sponging, while the rest of the body is immersed. Facial and palpebral lesions can be treated successfully this way. Infiltrations of hands and soles healed, but response was slow. Lesions in "shaded" regions such as axillae, inframammary areas and abdominal and gluteal folds and clefts are easily overlooked during treatment but respond when adequately exposed.

Histopathology of healed lesions

Biopsy specimens were examined at 3-month intervals (P. Westermarck, Dept. of Pathology, University Hospital, Uppsala). Lesions remaining clin-

ically healed for 1-2 months showed hyperkeratosis and slight atrophy. The papillary part of the dermis showed oedema, but only scattered lymphocytes and histiocytes, some of them containing melanin. No atypical cells were found, either in epidermis or in dermis.

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