Nodular malignant melanoma and multiple squamous cell carcinomas in a patient treated by photochemotherapy for psoriasis

We describe a patient suffering from psoriasis who developed a nodular malignant melanoma and three squamous cell carcinomas after treatment with psoralen and ultraviolet light A (PUVA). So far as we know this is the first report of invasive melanoma in a patient treated with this modality.

Case history

A 61 year old man had had a history of psoriasis for 40 years. Treatments had included tar, dithranol, and topical steroids, but he had never received x-rays, arsenic, or cytotoxic agents and had no cutaneous malignancy before starting PUVA. During the second world war he had spent three years in Egypt but subsequently worked as a clerk in London and did not expose himself to natural or artificial forms of ultraviolet light. Examination before photochemotherapy showed plaque psoriasis of 20 cm² of body surface. PUVA was instituted in March 1979. The dose of 8-methoxypsoralen was 50 mg and the starting dose of ultraviolet A 1 J cm⁻². He was treated two or three times weekly until the psoriasis cleared and then maintained with treatment once every two or three weeks. In February 1983, after a cumulative dose of ultraviolet A of 419 J cm² in 176 sessions, he developed three scaly lesions on the anterior chest. Histologically two of these were squamous cell carcinomas and the third a solar keratosis. Examination also showed many PUVA lentigines distributed widely. In May an area of Bowen's disease was excised from the V of the chest. Three months later one squamous cell carcinoma and three further solar keratoses were removed from the dorsa of the hands. PUVA was discontinued (cumulative dose 461 J cm² in 184 sessions). Unfortunately, control of his psoriasis proved impossible with topical treatment and PUVA was reintroduced in October for a further 10 sessions and 36 J cm². It was finally stopped in December 1983.

At follow up in April 1984 a symptomless, pigmented nodale 1 cm diameter was noted on the anterior shoulder. The lesion had been growing rapidly for eight weeks and he was not aware of a previous pigmented lesion on that site. The lesion was excised and proved to be a nodular malignant melanoma, with spread to the subcutaneous fat (Clark's level V). There were no excessive signs of actinic damage for the patient's age and sex. A wider excision was performed one week later.

Comment

Photochemotherapy with 8-methoxypsoralen and ultraviolet A is an effective treatment for severe psoriasis and is popular with patients, as it avoids the inconvenience of some topical agents. The long term hazards of the regimen, however, are unknown and remain to be quantified. Psoralens interact with pyrimidine bases to form cross linkages in the double helix of deoxyribonucleic acid (DNA). 8-Methoxypsoralen increases the incidence of skin tumours after simulated solar exposure in albino mice. Evidence is accumulating that PUVA is immunosuppressive, and it has been shown to have a proliferative effect on melanocytes. These melanocytes are often large and cytologically atypical and are found within the PUVA lentigines. The increased frequency of PUVA lentigines is associated with a greater number of PUVA treatments (~100), increasing age (~35), and male sex.²

There have been several reports of skin carcinoma in patients treated with PUVA. In a large series Stern et al found a 12-fold increased hazard of squamouscell carcinomas but not basal cell carcinomas in patients treated with PUVA compared with the general population.³ Marx et al reported the occurrence of malignant melanomas in situ induced by PUVA in patients with psoriasis.⁴ In addition, a patient with vitiligo receiving oral psoralen followed by solar exposure developed a malignant melanoma with spread to the upper dermis only (Clark's level III).⁵

The occurrence of malignant melanoma in our patient may have been coincidence. Marx et al estimated (using figures for the United States) that four melanomas might be expected to occur yearly worldwide in all patients who have received PUVA. While we cannot definitely incriminate PUVA in the aetiology of our patient's tumour, the fact that he had had three squamous cell carcinomas and an area of Bowen's disease, in the absence of any other known carcinogen, strongly suggests that PUVA was the oncogenic influence.

This case highlights the importance of careful supervision and the need for multicentre cooperation to determine the incidence of melanoma in patients with psoriasis treated with photochemotherapy.

Experience with routine reuse of plastic insulin syringes

The changeover to U100 insulin was scheduled by the British Diabetic Association to start in March 1983. From late 1982 our patients were told to bring all injection equipment to their first appointment after 1 March 1983 for replacement. Nearer that date we realised that new glass syringes would not be available. As plastic syringes can be reused safely by the same patient with probable financial saving¹ we agreed with our hospital pharmacist that our patients would receive plastic syringes to be used for one week each.

Patients, methods, and results

As patients were changed to U100 insulin we explained how to use the plastic syringes (Becton Dickinson 0·5 ml or Plastipak 1 ml insulin syringes, with fixed needles). Patients were told not to clean syringes or needles but to reinsert the needle into its cover after use and to store the syringe in a dry container in a refrigerator. At each clinic attendance patients received an internal hospital prescription for enough plastic syringes until their next visit at the rate of one syringe a week. Additional syringes could be bought from retail chemists if necessary.

One year later we completed a questionnaire with 118 consecutive patients. They had then been taking U100 for from three to 15 months (mean 9·8 months), having received insulin injections for from under one year to 43 years (mean 12·1 years). All were taking highly purified pork or beef insulin, 39 once daily and 79 twice daily. Sixty six patients used the plastic syringes for at least seven days and 44 patients for six days or less, and eight patients used glass, not plastic syringes. The mean duration of use of plastic syringes by patients in relation to number of injections a day and duration of use of insulin. (Figures are means (SD))

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<thead>
<tr>
<th>Patients taking once daily insulin (n=39)</th>
<th>Patients taking twice daily insulin (n=79)</th>
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<tbody>
<tr>
<td>All patients (n=118)</td>
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<tr>
<td>Patients using plastic syringes</td>
<td>Patients using plastic syringes</td>
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<tr>
<td>Time on U100 insulin (months)</td>
<td>Time on U100 insulin (months)</td>
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<td>6·70 (5·91)</td>
<td>6·40 (2·57)</td>
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<td>6·44 (4·45)</td>
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References