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Køebner Reaction Induced by Photodynamic Therapy Using Delta-aminolevulinic Acid

A Case Report

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We report a case of psoriasis reactivation following photodynamic therapy with delta-aminolevulinic acid. An 84-year-old woman received several UVB treatment sessions because of severe psoriasis at her crura in the period from 1960 to 1990. Since then her psoriasis had been inactive. In 1994 she was admitted to our out-patient clinic because of multiple dysplastic lesions as well as multiple carcinomas at her crura. Surgical intervention was impossible and retinoids were not tolerated. She was treated with photodynamic therapy, which provoked a Køebner reaction followed by a severe reactivation of the otherwise inactive psoriasis. Whether photodynamic therapy is used for the treatment of multiple dysplastic lesions in a psoriasis patient or for the treatment of psoriasis it seems important to be aware of this adverse effect. This is the first report of Køebner reaction following photodynamic therapy. ***Keywords: photochemotherapy; protoporphyrin IX; cancer; skin-neoplasms-drug-therapy; psoriasis.***

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Systemically administered Photofrin followed by laser irradiation has been used during the last twenty years in the treatment of various cancers. In spite of good and promising results photodynamic therapy (PDT) has never come into widespread use due to the unacceptable side-effects of generalized skin sensitization (1).

In order to avoid these side-effects, Kennedy et al. (2) introduced in 1989 topical application of delta-aminolevulinic acid (ALA) followed by illumination with visible light (ALA-PDT) in the treatment of cutaneous tumours. The therapy has shown good response rates for tumour treatment (3–5) and has lately been reported effective in the treatment of mycosis fungoides (6) and psoriasis (7). The treatment is promising, non-invasive, the side-effects are few, and it is cosmetically excellent. Some psoriasis patients treated with UVB, PUVA, superficial X-ray therapy and arsenic may develop multiple cutaneous malignancies (8). Multiple and disseminated tumours make surgical intervention difficult. Patients with multiple dysplastic lesions are controlled frequently, and usually only growing processes are removed. Since ALA-PDT has shown good response rates in the treatment of superficial tumours, it seems logical to apply this treatment to psoriasis patients with multiple therapeutically induced tumours. Since this therapy may be used in the future treatment of psoriasis and to psoriasis patients with skin malignancies, we find it necessary to report a severe case of psoriasis reactivation induced by ALA-PDT.

CASE REPORT

An 84-year-old woman had active psoriasis from 1960 to 1990. Psoriasis was primarily located to the lower legs, on which she was treated with local steroid as well as UVB for several years. Due to therapeutically induced multiple dysplastic lesions on the legs (Fig. 1), she was admitted to our out-patient clinic in 1994.

Histopathological representative biopsies from tumours on her legs demonstrated actinic keratoses, severe dysplasia, as well as squamous cell carcinomas. Surgical intervention was impossible and the patient did not tolerate treatment with retinoids.

Twenty per cent ALA in a cream based on polysorbat, glycerol and paraffin oil in water was applied to the tumour areas, from which representative biopsies were taken. Four hours later the lesions were exposed to an incoherent light source, a common slideprojector equipped with an Osram 250 W lamp emitting light with wavelengths ranging from 400 nm–850 nm, energy densities of 50 J/cm^2, 80,000 lux for 30 min. Only about 9% of the relative spectral power distribution for the lamp placed in the slideprojector is within the absorption action spectrum of Pp IX (635nm $\pm$5). During light exposure the patient reported pain similar to that of a sunburn at the ALA-treated area. No anaesthesia was needed. The sunburn sensations decreased during the irradiation period but lasted for 24 h after treatment. Inflammation at the treated areas was observed a few minutes after start of irradiation and lasted for 24 h. At the follow-up control 3 weeks later, we observed peeling at the treated areas. No other adverse effects were reported, and we proceeded to treat 4–6 tumours at the left crus using ALA-PDT.

Two days later several erythematous, confluent papules appeared in relation to the treated tumours at the left crus, with fast progression to the right crus and to both femora. Noticeable desquamation and inflammation were observed. The skin changes were compatible with a Køebner reaction induced by ALA-PDT in a psoriasis that otherwise had been inactive for years (Fig. 2).

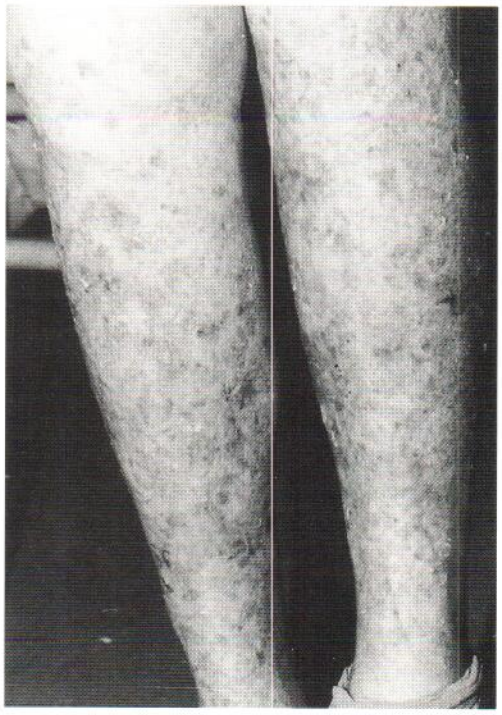

Fig. 1. Multiple carcinomas and multiple dysplastic lesions.

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DISCUSSION

Good response rates using ALA-PDT have been reported, and this treatment modality is becoming increasingly common in clinical trials against a range of dermatological disorders. It seems important to register possible adverse effects observed in relation to the treatment.

The effect of ALA-PDT is based on a cytotoxic photoactivation of accumulated porphyrins in the epidermal cells. When ALA is applied to abnormal skin it passes into the epidermal cells, in which it is enrolled in the intracellular biochemical synthesis of protoporphyrin IX (Pp IX). When cells accumulated with endogenous Pp IX are irradiated with visible light it causes cell death (2).

When tissue, photosensitized by ALA-induced Pp IX, is exposed to light, patients usually experience burning sensations which are usually noticed within 5 min and then gradually decrease within the irradiation period. Usually this discomfort vanishes within 48 h after treatment. The production of Pp IX takes a certain time, and even after the therapeutic exposure, additional Pp IX will be formed; consequently, protection from sun exposure 48 h following treatment seems necessary (9). Post-treatment peeling, superficial erosions as well as superficial ulcerations are described (10, 11).

In conjunction with psoriasis, traumas to the skin may sometimes cause lesions to develop at the site of injury. Surgical wounds, excoriations, sunburns are common types of trauma that might precede the development of psoriasis lesions. This phenomenon is called Køhner reaction. ALA-PDT has been well tolerated in several experimental treatments, with only minor adverse effects reported. However, the case of reactivation of psoriasis indicates that severe skin reactions can develop following ALA-PDT.

During illumination, the skin temperature at the ALA-PDT-treated area increased by 2–4 °C. This mild hyperthermia correponds to the rise in skin temperature seen when treating psoriasis patients with psoralen and UVA (PUVA). The mild rise in skin temperature seems not to be responsible for provoking the Køhner reaction. More cases of Køhner reactions may be expected as adverse effect when psoriasis or, even more frequently, when skin malignancies in psoriasis patients are treated with ALA-PDT. It seems important to inform the patient about this risk.

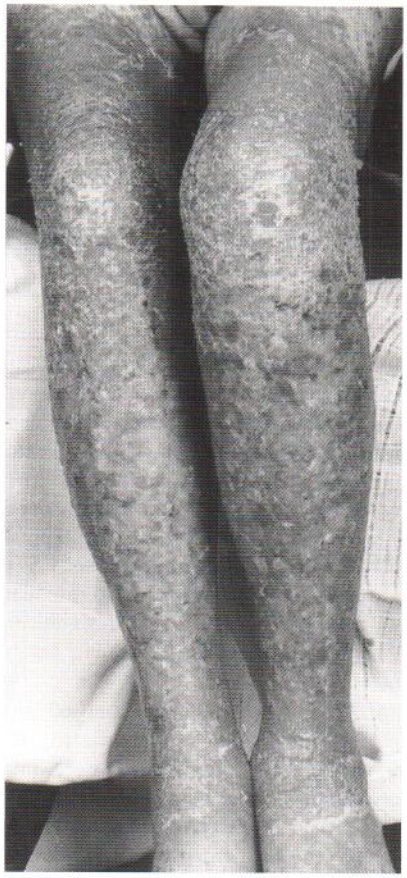

Fig. 2. Reactivated psoriasis after photodynamic therapy with δ-aminolevulinic acid.

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