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Persistent Light Reaction

Successful Treatment with Cyclosporin A

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A 53-year-old male patient who had suffered for several years from severe persistent light reaction possibly due to tribromsalan photosensitivity was treated with cyclosporin A after long-term low-dose administration of corticosteroids which had to be discontinued. PUVA therapy was impracticable due to the extraordinarily high UVA sensitivity. When cyclosporin A blood concentrations between 100 and 200 ng/ml were reached, the patient was nearly free from symptoms; the excellent clinical response was also documented by phototesting performed prior to and during therapy. Cyclosporin A may be a valuable therapeutic alternative to systemic corticosteroids for severe cases of persistent light reaction which cannot be controlled by photoprotective measures. (Received July 27, 1987.)

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Photoallergic contact dermatitis is common and may be caused by a variety of chemical agents such as coumarins, para-aminobenzoic acid, benzocain, musk ambrette and halogenated phenolic compounds (1). In most instances, the skin eruptions clear when exposure to the sensitizer is discontinued; in a minority of patients, however, persistent photosensitivity develops even if contact with the eliciting agent is carefully avoided (1, 2).

Persistent light reaction (PLR) (3) represents one of the most disabling disorders in photomedicine. Various therapeutic attempts have been performed in patients with persistent light reaction, with moderate success such as topical and systemic corticosteroids, 'sun blockers' and β-carotene (4). Oral photochemotherapy (PUVA), though offering high photoprotection due to melanin hyperpigmentation (4, 5, 6), fails if patients have an extremely low UVA threshold and thus cannot tolerate low-dose UVA after photosensitization with psoralens. Skin biopsies of patients with PLR show a predominance of Leu-3a-positive cells (i.e. T-helper cells) (7) whose activity can be successfully inhibited by systemic administration of cyclosporin A (8).

CASE REPORT

A 53-year-old male patient (skin pigmentation type: II (9)) had for several years suffered from severe eczematous lesions in UV-exposed skin areas. Allergologic examination and routine patch testing proved negative. Photopatch testing revealed a strong photoallergic reaction to tribromsalan. The disease worsened progressively and the patient was unable to continue with his normal outdoor activities even though tribromsalan was avoided carefully and 'sunblockers' and even 'shades' (titanium dioxide preparations) were used for topical photoprotection.

Photobiologic testing revealed marked erythema 24 h after irradiation with 0.5 J/cm^2 UVA (peak 365 nm, Dr Hönle blue light lamp, hl glass filter). Normal control individuals tested in an identical manner revealed slight erythematous reactions due to high-dose UVA irradiation after 30–70 J/cm^2. The minimal erythema dose to UVB as tested with the unfiltered blue light lamp in the patient was 3 s, corresponding to 20 mJ/cm^2 at 297 nm as measured with a UV meter (SGI, Greiter AG). Normal individuals develop erythema after 65–240 mJ/cm^2.

Histologic examination of an infiltrated eczematous lesion revealed a dense lymphocytic infiltrate in the upper and mid-dermis which by immunohistochemistry (Leu 1, Leu 2a, Leu 3a, Leu 14, Becton Dickinson, ABC Vectastain) was classified primarily of T helper cell origin. Atypical cells were not detected.

Photochemotherapy with oral administration of psoralens was initiated in order to afford photoprotection by melanine pigmentation. Due to his extremely low UVA threshold (0.5 J/cm^2 UVA) the patient was unable to tan. Administration of systemic corticosteroids (60 mg 6-methylprednisolone daily) and azathioprine (150 mg daily) led after several months to marked side effects such as facial swelling, skin atrophy and gastritis and offered only short periods of relief. Slow tapering of the corticosteroid dose (reduction from 60 mg daily to 20 mg/alternate day over 4 weeks) was regularly followed by a prompt relapse.

After discontinuation of corticosteroids, oral cyclosporin A (CyA) (Sandimmun®) was administered initially in a dose of 6 mg/kg body weight divided into two equal doses daily (8 a.m. and 8 p.m.). Blood levels of CyA were determined by high-pressure liquid chromatography twice a week. Blood samples were taken immediately before administration of the morning dose. The aim of dosimetry was to achieve CyA full blood levels between 100 and 200 ng/ml. Once a week the following laboratory parameters were determined and remained within normal limits: blood cell count, renal and liver function tests, serum protein and electrophoresis, blood sugar, triglycerides and cholesterin, C1 esterase inhibitor, creatinine clearance.

Four weeks after initiation of CyA treatment the eczematous lesions disappeared gradually and pruritus subsided. During the summer months the patient, still taking CyA, was advised not to use sunscreens but to avoid direct sun exposure. He could enjoy normal outdoor activities. Repeat of the phototest procedures demonstrated an increased UVA threshold dose from 0.5 to 16 J/cm^2, whereas the UVB threshold dose did not change. Six months after starting the CyA administration, CyA was tapered; the dose was reduced by 1 mg/kg body weight weekly and subsequently withdrawn after 6 weeks. Phototesting, performed 6 weeks and 6 months after discontinuation of CyA, revealed a decrease in the UVA threshold to 4 J/cm^2 and 2 J/cm^2, respectively. This was paralleled by a continuous deterioration of the skin disease.

DISCUSSION

Cyclosporin A (CyA) is a cyclic undekapeptide with potent immunosuppressive properties (8). The main indication for CyA at present is the immunosuppression of patients after organ transplantation. However, CyA has been tried in a variety of autoimmune diseases such as pemphigus vulgaris, lupus erythematosus and Behçet's disease (8). Though CyA does not cause myelotoxicity, a number of potentially serious side effects (nephrotoxicity, hepatotoxicity, malaise, tremor, hypertension, gingival hyperplasia, hirsutism and increased risk of malignant lymphoma) have been observed during long-term treatment. Hence, the application of CyA should be restricted to life-threatening or severely disabling disorders. All side effects, however, are dose related and most of them can be avoided by careful monitoring including regular determination of CyA blood levels.

Persistent light reaction (PLR) is a rare, disabling chronic disorder which is most frequently observed in middle-aged males and may be caused by photosensitivity to a chemical substance, e.g. musk ambrette or halogenized phenolic compounds (1). The

disease severely interferes with the outdoor activities of affected patients who due to extreme photosensitivity sometimes may be confined to a dark environment. Transition of PLR to actinic reticuloid, a dermatosis characterized by a dense dermal infiltrate simulating lymphoma has been observed and this leads one to suspect that these two entities may be regarded as transitional states of one disease (10).

In the present patient who exhibited extremely severe PLR, the threshold dose to UVA was strikingly low and thus PUVA could not be applied. The administration of high-dose systemic corticosteroids in combination with azathioprine led to marked side effects but only short periods of slight relief could be achieved; the patient was not able to undertake normal outdoor activities even in winter. Four weeks after administration of CyA, the lesions disappeared, pruritus subsided and the patient was able to enjoy normal outdoor activities.

His UVA threshold dose rose from 0.5 J/cm^2 prior to therapy to 16 J/cm^2 during treatment. Spontaneous remission appears to be unlikely as discontinuation of CyA was followed by a relapse of the disease paralleled by a definite decrease in the UV threshold.

The exact mode of action of CyA in PLR is not yet clear. Histologic examination of skin lesions induced by exposure to artificial or natural sunlight revealed a lymphocytic infiltrate which seems to be primarily of T helper cell origin. CyA acts by blocking the T cell signal to accessory cells and hence prevents the synthesis of interleukin 1. In addition, it blocks the generation of lymphokines, including interleukin 2, thereby inhibiting the proliferation of effector T cells (8), which obviously play an important pathogenic role in PLR. Cyclosporin A may be a valuable therapeutic alternative to systemic corticosteroids in severe cases of persistent light reaction which cannot be controlled by photoprotective measures.

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