# Squamous Cell Carcinomas in Relation to Cyclosporin Therapy of Non Malignant Skin Disorders

ANNEMETTE OXHOLM,[1] KRISTIAN THOMSEN[2] and TORKILD MENNE[1]

[1]*Department of Dermatology, Gentofte Hospital and* [2]*Department of Dermatology, University Hospital, Copenhagen, Denmark*

Oxholm A, Thomsen K, Menne T. Squamous cell carcinomas in relation to cyclosporin therapy of non malignant skin disorders. Acta Derm Venereol (Stockh) 1989; 69: 89–90.

Two patients with psoriasis and one with pityriasis rubra pilaris developed squamous cell carcinomas in relation to cyclosporin A therapy. Dermatological patients previously treated with ultraviolet radiation and other kinds of immunosuppressive therapy may represent a special risk group with respect to cyclosporin. A related malignancies. *Key words: Immunosuppression; Skin cancer; Dermatologic patients.* (Accepted August 10, 1988.)

A. Oxholm, Department of Dermatology, Gentofte Hospital, Niels Andersens vej 65, DK-2900 Hellerup, Denmark.

Cyclosporin A (CsA) is a cyclic endecaptide of fungal origin used as an immunosuppressant, primary in organ transplanted patients and patients with autoimmune diseases (1). CsA is also effective in the treatment of skin diseases where immunoinflammatory reactions are involved, especially in psoriasis (2). Mostly CsA is used in dermatologic patients when other therapies have failed.

Effective immunosuppression increases the risk of malignant tumours especially of the lymphoid system (3). Squamous cell carcinomas have also been reported in relation to immunosuppressive therapy including treatment with CsA (4).

We report three patients who, in relation to therapy with this drug, had diagnosed squamous cell carcinomas.

## CASE REPORTS

### *Case 1*

The patient was a 54-year-old male with severe psoriasis for 8 years. Previous treatments included coal tar, repeated courses of PUVA, retinoids and methotrexate; all measures resulting in only partial and short-lasting remissions in the disease. Treatment with CsA (5 mg/kg body weight per day) was successful as the psoriasis improved markedly. However, after 10 months on CsA a swelling of a right inguinal lymph node was observed. Excision and subsequent histological examination revealed metastasis from squamous cell carcinoma. One year previous to CsA treatment the patient had been treated surgically for a squamous cell carcinoma in the sacral region supplemented by radiotherapy with no signs of regional recurrence.

The CsA treatment was stopped and the patient was postoperatively treated with radiotherapy.

### *Case 2*

A 62-year-old male with psoriasis for 16 years previously treated with coal tar, repeated courses of PUVA, retinoids and methotrexate.

During the last two years the patient had suffered from polymyalgia rheumatica treated with prednisolone and azathioprin. Due to exfoliative erythroderma azathioprin was replaced by CsA (5 mg/kg body weight per day). This and continued prednisolone treatment (7 mg/day), was able to keep both diseases in acceptable remission.

After 5 months of therapy with this combination of CsA and prednisolone the patient developed a tumour on the right ear, histologically diagnosed as squamous cell carcinoma. This was radically treated by excision and the CsA treatment was withdrawn.

### *Case 3*

The patient was a 70-year-old male, with pityriasis rubra pilaris for 5 years. Treatment with PUVA, methotrexate, isotretinoin and prednisolone had not been able to control the disease, and thus CsA

therapy was initiated (2–5 mg/kg body weight per day). This treatment was stopped after 2 months as the skin disease did not improve. However, two weeks after cessation of therapy a circumscribed hard swelling of the right parotid gland was observed. The tumour was excised and histologic examination revealed a squamous cell carcinoma (originating from parotid duct). Postoperatively the patient was treated with radiotherapy. After elimination of the malignant tumour the skin disease seems to have improved considerably.

## DISCUSSION

In vivo and in vitro studies of the possible carcinogeneity of CsA have given conflicting findings. The risk of developing malignancies secondary to immunosuppressive therapy is probably not related to the specific drug but rather to the degree and duration of immunosuppression (3).

When dermatologic patients are treated with CsA they have often previously been treated with other immunosuppressive drugs. However, the dosage of CsA is usually lower than that employed for organ transplanted patients (5, 6).

The mean time for developing cancer following administration of CsA is shorter, about 20 months compared to conventional immunosuppressive therapy where it is about 60 months (3). In the patients we have presented, the tumours were observed two to 10 months after administration of CsA.

CsA is capable of promoting the survival and progression of UVR-induced skin tumours probably by its capacity to enhance the dominance of suppressor-cell-controlled immune responses (7). These observations could be of importance for dermatologic patients treated with CsA compared to patients treated with CsA for other diseases as these patients (especially psoriatic patients) very often have received UVR therapy for long periods.

Previous to CsA therapy, all the patients we describe had been treated with PUVA and other immunosuppressive drugs. The carcinomas in these patients were observed only few months after administration of CsA. These facts make it most likely that CsA has led to the progression of existing, but not yet clinically evident, tumours rather than being directly carcinogenic.

Skin cancers are slow-developing tumours and the follow-up of dermatological patients receiving CsA has been rather short as this drug has only recently been introduced in dermatology. However, skin cancers could very well turn out to be a major problem in dermatologic CsA-treated patients.

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