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Subpopulations of T Lymphocytes in a Patient with Fulminant Mycosis Fungoides

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Abstract. A patient with fulminant Mycosis fungoides was found to have a very high percentage of T lymphocytes with Fc receptors for IgG and a low percentage of T lymphocytes with Fc receptors for IgM. The total number of T lymphocytes was normal, but the *in vitro* function of the lymphocytes was depressed in short-term cultures, though not in cultures of 5 days' duration. T lymphocytes with Fc receptors for IgG are considered to have suppressor functions, and the immunological changes in this patient may be explained by an increased suppressor cell activity. Other investigators have proposed that the abnormal lymphocytes in Mycosis fungoides are T helper cells. After treatment with electron beam and transfer factor, our patient developed uraemia due to uric acid crystallization in the kidneys. This complication to the treatment given seems not to have been reported before.

Mycosis fungoides is characterized by an infiltration of lymphocytes in the skin. The cells are mostly large lymphocytes, immunoblasts, or Sézary cells (6). There is reason to believe that the 'mycosis cell' is derived from the thymus-derived

(T) lymphocyte population, and that the T-lymphocytes must be T helper lymphocytes characterized by an Fc receptor for IgM on their surface (2, 7).

We report here our studies on subpopulations of T lymphocytes and lymphocyte reactivity *in vitro* in a patient with a fulminant form of Mycosis fungoides.

CASE REPORT

A 73-year-old man was admitted with a universal erythrodermia and an itching eruption of brownish-red infiltrated patches and tumours. The symptoms were of 6 months' duration. The inguinal lymph nodes were enlarged, but histological investigation of these glands and of bone marrow showed no sign of involvement. A skin biopsy confirmed the diagnosis of Mycosis fungoides, stage III. The patient had light crural oedema, but apart from the skin changes the clinical findings were normal. Laboratory investigations showed a slight increase in the erythrocyte sedimentation rate, normal haemoglobin and a normal white blood cell count. The serum creatinine content was normal (1.0 mg per 100 ml of serum), serum uric acid was 8.4 mg per 100 ml of serum.

The patient was treated with potent steroid ointment, electron beam and transfer factor. Initially, he responded well, but a few months later, one week after a new course of electron beam therapy, he was admitted with uraemia, which apparently developed within the course of a few days. Serum creatinine was around 20 mg per 100 ml of serum, serum uric acid was 24 mg per 100 ml of serum, there was polyuria, proteinuria and erythrocyturia. The situation deteriorated in spite of treatment, and the patient died from bronchopneumonia and uraemia. Because of excessive cadaverositas a search for uric acid crystals in the kidneys failed.

Immunological investigations using our routine techniques (4) showed a normal number and percentage of T lymphocytes forming rosettes with sheep erythrocytes (Table I). However, the percentage of T lymphocytes carrying an Fc receptor for IgM was low. Actually, the ratio between these two populations was completely reversed at all investigations. Table II shows the results of the *in vitro* function of the lymphocytes. In unstimulated cultures the DNA synthesis was high during the first 3 days of culture after which it fell to normal levels at the 5-day culture. The PHA-stimulated cells

Table I. Subpopulations of T lymphocytes in a patient with mycosis fungoides

n.d.=not done, T-gamma=T lymphocytes with Fc receptors for IgG, T-mu=T lymphocytes with Fc receptors for IgM, E-AET=Estimates all T lymphocytes with receptors for sheep erythrocytes, E-a=Estimates a fraction of T lymphocytes

Date	Total no. of T lymphocytes per μ l blood	E-AET (%)	E-a (%)	T-gamma (%)	T-mu (%)
28.2.79	1496	83	44	25	7
6.3.79	n.d.	75	55	49	14
13.3.79	2451	77	48	65	7
21.3.79	1595	79	46	45	6
27.3.79	1855	83	49	31	7
Normal range	725-3 453	70-91	28-64	3-27	4-65

only expressed a weak DNA synthesis compared with unstimulated cultures after 3 days, but were stronger after 5 days.

Stimulation of lymphocytes with purified protein derivative of tuberculin (PPD) gave a very marked in vitro response. The patient had a strong non-specific suppressor cell activity, amounting to 41% suppression of DNA synthesis in a ConA-induced suppressor cell assay. Healthy persons have a mean of 25% suppression of DNA synthesis (range 2-83%, $n=13$ persons) (4).

DISCUSSION

Clinically and histologically our patient had Mycosis fungoides and not Sézary's Syndrome or acute leukaemia. Previous investigations have shown that lymphocytes in the skin of patients with Mycosis fungoides are T lymphocytes (1, 2). Worman et al. (7) have found a high percentage of T lymphocytes with Fc receptors for IgM in two patients with Sézary's Syndrome, whereas Gupta et al. (3) found normal or low levels of T cells with Fc receptors for IgM in three patients with the same

syndrome. These authors (3) also investigated 11 patients with Mycosis fungoides and in 4 of the patients they found an increase in the percentage of circulating T lymphocytes with Fc receptors for IgG. The percentage of T cells with Fc receptors for IgM was normal. In our patient we found a very marked change in the normal ratio between the subpopulations of T lymphocytes. The high percentage of T lymphocytes with an Fc receptor for IgG may reflect the high percentage of non-specific suppressor cells (5). The patient did also express strong non-specific suppressor cell activity in vitro. Although the total number of T lymphocytes was normal, the in vitro reactivity was clearly changed, in that the 3-day cultures showed no increase in DNA synthesis after PHA stimulation, whereas this did occur in cultures of 5 days' duration. On the other hand the DNA synthesis after PPD stimulation was very high. The results may be explained by the fact that mitogen stimulation is non-specific, involving many more cells than PPD stimulation. PHA stimulation in this patient apparently included non-specific suppressor cell stimulation.

It is conceivable that the intensive treatment of

Table II. In vitro reactivity of lymphocytes from a patient with mycosis fungoides

Cpm (counts per minute) is a measure of DNA synthesis. SI is stimulation index and is the ratio between stimulated and unstimulated cell cultures. Only the highest index obtained is included in the table

Date	Unstimulated cultures, cpm 3 days' duration	Unstimulated cultures, cpm 5 days' duration	PHA _{max} , SI 3-day culture	PHA _{max} , SI 5-day culture	PPD _{max} , SI 5-day culture
28.2.79	6700	2200	2.2	8.1	10.8
13.3.79	2400	1800	2.3	7.1	9.8
21.3.79	2000	1400	5.3	7.0	12.4
27.3.79	1800	1500	4.5	n.d.	15.2
3.4.79	7900	900	1.0	n.d.	13.4
Normal range	1 000-2 500	1 000-3 500	7.8-45.3	-	3.0-9.3

this patient led to a strong cell destruction with consequent release of large amounts of uric acid. This cause of uraemia is well known in the treatment of patients with leukaemia, but seems not to have been described before in a patient with Mycosis fungoides. Hence if patients with Mycosis fungoides present with a pronounced skin affection, then caution should be taken during therapy to avoid this complication.

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Normalized Light Reactions in Mycosis Fungoides Patients after Complete Remission of Skin Lesions

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Abstract: Eleven mycosis fungoides patients were photo-tested on apparently normal skin before treatment with mechlorethamine, typically in 8 patients and with methoxypsoralen followed by longwave ultraviolet light (PUVA) in 3 patients. Abnormal photosensitivity to UVB was seen before treatment in 4, to UVA in 4, and to visible light in one patient. The abnormal photosensitivity to all wavelength regions was normalized after complete remission of the cutaneous lesions. Two of the PUVA-treated patients demonstrated that special care should be taken during the initial phase of this treatment because of the light sensitivity, especially on lesional skin.

Key words: Mechlorethamine; Mycosis fungoides; Photochemotherapy; Photosensitivity

Abnormal photosensitivity is most pronounced on lesional skin in mycosis fungoides patients. Clinical evidence for this assertion is given by the observation that diseased skin in these patients very easily burned during photochemotherapy with psoralen and subsequent exposure to long-wave ultraviolet light (PUVA) (1, 3-6). Experimentally it is shown that the erythema threshold in apparently normal skin is lowest close to cutaneous lesions (10). These observations are important, considering the increasing use of PUVA treatment in mycosis fungoides patients.

The purpose of the present study was to explore the possibility of normalized light reactions in mycosis fungoides patients after complete remission of skin lesions induced by mechlorethamine in 8 patients and by PUVA in 3 patients.

MATERIALS AND METHODS

The material consisted of 11 mycosis fungoides patients, 5 women and 6 men, age range 45-72 years. Five of them are reported in a previous paper (10). All patients had clinical cutaneous lesions of mycosis fungoides and the diagnosis was confirmed histologically, before treatment was started. Eight were classified as stage II and three as stage III.