Acta Dermatovener (Stockholm) 60: 139–143, 1980

SUPPRESSOR T CELLS IN MYCOSIS FUNGOIDES AND SO-CALLED PREMYCOTIC ERUPTIONS

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Abstract. The proportions of suppressor T cells (T_G) and helper T cells (T_M) were determined in 5 patients with Mycosis fungoides (MF), 4 patients with parapsoriasis en plaques/poikiloderma atrophicans vasculare and 3 patients with generalized chronic dermatitis. All the MF patients showed increased proportions of suppressor T cells, whereas the others did not differ from age- and sex-matched healthy controls.

Key words: Mycosis fungoides; Parapsoriasis en plaques; Poikiloderma atrophicans vasculare; Chronic dermatitis; Lymphocytes; Suppressor T-cells

Lymphocytes with markers characteristic of T lymphocytes have been demonstrated in skin infiltrates of patients with Mycosis fungoides (MF) (3, 10). It is also now generally accepted that MF should be classified as a T-cell derived lymphoma. Concerning the number of T lymphocytes in the peripheral blood of the MF patients, there are conflicting reports in the literature (5).

Evidence has recently been presented that T lymphocytes can be divided into two major subpopulations: T-helper and T-suppressor cells. These two functional populations have been shown to possess Fc receptors for either IgG (suppressor T cells) or IgM (helper T cells) (7). Gupta et al. (5) have recently reported that some MF patients have higher proportions of cells with Fc receptors for IgG, while other MF patients have normal percentages of these cells.

In view of these observations it was considered of interest to examine total T lymphocytes as well as T lymphocyte subpopulations in patients with histologically verified MF as compared with patients with so-called "premycotic eruptions".

MATERIAL AND METHODS

Patients

Twelve patients were the subjects of the present study (Table I). Each patient had an age- and sex-matched healthy control. Five patients had MF; 4 patients had parapsoriasis en plaques and/or poikiloderma atrophicans vasculare and 3 had chronic generalized dermatitis. The 5 patients with MF were classified according to the criteria published by the Scandinavian Mycosis Fungoides Study Group (4). The histological pictures were the following: The patients with MF all had infiltrates consisting of atypical lymphoid cells in the corium. In the 4 patients with parapsoriasis en plaques/poikiloderma atrophicans vasculare, there were band-like or perivascular infiltrates of lymphocytes in the upper corium. In the patients with chronic generalized dermatitis there were histological changes corresponding to a subacute chronic dermatitis with dense variegated inflammatory cell infiltrates in the upper corium. The patients in the parapsoriasis and the dermatitis groups had all been referred to the clinic for suspicion of so-called premycotic eruptions. In none of those patients was it histologically possible to identify conclusively lymphoid cells with atypia characteristic of malignancy.

The histological examination (E. B.-A.) and the immunological tests were performed without any knowledge of either clinical or laboratory data concerning the patients under study. All patients had, prior to the laboratory testing, been periodically treated topically with glucocorticoid ointments. Otherwise, the treatment is as stated in Table I. The PUVA treatment was given according to the principles of the European Cooperative Clinical Trial (ECCT) described by Wolff et al. (11).

Immunological methods

Cell separations. Heparinized venous blood was centrifugated on Ficoll-Isopaque. Phagocytic cells were removed by iron powder and a magnet, and the lymphocytes were once again centrifugated on Ficoll-Isopaque (9).

T cells were separated from such purified lymphocyte preparations by a rosette sedimentation technique using neuraminidase-treated sheep red blood cells (SRBC) (1, 7). The SRBC–lymphocyte mixture was incubated over-

Table I

Case No.	Sex	Diagnosis	Born	Age (y.)	Duration (y.)	Case history	Histological features	Therapy prior to investigation
1	M	Mycosis fungoides stage III	1905	73	45	1933: parapsoriasis-like eruptions on trunk. 1948: first tumours on face and leg. Over the years, partly ulcerating tumours. Temporary regressions during treatment. Up to now (1979) remarkedly good general health	Dense infiltrate consisting atypical lymphoid cells	X-ray
2	M	Mycosis fungoides stage V	1913	65	11	1967: parapsoriasis-like eruptions on trunk. 1971: MF stage II. 1977: MF stage III with disseminated tumours. Dead 1978. Post-mortem examination: tumourous infiltrates in lung and liver	Dense infiltrate consisting atypical lymphoid cells	X-ray, cytostatics
3	F	Mycosis fungoides stage II	1921	57	12	1965: parapsoriasis-like eruptions on trunk. Regression after topical treatment with glucocorticoids. 1976: relapse of skin lesions. 1978: diagnosis of MF stage II. Free from skin lesions after PUVA treatment	Dense infiltrate consisting atypical lymphoid cells	PUVA
4	F	Mycosis fungoides stage II	1924	54	2	1976: isolated skin infiltrates on trunk. 1978: diagnosis of MF stage II. Regression of all skin lesions after PUVA treatment	Dense infiltrate consisting atypical lymphoid cells	–
5	M	Mycosis fungoides stage II	1907	72	1½	1978: isolated skin lesions on trunk. 1979: diagnosis of MF stage II. PUVA treatment started 1979	Dense infiltrate consisting atypical lymphoid cells	–
6	M	Poikilod. atroph. vascul.	1907	71	4	1974: first skin lesions. 1975: clinical and histological features corresponding to poikiloderma atrophicans vasculare	Band-like infiltrate of lymphocytes	–
7	F	Poikilod. atroph. vascul.	1907	71	32	1946: parapsoriasis-like eruptions. Since 1955 disseminated infiltrated plaques. Histologically on several occasions, strong suspicion of MF. The histological feature has, however, never been conclusive	Perivascular infiltrates of lymphocytes	X-ray PUVA
8	M	Parapsor. en plaques	1915	63	2	1976: parapsoriasis-like lesions on buttocks and leg. Skin lesions cleared after PUVA treatment	Band-like infiltrate of lymphocytes	–

Case No.	Sex	Diagnosis	Born	Age (y.)	Duration (y.)	Case history	Histological features	Therapy prior to investigation
9	M	Parapsor. en plaques	1945	34	16	1963: eczematous skin lesions on the belly. 1975: clinical and histological features of parapsoriasis en plaques. The skin eruptions healed after PUVA treatment	Band-like infiltrate of lymphocytes	PUVA
10	F	Chron. general. dermatitis	1922	56	6	Since 1970 disseminated eczematous skin lesions on the trunk. Patch test: sensitive to chromium and cobalt. Clinical and histological features: some suspicion of MF. Healed after PUVA treatment	Dermatitis with dense variegated inflammatory cell infiltrates in upper corium	X-ray, PUVA
11	F	Chron. general. dermatitis	1915	64	11	Since 1940 hand eczema. Since 1977 generalized dermatitis on extremities and trunk. Referred to skin clinic on suspicion of MF	Dermatitis with dense variegated inflammatory cell infiltrates in upper corium	–
12	F	Chron. general. dermatitis	1919	59	1	1978: eczematous oozing lesions on the feet. After some months, generalized dermatitis. Referred to skin clinic on suspicion of MF	Dermatitis with dense variegated inflammatory cell infiltrates in upper corium	–

night in 50% fetal calf serum (FCS) at +4°C. After gradient centrifugation, SRBC were lysed with NH_4Cl. The lymphocyte suspension contained 97–100% SRBC-rosette forming cells (E-binding cells).

Detection of Fc receptor bearing lymphocytes

T lymphocytes with receptors for the Fc portion of either IgG (T_G) or IgM (T_M) were determined by the method of Moretta and co-workers (7) as described previously in detail (1). Briefly, T_G cells were identified by their ability to form rosettes with bovine erythrocytes coated with rabbit anti-bovine erythrocyte IgG. T lymphocytes used for determination of the proportion of T_M cells were first incubated overnight at 37°C in RPMI 1670 medium supplemented with 20% FCS. T_M cells were identified by rosette formation with bovine erythrocytes coated with rabbit anti-bovine erythrocyte IgM. A rosette was defined as a lymphocyte with three or more red cells attached. 200–400 lymphocytes were scored for rosette formation. All tests were performed in duplicate.

Statistical analysis

The statistical difference between means was calculated using Student's *t*-test.

RESULTS

The total numbers of peripheral blood lymphocytes in patients with either MF or 'premycotic eruptions' were alike and were of the same order of magnitude as those in healthy persons of the same age group (data not presented).

The percentage of T lymphocytes in patient groups did not seem to differ from that of healthy controls (Table II). However, only 3 MF patients were examined, which does not permit us to draw any definite conclusion concerning this latter patient group.

The results of determination of T_G and T_M cells are given in Table III. The patients with MF had significantly ($p<0.001$) higher proportions of T_G cells than the patients with 'premycotic eruptions' and normal donors. On the other hand, there were no significant differences in the proportions of T_M cells among the three groups examined.

Table II. *Percentages of T lymphocytes in Mycosis fungoides (MF), Parapsoriasis en plaques/Poikiloderma atrophicans vasculare (P/P) and Chronic Dermatitis (CD)*

Case No.		Controls
	MF	
1	ND[a]	70
2	71	70
3	68	80
4	54	60
5	ND	ND
	P/P	
6	58	59
7	76	ND
8	38	ND
9	54	66
	CD	
10	57	65
11	70	75
12	63	73
Mean	59[b]	67

[a] ND=Not done.
[b] Mean of P/P and CD.

Table III. *Percentages of T_G and T_M lymphocytes in Mycosis fungoides (MF), Parapsoriasis en plaques/Poikiloderma atrophicans vasculare (P/P) and Chronic Dermatitis (CD)*

Case No.	T_G cells	T_M cells	Controls T_G cells	Controls T_M cells
	MF			
1	43	26	22	45
2	36	42	11	55
3	37	35	24	42
4	32	66	16	45
5	36	27	27	51
Mean	37	39		
	P/P			
6	19	41	18	48
7	7	65	ND[b]	ND
8	25	47	ND	ND
9	23	39	16	53
	CD			
10	21	37	15	46
11	18	63	17	54
12	11	51	15	59
Mean	18[a]	49[a]	18	50

[a] Mean of P/P and CD.
[b] ND=Not done.

DISCUSSION

The role of suppressor T cells or their products has recently been widely discussed. It has been shown that some forms of immunodeficiency may be associated with quantitative or qualitative abnormalities of these cells (6). Disturbances in cellular immunity present in some malignancies have been shown to be associated with altered proportions of T-lymphocyte subsets (6). Furthermore, experimental studies in mice strongly suggest a relationship between different types of tumours and the immunological system of the host, as expressed inter alia by the function of suppressor cells (8). It has been shown that both T lymphocytes and macrophages are involved (8).

Recently, quantitative and/or qualitative abnormalities of T_G and T_M cells have been reported in Sézary's syndrome (2). Gupta et al. (5) examined T_G and T_M cells in 14 patients with Mycosis fungoides and found normal proportions of total blood T lymphocytes, except in one patient. Three patients had a high frequency of T_G cells, whereas one patient had a high proportion of T_M cells. These findings indicate, according to Gupta et al., a heterogeneity of the distribution of T-lymphocyte subsets in patients with Mycosis fungoides.

Our results differ somewhat from those referred to above, as all 5 MF patients had high proportions of T_G cells and as there was no significant difference in the frequency of T_M cells between MF patients and the two control groups. Although the number of patients with MF was limited, it must be emphasized that stages II, III and V of the disease were represented and that all 5 patients demonstrated exactly the same type of imbalance in T_G cell subpopulations.

It is possible that the apparent disagreement between our results and those of Gupta et al. might be explained by differences in diagnostic criteria, clinical status, treatment or duration of the disease. However, since the untreated and treated MF patients in our material behaved in the same way it is less likely that the treatment itself has influenced the results. However, as no clinical data are available in the report by Gupta et al., it is not possible to compare the respective patients.

The significance of our findings is largely unknown. It remains to be clarified whether the atypical lymphoid cells in skin lesions of MF, which have been confirmed as being of T-cell origin (3, 10) have

Fc receptors for IgG. Furthermore, the functional ability of these cells should be examined. It is possible to speculate that the suppressive effect supposedly exerted by T_6 cells, demonstrated in MF, might permit the induction of the disease and/or promote the proliferation of neoplastic cells. Alternatively it is also possible that the induction of suppressor cells is secondary to the disease.

However, we know very little at present about the nature and function in vivo of these cells and any further knowledge depends on detailed characterization of their biological properties.

ACKNOWLEDGEMENTS

The authors wish to thank Miss Inger Vedin and Mr Ricardo Giscombe for their skilful technical assistance.

This work was supported in part by the Swedish Medical Research Council (project 16X-2380).

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Received June 20, 1979

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