ALTERATIONS OF THE CELLULAR IMMUNITY IN BEHÇET'S DISEASE

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SUMMARY : Several theories have been reported about the pathogenesis of Behçet's disease, and the studies have recently been focused on the cellular immunity.

In this study, we evaluated the role of cellular immunity in pathogenesis of Behçet's disease. The total T lymphocyte, T helper lymphocyte (T_4) and T suppressor lymphocyte (T_8) values and the Purified Protein Derivative (PPD) test as an important parameter of the cellular immunity, were examined.

In the patients with the active and inactive state; total T lyphocyte values were found to be significantly decreased, with negative PPD tests and normal T_4 values. T_8 levels were significantly increased only in the patients with the active state.

Our results suggest that the alterations in the cellular immune system play an important role in the pathogenesis of Behçet's disease. There is a close relationship between the activation of the disease and cellular immune system.

Key Words : *Behçet's Disease, Cellular Immunity.*

INTRODUCTION

Behçet's disease was described as a symptome triad, including oral and genital aphtous lesions and iridocyclitis in 1937 (Behçet, 1937). Nowadays, Behçet's disease has gained a multisystemic character involving the eye, joints, central nervous system, vascular system, pulmonary system, the alimentary tract and the mucocutaneous areas (Wong et al. 1984).

Studies on the etiopathogenesis of the disease are still being carried on. A viral infection, genetic factors, the differences in the activation of the fibrinolytic system and the toxic response against organic chemicals can be responsible (Sepici et al. 1988; Sezer, 1953).

The immunological theory based on the differences in the immune system, particularly in the cellular immunity, can play an important role in the etiopathogenesis of Behçet's disease (Lim et al. 1983).

In this study, the number of T lymphocytes and their subsets and to the results of PPD test have been investigated in the patients with Behçet's disease.

MATERIALS AND METHODS

This research project took place in the Department of Dermatology, Medical School of Gazi Uni-

versity and Immunology Laboratories of the Gülhane Military Medical School.

Patient groups : In this group, a total of 57 patients forming two groups, as active and inactive, were evaluated. There were a total of 26 patients : 9 female and 17 male, ages 16 to (mean age 33.846 ± 2.076) in the active group and there were a total of 31 patients : 14 female and 17 male, ages 8 to 69 (mean age 31.323 ± 3.429) in the inactive group. All patients had the clinical features of Behçet's disease.

The duration of the disease in the active group was one to fourteen years, while this period was one to fifteen years in the inactive group.

Healthy Control Group : A total of fifteen individuals : 7 female and 8 male, ages 16 to 52 (mean age 30.533 ± 2.550) from the hospital staff were evaluated as a control group.

Laboratory Techniques : The patients did not receive any medicine which might effect the cellular immunity, at least for four weeks. The same laboratory techniques were applied to the patient groups and the control group.

1- The PPD test : The classical Mantoux skin test was performed.

2- The determination of T lymphocytes were made by using E - rosette formation technique. A new modification, redefined by Jondal was used (Beveley, 1986).

3- The determination of T lymphocyte subsets : The lymphocytes were separated from the peripheral blood, and cell surface antigenes were examined by matching with monoclonal antibody (MoAb). T_4 lymphocytes were matched with OKT_4 MoAb (XXXIV-54, T-Helper, Kallstead Labs, U.S.A.) and T_8 lymphocytes were matched with OKT_4 MoAb (XLII-16, T-Suppressor, Kallstead Labs, U.S.A.). 200 cells were counted and the percentage of cells that had positive surface fluorescent were defined (%) (Reinherz et al. 1979).

4- Biostatistical Analysis : For the determination of the differences in the values of total T lymphocyte, T_4 lymphocyte, T_8 lymphocyte and T_4 / T_8 ratio of the patient groups and the control group were determined by using student-t test. The comparison of the PPD test results in the active, inactive and the control groups was made by Q-square (in percentile) test (Arkın and Calton, 1963).

RESULTS

The clinical properties of the patients in the active group are summarized on Table 1.

The PPD test is found to be positive in 10 patients and negative in 16 patients (61.5 %), in the active group. In the inactive group, the PPD test is found to be positive in12 patients and negative in 19 (61.2 %). In the control group, it is positive in 11 individuals and negative in 4 individuals (26.7 %). The comparison of the results of active and inactive groups to the control group shows that there is a statistically significant difference between these groups ($p<0.05$).

The PPD test results, and total T lymphocyte, T_4 and T_8 values are shown on Table 2.

Biostatistical analysis of these results indicated that, total T lymphocyte values were significantly decreased in both when active and inactive groups, compared with the control group ($p<0.05$). The difference between the mean T_4 values of two (active and inactive) groups and the control group was statistically meaningless ($p>0.05$). However, the mean T_8 values of all patients and the inactive group were statistically meaningless when compared to the control group, while the mean T_8 values of the active group was significantly increased when compared to the controls ($p<0.05$).

It can be seen that the mean number (±SD) of T_4 / T_8 ratio in the active group, is 1.45 ± 0.05; while it is 1.76 ± 0.08 in the control group. This suggests that the mean number of T_4 / T_8 ratio in the active group was significantly lower than the control group ($p<0.05$). In the inactive group, we find the mean number (±SD) of T_4 / T_8 ratio rising to 1.57 ± 0.10; so, the difference between them is not significant ($p>0.05$).

Total T lymphocyte, T_4, T_8 ratio values and T_4 / T_8 ratio of both active and inactive groups and the control group are shown on Table III.

DISCUSSION

Immunological process has been gaining increasing importance among the views put forward about the a etiopathogenesis of Behçet's disease.

No	Sex Age	Aphthae	G.U.	E.N.	Folliculitis	Ocular	Joint	Vascular	C.N.S.
1	M20	+				+			
2	F22	+	+	+					
3	F16	+	+						
4	F30	+	+						
5	M32	+	+	+					+
6	M32	+			+				
7	M29	+	+	+			+		
8	M29	+	+						
9	M42	+	+				+		
10	M40	+	+		+			+	
11	F18	+			+				
12	M36	+					+		
13	F13	+	+						
14	M44		+		+			+	
15	M42							+	
16	F45	+			+		+		
17	M29	+			+		+		
18	F18	+			+			+	
19	M55	+			+		+		
20	M57	+					+		
21	M32		+					+	
22	F26	+		+			+		
23	M35	+	+						
24	M38	+					+		
25	M35	+	+				+		
26	F35	+							

Table - 1 : Clinical symptoms and signs in patients with active Behçet's Disease.
(G.U. : Genital Ulcer, E.N. : Erythema Nodosum, C.N.S. : Central Nervous System).

Studies focusing the humoral immunity showed that serum immunoglobulin and complement levels could be high or normal in patients with Behçet's disease. High immunoglobulin levels, especially in the active state of the disease, were reported (Shimizu et al. 1973). The tissue specimens taken from the oral and genital aphtous lesions were examined with direct immunofluorescein technique and localized immunoglobulins, particularly IgG, on the vessel walls were reported. These results support the view that; Behçet's disease can be an autoimmune process (Williams and Lehner, 1977). A definite result relevant to a etiopathogenesis has not been obtained by the studies on the circulating immune complexes and B lymphocytes (Lim et al. 1983).

The PPD test, an important parameter of the cellular immunity, was found to be generally positive in the patient groups. This result suggested that no abnormalities on the cellular immune system could be determined (Müftüoğlu, 1980; Ural et al. 1986).

Many different and discordant results about T lymphocytes and T cell subsets were reported. This discordance could be partly attributed to the activation of the disease and technical mistakes (Raedler et al. 1986; Rimon et al. 1985). Total T lymphocyte values could be reported as normal; but, generally, there was a decrease in the total T lymphocytes and a suppression in the cellular immunity (Ahmed, 1982; Haim et al. 1976; Victorino et al. 1982). The reports about T_4 lymphocyte and T_8 lymphocyte values, had a contrary result (Lim et al. 1983; Sakane et al. 1982; Valesini et al. 1985). It seems that there is an immunological process in the etiopathogenesis of Behçet's disease, but the studies remained inadequate to explain this process.

In our study, we estimated the PPD test results highly negative in both of the active and inactive groups, compared with the control group. This reveals a cutaneous anergia and a suppression in the conflict immunity in Behçet's disease. Our results conflict with the studies reported before.

There is no statistically significant difference in the serum levels of T_4 lymphocytes, between both

ACTIVA PATIONTS					INACTIVA PATIENTS				
No.	PPD	Cells %			No.	PPD	Cells %		
		T	T_4	T_8			T	T_4	T_8
1	-	30	32	22	1	-	32	28	17
2	-	16	18	12	2	-	15	14	15
3	-	14	26	20	3	-	21	36	13
4	+	50	31	31	4	-	9	18	14
5	-	14	28	24	5	+	34	28	24
6	-	36	24	16	6	-	33	18	15
7	-	42	36	20	7	-	40	24	19
8	+	38	32	18	8	-	17	38	21
9	-	34	30	30	9	+	44	36	18
10	-	52	40	36	10	-	40	32	14
11	+	36	22	19	11	-	35	14	11
12	+	54	42	24	12	+	57	22	16
13	+	34	30	22	13	+	52	40	22
14	+	30	22	16	14	-	43	30	16
15	+	37	16	13	15	-	29	12	9
16	+	32	20	16	16	+	50	20	17
17	-	47	19	16	17	+	59	22	18
18	-	43	16	11	18	+	38	14	11
19	-	42	17	12	19	+	47	19	16
20	-	32	12	9	20	-	21	57	26
21	-	30	13	9	21	-	16	37	14
22	-	22	37	20	22	-	39	14	13
23	+	46	34	18	23	-	35	15	13
24	+	44	32	22	24	+	43	16	15
25	-	63	26	14	25	+	41	37	16
26	-	55	24	14	26	+	47	16	16
					27	-	48	24	16
					28	-	36	26	14
					29	+	64	27	26
					30	-	57	24	19
					31	-	65	25	18

Table - 2 : Specialities of the cellular immunity of the patients with active and inactive Behçet's disease.

	No of Patients	Mean Cell Values %			T_4 / T_8
		T	T_4	T_8	
All Patients with Behçet's Disease	57	38.298 ± 1.78	25.825 ± 1.25	17.368 ± 0.17	1.52 ± 0.06
Active Patients	26	37.423 ± 2.46	26.500 ± 1.64	18.615 ± 1.33	1.45 ± 0.05
Inactive Patients	31	39.032 ± 2.58	25.258 ± 1.84	16.323 ± 0.67	1.57 ± 0.10
Control Subjects	15	47.800 ± 3.15	27.200 ± 2.36	15.553 ± 1.13	1.76 ± 0.08

Table - 3 : The mean T cells, T cell subset values and T_4/T_8 rations of the patients with Behçet's disease.

of active and inactive groups, and the control group. This data suggests that T_4 lymphocytes do not play an important role in the immunopathogenesis of Behçet's disease.

The increase of the T_8 lymphocyte values of the active patients compared with the control group, results with the decrease of the T_4 / T_8 ratio, whereas this ratio is nearly the same in the control and inactive groups.

As a result; we detected a defect in the cellular immunity in Behçet's disease. A factor, which may increase the T_8 lymphocyte levels, deranges the T_4