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T-Lymphocyte Subpopulations in Schizophrenic Patients

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Summary. T-lymphocyte subpopulations were examined in the peripheral blood of 30 acute schizophrenic patients and compared with 30 age- and sex-matched patients with non-inflammatory neurological diseases. Significant increases in the numbers of Pan-T and T-helper cells were found in schizophrenic patients compared to the controls. The interindividual variability of values in the group of schizophrenic patients was greater than in the group of neurological patients.

Key words: Schizophrenia – T-lymphocytes – Autoimmune disease

Introduction

Schizophrenia has been hypothesized to be an autoimmune disease [3, 11]. Autoantibodies against brain tissue [7, 15] and other tissues have been described, including lymphocytes [8, 10]. Peripheral T-lymphocytes have been reported to be reduced in number [2, 14] and function [9, 13, 20] besides showing morphological changes [6, 19]. Other groups, however, did not find any differences between schizophrenic patients and controls [5] or found an increase of T-lymphocytes [4]. Therefore we examined T-lymphocytes and T-cell subpopulations in the peripheral blood of acute schizophrenic patients.

Patients and Methods

Thirty patients (18 ♂, 12 ♀) with normal blood cell counts suffering from an acute relapse of a known schizophrenic disease (DSM III) were included. Mean duration of the disease was 7.5 years; the mean number of relapses was 4.1. Of these patients, 93% showed acute paranoid-delusive, and 7% hebephrenic symptoms. Eighty-seven percent of the patients had no medication, 13% received haloperidol, and 7% biperiden in a medium dosage, when the tests were performed. Fourteen age- and sex-matched patients with noninflammatory neurological diseases (6 with disc prolapses, 3 cerebral insults, 3 epilepsies, 1 ocular myasthenia, 1 heredoataxia), and 16 staff members served as controls (Table 1).

Blood was drawn into heparinized tubes by venipuncture between 8.00 and 10.00 a.m. Lymphocytes were prepared by Ficoll gradient (Pharmacia, Stockholm) and differentiated by monoclonal antibodies in an indirect immunofluorescence assay [17]. In short, 1×10^6 cells in phosphate-buffered saline (+ 0.1% human serum albumine, + 0.02% Natriumazid) were incubated for 30 min at 4°C in the respective monoclonal antibody (CD11 marked pan-T, CD4 T-helper and anti-Leu2a T-suppressor cells; CD11 and CD4 were generous gifts from Professor Fleischer, Department of Immunology, Ulm, FRG; anti-Leu2a were from Becton and Dickinson, Rödermark, FRG). After three washes, cells were incubated in the same conditions in fluorescein-conjugated goat anti-mouse IgG

Table 1

Patients	Male			Female		
	Number (*n*)	Age		Number (*n*)	Age	
		x	SD		*x*	SD
Schizophrenia	18	37.7	12.5	12	47.2	11.8
Controls	18	37.8	12.1	12	47.1	11.7

Patients in the study; *x* = mean age, SD = standard deviation

Table 2

	Schizophrenics			Controls		
	x	SD	SD/*x*	*x*	SD	SD/*x*
T11 [%]	58.4	16.2	0.28	49.8	11.2	0.23
T4 [%]	40.3	13.5	0.33	33.8	8.6	0.25
T8 [%]	28.9	18.5	0.64	21.6	8.6	0.40
T4/T8	1.8	1.1	0.61	1.8	0.7	0.39

Percentages of lymphocytes reacting with a monoclonal antibody are given; T11 = pan-T, T4 = T-helper, T8 = T-suppressor cells, T4/T8 = helper/suppressor quotient

Pan-T and T-helper cells were significantly increased in the group of schizophrenic patients ($P < 0.05$). The helper/suppressor quotient was unchanged

SD/*x* (= measure for the interindividual variability) was increased in the group of schizophrenic patients

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(Ortho Diagnostic Systems, Raritan, NJ, USA). After washing, 200 lymphocytes were counted under a fluorescence microscope (Zeiss, Stuttgart, FRG). Patients and control samples were run in parallel; the evaluation was done "blindly". For evaluation Student's *t*-test was used.

Results

Comparing T cell subpopulations of schizophrenic patients and controls, we found a significant increase of pan-T and T-helper cells ($P < 0.05$) and a tendency for an increase of T-suppressor cells (Table 2).

A greater interindividual variability (standard deviation/mean value) was seen in the group of schizophrenic patients, which was due to a greater range of values compared with controls.

Discussion

T-cell subpopulations from the peripheral blood of 30 acute schizophrenic patients and 30 controls were determined. We were looking for changes that would support the hypothesis of an autoimmune mechanism in the pathogenesis of schizophrenia. Genetic studies [1], the relapsing-remitting course seen in this disease [11], and the finding that the blood-brain barrier is impaired in schizophrenic patients [12, 18] had pointed in this direction.

We found a significant increase in pan-T and T-helper cells. This was partly in agreement with a study by De Lisi et al. [4], who described an increase in B-cells, T-cells and T-suppressor cells. Other authors who described a decrease in T-lymphocyte numbers [2, 14] used another technique (T cell rosetting), which is not as sensitive as the immunofluorescence test and might be disturbed by several factors.

Generally, our results are compatible with an autoimmune disease in schizophrenia, but do not prove it. Changes of T-lymphocyte subpopulations in the peripheral blood have been described in several other autoimmune disorders (multiple sclerosis, lupus erythematosus, rheumatoid arthritis and others), but we cannot exclude an influence of previous drug therapy on the T-lymphocyte subpopulations (in most of the cases haloperidol). Some other laboratories, however, have described a decrease of T-cells after neuroleptics in mice and man [16, 21], which would not explain our results. De Lisi et al. [4] did not find differences in the increase of T-lymphocytes of medicated and unmedicated patients. The influence of age can be excluded, as well as cigarette smoking, since patients and controls showed similar habits.

Another interesting finding is the greater variability in population numbers in the patients. On the one hand, this might be a phenomenon that is often seen in autoimmune diseases, perhaps because of the relapsing-remitting courses. On the other hand it might be due to many different pathomechanisms. It might, however, also be explained by autoantibodies to lymphocytes that mask surface antigens, which are detected by monoclonal antibodies [8, 10]. The latter will be the subject of a future examination.

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