IMMUNOLOGICAL ASSESSMENT IN SPORADIC AMYOTROPHIC LATERAL SCLEROSIS (ALS)

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Introduction

The immune system may be able to contribute to the pathogenesis of ALS as it has to other neurological diseases such as experimental allergic encephalomyelitis, multiple sclerosis and lymphocytic choriomeningitis. The selective damage to upper and lower motor neurons in ALS might be regarded as a feature of a brain-confined, organ-specific autoimmune disease. The greater frequency of some histocompatibility antigens (HLA3, HLB12, HLBW35) may suggest the possible predisposition to autoimmune and infectious diseases[1-3].

Previous studies concerning humoral activities pointed out that values with regard to serum complement were normal[4] as they were for circulating immune complexes[5] and also for serum immunoglobulins[6]. On the contrary the incidence of antinuclear antibodies was higher than in normal controls even if only present in very low titers[7]. No specific humoral activity was proven against poliovirus[8] and common virus antigens[9], nor against spinal motor neurons[10] and myelin[11,12] nor against lymphocytes[13]. Only Gurney et al.[14] detected a serum immunoglobulin inhibiting the collateral sprouting in mice. Normal results concerning cell-mediated immunity were shown by Tavolato et al.[6] and Kott et al.[2] during skin tests and by Antel et al.[15] and Shout et al.[16] during activation tests with mitogens. The results obtained by Antel and Shou were not confirmed by Behan et al.[3] and Hoffman et al.[17].

The quantitative assessment of lymphocytic subpopulations by OK monoclonal antibodies was normal in small sporadic ALS groups[18]. On the contrary, Guam patients presented a reduction of T cells[17] and a low functional activity of these cells in the early course of the disease[18]. No specific cell-mediated activity against cerebral tissue was noted by Nemo et al.[19] nor against Ach muscular receptor by Antel[20]. Only Kott et al.[8] revealed cellular immune activity against poliovirus. Because of this conflicting evidence, the immunological system of ALS patients needs further research.
Methods

Out of 18 ALS patients, 13 were selected according to the following criteria:

(i) duration of illness from 2 to 26 months,
(ii) no history of autoimmune or infectious diseases,
(iii) absence of immunomodulating treatment,
(iv) no evidence of cancer,
(v) only patients with a low score on a modified Norris scale were selected.

The 13 patients included 6 cases with conventional, 4 with bulbar, 3 with pseudopolyneuritic ALS; 8 were males and 5 females, mean age 62 years.

The following immunological profile was evaluated:

(i) levels of circulating immune complexes (Clq binding activity),
(ii) organ and non organ specific antibodies,
(iii) serum immunoglobulins G,A,M,
(iv) lymphocyte subpopulations assessed with monoclonal OK antibodies,
(v) E-rosetting procedure.

Results

The following findings must be outlined (Figure 1):

(1) A statistically significant decrease of the percentage of E rosette forming cells (ERCF), i.e., T lymphocytes, was found.
(2) The high OKT4/OKT8 ratio due to a lower OKT8+ frequency and partly to a modest increase of OKT4+ cells, was detected.
(3) On the basis of the analysis of absolute values, the T cell reduction, i.e., ERFC 1018 ± 282/cumm vs. 1700 ± 419 of the normal controls (p<0.001), was shown. This was confirmed by lower OKT3+ subset in the ALS group (p<0.01), due to the decrease of OKT8+ cells.
(4) The number of circulating B cells (S-Ig+ lymphocytes) was found to be normal, as well as the serum levels of Ig subclasses, of complement fractions and of circulating immune complexes. Antibodies against striated muscles and against myocardium were detected in only one patient's serum.

Discussion

Although our ALS group was restricted to a few patients, the low number of similar cases available from previous studies may support the present investigation.

According to previous results, the humoral immunity was normal, as described by Whitaker et al.[4], Oldstone et al.[5,12], Tavolato et al.[6]. Vice-versa a striking involvement of the peripheral T compartment with reduction of the total number of T cells and OKT8 lymphocytes was found. These data do not seem to correlate in any way with age, sex, duration and clinical varieties of the disease. Our results do not confirm previous reports concerning small numbers of non-selected patients (Antel et al.[18], whereas our ALS patients underwent a defined selection as described above.

These data may support the hypothesis of an involvement of cell-mediated immunity in the development of the disease. They do not prove