P0485

Paper Poster Session II

Viral infections of the central nervous system

T CD8+ lymphocytes in the cerebrospinal fluid of patients with tick-borne encephalitis

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Objective: Pathogenesis of the central nervous system (cns) tissue damage in tick-borne encephalitis (TBE) is not well understood and probably includes both the direct cytopathic effect of the TBE virus on cns cells and the secondary immunopathology. Based on animal models of *Flavivirus* encephalitis and on human autopsy studies, cytotoxic T CD8+ lymphocytes have been hypothesized to mediate the cns immune-mediated damage, while Th CD4+ cells are considered protective and involved in TBE virus eradication. To verify that, we have compared the composition of the lymphocyte population in the cerebrospinal fluid (csf) of patients with different clinical forms of TBE.

Methods: Csf and venous blood samples were obtained from 9 TBE patients on admission to hospital: 6 with mild (meningitis) and 3 with severe clinical presentation (meningoencephalitis, with altered consciousness and/or focal neurologic deficits). Total csf pleocytosis and lymphocyte count were measured with standard laboratory techniques. Lymphocyte fractions in blood and csf were quantified cytometrically with a SimultestTM IMK-Lymphocyte kit, which employs pairs of fluorochrome conjugated antibodies to measure fractions of total CD3+, CD3+CD4+ (T helper), CD3+CD8+ (T suppressor/cytotoxic), CD3-CD19+ (B) and CD3-CD56/CD16+ (NK) cell populations. Non-parametric tests were used for statistical analysis.

Results: The median csf pleocytosis was 63 cells/ml and median lymphocyte count 43 cells/ml, with no difference between the meningitis and meningoencephalitis patients. Of csf lymphocytes 95% (median) were T CD3+ lymphocytes, the 79% being Th CD3+CD4+ and 16% T CD8+ cells. NK cells constituted 3% and CD19+ B lymphocytes only 1% of the lymphocyte population. In comparison with the peripheral blood lymphocytes, csf lymphocyte population was significantly enriched in T CD3+ and Th CD3+CD4+ cells. The median fraction of CD8+ cell in the csf of patients with meningoencephalitis was 28%, twice higher than in meningitis group (14,5%), at the expense of all the other cell populations, and the difference was statistically significant ($p<0.05$).

Conclusions: Th lymphocytes are preferentially attracted into csf in patients with TBE, irrespective of the clinical severity. T CD8+ cells constitute a minor fraction in csf of TBE patients, but their association with clinical symptoms of encephalitis supports the hypothesis that they are involved in the cns immunopathology in TBE.