

**O1111 The increased expression of the chemotactic receptor CCR5 on CD8+ T lymphocytes in tick-borne encephalitis**

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**Background:** In tick-borne encephalitis (TBE) the cerebrospinal fluid (CSF) and central nervous system (CNS) tissues contain infiltrates of mainly ThCD3+CD4+ and TcCD3+CD8+ lymphocytes. TcCD3+CD8+ cells have been implicated in intrathecal pathology, but also in TBE virus control and elimination. The chemotactic axes responsible for their migration into CNS in human TBE are not known. According to genetic association studies, the CCR5 chemokine receptor expression is protective against neurotropic flaviviruses, but it is unclear if this effect is mediated by a CCR5 role in lymphocyte migration.

**Materials/methods:** Blood and CSF from 31 patients with serologically confirmed TBE (20 with meningitis - M, 10 with meningoencephalitis - ME, 1 with meningoencephalomyelitis - MEM) and blood samples from 11 healthy donors (C) were studied. The lymphocyte fractions were assessed cytometrically with fluorochrome-stained monoclonal antibodies to CD3, CD4, CD8, CD16/56 and CD19. The chemokine receptors CCR5 and CXCR3 were detected on gated activated CD3+CD8+ and CD4+CD8+ lymphocytes with monoclonal antibodies and isotype controls. The data were analyzed with non-parametric tests with  $p < 0.05$  considered significant.

**Results:** In TBE, CD3+CD8+ lymphocytes constituted 24% (median) of the lymphoid population in blood (not different from C) and 21% in CSF. The CD3+CD8+ cells were more abundant in CSF in ME (median 16.4 cells/ $\mu$ l) than in M (10.4 cells/ $\mu$ l) and still more in patients with altered consciousness (35.2 cells/ $\mu$ l), following the analogous trend for the total lymphocyte count. The fraction of CD8+ within total lymphocytes did not differ significantly between these subgroups. However, two out of its three highest values ( $\geq 35\%$ ) were found in patients with the most severe TBE presentations: MEM and severe ME.

CCR5 was expressed on 48% (median) of CSF CD8+ lymphocytes, significantly higher fraction than blood CD8+ (22%) and CSF CD4+ cells (8%). CXCR3 expression did not differ between CD4+ and CD8+ cells and was not increased in CSF.

**Conclusions:** T CD8+ lymphocytes are present in CSF of TBE patients, but their association with clinical presentation is not evident and requires further study. CCR5 is strongly up-regulated on CSF CD8+ lymphocytes and likely involved in their migration into CNS from the periphery.

