Absence of CCR5 increases neutrophil recruitment in severe herpetic encephalitis.

The neuroinflammatory response aimed at clearance of herpes simplex virus-1 (HSV-1) plays a key role in the pathogenesis of neuroaxonal damage in herpetic encephalitis. Leukocytes activated in an adaptive immune response access brain tissue by passing through the blood-brain barrier. The chemokine CCL5/RANTES is involved in recruitment of these cells to the brain acting via the receptors CCR1, CCR3 and mainly CCR5. Here, we evaluated the role of CCR5 on traffic of leukocytes in the brain microvasculature, cellular and cytokines profile in a severe form of herpetic encephalitis. Wild type and mice lacking CCR5 (CCR5−/−) were inoculated intracerebrally with 104 PFU of neurotropic HSV-1. We evaluated the traffic of leukocytes in the brain microvasculature using intravital microscopy and the profile of cytokines by Enzyme-Linked Immunosorbent Assay at 1 day post infection. Flow cytometry and histopathological analyses were also carried out in brain tissue. Absence of CCR5 leads to lower viral load and an increased leukocyte adhesion in brain microvasculature, predominantly of neutrophils (CD11+ Ly6G+ cells). Moreover, there was a significant increase in the levels of MIP-1/CCL2, RANTES/CCL5, KC/CXCL1 and MIG/CXCL9 in the brain of infected CCR5−/− mice. These results suggest
that the absence of CCR5 may boost the immune response with a high neutrophil recruitment which most likely helps in viral clearance. Nonetheless, the elevated immune response may be detrimental to the host.

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