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Elevated levels of proinflammatory cytokines in cerebrospinal fluid of multiple sclerosis patients

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Abstract

© 2017 Khaibullin, Ivanova, Martynova, Cherepnev, Khabirov, Granatov, Rizvanov and Khaiboullina. Multiple sclerosis (MS) is an autoimmune neurodegenerative disease characterized by chronic brain inflammation. Leukocyte infiltration of brain tissue causes inflammation, demyelination, and the subsequent formation of sclerotic plaques, which are a hallmark of MS. Activation of proinflammatory cytokines is essential for regulation of lymphocyte migration across the blood-brain barrier. We demonstrate increased levels of many cytokines, including IL-2RA, CCL5, CCL11, MIF, CXCL1, CXCL10, IFNγ, SCF, and TRAIL, were upregulated in cerebrospinal fluid (CSF), whereas IL-17, CCL2, CCL3, CCL4, and IL-12(p40) were activated in MS serum. Interaction analysis of cytokines in CSF demonstrated a connection between IFNγ and CCL5 as well as MIF. Many cells can contribute to production of these cytokines including CD8 and Th1 lymphocytes and astrocytes. Therefore, we suggest that IFNγ released by Th1 lymphocytes can activate astrocytes, which then produce chemoattractants, including CCL5 and MIF. These chemokines promote an inflammatory milieu and interact with multiple chemokines including CCL27 and CXCL1. Of special note, upregulation of CCL27 was found in CSF of MS cases. This observation is the first to demonstrate CCL27 as a potential contributor of brain pathology in MS. Our data suggest that CCL27 may be involved in activation and migration of autoreactive encephalitogenic immune effectors in the brain. Further, our data support the role of Th1 lymphocytes in the pathogenesis of brain inflammation in MS, with several cytokines playing a central role.

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Keywords

C-C motive ligand, C-X-C motive ligand, Cerebrospinal fluid, Interferon, Interleukin, Multiple sclerosis

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