The Role of Th1 Lymphocytes in the Pathogenesis of Multiple Sclerosis (MS)

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Abstract

Th1 lymphocytes produce cytokines such as IL-2, IFN-γ, and TNF-α, TNF-β and GM-CSF and play an important role in the increase of delaying sensitivity and defense against intracellular pathogens. IFN-γ is the most important Th1 cell cytokine that induces the production of IgG, activation of macrophages, enhancing phagocytosis, and also increasing MHC class I and class II molecules. Increasing serum level of Th1 cytokines have also been observed in MS patients. Studies have also shown an increase in the serum level of IFN-γ in mice with EAE. It has also been proven that in humans, exacerbation of MS disease is often accompanied by the increase of myelin-specific Th1 cells in the CSF and according to pathological observations, in thrombolytic plaques, the accumulation of Th1 cells and the production of IFN-γ is directly linked to the demyelination process, which also proves the pathogenicity of Th1 cells. Moreover, the treatment of multiple sclerosis with IFN-γ increases the severity of the disease; while treatment with an anti-IFN-γ antibody improves the disease. Th1 cells cytokines activate macrophages, and activated macrophages cause damage to myelin and subsequently oligodendrocytes and can also produce other inflammatory cytokines that can exacerbate tissue damage. Macrophages and activated microglia cells secrete a number of cytokines such as IL-1, IL-6, IL-12, IL-23 and TNF-α, that high concentrations of these cytokines may damage the oligodendrocytes and neurons. According to studies, Th1 lymphocytes seem to play an important role in immuno-pathological reactions in MS. Preventing the entry of Th1 cells into the CNS, differentiation of native T-cell into Th1 cells, and also activation of Th1 cells, and in the other hand targeting cytokines secreted from Th1 cells or their receptors can significantly reduce the process of demyelination in MS. This review study aimed to investigate the role of Th1 Lymphocytes in the Pathogenesis of Multiple Sclerosis.

Keywords: Multiple Sclerosis, Th1 Lymphocyte, IFN-γ, Macrophage

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