Turk J Gastroenterol *2017; 28: 115-6*

Re: The role of Th1/Th2 cells and associated cytokines in autoimmune hepatitis

Autoimmune hepatitis (AIH) is a serious autoimmune liver disorder. The World Health Organization reported that, AIH has an annual incidence of approximately 2 in 100,000 individuals and a prevalence of 15 cases in 100,000 individuals worldwide (1,2). AIH is characterized by progressive destruction of the liver parenchyma and chronic fibrosis. Clinical manifestations of AIH range from asymptomatic to severe clinical presentations. For histological analysis and diagnosis, specific autoantibodies are used as liver and serum biomarkers; however, it is difficult to identify the disease in various cases due to lack of additional biomarkers (3).

The immunopathogenesis of AIH is still controversial. The presence of autoantigen-specific antibodies and T cells specifically in the liver are the signs of AIH. This autoimmune attack results in liver damage as an organ-specific manner. One of the major autoantigens in AIH type 2 is CYP2D6, which is a cell-surface protein on hepatocytes (4,5). As seen in peripheral and organ-specific local immune responses show cellular differences in the immune-mediated disease, in AIH, CD4+ and CD8+ T cells show different localization patterns. In the blood, which is referred as the peripheral immune area, the dominant liver autoantigen-specific T-cell population has a CD4+ α/β T-cell phenotype, whereas in the liver, either CD8+ α/β T cells or CD4/Cd8 γ/δ T cells are mainly found (6).

In this issue of the Turkish Journal of Gastroenterology, Behfarjam et al. (7) have shown the relationship between Th1 and Th2 cell balance in AIH (7). When overstimuated, helper Th1 and Th2 cells secrete different cytokines, leading to autoimmunity and allergic diseases, respectively (8). In this study, 18 AIH patients and 18 healthy controls were enrolled with an average age of 41-42 years. All analyses were performed from peripheral blood mononuclear cells (PBMCs).

As the dsyregulation of T cells are evident in the immunopathogenesis of autoimmune diseases, the researchers analyzed T-cell associated transcription factor (T-bet) and Interferon-γ (IFN-γ) mRNA expression levels associated with Th1 immune deviation, as well as GATA-3 and IL-4 mRNA expression to show Th2 immune activity. Their findings clearly showed that, PBMCs from the AIH patients had increased levels of T-bet and IFN-γ mRNA expression compared to healthy subjects, suggesting dominant Th1 immunity. This observation is unique to Th1 cells and differences in gene expression were not observed for Th2 cells. The main role of IFN-γ is to stimulate CD8+ T cells in cytotoxic attack to hepatocytes. These increased expression of Th1 transcription factors and IFN-γ protein clearly explain the overactivation of CD8+ T cells in AIH.

Behfarjam et al. (7) monitored PBMCs of AIH patients for mRNA expression of various immune factors. Their results may not definitively reveal the immune mechanism of the disease, and further cell culture and animal studies are required. As immunoregulatory activity is important in immune-mediated diseases, CD4+CD25+Foxp3+ regulatory T (Treg) cells need to be investigated in later studies.

In conclusion, the balance between Th1 and Th2 cells are critical in the immunopathogenesis of AIH. In particular, the Th1 immune response has been shown to be responsible for hepatocellular damage. Behfarjam et al. (7) further demonstrated the imbalance between Th1 and Th2 imbalance in AIH at the level of mRNA expression. These results highlight the importance of a dominant Th1 immune response in AIH.

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Received: 10.02.2017 **Accepted:** 15.02.2017

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