T cell Function in Patients with Dilated Cardiomyopathy

Avhandlingen baseras på följande delarbeten:


T cell Function in Patients with Dilated Cardiomyopathy

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Abstract

Dilated cardiomyopathy (DCM) is a heart muscle disease characterized by dilatation of one or both ventricles together with decreased systolic function. Its etiology is still largely unknown. However, immunological alterations such as the presence of autoantibodies, elevated cytokines in plasma, and viral genomes in the myocardium have been frequently reported. The aim of this thesis was to examine T cell function in patients with DCM.

First, cytokines in plasma were measured. In accordance with previous reports, plasma cytokines of TNF-α, IL-6, IL-10, and CRP were significantly elevated in patients with heart failure. Incorporating an etiology of DCM or ischemic heart disease together with clinical variables in a multivariate analysis, a diagnosis of DCM was found to be independently associated with lower IL-10 levels. Next, specific CD4+ T cell response, accumulated cytokines in supernatant, and lymphocyte proliferation were measured using flow cytometry-based methods following culture of isolated peripheral blood mononuclear cells, and stimulation with Staphylococcus enterotoxin B or phytohaemagglutinin. The frequency of IFN-γ-producing CD4+ (Th1) cells was significantly lower in patients than in healthy controls. In contrast, no difference was found in the number of IL-4-producing CD4+ (Th2) cells. In addition, IL-10 production in the supernatant and lymphocyte proliferation were both significantly lower in patients. To conclude, these impairments of IFN-γ and IL-10 are both consistent with an increased susceptibility to chronic infections and autoimmunity.

Finally, we investigated the frequency of a single nucleotide polymorphism in the IFN-γ gene, which alter the transcription level. We found a significant association between the IFN-γ polymorphism and susceptibility to DCM. This previously unreported finding could be the first diagnostic marker of a DCM of autoimmune etiology.

In its entirety, this thesis supports the concept that DCM is a late sequela of myocarditis leading to a disease of autoimmune character.

Keywords: Cardiomyopathy, Lymphocytes, Cytokines, Autoimmunity, Infection.