INVESTIGATION OF IMMUNOREGULATORY DISORDERS IN SYSTEMIC AUTOIMMUNE DISEASES

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The results of our study in Sjögren's syndrome (SSc) indicate that cells with certain regulatory activity are involved in the pathological immune mechanisms both at the level of innate and adaptive immune system. The increased percentages of peripheral NK, NKT and Tr1 cells may be part of an increased counter-regulatory reaction, presumably compensating the derailed, disproportional immune responses. Contrary to the other cell types, peripheral CD4+ CD25+ Treg cells showed decreased percentages in SSc. We were the first to report the decreased suppressor activity of CD4+ CD25+ Treg cells in primary Sjögren's syndrome. We demonstrated elevated IL-6 and TNF-alpha levels in the sera of the patients, which may be at least partially responsible for the functional defect in the suppression capability of these cells. In summary, our observations indicate that not only the decreased peripheral CD4+ CD25+ Treg cell percentages, but also their altered function may be responsible for their insufficient regulatory operation in pSS.

In systemic sclerosis (SSc), we observed increased Th17 cell percentages, while the ratios of the regulatory cells, such as IL-10-producing Tr1 and CD4+ CD25+ Treg cells were decreased. The levels of IL-10 and the suppressor activity of CD4+ CD25+ Treg cells were also lower in patients. Moreover, we revealed a negative correlation between the modified Rodnan skin score and Tr1 cell percentages, which indicates that beside the altered Th17/CD4+ CD25+ Treg ratio, the role of Tr1 cells may be also important in the progression of disproportionate immune responses in SSc.

During the investigation of the clinical efficacy of extracorporeal photopheresis (ECP) in SSc, in accordance with the earlier studies, we observed significant amelioration of symptoms. Since the immunobiological effects of ECP have not been investigated in SSc before our study, all of the laboratory results are novel observations in the international literature.

According to our results, ECP treatments reduce the number of Th17 cells, and increase the number of Tr1 and CD4+ CD25+ Treg cells in the peripheral blood. Moreover, the therapy improves the suppressor capacity of Treg cells in SSc patients. Levels of CCL2 and TGF-beta decreased, while levels of IL-1Ra, IL-10 and HGF increased. Thus ECP contributes to the restoration of the balance between regulatory and effector immune mechanisms leading to the deceleration of disease progression.

Tárgyszavak: Sjögren-szindróma, szisztémás sclerosis, extrakorporális fotoferezis
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