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THE IMMUNOMODULATORY AND CLINICAL EFFECT OF EXTRACORPOREAL PHOTOCHEMOTHERAPY IN PATIENTS WITH CHRONIC GVHD AND CTCL. THE ROLE OF DENDRITIC CELLS IN THE PROCEDURE

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**Background:** Extracorporeal photochemotherapy (ECP) is a method in which the pathogenic or autoreactive T-lymphocytes of the patient are ex-vivo exposed to photoactivated 8-MOP (8-methoxypsoralen) and transfused to the patient. ECP has been used worldwide since its first application in the treatment of cutaneous T-cell lymphoma (CTCL) in 1987. The effect of ECP is further evaluated in a variety of T-cell mediated diseases including the therapy of acute and chronic GVHD.

**Aims:** We tried to verify the immunomodulatory and clinical effect of ECP in six patients with chronic extensive GVHD and in 2 patients with CTCL (cutaneous T-cell lymphoma) / Mycosis fungoides with generalized erythrodermia.

**Methods:** We evaluated the clinical and immunomodulatory effect of 279 ECP procedures, which were performed by means of the „off line” regimen using two separated devices for mononuclear cell (MNC) collection and for photomodification - Cobe Spectra, Gambro and UV-A irradiator Psorilux 3070, Heraeus. We assessed the influence of the ECP on levels of T cell subsets, B and NK cells in blood and in mononuclear cell concentrates, on the serum levels of IgG, parameters of blood counts, renal and liver functions. We also studied the characteristics of dendritic cells (DC), which were proved in photopheresis product.

**Results:** We observed a good clinical response in patients with c-GVHD as in patients with CTCL. In five of six patients with c-GVHD the improvement of sclerodermatous skin changes, joint mobility, and the reduction of joint pain was found. The patients with CTCL responded to ECP with rapid improvement of the skin changes. In patients with c-GVHD and CTCL we observed the similar tendency to increase in the number of CD 3/8+ T-lymphocytes and the decrease of CD4/8 IRI. ECP did not cause any significant changes in levels of IgG and parameters of liver and renal functions in both groups of patients. In MNC concentrates in patients with cGVHD we proved the myeloid immature DC, which produced the significant amount of IL- 10. ECP also induced rapid and massive apoptosis of alloreactive lymphocytes. They are then captured by immature DC that subsequently present their antigens to the host immune system. IL-10 produced by DC prevents their maturation and immature DC induce antigen specific regulatory T-cells. Regulatory T cells could then participate in the downregulation of the harmful immune reaction.

**Conclusions:** Findings of our study thus contribute to the spectrum of already known effects of ECP. It is conceivable that the reinfusion of large numbers of apoptotic T cells could modulate either their number or function. It is recently suggested that immature DC could be able to activate regulatory T lymphocytes with the subsequent suppression of the autoimmune symptoms of the disease. ECP is accepted as an efficient method that is able to mediate immune system of the patient without generalized immunosuppression. No serious adverse reactions in patients have been observed. The study was supported by the Grant Agency of the Ministry of Health Czech Republic, Grant No. NC / 7542-3