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Treatment of chronic GVHD with extracorporeal photochemotherapy

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Extracorporeal photochemotherapy (ECP) is an immunomodulatory therapy which has been used in treatment of chronic GVHD (cGVHD). ECP involves separation of the mononuclear cells (MNC) with leukapheresis, followed by ex vivo administration of a photosensitizer 8-methoxypsoralen (8-MOP) and ultraviolet A (UV-A) radiation, before reinfusion to the patient.

1. Aim

The aim of the study was to evaluate clinical and immunomodulatory effect of ECP procedures performed in patients with cGVHD. The frequency of adverse reactions associated with ECP was also evaluated.

2. Patients and methods

We analyzed 351 ECP procedures performed in 6 patients with cGVHD; median ECP per patient was 52 (range 13–127). Patients' median age was 29 years (range, 12–76 years). The patients suffered from generalized sclerodermatous skin changes, impaired join mobility and one patient had symptoms of oral disease. In all patients concomitant immunosuppressive treatments for cGVHD were used as necessary.

ECP procedures were performed for two consecutive days: in initial phase weekly, followed every two weeks and then monthly according to clinical response. ECP was performed using the "off line" technique. MNCs were collected using COBE Spectra cell separator (Caridian BCT). In all leukapheresis 2 patient's total blood volumes were processed. Collected MNC concentrate was transferred to Extracorporeal UV-A Bag Set (Cell Max GmbH) and diluted with saline solution. 8-MOP (Gerot) was injected into the UV-A Bag Set and bag was irradiated by PUVA Combi-Light UVA Illuminator at wave length of 350 nm with the irradiation dose of 2 J/cm^2. Irradiated cells were reinfused back to the patient. During apheresis and reinfusion of irradiated cells patients were monitored for adverse reactions. Number of T-lymphocyte subsets (CD3+, CD3 + 4+, CD3 + 8+, CD4 + CD8 + ratio) and B-lymphocytes (CD 19+), in patient's peripheral blood were tested monthly.

3. Results

The effect of ECP in patients with cGVHD with skin and joint involvement was mostly beneficial. Five patients experienced either improvement or stabilization in sclerodermatous skin changes and joint mobility. The overall cutaneous response rate was 83% (complete response rate 50% 3/6 pts), and partial response rate 33% (2/6 pts). In patient who suffered from oral disease, the total recovery was observed. Clinical response was typically delayed until 2–3 months. In patients who responded to ECP efficiently, the influence of ECP on T-cell subsets leads to the suggestion that interactions between T-cell subsets may participate in the process of ECP.

In general ECP was well tolerated. No increased incidence of infections and no serious adverse reactions have been observed. After reinfusion of MNCs, one patient experienced increase in body temperature, likely due to the release of cytokines from photo modified cells.

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4. Conclusion

ECP proved to be efficient and safe procedure that may be recommended for patients with cGVHD who do not respond to conventional therapy. ECP is relatively long-term therapy, and a proper function of the venous access is necessary. Due to the higher risk of infectious complications related to the long-term positioning of central venous catheters we preferred the use of peripheral veins, but in two patients insertion of central venous catheters were necessary.