Relative resistance of CD4+CD25 high CD127low regulatory T cell subpopulation in the peripheral blood to the treatment of different types cancers

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Background. Very important factor in curing cancer is an efficient immune system. Regulatory T cells (Tregs) are currently under extensive investigation in different forms of human cancers. Tregs maintain the immune cell homeostasis. Recent papers have demonstrated previously elevated number of Tregs in lung, breast, pancreatic, ovarian, melanoma, digestive system cancers, CLL, T cell ALL, and B cell NHL. Elevated number and increased suppressor properties of Tregs are sometimes observed after cancer treatment. Therefore, an further intensive study sensitivity of Tregs to the toxic effects of chemo(radiation)therapy and combine therapy is necessary.

The objective of research

Purpose of this investigation - determination of the level of Tregs in the peripheral blood of patients before and after treatment of different forms of human cancers.

Materials and methods. This study was approved by the A. Tsyb MRRC, Obninsk. The peripheral blood were obtained at diagnosis and after chemo(radiation) therapy for lymphoproliferative disorders (Hodgkin lymphoma, LH; non-Hodgkin lymphoma/B-cell chronic lymphocytic leukemia, NHL/CLL,140 tests) and after combined therapy for colorectal cancer, CC, 108 tests. In our work, we studied the population of CD4+CD25highCD127low/– Tregs of peripheral blood. In addition, their level was compared with the dynamics of the relative and absolute number of T- (CD3+CD19-) and B- (CD19+CD3-) cells. All of the antibodies were obtained from BD Bioscience, USA. In the control group 50 peripheral blood samples were tested. Data were analyzed using Statistica software version 8.0. Parametric Student's t-test was used. Significance level was $p < 0\ 05$.

Results The aim of our study was to confirm the observation of an increased level of Tregs in the peripheral blood of patients with LH, NHL/CLL and CC made by other researchers. Statistical analysis revealed the untreated patients showed an increase in the relative and absolute numbers of Tregs than control number of regulatory lymphocytes. We assessed the response of circulating Tregs following chemo(radiation) therapy for LH, NHL/CLL and combined therapy for CC (Fig.). It has also been shown that the sensitivity of Tregs to chemotherapy of lymphoproliferative diseases and to the combined treatment of CC was less than other types of immunocompetent cells (T and B cells). Therefore, they can be considered more resistant cells in relation to the implemented treatment.

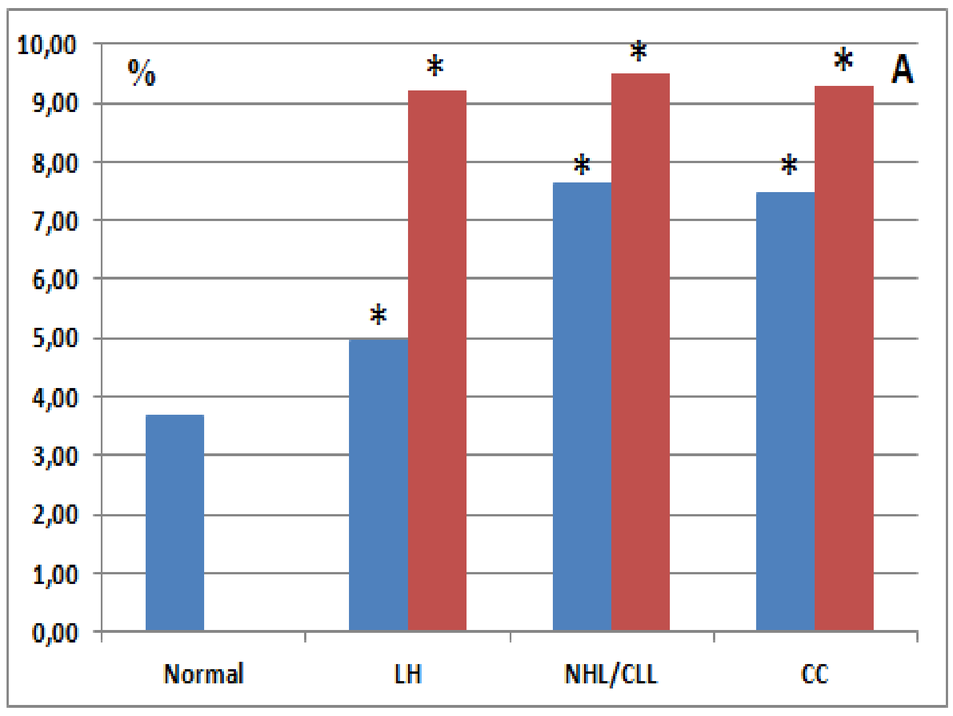

Fig. Tregs in patients with LH, NHL/CLL and CC before (A) and after (B) treatment

*- *Differences are statistically significant to the norm, p<0,05*

Conclusion Tregs are group of cells that might play important role in the development of cancer including LH, NHL/CLL and CC. Their elevated in peripheral blood might be linked to the development of the disease. Tregs can be considered more resistant cells in relation to the implemented treatment. These results indicate that the level of Tregs may influence on the final therapeutic effect. Tregs are a potential target of immunotherapy. Targetting their might represent as therapeutic option to enhance the final antitumor effect. Larger studies are now warranted to validate these findings and determine their clinical implications.

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