Lymphocytes T and Treg as prognostic factors of newly diagnosed DLBCL patients

Diffuse large B-cell lymphoma (DLBCL) is an aggressive and most common form of non-Hodgkin lymphoma. The mechanism of DLBCL pathogenesis is not fully understood. Malignant B-cells responsible for lymphoma formation are believed to arise from different stages of development and differentiation of normal B-cells present are in location nodes and extranodal. Both the development and differentiation of B-cells contain steps were the double stranded DNA is broken, therefore – genetic errors are more likely to occur. Several B-cell lymphomas have translocations of the immunoglobulin and an anti-apoptotic protein, resulting in constitutive expression and leaving the B-cell less sensitive to apoptosis. Examples of such translocations include the t(14;18) resulting in Bcl-2-IgH that can be found in some patients with DLBCL. Most DLBCLs express pan-B antigens ($CD19^{+}CD20^{+}CD22^{+}CD79a^{+}$). These proteins have been found on the surface of both normal and cancerous B cells. However, it is believed that lymphoma B cells have a higher CD19, CD20, CD22 antigen expression compared with normal B lymphocytes. At the same time, as opposed to normal B lymphocytes, lymphoma B cells do not exhibit the CD23 ($CD19^{high}CD20^{high}CD22^{high}CD23^{-}$) antigen expression. In about 20-50% patients, together with pan-B antigen expression, CD10 antigen expression is also recognized. The same goes for about 10% of patients and the CD5 antigen.

According to the latest data regulatory T cells (Tregs) seem to be playing an important role in the regulation of both - normal B-cells and malignant B-cells. These cells are characterised by the presence of CD4, CD25, CD3, CTLA4, and Foxp3. Among Tregs there is a population of virgin and/or resting cells with antigen expression: $CD4^{+}CD25^{+++}Foxp3^{low}$ and there are effector and/or activated Tregs with $CD4^{+}CD25^{+++}Foxp3^{high}$ expression. Foxp3 expression determines the Tregs' ability to form the Fas complex with the FasL (CD95L) receptor, which initiates the apoptosis and lysis of the final cell. Interestingly, it has been recently found that lymphopenia predicts preclinical relapse of patients with diffuse large B-cell lymphoma. To date, however, it has remained obscure what quantitative changes within B, T, and Treg cell lymphocyte subpopulation accompany the decreased number of lymphocytes in peripheral blood.

The aim of the study was to investigate whether the absolute number of peripheral blood $CD19^{+}CD20^{+}CD22^{+}CD79a^{+}$ B cells, $CD3^{+}CD4^{+}CD5^{+}CD8^{+}$ T cells and $CD4^{+}CD25^{+++}FOXP3^{high}$ Treg cells assessed at the time of diagnosis can improve prognostication of newly diagnosed DLBCL patients. We also evaluated the influence of applied chemotherapy on the level of peripheral blood B, T and effector/activated Treg cells.

The absolute count of lymphocytes, B-cells, T-cells and Treg-cells as well as the percentage of apoptotic cells were assessed by means of flow cytometry in all studied subjects.

Significantly lower level of ALC and the percentage of apoptotic cells have been observed

exclusively in DLBCL patients with HR. We also showed, that in comparison with LR, in HR and MR groups, there is a significant decrease in the absolute number of T-cells and Tregs. The applied treatment does no normalize the number of B-cells, Tregs and apoptotic cells only in the case of HR patients.

Lymphopenia, the decreased absolute number of T cells, Tregs, and a percentage of apoptotic cells, correlates with clinical staging in DLBCL patients. The increased number of B cells and the decreased level of Tregs and apoptotic cells after treatment might predict a poor clinical outcome in patients treated with RCHOP. Thereby, evaluation of peripheral blood lymphocytes may be useful in prognostication of newly diagnosed DLBCL patients.

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Publication

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