8. Streszczenie w języku angielskim

Gastric cancer is one of the most deadly and aggressive cancer, being the third leading cause of cancer-related deaths in the world. Despite significant progress in treatment options, the prognosis in patients with stomach cancer is still poo becouse most patients are in an advanced stage at the time of diagnosis. Therefore, it is necessary to explore further the biology of this cancer, as it can help develop new therapies and thus improve the survival of patients with gastric cancer.

Current data suggests that the presence of tumor infiltrate lymphocytes (TILs) may be an important marker for predicting the survival of cancer patients. These cells include but are not limited to, tumor infiltrating cytotoxic T cells– CTLs, whose role is to recognize modified or mutated antigens and eliminate malignant cells. Put forward hypotheses suggest that CTLs have a major impact on the development and progression of the cancer process. Therefore, it seems interesting to examine whether CTLs can contribute to the determining the prognosis and serve as prognostic biomarkers in stomach cancer.

The purpose of this work was to assess inflammatory of cytotoxic T lymphocytes (CTLs) in gastric cancer, assess the percentage of cytotoxic T lymphocytes in relation to the entire T-cell population and in relation to their subpopulations (helper and regulatory lymphocytes) in gastric inflammatory infiltration, assessing the relationship between the number CTLs infiltrating the tumor and selected clinical-pathological parameters, an assessment of the relationship of inflammatory infiltration on CTLs in gastric cancer accompanied by Helicobacter pylori infection and an assessment of inflammatory infestation of cytotoxic T lymphocytes in gastric cancer in correlation with patients survival.

The study included a group of 87 patients who were surgically treated for stomach cancers in the years 2005-2015 at the II Department of General and Gastroenterological Surgery at the Medical University of Bialystok. The material was subjected to histopatological processing and analysis at the Department of General Pathomorphology at the Medical University of Bialystok. Paraffin blocks with embeded tissue material were cut into sections of 4 μm thickness and stained with hematoxylin-eosin (H+E). Immmunohistochemical studies were carried out using specific antibodies: anti - CD3, CD4, CD8, CD103, Foxp3. The IHC automatic method was used for CD3, CD4 and CD8 antigens, manual staining was performed for CD103 and Foxp3. The obtained results were subjected to statistical analysis using the Spearman rank correlation test. Survival analysis was performed

using the Kaplan-Meier test. A significance level of $p < 0.05$ was adopted. Missing data were removed in pairs.

It was shown that the average number of CTLs was similar in the stroma in the invasion front with their number in the stroma in the main mass of gastric cancer. Statistical analysis of the percentage of cytotoxic $CD8^+$ and $CD103^+$ T cells infiltrating the tumor in relation to the remaining T lymphocyte subpopulations ($CD3^+$-entire T lymphocyte population, $CD4^+$-helper T lymphocytes, $Foxp3^+$-regulatory T lymphocytes) showed that the infiltrate intensity correlates with these lymphocytes themselves positively (an increase in the CTLs population is associated with an increase in other T cell subpopulations). In addition, the results of statistical analysis showed a significant relationship between stronger CTLs infiltration and male sex ($p=0.021$). A higher number of $CD103^+$ lymphocytes was also observed in gastric cancers located in 1/3 of the lower stomach ($p=0.020$). In addition, the average number of CTLs $CD8^+$ and $CD103^+$ CTLs increased with the extent of tumor invasion deep into the stomach wall (pT). In addition, the infiltration of the cytotoxic lymphocytes tested positively correlated with the presence of perineural infiltration by tumor cells ($p=0.011$).

This study indicates that cytotoxic T cell infiltration may depend on the constitution of the body. In addition, the intensity of infiltration with CTLs is associated with the location of the tumor. The infiltration of cytotoxic T lymphocytes deep into the stomach wall at the site of the tumor process may also be conditioned by the time it takes to activate their cytotoxic mechanisms/activity or the time that must pass for CTLs to penetrate deeper layers of the tumor. In addition, the statistical relationship observed in this study between the number of CTLs and perineural infiltration may indicate that there is signaling recruiting cytoxic T cells during perineural infiltration by cancer cells in gastric cancer. More extensive research on cancer infiltrating cytotoxic T lymphocytes may be helpful in the diagnosis of gastric cancer and may become potential targets for the immunotherapy of this cancer.