**UNIWERSYTET MEDYCZNY W BIAŁYMSTOKU**

**WYDZIAŁ FARMACEUTYCZNY Z ODDZIAŁEM MEDYCYNY LABORATORYJNEJ**



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**Udział rozpuszczalnych selektyn (sP-, sE- i sL-) oraz płytek krwi w zapaleniu towarzyszącym rakowi jelita grubego**

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**VIII. SUMMARY**

Colorectal cancer is one of the most common diagnosed cancers in the world. Because of lack of early symptoms CRC is often diagnosed when metastasis to other organs are present. For this reason, colorectal cancer is the third leading cause of cancer-related deaths on the world. Research shows that a major of malignancies develops on the basis of inflammation of the colon mucosa. It is suggested that prolonged activation of inflammatory cells and release of proinflammatory proteins can lead to the induction of angiogenesis and lymphangiogenesis, stimulating the processes of DNA damage and remodeling of extracellular matrix and consequently the malignant transformation. Therefore, it appears appropriate to assess the relationship between the severity of inflammation and progression of cancer and correlations between markers of inflammation and cancer progression and platelets role in those process.

The aim of this study was to evaluate the concentration of inflammation markers such as IL-6, soluble CD40 ligand and selectins (sP-, sE- and sL-) and the platelet count in patients with colorectal cancer. The relationships between measured parameters and the stage of disease and location of the tumor in the colon were also assessed.

The study was conducted in 53 patients (24 women and 29 men, average age 66.9) with colorectal cancer (CRC), diagnosed and hospitalized in the II Department of General Surgery and Gastroenterology USK in Białystok and in 25 healthy control group. The study group was divided according to tumor stage into three subgroups: I - TxN0M0 (I / II ° grade), II - TXN+M0 (III° grade) and III - TXN + M + (IV ° grade) and also due to the location of the tumor in colon, sigmoid colon and rectum.

The study was approved by the Bioethics Committee of the Medical University of Bialystok (Permission No. R-I-002/246/2014)

The measurement of IL-6, sCD40L, sP-, sE- and sL-selectin were carried out in the plasma by using the ELISA kits (R&D Systems). The platelet count was determined in venous blood, on hematology analyzer ADVIA 2120i (Siemens).

The results were statistically analyzed using SPSS 21 statistical package and STATISTICA 10. For the features follow the normal distribution, rated by Shapiro-Wilk test, Student's t-test was used, and features incompatible with the normal distribution were evaluated using the U Mann-Whitney test. For comparison of more than two groups were used analysis of variance or Kruskal-Wallis test. Also calculated the Spearman correlation coefficient and ROC curve analysis was performed. The calculations assume significance level of p<0.05 as statistically significant.

Analysis of result of patients with colorectal cancer showed a significant increase of the average concentration of inflammation markers. It has been shown more than 4-fold increase in IL-6 and more than 2-fold increase in the level of sCD40L in the study group compared to healthy subjects. With the progression of the disease an increase in the concentration of inflammatory cytokines was observed, but only in the case of sCD40L obtained differences were statistically significant (group I and II, p = 0.05). On the other hand IL-6 level was correlated with the location of the primary tumor, demonstrating significantly higher concentrations in patients with colon cancer as compared to patients with tumor localized in the rectum. In the study group was also observed a significant increase in platelet count relative to the control group. Analysis of PLT, depending on the severity of the disease, showed the highest number of platelets in patients with IV stage in total (group III). The differences between group I and II and patients from group III were statistically significant. The results of determinations of soluble selectins showed significantly higher levels of sP-, sE- and sL-selectin in patients with colorectal cancer as compared to healthy subjects. Level of sP-selectin and sE-selectin increased with cancer progression. However, sP-selectin concentration was highest in patients with distant metastases (group III, p = 0.01), while sE-selectin in patients with lymph node metastasis (group II). Moreover, the level of sE-selectin correlated with the location of the tumor, with the highest value in patients with sigmoid colon cancer and lowest in patients with rectum tumors (p = 0.02). There was a positive correlation between the size of the tumor and the concentration of IL-6 and platelet count (p = 0.05 and p = 0.01). PLT, sCD40L and sE-selectin correlated with metastases (p = 0.01).

 Analysis of the area under the ROC curve (AUC) of the test parameters showed that IL-6 has the highest area under the curve, which demonstrates its excellent effect in the differential diagnosis cancer patients from healthy subjects. On the other hand, sCD40L and SP-selectin had good diagnostic power (AUC 0.895 and 0.887). Both parameters were characterized with similar diagnostic sensitivity and specificity, suggesting that they may be used interchangeably as a marker of platelet activation.

The research indicates the severity of inflammation with progression of colorectal cancer, which is reflected by elevated levels of pro-inflammatory proteins like: IL-6 and sCD40L. High levels of sCD40L, sP-selectin and sE-selectin indicate that activation of platelets and endothelial cells in the course of cancer. Increase in the level of these proteins with metastases may indicate their potential role in the metastasis. Test results of IL-6, sCD40L and SP-selectin suggest the possibility of their use as potential indicators of inflammation, platelet activation due to cancer progression.