Summary

Chemokines are low molecular chemotactic proteins which activate various leukocyte populations through binding to G protein coupled receptors. It has been shown that chemokines and their receptors play a significant role in numerous physiological and pathological processes. These proteins may also be important in the development of malignant tumors including pancreatic cancer. Pancreatic adenocarcinoma (PC) is characterized by rapid progression and poor prognosis, which is often diagnosed at an advanced stage, with metastases to regional lymph nodes or distant organs. The average survival time of PC patients from the time of diagnosis is 3-6 months.

It is suggested that the chemokine CXCL8 and its receptor CXCR2 are involved in the development of pancreatic adenocarcinoma. Immunohistochemical studies have shown increased expression of CXCL8 and CXCR2 in PC tissues. In addition, overexpression of CXCR2 correlated with the severity of this tumor. However, the diagnostic usefulness of the determination of CXCL8 and CXCR2 concentrations in the sera of patients with PC, especially in comparison with classical tumor markers of PC, i.e. tumor antigen 19-9 (CA 19-9) and carcinoembryonic antigen (CEA), have not been evaluated so far.

Therefore, the aim of this study was:

1. Determination of concentrations of CXCL8 and CXCR2 in the blood of patients with pancreatic cancer and comparison of these concentrations with the control group.
2. Analysis of relationship between serum CXCL8 and CXCR2 concentrations and tumor stage of cancer as well as clinico-pathological features of PC.
3. Comparison of serum levels of CXCL8 and CXCR2 with concentrations of CEA and CA 19-9 in the sera of PC patients as well as with markers of inflammation – C-reactive protein (CRP) and C-X-C chemokine receptor type 4 (CXCR4).
4. Determination of diagnostic criteria, such as diagnostic sensitivity and specificity, positive and negative predictive values as well as the area under the ROC curve of CXCL8 and CXCR2.

The study group consisted of patients with pancreatic adenocarcinoma and healthy volunteers as a control group. Serum samples in PC patients were collected before treatment. CXCL8, CXCR2 and CXCR4 concentrations in the sera of PC patients and healthy subjects were determined by the microimmunoenzymatic ELISA method, whereas the levels of CA 19-9, CEA and CRP were determined on Abbott Architect 8200 analyzer using commercially available assay kits. Differences in the concentrations of the tested proteins between PC patients

and the control group were subjected to statistical analysis with methods selected according to the distribution of the results obtained.

Serum levels of CXCL8 and CXCR2 were significantly higher in PC patients than in healthy controls. CXCL8 concentrations were also significantly higher in patients with lymph node metastases than in N0 patients and positively correlated with the presence of lymph node metastases and CRP levels. Moreover, the diagnostic sensitivity of CXCL8 was the highest among the proteins tested, while the combined analysis of CXCL8 and CXCR2, as well as with CEA and CA 19-9 increased the diagnostic sensitivity of the assays up to 100%. Furthermore, the highest area under the ROC curve was obtained for CXCL8. The concentration of this chemokine proved to be an independent, significant risk factor of PC in multivariate regression analysis.

Obtained results suggest the contribution of the CXCL8-CXCR2 axis to the development of pancreatic adenocarcinoma and the role of CXCL8 in the progression of this malignancy, while the correlations of CXCL8 with CRP serum levels indicate the participation of the inflammatory process in the growth of pancreatic cancer. Furthermore, presented results suggest the usefulness of the determination of CXCL8 in the diagnosis of patients with pancreatic adenocarcinoma and in the evaluation of tumor progression, especially in combination with commonly used markers of PC, such as CA 19-9 and CEA, as well as with CRP.