Streszczenie w języku angielskim

Endometrial cancer is the most common malignant neoplasm of the female reproductive system. In Poland, it ranks 3rd among malignant neoplasms incidence and 6th in terms of mortality. Both prophylactic measures and the improvement of diagnostic tests and therapy of this cancer are important, therefore research is still ongoing on the search for specific markers and therapeutic targets for endometrial cancer.

The cadherins are the most important adhesion molecules that mediate cell-to-cell intercellular adhesion. In most cancers of epithelial origin, loss of E-cadherin mediates the acquisition of an invasive and aggressive phenotype by the tumor cells. In contrast, the P-cadherin expression is strongly associated with cells of undifferentiated epithelial tissues and poorly differentiated cancers. N-cadherin is involved in maintaining microvessel stability and plays a role in blood vessel formation. Inversely, the EpCAM adhesive protein mediating homophilic cell-cell adhesion interactions prevents metastasis. In tumors, EpCAM appears to act as a protective molecule. Deletions of EpCAM lead to an increased risk of cancer development, while the overexpression of EpCAM in cancer cells inhibits metastasis. The fascins represent a group of proteins responsible for maintaining the correct internal structure of the cellular cytoskeleton. They also play an essential role in cell migration. One of the proteins belonging to this group is Fascin-1, which expression is not usually observed in healthy cells, but its overexpression has been shown in many cancers.

Understanding the role and functioning of proteins involved in cell adhesion and migration in tumors is an important research area. Considering the functions of the described proteins, it seems interesting to analyze their expression in endometrial carcinomas. Therefore, the aim of this study was to evaluate expression of the adhesion proteins: E-cadherin, N-cadherin, P-cadherin, EpCAM and Fascin 1 in endometrial cancers, and to correlate the expression of these proteins with selected histo-clinical parameters.

The study included a group of 38 patients surgically treated for endometrial cancer at the Żelazna Medical Center in Warsaw in 2008-2015. Immunohistochemical studies for the proteins EpCAM, Fascin-1, E-cadherin, N-cadherin and P-cadherin were performed on 38 primary endometrial tumor tissues and 20 metastatic tissues. Data obtained from the immunohistochemical analysis were presented as the mean percentage of the expression level. Statistical analyzes were performed using Statistica 11 (version 4.0; StatSoft; TIBCO Software, Inc.) and GraphPad Prism (version 5.04; GraphPad Software, Inc.).

In the study, the E-, N- and P-cadherin proteins in hyperplastic lesions of the endometrium showed poor cytoplasmic expression, while the expression of these cadherins in endometrial cancer was localized in membrane and/or cytoplasm. A stronger reaction of the three cadherins was observed in the tumor front than in the main mass of endometrial cancer. It was shown that the levels of membrane cadherin expression were lower in metastatic cancer cells as compared to the levels in primary cancer cells. In the hyperplastic epithelium of the endometrium expression of the EpCAM protein was weak, while the expression of Fascin-1 was not observed. While in endometrial cancers, the expression of the EpCAM and Fascin-1 proteins increased. Statistical analyses showed no correlation between EpCAM and Fascin-1 protein' expression and clinical and pathological factors of endometrial cancer. However, significantly elevated cytoplasmic E-cadherin expression level and increased membrane and cytoplasmic P-cadherin expression were associated with a high degree of tumor budding. Moreover, a higher percentage of membrane P-cadherin expression was associated with a poorly differentiated type of endometrial cancer. Increased level of membranous E-cadherin expression was associated with the presence of metastases to the local lymph nodes.

The results of current studies indicate that the increase in E-, N-, P-cadherin expression in the front of tumor invasion may imply a specific mechanism of local spread of endometrial cancer. High expression of membrane P-cadherin is associated with high-grade tumor budding and a low degree of histological differentiation in endometrial cancer. The increase in the membrane expression of E-cadherin in the primary tumor of endometrial cancer is associated with the presence of metastases to the lymph nodes. While the lower membrane expression of E-, N-, P-cadherins in metastatic cells compared to the primary tumor of endometrial cancer may indicate their metastatic potential. Moreover, differences in the localization of adhesion proteins expression in endometrial cancer may be related to the differentiation of the histological type of the tumor and its aggressiveness.