SUMMARY

The increase in morbidity and mortality caused by cancers makes research on them one of the most important issues in the modern pathology of humans and animals. In dogs and cats, nearly 20% of deaths and euthanasia performed for medical reasons are directly related to cancers. Neoplasms of the mammary gland in cats rank third after skin and hematopoietic system neoplasms, in terms of their frequency. Malignant neoplasms of the mammary gland in female cats are characterized by similar microscopic structure and clinical course to human breast cancers, which, combined with the shorter life span of the animals, makes them useful in comparative studies as natural experimental models. The results obtained in these studies can be used both in human and veterinary medicine. The main risk factors for developing mammary tumours in female cats are: the lack of sterilization performed up to the age of one year, long-term use of oestrus cycle blockers, older age, obesity and an unbalanced, high-calorie diet. From 80% to 90% of surgically removed mammary tumours in female cats are malignant, resulting in a high rate of recurrences and metastases. This implies the need for postoperative adjuvant chemotherapy. The results of clinical trials show that adjuvant chemotherapy with the use of doxorubicin and its derivatives, classified as anthracyclines, supporting surgical treatment may extend time of disease remission and the overall survival time of animals. This indicates a need to the search for prognostic factors on the basis of which it would be possible to determine course of the neoplastic disease after surgery and predictive indicators enabling to predict the response to treatment with the use of cytostatic drugs.

Most cytostatic drugs affect actively dividing cells, therefore the basic indicator of cancer chemosensitivity is the determination of the fraction of cells in an active cell cycle. In histopathological studies the evaluation of the immunoexpression of regulatory proteins, the level of which changes depending on the phase of the cell cycle, is used in addition to the traditional method of counting cells showing mitotic figures. One of the most frequently measured markers of proliferation is a Ki-67 antigen. Another marker of proliferation is a topoisomerase IIα (Top IIα), which is also a molecular target for anti-cancer drugs from the group of its inhibitors, including doxorubicin. Inhibition of Top IIα function by doxorubicin leads to the formation of numerous intra-strand bonds that block basic life processes - transcription and replication. Cells with damaged DNA are then eliminated by apoptosis. The results of recent studies on breast cancer in

women indicate a relationship between the increase in immunohistochemical expression of Top IIα in tumour cells and sensitivity to drugs from the group of its inhibitors.

The research was carried out on a group of 70 malignant epithelial neoplasms of the mammary gland from female cats undergoing mastectomy. Tissue samples were fixed in 10% formalin and then processed by increasing concentrations of alcohol solutions and xylene into paraffin blocks. Tissue samples were sectioned on the sledge microtome and stained with hematoxylin and eosin, mucicarmin and p.a.S., and then assessed according to the classification of feline mammary gland tumours, taking into account the grading of histological malignancy. An antigen-antibody complex detection system based on secondary antibodies combined with biotin directed against the mouse primary monoclonal antibodies was used for immunohistochemical studies. The enzyme marking the reaction site was horseradish peroxidase conjugated with streptavidin, and as chromogen 3,3'-diaminobenzidine tetrahydrochloride was used. In the studies, the immunohistochemical expression of the Top IIα was determined and compared with the immunoexpression of the Ki-67 and the number of cells showing mitotic figures in various histological types of diagnosed tumours. The selection of proliferation indicators was made taking into account their function in the cell cycle, the mechanisms of action of cytostatic drugs and the principles of cancer chemotherapy, as well as the results of the novel research on their prognostic value. In addition, the relationship of studied proliferation markers with prognostic indicators such as the size of the primary tumour (pT), the presence of neoplastic cells in lymph vessels and organs, and the degree of histological malignancy as well as immunoexpression of the E-cadherin, protein responsible for cell adhesion were assessed. The application the investigated markers of proliferation as elements of the prognosis and the qualification of female cats with mammary tumours for systemic chemotherapy with the use of anthracyclines were taken into account.

The results obtained in the conducted studies, were analyzed statistically and compared with the literature data. The study confirmed the value of studied cell proliferation as prognostic indicators in feline malignant mammary tumours. In the conducted studies, the marker of proliferation with the greatest prognostic value was the immunoexpression of Ki-67 antigen. Immunoexpression of Ki-67 antigen correlated significantly positively with the values of immunoexpression of Top IIα and the number of cells with mitotic figures, and significantly negatively with immunoexpression of E-cadherin. Moreover, a statistically significant relationship was demonstrated between

Ki-67 immunoexpression and the size of the tumour, the invasiveness of tumour cells into lymphatic vessels, as well as the histological malignancy grade. The obtained results related to Top IIα immunoexpression do not allow to consider this assay as a prognostic indicator. In contrast, this assay may serve as a marker of proliferative activity in feline mammary tumours. At the same time, by analogy to the results obtained in breast cancer in women, it can be assumed that mammary tumours in female cats with high Top IIα expression should respond better to pharmacological treatment with anthracyclines than tumours with low expression of this enzyme. It can therefore be hypothesized that the immunohistochemical determination of Top IIα expression in feline malignant mammary tumours could be a valuable predictive indicator for adjuvant treatment with anthracyclines and help in the selection of patients for chemotherapy. Nevertheless, clinical trials aimed at assessing the relationship between Top IIα expression and treatment response in correlation with other prognostic and predictive indicators are needed.