Abstract

Nearly 90% of hematological malignancies and about 5–7% of all neoplasia in dogs are malignant lymphomas. The main diagnostic test for suspected lymphoma is cytopathological examination of fine needle aspiration, collected from enlarged lymph nodes and, according to the WHO guidelines, histopathological examination of the surgically removed lymph nodes supplemented with the immunophenotype assessment. The most common lymphoma in dogs is diffuse large B-cell lymphoma (DLBCL). Lymphomas are neoplasms with high chemosensitivity. The chemotherapy of canine lymphoma involves single or multi-drug protocols which allow for complete or partial remission and, in some cases, can extend a dog's life up to 36 months . At the same time, despite confirmed diagnosis and numerous available therapeutic regimens, it is difficult to determine the prognosis, choose the optimal method of treatment, and predict the response to treatment in each individual patient. Due to the high cytotoxicity and side effects of drugs used in chemotherapy and the varied response to the treatment protocols, attempts are being made to implement individualized treatment. Targeted therapy aims to adapt the treatment regimen to the type of neoplasia as well as to the individual patient. The potential predictive value of protein markers whose expression changes in the course of neoplastic transformation is of particular interest. Counting of mitotic figures and the assessment of the expression of regulatory proteins, such as Ki67, are most commonly used to assess the proliferative activity. A new proliferation marker of prognostic and predictive value is topoisomerase IIα (TOPIIα). TOPIIα expression is variable, associated with the phase of the cell cycle. TOPIIα expression increases in S phase, reaching peak in G2 and M phase, and then decreases at the end of mitosis (G1 phase). Moreover, TOPIIα is a molecular target for antineoplastic drugs such as anthracyclines, which are TOPIIα inhibitors. The inhibition of the TOPIIα function results in permanent links between the DNA strands, and finally in blocking of transcription and replication. Cells with damaged DNA are eliminated by apoptosis. The most commonly used drug belonging to this group is doxorubicin. Doxorubicin (Dox) exhibits a broad spectrum of antineoplastic activity and is used in the treatment of many types of neoplasia, including as a monotherapy drug or as one of the components of multiple CHOP. The aim of this study was to determine the predictive and prognostic value of the expression of TOPIIa and the relationship between TOPII_expression, mitotic count (MC), and Ki67 antigen index in canine malignant lymphomas (especially DLBCL), taking into account the applicability of the determined parameters to select the optimal chemotherapy protocol with

emphasis on the use of anthracycline drugs. The conducted studies showed a positive correlation between the expression of topoisomerase IIα and the number of mitotic cells (MC), with no correlation with the expression of the Ki67 antigen. The relationship between the expression of TOPIIα and the course of the disease, justify the conclusion that that immunohistochemical determination of TOPIIα expression in DLBCL in dogs treated with CHOP protocol may be a prognostic indicator and at the same time may be useful in selecting patients for therapy with the use of anthracyclines. The limitations of the study result from the small number of patients, and the lack of standardized, uniform schemes for assessing the expression of individual proteins in the cell cycle, imply the need for further research in this area.