1. ABSTRACT

INTRODUCTION: Astrocytomas are one of the most frequent and malignant brain tumors. Furthermore, they can be characterized by a high level of viariability in terms of clinical presentation, prognosis and resistance to treatment. The malignancy together with the variance and inefficiency of available therapy are the reasons why the diagnostic process for astrocytomas has to be improved and why new methods of treatment have to be found. A key epigenetic modification attributed to astrocytoma treatment resistance is *MGMT* gene promoter methylation. *IDH, p53* and *EGFR* mutations are hallmark drivers of astrocytoma formation and growth. Activation of JAK/STAT signaling pathway is a less known aspect of gliomagenesis.

AIM: Evaluation of IDH1/2, p53, MGMT, EGFR, pJAK2, pSTAT3 protein expression in grade II, III and IV astrocytomas and statistical assessment of relations between expression of these proteins. Analysis of expression dependency on patients' age, sex and localization of the tumor.

MATERIAL AND METHOD: The study grup comprised 100 patients with a diagnosis of astrocytoma: 60 patients diagnosed with astrocytoma stage IV (glioblastoma), 20 patients diagnosed with anaplastic astrocytoma (stage III) and 20 patients diagnosed with diffuse astrocytoma (stage II). The study material consisted of 100 formalin-fixed, paraffin-embedded tumors. Immunohistochemistry with IDH1/2, p53, MGMT, EGFR, pJAK2 and pSTAT3 specific antibodies was used as a technique of visualising protein expression.

RESULTS: IDH expression was positive in 86% of patients, p53 expression in 97%, MGMT expression in 50%, EGFR expression in 89%, pJAK2 expression in 87%, pSTAT3 expression in 91% of patients. There was statistically significant association between EGFR and pJAK2 expression, EGFR and pSTAT3 expression and between pJAK2 and pSTAT3 expression ($p<0,05$). There was statistically significant association between expression of EGFR, MGMT, pJAK2 and pSTAT3 and tumor grade ($p<0,05$). We haven't found any association of the protiens expression with patients' age ($p>0,05$). Furthermore, we haven't found an association of IDH, MGMT, EGFR, pJAK2 and pSTAT3 expression with sex. There wasn't an association of MGMT protein expression and tumor localization.

CONCLUSIONS: IDH1/2-wt immunohistochemistry is not a valid method for diagnosing astrocytomas. MGMT, p53 and EGFR expression is present in II grade astrocytomas, anaplastic astrocytomas and glioblastomas; MGMT and EGFR expression is associated with tumor grade. JAK/STAT signalling pathway shows activity in II, III and IV grade astrocytomas and phosphorylated JAK2 and STAT3 expression is associated with tumor grade. JAK/STAT activity in astrocytomas may indicate an association with aggressive tumor traits typical for high-grade glioma. Co-expression of EGFR and pSTAT3, EGFR and pJAK2, pSTAT3 and pJAK2 suggests STAT3 signalling being promoted by both EGFR overexpression and JAK2 activity. IDH1/2, p53, MGMT, EGFR, pJAK2 and pSTAT3 expression is not dependent on patients' age. IDH1/2, p53, MGMT, EGFR, pJAK2 and pSTAT3 expression is not dependent on sex. Tumor localization does not influence MGMT protein expression.