p27 and p21 Protein Expression in Gliomas and Their Prognostic Relevance

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Introduction. p21 and p27 are cell cycle inhibitors which can bind to cyclin-cyclin dependent kinase complexes and induce cell cycle arrest (Coqueret et al., 2003). p21 plays multiple roles in cell cycle regulation and can show opposite effects, functioning both as tumour suppressor and oncoprotein. Expression of p21 was found to be more frequent in high-grade than low-grade gliomas (Zolota et al., 2008). In contrast to other tumour suppressors, p27 is frequently deregulated in human cancer. Reduced levels of p27 have been described in different types of neoplasia (Slingerland et al., 2000). To the best of our knowledge, loss of nuclear p27 expression correlates with poor prognosis in many human cancers (Chetty et al., 2003). Expression of p21 and p27 has been extensively studied in many human malignancies; however, there is limited number of studies regarding p21 and p27 expression and their prognostic relevance in gliomas.

Aim, Materials and Methods. The aim of the study is to evaluate the expression of p21 and p27 proteins in gliomas by immunohistochemistry (IHC) as well as access their prognostic significance. 146 patients diagnosed with glioblastoma (GBM) and 19 cases of diffuse astrocytoma (DA) were included in the study. Immunostaining was performed with anti-p21 (clone SX118) and anti-p27 (clone SX53G8) monoclonal antibodies. Nuclear expression of p21 and p27 was measured quantitatively by the proportion (%) of positive neoplastic cells. Survival was evaluated by Kaplan-Meier analysis. For survival analysis, the cut-off points at 70 % for p27 (Faria et al., 2007) and 20 % for p21 protein (Trabelsi et al., 2016) expression have been selected. Descriptive statistical analysis was performed including calculation of 95 % confidence interval (CI) by CIA software according to Altman et al. (Altman et al., 2000).

Results. Expression of p27 was common in both GBMs and DAs. However, the mean value of p27 expression was significantly lower in GBMs than in DAs: 69.7 % (95 % CI = 65.8–73.7) *vs.* 86.6 % (95 % CI = 81.6–91.7) of neoplastic cells. Using the selected cut-off point, high p27 protein expression was found in 60.1 % (95 % CI = 50.9–68.7) of GBMs and 86.9 % (95 % CI = 67.8–95.4) of DAs. In contrast, expression of p21 was significantly more marked in GBMs than in DAs: 21.2 % (95 % CI = 18.7–23.6) vs. 6.9 % (95 % CI = 2.4–11.4) of tumour cells. By the selected cut-off value, 49.3 % (95 % CI = 41.3–57.4) of GBMs and only 15.0 % (95 % CI = 5.2– 36.0) of DAs showed high expression of p21 protein. There were no survival differences in patients with both GBMs and DAs regarding the expression of p21 and p27 proteins.

Conclusions.

1. Expression of p27 is common in both GBMs and DAs. However, loss of p27 expression is more frequent and significantly more widespread in GBMs.
2. In contrast, p21 is significantly upregulated in GBM, compared with DA.
3. p21 and p27 protein expression show no prognostic significance in gliomas. However, due to the different expression levels, these proteins may serve as diagnostic adjuncts.