Prognostic Role of Platelet Derived Growth Factor Receptor Alpha Expression in Diffuse Gliomas

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Introduction. Platelet derived growth factors (PDGFs) are the family of growth factors involved in numerous biological functions such as cell growth and development, proliferation, and angiogenesis. Platelet derived growth factor receptor alpha (PDGFRA) signalling is important in high-grade gliomas. Furthermore, *PDGFRA* gene amplifications resulting in overexpression of receptors were found in 5–10 % of glioblastomas (Puputti et al., 2006). Clinical impact of PDGFRA in gliomas is debated in several studies. As there is no consensus on its prognostic role, additional research is important.

Aim, Materials and Methods. The aim of the study is to evaluate expression of PDGFRA in gliomas at protein level by immunohistochemistry (IHC) as well as access the prognostic significance of PDGFRA. 146 patients diagnosed with glioblastoma (GBM) and 19 cases of diffuse astrocytoma (DA) were included in the study. IHC was performed with polyclonal rabbit anti-PDGFRA antibody (1 : 50). The cytoplasmic or membranous expression of PDGFRA was evaluated quantitatively. Survival was evaluated by Kaplan-Meier analysis. For survival analysis, expression of PDGFRA was classified into high and low expression using cut-off of 50 % (Popova et al., 2014). 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. The range of PDGFRA expressing cells in GBMs was between 0–90 %, mean 7.9 % (95 % CI = 5.0– 10.7). PDGFRA expression in DAs ranged from 1 % to 95 %, mean 42.3 % (95 % CI = 25.7–59.0). By the selected cut-off level, high PDGFRA protein expression was observed in 6.2 % (95 % CI = 5.0–10.6) of GBMs and 52.6 % (95 % CI = 30.1–75.0) of DAs. PDGFRA in most cases was expressed in cytoplasm and membrane of neoplastic cells; however, some rare cases showed nuclear labelling. A trend towards a difference in overall survival (OS) was found in patients with GBMs by PDGFRA expression (log-rank; p = 0.066). Thus, the median OS of patients with high PDGFRA expression was 6.4 (95 % CI = 2.8–9.9) months vs. 8.3 (6.4–10.1) months in patients with low PDGFRA expression. A statistically significant survival difference was found in patients with DAs (log-rank; p = 0.017). The median OS in patients with DAs showing low PDGFRA expression was 61.4 months (95 % CI = 9.9–112.0). The median OS in patients with high PDGFRA expression could not be calculated because of few death cases (n = 1). Finally, at the end of study 1/10 (10 %; 95 % CI = 1.8–40.4) of patients with DA had died within tumour group with high PDGFRA expression compared with 5/9 (55.6 %; 95 % CI = 26.7–81.1) of patients with DA that had died in tumour group with low PDGFRA expression.

Conclusions.

1. PDGFRA expression is significantly more frequent in DAs than in GBMs. This finding may point at the importance of PDGFRA in the development of gliomas.
2. PDGFRA expression has prognostic significance in gliomas. Low expression in GBMs and high expression in DAs is associated with better overall survival.