Prognostic Role of CD44 Expression in Diffuse Gliomas

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Introduction. CD44 is a transmembrane glycoprotein that serves as a major surface hyaluronic acid receptor and is involved in cell-matrix adhesion, cell migration and various cellular signalling pathways. In addition, CD44 has been identified as a marker of neural stem cells as well as astrocyte and oligodendrocyte precursors. Clinical impact of CD44 in gliomas has been 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 present study was to evaluate expression of CD44 in gliomas at protein level by immunohistochemistry (IHC) as well as assess the prognostic significance of CD44.

Performing retrospective archive search for consecutive glioma cases, 146 patients diagnosed with glioblastoma, grade IV (GBM) and 26 cases of diffuse astrocytoma, grade II (DA) were included in the study. IHC was performed with monoclonal mouse anti-CD44 antibody (1 : 50). The cytoplasmic or membranous expression of CD44 was evaluated quantitatively as the fraction (%) of neoplastic cells. Survival was evaluated by Kaplan-Meier analysis. For survival analysis, expression of CD44 was classified into high and low expression using cut-off value of 50 %. In addition, other cut-off values, which were based on median CD44 expression, were tested. Descriptive statistical analysis was performed including calculation of 95 % confidence interval (CI) by CIA software, according to Altman et al., 2000. In addition, clinical data such as patient's age, gender and tumour's size by magnetic resonance imaging were used in statistical analysis by Mann-Whitney test and Spearman's rank order correlation.

Results. The range of CD44 expressing cells in GBMs was from 5 % to 100 %, mean 74.1 % (95 % CI = 69.6–78.7), median – 86.6 % [interquartile range (IQR) = 36]. CD44 expression in DAs ranged from 1 % to 50 %, mean 13.5 % (7.7–19.2), median 8.5 % [IQR = 15]. Using cut-off level of 50 %, high CD44 protein expression was observed in 119/146 (81.5 %; 74.4–86.9) of GBMs and 1/26 (3.8 %; 0.1–19.6) of DAs. There were no survival differences within GBM and DA groups regarding the expression of CD44. Considering clinical characteristics, associations between CD44 level, GBM size and patient's gender were found. Thus, expression of CD44 was significantly more marked in females ($p = 0.026$) and patients affected by smaller tumours ($p = 0.018$). There were no associations regarding clinical characteristics in patients diagnosed with DAs.

Conclusions. CD44 expression is significantly more marked in GBMs than in DAs. This finding may point at the importance of CD44 in the development of high-grade gliomas. Additionally, CD44 expression shows no further prognostic significance within gliomas of the same grade. However, it must be acknowldged that CD44 expression in GBMs is higher in females, indicating that glioma stem cell population may be altered by gender specific factors. Higher CD44 expression values more frequently are found in smaller GBMs, indicating that expansion and rapid growth of tumour may lead to depletion of stem cell population in glioma.