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Cyclin D1 gene and protein expression in intracranial ependymomas: correlation with supratentorial localization

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Ependymomas are rare tumors more common in children and intracranial localization. Cyclin D1 is an important regulator of cell cycle and its overexpression has been related with several cancers. The prognostic value of increased *CCND1* expression in intracranial ependymomas has not yet been established.

We performed *CCND1* RNA expression in 22 cases and protein expression by immunohistochemistry of a TMA in 82 samples of intracranial ependymomas, corresponding to 60 patients (including relapses). Thirty-six patients were under 18 years and 24 patients were adults (mean 18 years). There were 26 supratentorial and 34 infratentorial, of which 46 grade II and 14 grade III. Gross total resection was achieved in 55% of cases and relapse was confirmed in 62.5%. Immunohistochemical reactions were analyzed by two observers independently and final labeling indices (LI) were calculated as the percentage of the positively stained nuclei (negative=0, 0-25%=1, 26-50%=2, 51-75%=3, >75%=4, and focal=F) over the intensity (weak=1, moderate=2, strong=3).

Higher *CCND1* RNA expression levels were observed in anaplastic cases (p=0.003) and supratentorial localization (p=0.003). Cyclin D1 protein expression was considered as negative in 3.8% (LI=0), focal in 16.3%, weak in 15% (LI=1, 2 or 3), moderate in 16% (LI=4 or 6) and strong in 45% (LI=9 or 12). There was a correlation between mRNA and protein expression levels (p=0.017). Statistically significant correlations between cyclin D1 LI score and tumor location (p<0.0001) and histological grade (p=0.0001) were also observed. Stratified analysis demonstrated that cyclin D1 expression was strong in supratentorial tumor location in grade II (8/12 p=0.002) and grade III (23/26 p=0.001). Progression free survival (Kaplan-Meier method and log-rank test) was correlated with age (p=0.026) but not with *CCND1* expression (p=0.805).

Overexpression of cyclin D1 had association with supratentorial tumors and this finding could be used to the development of specific therapeutic targets for these tumors.