MGMT Promoter Hypermethylation in a Series of 104 Glioblastomas.


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Aim: To evaluate MGMT promoter hypermethylation as prognostic factor in a retrospective study of 104 cases of glioblastoma multiforme (GBM). MATERIALS AND METHODS: The O(6)-methylguanine-DNA methyltransferase (MGMT) status was evaluated by methylation-specific PCR (MSP), immunohistochemistry and Western blotting analysis in formalin-fixed paraffin-embedded surgical samples. RESULTS: The MGMT gene was found to be methylated in 29 of 101 tumors (28.7%) by MSP, according to the evaluation methods employed. By immunohistochemistry, different categories were identified on the basis of reaction intensity, percentage of positive cells and homogeneous or heterogeneous distribution. MSP did not correlate with immunohistochemistry, with the exception of the category with the highest percentage of positive cells and homogeneity of immunostaining. Western blotting analysis correlated with immunohistochemical findings (Pearson's correlation coefficient r=0.268, p=0.0211), but not with MSP. By Kaplan-Meier survival analysis, radiotherapy was a significant prognostic factor (p=0.0001). When uncensored patients alone were considered, MGMT methylation status showed a significant correlation with survival (p=0.026). Temozolomide therapy correlated with survival (p=0.022), but not with MGMT methylation. After multivariate Cox regression analysis, only radiotherapy remained as an independent prognostic factor (p=0.0001). CONCLUSION: Correlation was inconclusive among MSP, immunohistochemistry and Western blotting analysis, despite the sophisticated score system for the immunohistochemical quantitative evaluation. MGMT expression is a complex event in which many factors beside epigenetic silencing are implicated.

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