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O (6)-Methylguanine DNA methyltransferase determined by promoter hypermethylation and immunohistochemical expression is correlated with progression-free survival in patients with glioblastoma.

Sonoda Y, Yokosawa M, Saito R, Kanamori M, Yamashita Y, Kumabe T, Watanabe M, Tominaga T.

Department of Neurosurgery, Tohoku University Graduate School of Medicine, 1-1 Seiryomachi, Aoba-ku, Sendai, 980-8574, Japan, sono@nsg.med.tohoku.ac.jp.

Abstract

OBJECTIVE: The prognostic significance of O (6)-methylguanine DNA methyltransferase (MGMT) was evaluated by analysis of both MGMT promoter methylation and protein expression in a series of patients with newly diagnosed glioblastoma. **METHODS:** Seventy-three patients with glioblastomas treated with alkylating agents were analyzed for MGMT expression by immunohistochemistry. Genomic DNA was isolated from frozen surgical specimens obtained from 62 of 73 patients. MGMT promoter methylation was determined by methylation-specific polymerase chain reaction. The prognostic significance of MGMT was evaluated together with other well-known prognostic factors. **RESULTS:** MGMT promoter hypermethylation was detected in 35 of 62 patients (56.4%). MGMT immunoreactivity was low in 26 (35.6%) tumors, moderate in 24 (32.9%), and high in 23 (31.5%). Significant correlation was observed between MGMT expression and MGMT promoter methylation ($P < 0.001$). Both MGMT promoter methylation and low MGMT expression were independently associated with better progression-free survival but not with longer overall survival. However, in the subgroup analysis, MGMT promoter hypermethylation was significantly associated with longer overall survival in patients treated with temozolomide (TMZ) after nimustine hydrochloride (ACNU) treatment. **CONCLUSIONS:** Low MGMT expression and MGMT promoter methylation are both predictive markers for slower tumor progression in patients with glioblastoma.

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