Prognostic significance of loss of O\(^6\)-methylguanine-DNA methyltransferase expression in supratentorial diffuse low-grade astrocytoma

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Abstract
Background
\(O^6\)-Methylguanine-DNA methyltransferase is a DNA repair protein. Epigenetic silencing of MGMT function by its promoter hypermethylation is considered to contribute to carcinogenesis. If loss of function in MGMT is related to tumor progression, the immunohistochemical method may predict the malignant change of gliomas.

Method
We investigated the expression of MGMT by immunohistochemical method in 28 supratentorial hemispheric diffuse astrocytomas. The prognostic significance of MGMT expression, proliferation index (MIB-1), and various clinical factors was evaluated.

Results
There were 19 MGMT-positive and 9 MGMT-negative astrocytomas. Their rates of malignant transformation at 5 years were 12.3% and 51.4%, respectively. The difference was significant in the univariate (\(P = .004\)) and multivariate analyses (\(P = .044\)). Age, sex, extent of surgery, MIB-1 value, and radiation therapy at initial treatment did not correlate with the malignant progression. The 10-year overall survival rates were 71.8% and 58.3% in the patients with MGMT-positive and MGMT-negative tumors, respectively, and were not significantly different between these 2 groups (\(P = .079\)). Two long-term survivors with MGMT-negative tumor responded well to nitrosourea-based chemotherapy and lived more than 8 years after malignant transformation. The patients' age (\(P = .0047\)) and the degree of surgical removal (\(P = .0082\)) affected the overall survival in the univariate analysis. In the multivariate analysis, none of these factors reached significance.

Conclusion
Although the status of MGMT did not affect the overall survival, immunohistochemical evaluation of MGMT expression may be a good marker for tumor progression.

Abbreviations: CT, computed tomography, DAB, diaminobenzidine, KPS, Karnofsky performance score, MGMT, \(O^6\)-methylguanine-DNA methyltransferase, PBS, phosphate buffer saline, SI, staining index

Keywords: Diffuse astrocytoma, Immunohistochemistry, Malignant transformation, \(O^6\)-Methylguanine-DNA methyltransferase

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