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MGMT Promoter Methylation Status Can Predict the Incidence and Outcome of Pseudoprogression After Concomitant Radiochemotherapy in Newly Diagnosed Glioblastoma Patients

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Purpose: Standard therapy for glioblastoma (GBM) is temozolomide (TMZ) administration, initially concurrent with radiotherapy (RT), and subsequently as maintenance therapy. The radiologic images obtained in this setting can be difficult to interpret since they may show radiation-induced pseudoprogression (psPD) rather than disease progression.

Methods: Patients with histologically confirmed GBM underwent radiotherapy plus continuous daily temozolomide (75 mg/m²/d), followed by 12 maintenance temozolomide cycles (150 to 200 mg/m² for 5 days every 28 days) if magnetic resonance imaging (MRI) showed no enhancement suggesting a tumor; otherwise, chemotherapy was delivered until complete response or unequivocal progression. The first MRI scan was performed 1 month after completing combined chemoradiotherapy.

Results: In 103 patients (mean age, 52 years [range 20 to 73 years]), total resection, subtotal resection, and biopsy were obtained in 51, 51, and 1 cases, respectively. *MGMT* promoter was methylated in 36 patients (35%) and unmethylated in 67 patients (65%). Lesion enlargement, evidenced at the first MRI scan in 50 of 103 patients, was subsequently classified as psPD in 32 patients and early disease progression in 18 patients. PsPD was recorded in 21 (91%) of 23 methylated *MGMT* promoter and 11 (41%) of 27 unmethylated *MGMT* promoter ($P = .0002$) patients. *MGMT* status ($P = .001$) and psPD detection ($P = .045$) significantly influenced survival.

Conclusion: PsPD has a clinical impact on chemotherapy-treated GBM, as it may express the glioma killing effects of treatment and is significantly correlated with *MGMT* status. Improvement in the early recognition of psPD patterns and knowledge of mechanisms underlying this phenomenon are crucial to eliminating biases in evaluating the results of clinical trials and guaranteeing effective treatment.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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