Tumori, 93: 248-256, 2007

PROGNOSTIC IMPLICATION OF CLINICAL AND PATHOLOGIC FEATURES IN PATIENTS WITH GLIOBLASTOMA MULTIFORME TREATED WITH CONCOMITANT RADIATION PLUS TEMOZOLOMIDE

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Aims and background: **Glioblastoma multiforme is the most common and most malignant primary brain tumor in adults. The current standard of care for glioblastoma is surgical resection to the extent feasible, followed by adjuvant radiotherapy plus temozolomide, given concomitantly with and after radiotherapy. This report is a prospective observational study of 43 cases treated in the Department of Radiotherapy, University of Rome La Sapienza, Italy. We examine the relationship between pathologic features and objective response rate in adult patients treated with concomitant radiation plus temozolomide to identify clinical, neuroradiologic, pathologic, and molecular factors with prognostic significance.**

Methods: **Forty-three consecutive patients (24 males and 19 females), ages 15-77 years (median, 57) with newly diagnosed glioblastoma multiforme, were included in this trial between 2002 and 2004 at our department. All patients were treated with surgery (complete resection in 81%, incomplete in 19%) followed by concurrent temozolomide (75 mg/m^2/day) and radiotherapy (median tumor dose, 60 Gy), followed by temozolomide, 200 mg/m^2/day for 5 consecutive days every 28 days. Neurologic evaluations were performed monthly and cranial magnetic resonance bimonthly. We analyzed age, clinical manifestations at diagnosis, seizures, Karnofsky performance score, tumor location, extent of resection, proliferation index (Ki-67 expression), p53, platelet-derived growth factor and epidermal growth factor receptor immunohistochemical expression as prognostic factors in the patients. The Kaplan-Meier statistical method and logrank test were used to assess correlation with survival.**

Results: **Fourteen patients (32%) manifested clinical and neuroradiographic evidence of tumor progression within 6 months of surgery. In contrast, 5 patients (12%) showed no disease progression for 18 months from the beginning of treatment. Median overall survival was 19 months. Multivariate analysis revealed that an age of 60 years or older (P <0.03), a postoperative performance score ≤70 (P = 0.04), the nontotal tumor resection (P = 0.03), tumor size >4 cm (P = 0.01) and proliferation index overexpression (P = 0.001) were associated with the worst prognosis. p53, PDGF and EGFR overexpression were not significant prognostic factors associated with survival.**

Conclusions: **The results suggest that analysis of prognostic markers in glioblastoma multiforme is complex. In addition to previously recognized prognostic variables such as age and Karnofsky performance score, tumor size, total resection and proliferation index overexpression were identified as predictors of survival in a series of patients with glioblastoma multiforme.**

Key words: EGFR, glioblastoma multiforme, Ki67, p53, PDGF, prognostic factor, temozolomide.

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Received September 7, 2006; accepted January 16, 2007.