Glioblastoma in elderly patients

Newly diagnosed elderly patients (age > 65-70 years) with glioblastoma should be treated with a patient-centred approach by a multi-disciplinary team. Chronological age alone should not be considered as a contraindication to treatment with maximal safe surgical resection. A 3-week course of adjuvant radiation and chemotherapy is appropriate in selected elderly patients with favourable Karnofsky performance status (KPS) who cannot tolerate a longer 6-week course of fractionated radiotherapy. The presence or absence of 06-methylguanine-DNA methyltransferase (MGMT) promoter methylation can be used to guide clinical decision-making as both prognostic and predictive biomarkers [1].

The clinical paradigm for the treatment of elderly patients with glioblastoma multiforme (GBM) remains controversial [2] [3] [4] [5] [6].

Elderly patients often have more medical comorbidities and lower Karnofsky Performance Scales (KPS) than their younger counterparts. This has led to an increased focus on utility and efficacy of surgical and medical treatment in geriatric patients, with some studies showing increases in life expectancy with aggressive management [7] [8] [9] [10] [11] [12] , possibly correlated to a higher extent of resection [13] [14].

The decision to proceed with surgical resection of glioblastoma in an elderly patient requires an informed understanding of potential outcomes and perioperative morbidity. This can be particularly challenging in patients who are substantially older than the patient population that is most commonly reported upon. Often times, “geriatric” patients are referred to as age 65 or 70 “onwards”. However, the practical and clinical features of patients in their late 6th decade are most likely very different than those of patients in their late 8th decade. Even in the light of recent studies that reveal that both surgical resection (versus biopsy) and aggressive treatment with chemoradiation may prolong life in a geriatric population, the decision to proceed with glioblastoma resection in an octogenarian can be particularly complex [15].

Although glioblastoma occurs mostly in elderly patients, there is a paucity of trials addressing patients older than 70 years of age.

The data available on outcomes of patients greater than 80 undergoing resection is also limited.

Age, by itself, constitutes an unfavorable prognostic factor, which is probably due to unpropitious genetic features, but also due to iatrogenic defeatism. However, many retrospective studies report a survival benefit achieved by aggressive surgical resection seeking gross total removal of contrast-enhancing tumor according to preoperative MRI. Combined radiochemotherapy with concomitant and adjuvant temozolomide has not been investigated in prospective trials. Numerous retrospective studies and a meta-analysis suggest benefit from combined treatment. Prospective randomized trials only evaluated either temozolomide or radiotherapy. Single-treatment hypofractionated radiotherapy performed superior to conventional fractionation. In patients with methylated MGMT promoter, first-line dose-dense temozolomide facilitates prolonged survival. However, there is no comparison with combined radiochemotherapy as the standard-of-care in adult patients. Comorbidity is more frequent in elderly patients, but does not correlate with preterm termination of temozolomide treatment [16].

In a study, factors linked to increased survival in patients over the age of 80 were analyzed. A retrospective chart review of all patients over the age of 80 with a new diagnosis of glioblastoma and who underwent surgical resection with intent for maximal resection were examined. Patients who had only stereotactic biopsies were excluded. Immunohistochemical expression of oncogenic drivers (p53, EGFR, IDH-1) and a marker of cell proliferation (Ki-67 index) performed upon routine neuropathological examination were recorded. Stepwise logistic regression and Kaplan Meier survival curves were plotted to determine correlations to overall survival. Fifty-eight patients fit inclusion criteria with a mean age of 83 (range 80-93 years). The overall median survival was 4.2 months. There was a statistically significant correlation between Karnofsky Performance Status (KPS) and overall survival ($P < 0.05$). There was a significantly longer survival among patients undergoing either radiation alone or radiation and chemotherapy compared to those who underwent no postoperative adjuvant therapy ($p < 0.05$). There was also an association between overall survival and lack of p53 expression ($p < 0.001$) and lack of EGFR expression ($p <0.05$). In this very elderly population, overall survival advantage was conferred to those with higher preoperative KPS, postoperative adjuvant therapy, and lack of protein expression of EGFR and p53. These findings may be useful in clinical decision analysis for management of patients with glioblastoma who are octogenarians, and also validate the critical role of EGFR and p53 expression in oncogenesis, particularly with advancing age [17].

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