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Cerebellar gliobastomas multiforme in adults: a rare cancer network study on 31 patients

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Purpose: To assess the outcome in patients with cerebellar glioblastoma (GBM) treated in 10 institutions of the Rare Cancer Network.
Methods and materials: Data from a series 31 (16 male, 15 female) adult patients with cerebellar GBM, consecutively treated between 1977 and 2004, were collected in a retrospective multicenter study by the Rare Cancer Network. All patients had a histological diagnosis of GBM in the cerebellum. These tumors were classified as: GBM (28 cases), GBM with an oligodendroglial component (2 cases) and giant cell GBM (1 case). Tumor size ranged from 2.4 to 82.1 ml (median 11.4). Median age was 51.4 years (range 21.9–83.2). Initial clinical manifestations were gait and imbalance disorders in all patients. Pre-surgery median KPS and NFS scores were 80 (range 30–100) and 1 (range 0–1), respectively. Tumor resection was subtotal and gross total in 21 and 5 patients, respectively. Three patients had a biopsy only and diagnosis was made at autopsy in another 2 patients. RT was administered to 23 patients (with concomitant chemotherapy, 2 patients). Adjuvant chemotherapy after RT was administered in 1 patient. Chemotherapy only was administered in 2 patients. Six patients could not be treated as a result of rapid clinical progression (3 cases) or sudden death (3 cases) during hospitalization. Median RT dose was 58 Gy (range 12.6–68), using a median of 2 Gy (range 1.8–3) per fraction. RT had to be interrupted in 1 patient after 16.2 Gy as a result of listerial meningitis. No patient progressed during RT, whereas all patients progressed while receiving up-front chemotherapy.
Results: After a median FU of 10.2 months (range 1–222.3) for patients terminating their treatment, 27 patients died, 3 patients are alive without evidence of disease and 1 patient has stable disease. All but 5 patients died of their disease. Three patients died of cardiovascular or pulmonary illnesses, 1 patient died of sepsis and another died of listerial meningitis. All but 5 patients recurred locally (local and brain 3; local and spinal 1; local, brain and spinal 1 patient). No isolated spinal relapse was observed. Salvage therapy was administered to 6 patients (surgery 2; RT 1; chemotherapy 1; RT and chemotherapy 1; surgery, brachytherapy and chemotherapy 1). Median and 1 year-overall survival were 7.2 months and 32.7%, respectively.
Conclusions: Initial clinical manifestations of cerebellar GBMs are gait and imbalance disorders. Treatment could not be initiated in a substantial number of patients as a result of rapid clinical progression or lethal events during initial hospitalization. The pattern of failure is local in a majority of cases. No isolated cranio-spinal recurrence was observed. After RT with or without surgery and/or chemotherapy, the overall prognosis is poor and may be inferior to that of supratentorial GBMs. If clinically appropriate, RT should be initiated rapidly and before chemotherapy, as all patients progressed during up-front chemotherapy.

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Women with brain metastases from non-small cell lung cancer live longer than men: an outcomes study utilizing the RTOG RPA class stratification

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Purpose: Women with lung cancer are reported to have a better prognosis than men. In patients (pts) with non-small cell lung cancer (NSCLC) metastatic to brain, female sex may favor survival but this association is less well described. To explore this potential interaction, our single-institution brain database was analyzed. The RTOG recursive partitioning analysis (RPA) brain metastases classification was used to create pt cohorts.
Methods: A retrospective review of a single institution brain metastasis database for pts treated between 1/82 and 9/04 was performed. This yielded 831 NSCLC pts with brain metastases for analysis. RPA criteria used for class assignment were: class I – Karnofsky performance status (KPS) $\geqslant$ 70, age < 65 years, primary tumor controlled, no extracranial metastases; class III – KPS< 70; class II – all others.
Results: Median follow-up was 5.4 months (mos) (range 0–122.9). Median age was 62.4 (range 25–90). Median KPS was 80 (range 20–100). There were 485 males (58.4%) and 346 females (41.6%). Comparing female vs. male, there were no differences in: number of treatments [one vs. multiple, p = 0.68]; use of whole brain therapy [88.8% vs. 88.7%, p = 0.97]; other forms of treatment used including surgery (p = 0.3), radiosurgery (p = 0.6), and chemotherapy (p = 0.8). There was no significant gender imbalance (female vs. male) when 806 (97%) pts were ranked by RTOG RPA classification: class I – 12.5% vs. 10.7%; class II – 66.5% vs. 69.9%; class III – 21.1% vs. 19.4% (p = 0.56). Overall survival (OS) from time of brain metastasis diagnosis was 5.8 mos, with female living longer than male, 6.3 mos vs. 5.5 mos, p = 0.013. Considering RPA classes, females trended to improved survival over males in I and II but not III: 17.1 mos vs. 9.5 mos (p = 0.11); 6.8 mos vs. 6.0 mos (p = 0.09), 2.7 mos vs. 2.5 mos (p = 0.42), respectively. OS for pts with multiple treatments favored females over males: 13.2 mos vs. 8.5 mos, p = 0.0037. On multivariable analysis, significant variables were sex (p = 0.041; RR 0.83); RPA class (p < 0.0001; RR = 0.28, for I vs. III; p < 0.0001; RR = 0.51, for II vs. III); single vs. multiple treatments (p < 0.001, RR = 2.1). There were 17 long-term survivors (> 5years); 8 females and 9 males, with median survival favoring women: 121.2 mos vs. 65.3 mos, p = 0.0062.
Conclusions: Women with brain metastases from NSCLC survive longer than men. Multivariable analysis identifies sex and RTOG RPA classification as highly significant variables with respect to survival.

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High-grade glioma treated with 3d external beam radiotherapy (3DCRT) and sterotactic radiotherapy combined with concurrent temozolomide and carboplatin

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Background: The standard of care for patients with high grade glioma is surgery followed by adjuvant radiotherapy. The benefit of temozolomide-based concurrent chemo-radiotherapy has been recently shown. In this study we have evaluated the toxicity and efficacy of temozolomide/carboplatin-based chemotherapy and high-dose radiation in patients with malignant gliomas.
Material and methods: Radiation was initially delivered with 3DCRT to the PTV1 defined as the GTV (T1 weighted MRI scan) with a margin of 2 cm to a total dose of 50 Gy in 25 daily treatments. This was followed by a cone-down boost to the PTV-2 (GTV+0.7 cm (delivered with sterotactic radiotherapy (SRT) to reach a boost dose of 20 Gy using the same fractionation. Concurrent chemotherapy consisted of temozolomide (50 mg/m^2 p.o., 5 days per week) and carboplatin (AUC = 1.5 once a week). Toxicity has been evaluated using the RTOG criteria. The patterns of failure has been classified in local (within PTV1), marginal (adjacent to PTV1) and distal (farthest to PTV1).
Results: Between November 2000 and June 2004, 30 pt (23 males and 7 females with a median age of 57 years) were included in the study. The type of resection was biopsy-only in 14 pt, subtotal resection in 10 pt and total resection in 6 pt. Nineteen pts (63.3%) with bulky residual tumor burden after surgery received 2–4 cycles of postoperative chemotherapy prior to the start of chemoradiation. Eight pt had anaplastic astrocytoma (AA) (25%) and 22 pt glioblastoma multiforme (GBM) (75%). Patient distribution according to RPA class were: RPA I-III (30%) and RPA IV-VI (70%). Eighteen patients (60%) completed the prescribed chemotherapy and radiotherapy protocol. The toxicity was mild with haematologic toxicity grade 3–4 in 23%. Grade 3–4 late toxic events has not been observed in long-term survivors. Patterns of local failure: local (20%), marginal (7%), distal (10%) and mixed (30%). With a median follow-up of 31 months (mo) (range 5–55+), the 4-year disease-free survival and overall survival were 6% and 22% respectively. Median survival according to the RPA class, histology and treatment compliance was: RPA I-III, 25.9 months vs. RPA IV-VI, 12.5 mo (p = 0.04); AA, 26 mo vs. GBM, 15 mo (p = ns); completed treatment, 25.9 mo; did not complete 15.4 mo (p = ns).
Conclusions: High dose 3DCRT+SRT concurrent with carboplatin-temozolomide chemotherapy is feasible with mild toxicity. Some patients achieve long-term survival in spite of a large number of biopsy-only patients.