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Background

Treatment of high-grade glioma consists of fractionated radiation therapy (RT) ± chemotherapy. The incidence/significance of neurological toxicity (NT) in this disease is not known. We evaluated the relationship between acute and chronic NT, and ultimate outcome, as well as risk factors for NT from the RTOG database.

Methods

Acute (≤ 90 days of RT start) and late (> 90 days) NT events ≥ grade 3 were analyzed amongst 2,761 patients from 14 RTOG RT glioma studies, accrued from 1983-2003. Scoring schema used were RTOG Acute Morbidity Scoring Criteria, RTOG/EORTC Late Radiation Morbidity Scoring Schema and NCI-CTC version 2.0. The incidence of acute and late NT, the risk factors for these, correlation between acute and late NT, and eventual outcome were analyzed. Statistical methods included Chi squared test, McNemar's test, logistic regression, and Cox proportional hazards model. Two sided test was used, significance level 0.05.

Results

Of 2,610 analyzable patients, 86% had glioblastoma, and 10% anaplastic astrocytoma. All received a systemic agent during RT (78% BCNU, 5% thalidomide, 5% tirapazamine, 12% other agents). Median RT dose: 60 Gy. There were 182 acute and 83 late NT events. On univariate analysis age > 50, poor performance status, more aggressive surgery, poor neurological function, poor mental function and twice daily RT were associated with increased acute NT. All these variables, except age, were also associated with acute NT on multivariate analysis. There was a statistically significant correlation between acute and chronic NT ($p < 0.0001$). In a step-wise logistic regression model considering once daily RT, use of chemotherapy, total RT dose (BED) and acute NT, the occurrence of acute NT was significantly associated with late NT (OR = 2.48; 95% CI = 1.2-5.0; $p = 0.01$). The presence of acute NT (HR = 1.43; 95% CI [1.2, 1.7]; $p < 0.0001$) was also found to predict poor overall survival, independent of RPA class (median survival 7.8 vs. 11.8 months).

Conclusion

Acute NT is significantly associated with both chronic NT and overall survival.

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