Prognostic factors and outcomes in anaplastic gliomas: An institutional experience

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Abstract

Background: There is lack of clear evidence and treatment guidelines for anaplastic gliomas (AGs) with very few studies focusing exclusively on these patients. The aim of the study was to analyze the clinical profile and survival in these patients. Materials and Methods: Patients of AGs treated with radiation and concurrent ± adjuvant chemotherapy from January 2010 to December 2015 were analyzed. Statistical analysis was done using SPSS version 20 software. Results: A total of 100 patients were included in the study. The median age was 35 years (range 6–68 years). Eighty-four patients had follow-up details and were included for survival analysis. The 5-year overall survival (OS) was 58%. Age, presentation with seizures, and focal neurological deficit were not found to significantly influence survival. The 5-year survival for oligodendroglioma and astrocytoma was 69% and 52%, respectively. Patients with Karnofsky Performance Score (KPS) of ≥70 had a significantly better 5-year OS (65%) as compared to those with KPS <70 (33%) (P = 0.000). The use of adjuvant temozolomide (TMZ) showed longer 5-year OS of 67.7% compared to 36% in patients who did not receive adjuvant chemotherapy (P = 0.018). Patients receiving both concurrent and adjuvant TMZ showed longer 5-year OS (68.5% vs. 40%; P = 0.010). Twenty-two patients had recurrence with average time to recurrence being 37 months. Fourteen patients underwent salvage surgery and two patients received reirradiation. Conclusions: OS significantly correlated with KPS and receipt of concurrent and adjuvant chemotherapy with TMZ. Therefore, adjuvant radiation with concurrent and adjuvant TMZ should be the standard of care for AGs.

Key words: Anaplastic glioma, chemoradiation, survival, temozolomide

Introduction

Gliomas account for 80% of primary malignant brain tumors. Anaplastic gliomas (AGs) constitute 6.1% of primary central nervous system gliomas. AGs are typically treated with maximal safe resection, followed by external beam radiation therapy (RT). This approach is supported by observational data that suggest that the survival of patients with AGs is longer after complete or near-total resection (compared to biopsy alone). Randomized controlled trials of patients with high-grade glioma suggest that RT is associated with longer survival. Currently, there limited evidence for AG despite the widespread use of chemotherapy to treat these cancers. No consensus has been derived from a previously conducted survey of recommendations for treatment of newly diagnosed AG. The aim of the study was to analyze the clinical profile, and treatment outcomes of patients with AGs treated with concurrent chemoradiation (CRT) at our institute.

Materials and Methods

Medical records of patients with histopathological diagnosis of AGs treated with adjuvant radiotherapy with or without concurrent and adjuvant chemotherapy between 2010 and 2015 were reviewed. Clinical data such as age, performance status, and extent of resection were collected. The extent of surgery was identified as gross total resection, subtotal resection or biopsy by operative and clinical notes and when available by postoperative imaging. Patient-, tumor-, and treatment-related variables were recorded and used to assign patients to an RT Oncology Group recursive partitioning analysis (RTOG RPA) classification. All patients received external beam RT to a total dose of 60 Gy, 2 Gy per fraction for 30 fractions. Most patients were treated using intensity-modulated radiotherapy technique. All patients completed the planned course of radiation without any significant interruptions. Concurrent chemotherapy regimen prescribed was temozolomide (TMZ) to a dose of 75 mg/m²/day PO for the entire course of radiation. Following CRT, all patients were advised adjuvant TMZ (150–200 mg/m²) 5 days a week every 28 days for 6–12 cycles.

Data that were unavailable in the medical records due to follow-up loss were obtained via a telephone interview with the patient or, if the patient was deceased, with his or her relatives with their permission. Overall survival (OS) was defined as the time from the date of diagnosis to the date of death or last contact.

Statistical analysis

Kaplan–Meier estimates were used to analyze OS estimates with the comparison of rates among the groups performed using the two-tailed log-rank test. A two-sided P < 0.05 was considered statistically significant. The analysis was done using SPSS version 20 software (IBM corporation).

Results

A total of 100 patients were included in this analysis. The median age was 35 years ranging from 6 to 68 years. Nine patients were <18 years of age, 48 patients were <35 years of age and 52 patients were 35 years or above. About 61% were males and 39% were females with male:female ratio of 1.6:1. Most common presentation was with headache (65%), seizures (44%), vomiting (21%), or hemiparesis (19%). Average duration of symptoms was 8 months. Twenty-nine patients had focal neurological deficit at the time of presentation. Most common location of tumor was the frontal lobe followed by temporal lobe. Fifty-seven patients had tumors with contrast enhancement. Majority of the patients belonged to RTOG RPA class I. Patient characteristics are tabulated in Table 1.

Based on the surgical notes, gross total resection was done in 22 patients, near-total resection in 29 patients, subtotal resection in...
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38 patients and biopsy/decompression in 11 patients. Most of the histopathological diagnosis was morphological. Sixty‑three patients had AA histology, three cases were reported as oligoastrocytoma and 37 patients had AO histology. Fourteen patients were tested for IDH mutation of whom nine were positive. Three out of six patients tested for 1p19q codeletion were positive.

Out of 100 patients, 82 received concurrent chemotherapy with TMZ and 62 patients received concurrent and adjuvant TMZ. Median number of adjuvant chemotherapy cycles was five. Treatment details are tabulated in Table 2.

Out of 100 patients, follow‑up details were available for 84 and these patients were included in the survival analysis. Median OS was not yet reached at the time of analysis. The 5‑year OS was 58% [Figure 1a]. The Kaplan–Meier survival estimates for other cofactors are tabulated in Table 3.

Younger age, female sex, presentation with seizures, and no focal neurological deficit showed a trend to longer survival but were not statistically significant. Surgical extent defined by operating surgeon did not correlate with survival. Probable explanation for this observation could be that the extent of resection might be overestimated at the time of surgery and immediate postoperative magnetic resonance imaging (MRI) could not be done in all cases. Patients with postoperative residual tumor on imaging had a shorter survival.

Patients with AO histology had 5‑year OS of 65.7% compared to 51.9% for AA (log‑rank $P = 0.27$). The use of concurrent chemotherapy with TMZ showed a longer 5‑year OS compared to only RT (59.1% vs. 53.8%, log‑rank $P = 0.63$). The use of adjuvant chemotherapy with TMZ showed longer 5‑year OS of 67.7% compared to 36% in patients with no adjuvant chemotherapy (log‑rank $P = 0.018$). Patients receiving both concurrent and adjuvant TMZ also showed longer 5‑year OS (68.5% vs. 40%, $P = 0.010$) [Figure 1b]. There were no grade 3 or higher toxicities noted with this regimen.

Patients with preradiotherapy Karnofsky Performance Score (KPS) ≤70 had 5‑year OS of 33.3% and those with KPS ≥70 had 5‑year OS of 65.1% (log‑rank $P = 0.000$) [Figure 1c]. A follow‑up MRI done at 6‑month post‑RT showed residual tumor in 56 patients. Patients with no residual had 5‑year OS of 66.7% and patients having residual on follow‑up scan had 5‑year OS of 54.3% (log‑rank $P = 0.19$). Twenty‑three patients had documented recurrence during with average time to recurrence being 37 months. Fourteen patients underwent salvage surgery and 3 patients received reirradiation. The average survival after recurrence was 12.7 months.

Table 1: Patient characteristics

| Characteristics          | Number of patients |
|-------------------------|--------------------|
| Age                     |                    |
| Median                  | 35 years           |
| Range                   | 6‑68 years         |
| <35 years               | 48                 |
| ≥35 years               | 52                 |
| Sex                     |                    |
| Male                    | 61                 |
| Female                  | 39                 |
| Ratio                   | 1.56:1             |
| Clinical presentation   |                    |
| Headache                | 65                 |
| Seizures                | 44                 |
| Vomiting                | 21                 |
| One‑sided weakness      | 19                 |
| Blurring vision         | 10                 |
| Focal neurological deficit |            |
| Yes                     | 29                 |
| No                      | 71                 |
| Location on MRI/CT scan |                    |
| Frontal lobe            | 54                 |
| Temporal lobe           | 20                 |
| Parietal lobe           | 15                 |
| Thalamus                | 6                  |
| Cerebellum              | 5                  |
| RTOG RPA class          |                    |
| I                       | 79                 |
| II                      | 2                  |
| III                     | 5                  |
| IV                      | 10                 |
| V                       | 4                  |

RT0G=Radiation therapy oncology group, RPA=Recursive partitioning analysis, MRI=Magnetic resonance imaging, CT=Computed tomography

Table 2: Treatment details

| Other characteristics            | Number of patients |
|----------------------------------|--------------------|
| Surgery                          |                    |
| GTE                              | 22                 |
| NTE                              | 29                 |
| STE                              | 38                 |
| Biopsy/decompression             | 11                 |
| Histopathology                   |                    |
| AO                               | 37                 |
| AA                               | 60                 |
| OA                               | 3                  |
| Postoperative residual           |                    |
| Yes                              | 70                 |
| No                               | 30                 |
| RT technique                     |                    |
| 2D                               | 11                 |
| 3DCRT                            | 22                 |
| IMRT                             | 67                 |
| Chemotherapy                      |                    |
| Concurrent                       | 82                 |
| Concurrent + adjuvant             | 62                 |
| Average adjuvant cycles           | 5.2                |
| Residual on follow‑up scan       |                    |
| Yes                              | 34                 |
| No                               | 66                 |

RT=Radiotherapy, IMRT=Intensity modulated radiation therapy, 2D=Two‑dimensional, AA=Anaplastic astrocytoma, AO=Anaplastic oligodendroglioma, OA=Oligoastrocytoma, GTE=Gross total excision, STE=Sub total excision, NTE=Near total excision

Figure 1: (a) Overall survival by Kaplan–Meier method. (b) Kaplan–Meier survival analysis by chemotherapy. (c) Kaplan–Meier survival analysis by Karnofsky Performance score
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Dear Editor,

A large cystic gastrointestinal stromal tumor within lesser sac: A diagnostic dilemma

A 52-year-old male presented with intermittent left upper quadrant pain and fullness. There was no history suggestive of pancreatitis. On physical examination, there was an abdominal mass, which was hard, immobile, and nontender. The mass was located along with amber colored ascites. Ascitic fluid analysis showed normal amylase, lipase, and cytology. Cyst wall biopsy showed cystic lesion in lesser sac adherent to surrounding viscera oncosurgeon, endoscopist, and radiologist. Exploration showed highly anaplastic astrocytoma with mitoses suggestive of GIST on frozen high-grade tumor with mitoses with pancreatic atrophy with intact pancreatic duct and preserved sac 22 cm × 20 cm × 12 cm in size pushing adjacent viscera.

The patient underwent wedge resection of greater curvature along with the mass

There are no conflicts of interest.

Nil.

Conflicts of interest

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