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Original Research

Stereotactic radiosurgery for recurrent high-grade gliomas

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Highlights

- High-grade gliomas (WHO Grade III and IV) invariably recur.
- Stereotactic Radiosurgery (SRS) may be beneficial in the recurrent treatment setting.
- We conducted a retrospective cohort study consisting of 33 patients with rHGGs treated with SRS.
- Median overall survival (OS) and progression free survival (PFS) were consistent with previous literature.
- MGMT methylation status predicted improved OS.

Abstract

Introduction

High-grade gliomas (WHO Grade III and IV) invariably recur. Standardized management in the recurrent setting is ill defined. Stereotactic radiosurgery (SRS) represents a non-invasive

treatment modality. Evidence to date is limited and therefore further evaluation of the role of SRS in recurrent high-grade-gliomas (rHGG) is warranted.

Methods

We conducted a retrospective cohort study consisting of 33 patients with rHGGs treated with SRS from January 2020 to June 2024. Baseline demographics, radiosurgical parameters, and outcomes/toxicity data were collected. Descriptive statistics were calculated for all continuous variables. Survival analysis was performed using the Kaplan Meier method. Univariate analysis was performed using Cox proportional hazard model. All statistics were performed in GraphPad Prism (V.10).

Results

Thirty-three patients with 44 rHGG lesions underwent Gamma Knife SRS with a median of 5 fractions (range:1–5). Overall local control at 3-,6-, and 12-months was 69.9%, 45.9%, and 31.9% respectively. Distant tumor control at 3-,6-, and 12-months was 71.7%, 48.2%, and 42.2%. Global tumor control was at 3-,6, and 12-months was 69.9%, 45.9%, 31.9% respectively. Median OS from the time of SRS was 7 months (95% CI: 6.65–17.23). Median PFS from the time of SRS was 5.5 months (95% CI: 4.79–14.31). MGMT methylated status was associated with improved OS (HR: 0.24 95% CI: 0.07–0.60, P=0.01).

Conclusions

SRS affords reasonable local control in the short term for patients with recurrent HGG who are otherwise poor surgical candidates. Local failure is more common than distant failure, albeit global control is critical in increasing PFS. MGMT methylated status is associated with increased overall survival.

Introduction

Despite maximal safe resection followed by concurrent chemoradiation, high grade gliomas (HGGs) have a propensity for recurrence [1], [2], [3]. Furthermore, recurrent high-grade gliomas (rHGGs) are aggressive in nature and demonstrate a tendency towards radiation and chemotherapy resistance [1], [2]. Therefore, managing recurrent HGGs is extremely challenging. This is exemplified by a relative lack of high-level treatment evidence in this setting [1], [2].

In a recent report by the Response Assessment in Neuro-Oncology (RANO) resect group, repeat surgical resection was superior to non-surgical management of rHGG lesions (HR: 0.69, 95% CI: 0.6–0.8, P=0.001) [4]. However, this finding applies to lesions in which a post-surgical volume of <1 cm^3 can be achieved [4]. Furthermore, not all regions of recurrence are discreet nor are they amenable to re-resection. Furthermore, additional radiation and chemotherapy is imperative in those with rHGGs who do undergo repeat resection. Systemic chemotherapy is one option, however the majority of rHGG patients have previously undergone extensive chemotherapy and may not be amenable to additional agents or the associated side effects. While immunotherapy

has received increased attention over the past few decades as a candidate therapeutic modality, experience with such therapies in this setting is limited. Finally, additional doses of conventional radiotherapy may carry an unacceptable side effect/toxicity profile [1], [2].

Stereotactic radiosurgery (SRS) enables radiation delivery with a greater therapeutic index compared to conventional external beam radiation therapy (EBRT) [5]. Additionally, SRS is less invasive than surgery and may be consistent with greater quality of life outcomes compared to patients undergoing repeated resection and multiple rounds of chemotherapy/immunotherapy [1], [2], [6].

Overall, there is no consensus regarding standardized management of rHGGs and literature on the role of SRS is sparse. Given this we sought to examine our single institution cohort and report the associated outcomes. Our work primarily focused on survival, progression, and tumor control outcomes. Furthermore, an exploration of variables associated with survival and progression was conducted.

Section snippets

Study cohort inclusion criteria

Approval from the Institutional Review Board at AHN was obtained for this study. We retrospectively analyzed patients with rHGGs defined as those with a pathologically confirmed WHO grade III or IV lesions (based on 4th (2016) and 5th (2021) editions of the WHO classification system) who were treated initially with either biopsy or resection who demonstrated radiographic recurrence on routine follow up MRI after conventional chemoradiation. We then selected patients whose care in the recurrent …

Cohort characteristics

In total 33 patients with primary WHO grade III or IV gliomas were initially treated with a standard maximal safe resection followed by concurrent EBRT/TMZ. The 33 treated index lesions subsequently underwent progression at median time of 12 months (IQR: 9.0–18.5) resulting in 44 total recurrent lesions managed with SRS. The median age of the cohort was 60 yrs (IQR: 51.5–68.0), with a 42.8% male and 58.6% female distribution. Across the 44 lesions treated with SRS 6 (18.1%) and 11 (33.3%) …

SRS outcomes

At the time of clinical follow-up radiation toxicity occurred in 2 (6.1%) patients following SRS. One (3.0%) event was an acute grade 1 seizure with an onset 5 days after initiation of radiation therapy. The other toxicity event was a chronic grade 3 radiation necrosis with an onset >90 days after initiation of SRS which resolved with dexamethasone. After treatment of the index lesions,

4 (9.1%) lesions demonstrating further progression or recurrence were treated with additional SRS. …

Discussion

In our paper we demonstrated an OS and PFS rate of 7.0 months and 5.5 months respectively. Furthermore, we showed that MGMT methylated status was significantly associated with OS and borderline significantly associated with PFS. These outcomes are consistent with prior literature [8]. Through this effort we have corroborated previous literature delineating similar patterns of genetic predictors of survival and progression outcomes [8]. Furthermore, our work is one of few detailing both local …

Conclusion

SRS in the setting of rHGGs can prolong life while preserving quality of life. Existing literature demonstrates a trend toward prolonged overall and progression free survival consistent with chemotherapy or resection with adjuvant chemotherapy Therefore, SRS presents an enticing option for those not fit for continued chemotherapy or repeat surgery. Additionally, while SRS may be beneficial as monotherapy, adjuvant therapies like BVZ may augment responses to SRS, however, to date the evidence is …

Ethical approval

IRB approval was obtained for this study. …

CRediT authorship contribution statement

Trent Kite: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Vineetha Yadlapalli:** Data curation. **John Herbst:** Writing – review & editing. **Stephen Karlovits:** Writing – review & editing. **Rodney E. Wegner:** Writing – review & editing, Resources. **Matthew J. Shepard:** Writing – review & editing, Writing – original draft, Supervision. …

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Matthew Shepard is a consultant for GT Medical Technologies. All other authors have no potential conflicts to declare. …

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None. …

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