Reviewer's report

Title: Multiple Courses of Stereotactic Reirradiation Are Tolerable: Case of a Long Term Survivor with Recurrent Oligodendroglioma

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Reviewer: David Roberge

Which of the following following best describes what type of case report this is?: Other

If other, please specify:

Undereported and infrequent treatment.

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: No

Does the case report have explanatory value?: No

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

General

• This is a case report of a patient with a malignant oligodendroglioma treated with 4 courses of radiation over the span of 7 years. The relevance of this report can be summarized by the authors statement that: “This case not only illustrates the importance of individualizing care and maintaining a balance between the benefits and detriments of treatment. In the case of this patient, multiple courses could be delivered to a variety of areas along the periphery of the tumor bed as
noted with minimal effect to the patients well being.”

- The general background and context given to the report is that of the more common glioblastoma multiforme, if may be interesting to at least partially refocus this on the pathology treated
- In general the strength of the evidence supporting re-irradiation as a life-extending treatment and the benefits ascribed to the treatment in the specific case are probably overstated and may benefit from more nuance

Abstract

- The pathology treated should be mentioned in the abstract
- “High grade gliomas are an insidious disease associated with an extremely poor” although this statement is true, it may not apply to many patients with Grade III oligodendrogliomas and a more focused background statement may be more appropriate
- Randomized studies (plural), the reviewer is unaware of any randomized studies of re-irradiation, if they do exist please list them in the references

Introduction

- If the case presented is a Grade III oligodendroglioma (by the current WHO classification) the standard of care is arguably not the so-called “Stupp regimen”
- It may make some sense to give some background on the natural history of oligodendroliomas (in young patients).
- Mention should be made of the updated RTOG 94-02 results as they perain to this case
- Arguably, the treatments delivered to this patient have been available for 20 years and there has, in the big picture, been rather little advance in radiosurgery technology (“novel imaging” does not seem to have been used in treatment planning for this case). It is of interest that the references quoted in support advances in radiosurgery include patients treated more than 20 years ago as well as a familiar 1995 statement “In recent years, new treatment options of focal radiation dose escalation have become available as a result of advances in radiographic imaging”. One could argue that there have rather been advances in widespread availability of focused radiation treatments.
- It may be worth some mention that high-grade gliomas are by nature infiltrative and thus difficult to target with high precision (thus relatively large margins are typically added in standard external beam radiation)
- It should be made clearer early in the manuscript that the limited use of multiple courses of radiation is in part due to the lack of good evidence for efficacy and the limited number of cases with focal recurrences technically amenable to radiosurgery and not only because of concerns regarding potential toxicity
- Some comment may need to be made on the interval between treatments in the decision to re-irradiate
- * It may also be good to clarify for readers that current “maximum tolerated dose”
levels for radiosurgery are meant to take into account 1 course of prior radiation as RTOG 90-05 patients all had prior external beam radiotherapy.

- “Retrospective reviews have indicated that re-irradiation to the tumor bed is feasible and can lead to improvement in survival with improved quality of life;” can be a controversial statement. There should be a reference provided and some indication that this may be a statement of opinion rather than fact.

Case

- “(WHO) grade IV oligodendroglioma”, it would be preferable to frame the pathology in terms of a specific and current version of the WHO classification (likely a Grade III Oligodendroglioma in the 2007 revision).
- What was the 1p19q status of the tumor?
- “1999 in the tumor bed at which point a second resection was performed” what were the pathological findings? was there visible residual disease at the time of irradiation? what was the irradiation target volume?
- It may be of interest to know the volume of the radiosurgery treatments and the isodose prescribed to.
- It may be better to either mention both radiosurgery devices or omit the branding for both.
- When did the patient die? When did he progress before death? Did he never receive a second course of chemotherapy?

Discussion

- ‘It is more commonly used for smaller treatment volumes and has also demonstrated improved survival times following re-irradiation[5, 7, 8]. Radiation-induced necrosis in these studies was prevalent in studies where larger tumor volumes were treated.”, the notion that radiosurgery improves survival (as opposed de reasonable median survival times are seen after radiosurgery in very highly selected patients) may need more nuance, this is the case in the Heidelberg papers and the Bringham’s report may reflect pre 93-05 enthusiasm for glioma radiosurgery.
- “The largest study examining the efficacy and tolerability of fractionated radiation therapy consisted of 172 patients and demonstrated higher rates of survival when compared to historical norms with minimal rates of radiation induced side effects[9].” Unless I am misreading the reference quoted, there is no formal comparison to matched historical controls and no claim of survival benefits. The Heidelberg group acknowledges the biases associated with retrospective reviews of selected radiosurgery-eligible patients.
- “While the patient developed necrosis within the tumor bed, it is important to recognize that necrosis is considered a therapeutic effect of radiosurgery and the important component of treatment with respect to clinical outcomes is the sparing of normal tissue”, when did this occur, could it be detailed in the case report?
- There could be a brief mention of the therapeutic options for recurrent gliomas
There could be a brief mention of the authors estimate of the risk of symptomatic radiation necrosis for their patient and the potential difficulty in discriminating treatment effect from tumor recurrence (or a mix of both).

Conclusions

“While the patient’s age and histologic diagnosis make his prognosis better compared to other patients with high grade tumors, his extended survival is in part due to controlling his tumor with both surgery and multiple courses of irradiation.”, “may in part be due” may be more realistic than “are in part due”

Form/typographical

“fear of surpassing normal Central Nervous System tissue toxicity” tolerance

“Dilantin which resolved when switched to Depakote.” Use generic names

Figures

Figure 2 could be cleaned up, removing some of the extraneous windows on the left and right of the BrainScan screen.

Quality of written English: Acceptable

Declaration of competing interests:

I declare that I have no competing interests