Polymodal Therapy for High Grade Gliomas: A Case Report of Favourable Outcomes following Intraoperative Radiation Therapy

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SUMMARY

High grade gliomas, frequently with their infiltrative nature, often make the outcome from neurosurgical intervention alone unsatisfactory. It is recognized that adjuvant radio-chemotherapy approaches offer an improved prognosis. For these reasons, we opted for surgical debulking, intraoperative radiation therapy (IORT) in combination with whole brain irradiation therapy and chemotherapy (temozolamide cycles) in the management of a 42 year-old lady with Glioblastoma Multiforme (GBM). Her troublesome symptoms improved after 3 months of this polymodal therapy and remained independently functional for more than two years.

KEY WORDS:
Intraoperative radiation therapy, High grade gliomas, Temozolamide

INTRODUCTION

Several factors are known to influence the prognosis of high grade gliomas, include tumour resection without causing deterioration in patient's neurological functions, adjuvant radiotherapy and chemotherapy with temozolamide. Since high grade gliomas tend to be infiltrative in nature. Radiation therapy targets both the tumour and its infiltrative margin. Hochberg and Pruitt performed a series of autopsy studies in patients with high grade gliomas, where the microscopic margin of tumour was within 2 cm of the enhanced region [1]. This rule of 2 - 3 cm margin from the tumour in radiation therapy seems practical with intraoperative radiation therapy (IORT). We reported our first experience of treating Glioblastoma Multiforme with IORT.

CASE REPORT

A 42 year-old lady presented with 3 months history of right limbs weakness, recurrent seizure, persistent mild headache and blurring of vision. On admission, she appeared alert but had global aphasia, features of Gerstmann syndrome and marked right upper motor neuron facial and ipsilateral limbs weakness. The subsequent MRI brain revealed a left temporoparietal high grade tumoral lesion (figure 1A and 1B) that prompted the plan for surgical debulking, IORT in combination with whole brain irradiation therapy and chemotherapy using temozolamide. At surgery, the tumour appeared infiltrative, with poor demarcating plane from adjacent normal brain tissues. Nearly 80% of the tumoural bulk was successfully removed (figure 2A) and confirmed as Glioblastoma Multiforme on histopathology. The tumoral bed was subjected to IORT, scheduled 2 weeks after the debulking surgery.

Surgical procedure

The procedure was performed under general anaesthesia. Patient's head was fixed with Mayfield head clamped and rotated to the right. Skin incision was made following a previous scar. Previous craniotomy flap was raised, dura reopened, previous corticotomy and the tumoural bed were identified and prepared for the placement of radiation source. The 2.5 cm probe was fixed to the Zeiss intraoperative radiation source, 10 Gy of focal irradiation therapy was administered (figure 1C). After completion of the procedure, absolute hemostasis was achieved, dura was closed primarily and the wound was closed in layers.

Clinical progress

The intraoperative radiation therapy procedure was uneventful. Further external whole brain irradiation therapy (40 Gy) was given in fractionated dose for 6 months, followed by chemotherapy with temozolamide. The weakness

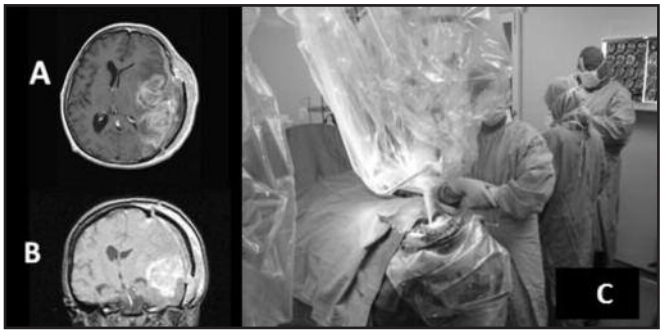

Fig. 1: A and B: Axial and coronal slices of MRI brain show left frontotemporal high grade gliomas. C: An intraoperative radiation therapy procedure.

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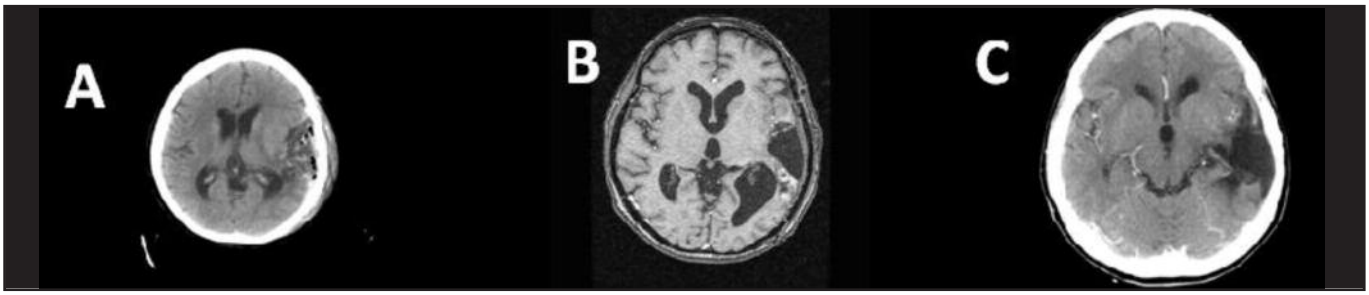

Fig. 2: A: CT brain immediately after the surgery shows residual tumours. B and C: Follow-up MRI (1 year after therapy) and CT brain (2 years after therapy) show areas of encephalomalacia and no tumour recurrence.

gradually improved and she gained functional independence (Barthel's index score of 100) 3 months after the polymodal therapy. Series of follow-up brain imaging (figure 2B and 2C) showed some areas of encephalomalacia and no recurrence. She remained healthy for more than 2 years since the therapy, and is currently under our regular follow-ups.

DISCUSSION

Stereotactic radiosurgery (SRS), stereotactic radiotherapy (SRT) and IORT are three techniques of precision radiation therapy to treat high grade gliomas. In many instances, surgical resection of the tumour is required to reduce the tumour bulk to suit for adjuvant therapy, but radiating the 'empty' tumoural bed with SRS seems inappropriate. Besides, size of the tumour is also a limiting factor for SRS. As for the time-consuming SRT technique, it is potentially inaccurate because of the different timing of radiation with non-fixed referral points. Thus, such limitations of the two techniques made IORT a more favourable option. The key advantages of IORT are a) radiation to the tumoural bed is administered directly after surgical resection; b) radiation can be given circumferentially from the centre of the 'empty' tumoural bed whereby the plan tumour volume is better defined and irradiated; and c) size of the tumour is not a hindrance for high dose irradiation therapy [2].

Previous study has indicated that the median survival for high grade gliomas without adjuvant therapy is 6 – 9 weeks, compared with adjuvant radiotherapy and/or chemotherapy of 23 – 45 weeks [3]. After surgical resection, residual high grade gliomas tend to lie peripherally, infiltrating the normal brain tissues. Consequently, the recurrence rate is high in cases where no adjuvant therapy is given to cover these residuals. In our institution, we regularly add IORT to irradiate the periphery of the tumoural bed. IORT with various applicator sizes fixable to the radiation source offers promising tool in radiating the periphery of the tumoural bed. In this case, we used a 2.5 cm applicator to deliver 10 Gy irradiation at the periphery of the tumoural bed. To date, we had acquired a satisfactory outcome with no recurrence after more than 2 years of follow-up with Barthel's index score of 100 (fully functional and independent).

CONCLUSIONS

Currently, the therapeutic strategy to treat high grade gliomas is evolving rapidly. Combination of various modes of adjuvant therapy together with intraoperative adjuncts has significantly improved prognostic outcomes. Our case report of Glioblastoma Multiforme illustrates the use IORT as a promising and feasible mode of therapy for such a diffuse and infiltrative high-grade glioma.

REFERENCES

1. Hochberg FH, Pruitt A. Assumptions in the radiotherapy of glioblastoma. Neurol 1980; 30: 907-11.
2. Kalapurakal JA, Goldman S, Stellpflug W, Curran J, Sathiaseelan V, Marymont MH *et al*. Phase I study of intraoperative radiotherapy with photon radiosurgery system in children with recurrent brain tumors: preliminary report of first dose level (10 Gy). Int J Radiat Oncol Biol Phys. 2006 Jul 1; 65(3): 800-8.
3. Mohan DS, Suh JH, Phan JL, Kupelian PA, Cohen BH, Barnett GH. Outcome in elderly patients undergoing definitive surgery and radiation therapy for supratentorial gliobalstoma multiforme at a tertiary care institution. Int J Radiat Oncol Biol Phys 1998; 42: 981-7.