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REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY

ISSN: 1507-1367

e-ISSN: 2083-4640

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DOI: 10.5603/rpor.104738

Article type: Clinical vignette

Published online: 2025-02-27

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Recurrent glioblastoma: a typical example of a complex approach

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Keywords: glioblastoma; relapse; re-irradiation

Glioblastoma is the most common malignant tumor of the central nervous system, accounting for 45% of all gliomas [1, 2].

It is considered an incurable disease with a poor prognosis, and a median survival exceptionally exceeding 15 months from diagnosis [1].

Recurrence further increases mortality and occurs around 6 to 9 months after the first treatment [2].

The case was about a 68-year-old patient who has been followed for World Health Organization grade 4 glioma.

The initial magnetic resonance imaging (MRI) revealed a right parietal process for which the patient underwent a partial resection surgery. Anatomo-pathological results confirmed

glioblastoma. Molecular study using polymerase chain reaction (PCR) techniques showed no *MGMT* gene methylation.

Treatment was continued following Stupp protocol. It was a radiotherapy treatment using volumetric modulated arc therapy (VMAT) technique with Novalis Truebeam STX linear accelerator, at a dose of 60 Gy (2 Gy/fraction) with daily concomitant temozolomide intake (75 mg/m^2). Target volumes were defined according to the recommendations of the Radiation Therapy Oncology Group (RTOG).

Temozolomide was followed as an adjuvant therapy six months, then extended for further 6 months. 8 months after the end of radiotherapy the brain-MRI showed a 41% reduction in the size of the tumor.

Then, one year after the end of chemotherapy, an ectopic re-growth in the right occipito-temporal lobe, was identified on brain MRI marking a relapse of the disease.

The patient benefited from targeted therapy; bevacizumab combined to hypofractionated radiotherapy under stereotactic conditions using Novalis Truebeam STX linear accelerator at a dose of 30 Gy (5 Gy/fraction).

A second relapse was detected around 4 months later in the right parietal lesion, for which the same treatment was initiated (Fig. 1). The cumulative equivalent dose in 2 Gy fractions (EQD2) dose to the healthy brain was less than 130 Gy (Tab. 1).

A follow-up MRI one month later showed a 28.5% regression of the right parietal lesion, with a stable appearance of the right occipito-temporal lesion.

3 months later, the volume of the right occipito-temporal lesion increased by 36%, indicating progression of the disease.

It was decided to change the therapeutic strategy and opt for Trametinib, which the patient tolerated poorly. The patient has remained under palliative care only to pass away 42 months after his diagnosis.

The patient studied was over 65 years and had glioblastoma without MGMT promoter methylation. These are poor prognosis factors and predict increased resistance to treatment [3]. It was therefore of particular interest to extend the duration of adjuvant temozolomide by 6 months. According to Hegi et al, prolonged treatment with temozolomide leads to a

decrease in MGMT levels, thereby weakening tumor cells and reinforcing the effects of treatment [4]. In 2021, a study of 319 patients by Huang et al. showed that patients who received long-term adjuvant chemotherapy had a statistically significant progression-free survival ($p = 0.008$) [5].

Re-irradiation combined with bevacizumab was associated with longer progression-free survival in recurrent glioblastoma. A phase II trial confirmed this benefit, showing improved progression-free survival (7.1 *vs.* 3.8 months) without affecting overall survival [6].

But the main toxicity feared is cerebral necrosis, which occurs at a risk of 7–13% after stereotactic hypo-fractionated radiotherapy at a cumulative EQD2 dose of between 102 and 130 Gy [7]. The most commonly used treatment regimens range from 25 to 35 Gy, delivered in 5 to 7 Gy fractions. Numerous studies have demonstrated their efficacy, with an overall survival up to 12.5 months and a radiological response rate of 40% [7].

For the last relapse, the patient received Trametinib because of its somatic BRAF V600E mutation. A Phase II trial evaluated the combination of dabrafenib and trametinib in recurrent or refractory high-grade gliomas with BRAF V600E mutation. The results showed a 33% objective response rate and a median progression-free survival of 12.7 months [8].

Although glioblastoma is a tumor with a poor prognosis, re-irradiation combined with bevacizumab remains an option for controlling the disease, pending the emergence of new therapies.

Ethical permission

There was full compliance with ethical standards including informed consent. The patient has provided verbal consent for the publication of this report and any accompanying images.

Conflict of interest

The authors have no relevant financial or non-financial interests to disclose.

Author contributions:

M.N. conceived the clinical vignette and wrote the manuscript. S.B. collected and analyzed the data and contributed to the writing of the manuscript. S.ElM., A.N. and N.I. reviewed and

edited the manuscript, provided critical feedback. All authors have read and approved the final version of the manuscript.

Funding

This publication was prepared without any external source of funding.

References

1. Alifieris C, Trafalis DT. Glioblastoma multiforme: Pathogenesis and treatment. Pharmacol Ther. 2015; 152: 63–82, doi: 10.1016/j.pharmthera.2015.05.005, indexed in Pubmed: 25944528.
2. Cantidio FS, Gil GO, Queiroz IN, et al. Glioblastoma - treatment and obstacles. Rep Pract Oncol Radiother. 2022; 27(4): 744–753, doi: 10.5603/RPOR.a2022.0076, indexed in Pubmed: 36196416.
3. Śledzińska P, Bebyn MG, Furtak J, et al. Prognostic and Predictive Biomarkers in Gliomas. Int J Mol Sci. 2021; 22(19), doi: 10.3390/ijms221910373, indexed in Pubmed: 34638714.
4. Hegi ME, Diserens AC, Gorlia T, et al. MGMT gene silencing and benefit from temozolomide in glioblastoma. N Engl J Med. 2005; 352(10): 997–1003, doi: 10.1056/NEJMoa043331, indexed in Pubmed: 15758010.
5. Huang B, Yu Z, Liang R. Effect of long-term adjuvant temozolomide chemotherapy on primary glioblastoma patient survival. BMC Neurol. 2021; 21(1): 424, doi: 10.1186/s12883-021-02461-9, indexed in Pubmed: 34724914.
6. Tsien CI, Pugh SL, Dicker AP, et al. NRG Oncology/RTOG1205: A Randomized Phase II Trial of Concurrent Bevacizumab and Reirradiation Versus Bevacizumab Alone as Treatment for Recurrent Glioblastoma. J Clin Oncol. 2023; 41(6): 1285–1295, doi: 10.1200/JCO.22.00164, indexed in Pubmed: 36260832.
7. Minniti G, Niyazi M, Alongi F, et al. Current status and recent advances in reirradiation of glioblastoma. Radiat Oncol. 2021; 16(1): 36, doi: 10.1186/s13014-021-01767-9, indexed in Pubmed: 33602305.

8. Wen PY, Stein A, van den Bent M, et al. Dabrafenib plus trametinib in patients with BRAF-mutant low-grade and high-grade glioma (ROAR): a multicentre, open-label, single-arm, phase 2, basket trial. Lancet Oncol. 2022; 23(1): 53–64, doi: 10.1016/S1470-2045(21)00578-7, indexed in Pubmed: 34838156.

Table 1. Doses received in the healthy brain in physical and equivalent dose in 2 Gy fractions (EQD2) doses

Figure 1. Treatment planning; first irradiation (**A**), second irradiation (**B**) and third irradiation (**C**)