^{177}Lu-/^{68}Ga-PSMA Theranostics in Recurrent Glioblastoma Multiforme

Proof of Concept

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Abstract: A 37-year-old man, treated case of left temporal glioblastoma presented with headache, seizures, and progressive right-sided weakness with MRI evidence of recurrence. Exploratory ^{68}Ga-PSMA PET/CT demonstrated PSMA expression in the recurrent lesion; it was decided to treat this patient with ^{177}Lu-PSMA-617. After 3 cycles of ^{177}Lu-PSMA-617, ^{68}Ga-PSMA PET/CT showed significant reduction in PSMA uptake and regression in size of lesion on MRI with improvement in patient's symptoms and performance status. ^{177}Lu-/^{68}Ga-PSMA theranostics has potential in patients with recurrent glioblastoma multiforme when other therapeutic options are not feasible.

Key Words: ^{177}Lu-PSMA-617, ^{68}Ga-PSMA, GBM, radioligand therapy, recurrent glioblastoma

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REFERENCES

1. van Linde ME, Brahm CG, de Witt Hamer PC, et al. Treatment outcome of patients with recurrent glioblastoma multiforme: a retrospective multicenter analysis. *J Neurooncol*. 2017;135:183–192.
2. Stupp R, Hegi ME, Mason WP, et al. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial. *Lancet Oncol*. 2009;10:459–466.
3. Wernicke AG, Edgar MA, Lavi E, et al. Prostate-specific membrane antigen as a potential novel vascular target for treatment of glioblastoma multiforme. *Arch Pathol Lab Med*. 2011;135:1486–1489.
4. Van de Wiele C, Sathekge M, de Spiegeleer B, et al. PSMA-targeting positron emission agents for imaging solid tumors other than non-prostate carcinoma: a systematic review. *Int J Mol Sci*. 2019;20:4886–4896.
5. Mahzouni P, Shavakhi M. Prostate-specific membrane antigen expression in neovasculature of glioblastoma multiforme. *Adv Biomed Res*. 2019;8:18–24.
6. Kunikowska J, Kuliński R, Muylle K, et al. ^{68}Ga-prostate-specific membrane antigen-11 PET/CT: a new imaging option for recurrent glioblastoma multiforme? *Clin Nucl Med*. 2020;45:11–18.
7. Bertagna F, Albano D, Cerudelli E, et al. Potential of radiolabelled PSMA PET/CT or PET/MRI diagnostic procedures in gliomas/glioblastomas. *Curr Radiopharm*. 2020;13:1–5.
8. Sathekge MM, Bruchertseifer F, Lawal IO, et al. Treatment of brain metastases of castration-resistant prostate cancer with ^{225}Ac-PSMA-617. *Eur J Nucl Med Mol Imaging*. 2019;46:1756–1757.
9. Wei X, Schlenkhoff C, Schwarz B, et al. Combination of ^{177}Lu-PSMA-617 and external radiotherapy for the treatment of cerebral metastases in patients with castration-resistant metastatic prostate cancer. *Clin Nucl Med*. 2017;42: 704–706.

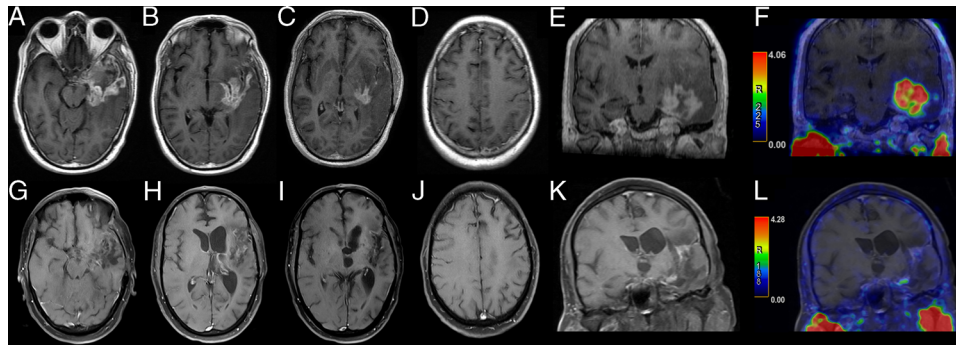

FIGURE 1. A 37-year-old man treated for left temporal glioblastoma multiforme (GBM) with total tumor excision, radiotherapy, and adjuvant temozolomide presented with headache, seizures, and progressive right-sided weakness within 1 month of therapy completion. Serial MRI showed progressive left temporal nodular enhancing lesion extending to involve left gangliocapsular region posteriorly with perilesional edema and leptomeningeal enhancement (**A–E**). After being refused surgery and radiation therapy and financial constraints limiting bevacizumab therapy, the patient was taken up for ^{68}Ga–prostate-specific membrane antigen (^{68}Ga-PSMA-11) PET. Fused ^{68}Ga-PSMA PET/MR images demonstrated intense PSMA expression in the enhancing areas on MRI (F). Written and informed consent of the patient was obtained, and he underwent 3 cycles of 3700 MBq ^{177}Lu-PSMA-617 therapy at 2 monthly intervals with no significant adverse events in the post-treatment period. The patient showed improvement in performance score (ECOG 4 to 3) and symptoms. Post-therapy MRI (**G–K**) and fused PET/MR (**L**) showed significant reduction in lesion size (volume decreased from 18 to 5.4 mL using brain tumor image analysis, https://www.nitrc.org.projects/bratumia software) with minimal residual enhancement and PSMA expression with no new lesion elsewhere. Recurrent glioblastoma is associated with a poor prognosis, limited treatment options, and a median survival of 12 to 15 months.[1,2] The expression of PSMA has been demonstrated in neovasculature of high-grade gliomas,[3–5] and ^{68}Ga-PSMA-11 PET has been suggested as a useful imaging option in recurrent GBM.[6,7] As PSMA is highly overexpressed in prostate cancer cells, successful targeted radioligand therapy with ^{177}Lu-PSMA-617 has been reported in cases of brain metastases from the carcinoma prostate.[8,9] Because no further therapy options were available to our case, we offered him ^{68}Ga-PSMA-11 followed by ^{177}Lu-PSMA-617 theranostics, which resulted in symptomatic improvement and good imaging response. This case therefore demonstrates the potential for ^{177}Lu-PSMA thernostics in recurrent GBM. Further multicentric studies with prospective data collection would be useful to determine the usefulness of this salvage option in this aggressive disease with high mortality.