ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Clinical Professor of Neurological Surgery, School of Medicine, State U. of NY at Stony Brook.

SNI: Neuro-Oncology

Editor
Mitsutoshi Nakada, MD
Kanazawa University, Ishikawa, Japan

SNI
Open Access

Case Report

Prolonged survival after laser interstitial thermal therapy in glioblastoma

A. Basit Khan[1], Carlos Kamiya Matsuoka[2], Sungho Lee[1], Maryam Rahman[3], Ganesh Rao[1]

[1]Department of Neurosurgery, Baylor College of Medicine, [2]Department of Neuro-Oncology, MD Anderson Cancer Center, Houston, Texas, [3]Department of Neurosurgery, University of Florida, Gainesville, Florida, United States.

E-mail: A. Basit Khan - abdulk@bcm.edu; Carlos Kamiya Matsuoka - ckamiya@mdanderson.org; Sungho Lee - sungho.lee@bcm.edu; Maryam Rahman - maryam.rahman@neurosurgery.ufl.edu; *Ganesh Rao - grao@bcm.edu

***Corresponding author:**
Ganesh Rao, MD
Department of Neurosurgery,
Baylor College of Medicine,
7200 Cambridge, Houston - 77030, Texas, United States.

grao@bcm.edu

Received : 18 February 2021
Accepted : 23 March 2021
Published : 17 May 2021

DOI:
10.25259/SNI_174_2021

Quick Response Code:

ABSTRACT

Background: Glioblastoma (GBM) is the most common primary malignant brain tumor in adults. Management includes surgical resection followed by chemoradiation, and prognosis remains poor. Surgical resection is not possible for some deep-seated or eloquent tumors. Laser interstitial thermal therapy (LITT) has emerged as a new, minimally invasive surgical option for deep-seated GBM.

Case Description: We report a case of newly diagnosed thalamic GBM managed with LITT followed by radiation and chemotherapy.

Conclusion: The patient remains well at 50-month post-LITT, indicating a potentially unique durability of LITT treatment in GBM.

Keywords: Glioblastoma, Laser interstitial thermal therapy, Survival

INTRODUCTION

Glioblastoma (GBM) is the most common primary malignant brain tumor in adults with an age-adjusted annual incidence of 3.22/100,000 population.[12] GBM is defined pathologically as a glial tumor with an abundance of mitoses, necrosis, and neovascularization.[6] The standard management of these tumors is maximal safe resection followed by concurrent chemoradiation with subsequent adjuvant chemotherapy.[15,17] Prognosis remains poor with median survival of 14 months.[15,17] Extent of surgical resection is an important treatment factor for this disease.[13] Deep seated or eloquent tumor locations pose increased risk of surgical morbidity. Depending on tumor location, even subtotal resection may not be safely possible.

Laser interstitial thermal therapy (LITT) is a technique used to thermally ablate tumors in a minimally invasive fashion. The use of laser-mediated interstitial thermal ablation was first demonstrated in 1983, and the clinical utility of this technology was improved by the development of magnetic resonance (MR) thermography.[1,2] The main mechanism of LITT is to impart thermal damage on local tissue.[14] Irreversible heat-induced necrosis occurs at or above 46°C.[8] LITT has been utilized in diverse disease processes in neurological surgery.[9] As of yet, no randomized controlled trials have been performed regarding intracranial LITT, but retrospective

series show positive results for LITT.[16,18] Given its minimally invasive nature, LITT offers a surgical option for GBM located in areas of high surgical risk. Here, we report a case of prolonged survival in a patient with a thalamic GBM treated with LITT, which serves to highlight the potentially durable nature of LITT treatment for this disease.

CLINICAL CASE

A previously healthy 32-year-old man presented to our institution for a second opinion after undergoing biopsy of a left thalamic lesion which revealed GBM. He initially presented to an outside hospital with a complaint of progressive clumsiness of the right hand and foot. MRI of the brain revealed a solitary ring-enhancing lesion with associated increased FLAIR signal in the left thalamopeduncular region [Figure 1a]. Stereotactic biopsy of the lesion was performed at the outside institution, and neuropathology analysis revealed the WHO Grade IV GBM. Immunohistochemistry showed no mutation in *IDH1*, *ATRX*, or *BRAF* genes. Subsequent molecular analyses showed indeterminate O(6)-methylguanine-DNA methyltransferase (MGMT) promoter methylation and no mutation or copy number alteration in *IDH1*, *IDH2*, *EGFR*, or *PDGFR*. Histone H3F3 (H3K27M) mutation was absent, and H3K27me3 shows retained trimethylation mark. He presented to our institution for a second opinion. At that time, he had a normal neurologic examination. Given the deep-seated location of the tumor and eloquence of surrounding structures, we elected for LITT followed by radiation alone and adjuvant temozolomide. The patient continues to do well at last follow-up [Figure 1b].

The LITT procedure was performed in our intraoperative MRI suite using image-guided stereotactic lead placement using the ClearPoint system (Clearpoint Neuro). For the ablation, we utilized the NeuroBlate system (Monteris). The laser ablation was carried out under real-time MR thermography [Figure 2a]. We began thermal lesioning 5 mm superior to target along our trajectory following the long axis of the tumor, advancing 5 mm at a time until the entire lesion was affected by adequate thermal damage. Total laser on time was approximately 7 min. Nearly, total ablation of the tumor was achieved with the vast majority of the tumor. There was a sharp drop in temperature across the enhancing surface of the tumor, allowing adequate tumor ablation without damaging the corticospinal tracts. Immediate postoperative MRI showed diffusion restriction within the tumor and increased enhancement within the necrotic core [Figure 2b]. He was given a short course of dexamethasone to prevent postoperative perilesional edema and discharged home on postoperative day 1 with no neurologic deterioration.

Postoperatively, the patient received intensity-modulated radiation therapy to the resection cavity with a total dose of 60 Gy in 30 fractions starting on postoperative day 13. He did not receive concurrent chemotherapy. Thereafter, he was given adjuvant temozolomide at 200 mg/m^2/day, days 1–5 every 28-day cycle, for 12 cycles. Most recently, his MRI from 47.5

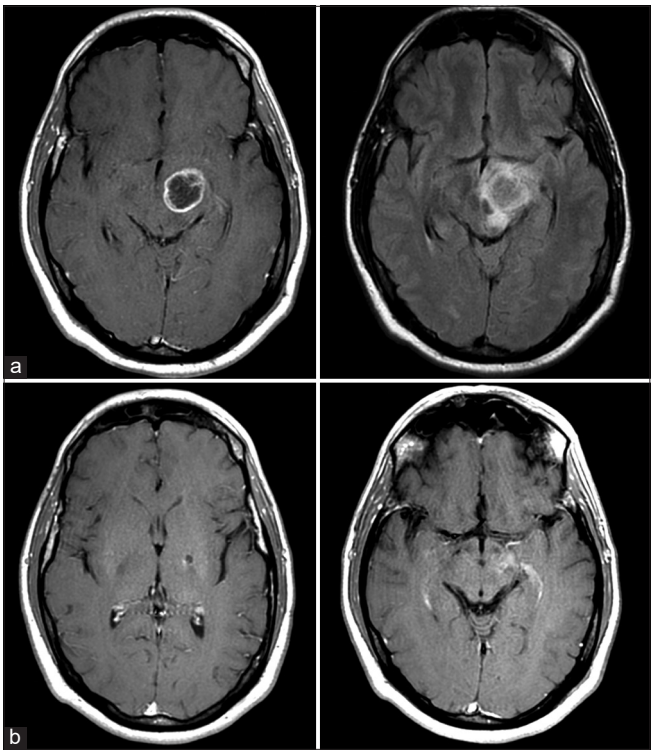

Figure 1: Pre and postoperative MRI. (a) Representative preoperative T1 contrast enhanced (left) and FLAIR (right) images. (b) Representative 46.9-month post-LITT T1 contrast enhanced (left) and FLAIR (right) images.

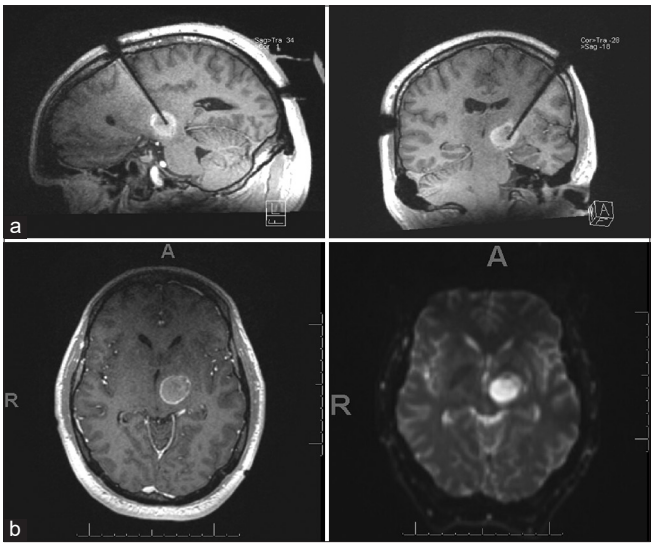

Figure 2: Intraoperative and immediate postoperative MRI. (a) Intraoperative MRI demonstrating laser probe position. (b) Immediate postoperative T1-weighterd post-contrast and diffusion-weighted images.

months after initial biopsy and 46.9 months after LITT showed only a small cavitation with minimal enhancement and FLAIR signal, likely as a result of LITT [Figure 1b]. His neurologic examination remains normal at 51 months after initial biopsy.

DISCUSSION

Observations

Here, we report a case of prolonged survival of a patient with thalamic GBM treated with LITT and subsequent adjuvant treatment that concluded 1 year after diagnosis. The patient remains disease free over 50 months from diagnosis. While an outlier, this case represents the potential durable treatment effect of LITT in newly diagnosed GBM.

Lessons

The use of LITT for treatment of GBM, whether primary or recurrent, is an emerging surgical option for tumor control. When considering deep-seated tumors, a reasonable comparison is to patients who were previously allocated to biopsy-only options. Patients undergoing concurrent chemoradiation after biopsy only had a median overall survival (OS) of 9.4 months versus 15.8 months in patients who underwent tumor resection.[15,17] Initial early-stage single-center retrospective studies showed minimal efficacy of LITT in newly diagnosed GBM with median OS of 8 months and median progression-free survival (PFS) of 2 months but more favorable result in recurrent GBM.[16,18] This trend has been replicated in larger series.[4,11] More recently, a meta-analysis of 25 patients with newly diagnosed high-grade glioma treated with LITT showed median OS of 14.2 months and PFS of 5.1 months, both of which are superior to biopsy-only data.[3] A matched cohort multicenter study comparing LITT to biopsy alone in unresectable glioma in 24 patients showed no difference in median OS or PFS but improved outcomes in disease-specific OS and PFS in the subset of LITT patients that had adequate thermal ablation as compared to biopsy only.[10] Ultimately, data regarding LITT in GBM are limited to retrospective analyses with mixed results in treatment of newly diagnosed GBM. Clearly, our patient who has survived over 50 months is an outlier. Nonetheless, our patient's prolonged survival indicates that LITT treatment may offer durable disease control in GBM. More research is needed to delineate the effect of LITT in newly diagnosed GBM and its effect on survival of patients with unresectable tumors.

Beyond direct tumor control, alterations in GBM pathobiology in response to LITT are actively being studied. One of the challenges to treating GBM is delivering chemotherapy across the blood–brain barrier. Recent studies have shown that LITT treatment can increase permeability of the blood–brain barrier in a time-dependent fashion.[5] This suggests that for some time after LITT, GBM may be more susceptible to chemotherapy. It is standard at our institution to administer concurrent chemoradiation starting at postoperative day 14. In this case, we withheld temozolomide to reduce potential for developing symptomatic treatment effect in a neurologically normal patient given the tumor location. In addition, early data to suggest LITT may sensitize GBM to radiation by inhibiting AKT signaling.[7] It is notable that our patient did begin radiation on postoperative day 13, potentially within a window of increased tumor susceptibility to radiation. These concepts lend to the notion that the effect of LITT in GBM treatment may be multifactorial beyond pure cytoreduction.

The genetic landscape of GBM is diverse with certain genetic alterations portending variably good or bad prognoses. Per the WHO 2016, GBM diagnoses are segregated on the basis of IDH mutational status.[20] Mutant IDH is more commonly present in secondary GBM, and these patients typically have better prognoses.[6] Our patient did not have an IDH mutation consistent with his primary GBM diagnosis, however, his prolonged survival defies the common expectation of IDH wildtype patients. MGMT is a DNA repair enzyme, and methylation of the MGMT promoter indicates heightened response to chemoradiation in glioma.[19] The methylation status of MGMT in our patient was indeterminate. H3K27M mutations are most commonly found in diffuse midline glioma in pediatric patients but are also encountered in a subset of adult tumors characterized by midline location, low MGMT promoter methylation rate, and poor prognosis.[10] Our patient did not have an H3K27M mutation, consistent with his prolonged survival. In addition, our patient did not have mutation or copy number alteration in IDH2, EGFR, or PDGFR. Ultimately, the IDH wildtype status of our patient suggested a poor prognosis without evidence of any favorable molecular factors, yet he remains clinically well at 51 months. This highlights the need for further molecular analyses regarding GBM.

CONCLUSION

In summary, we report a unique case of prolonged survival and excellent radiographic response using LITT to treat a thalamic GBM. GBM in deep-seated locations remains challenging neuro-oncological problems as resection is often not possible. The published data regarding LITT are sparse with mixed result. This case highlights the need for higher quality research regarding LITT in GBM. Moreover, this report suggests that LITT treatment in GBM may offer durable treatment response beyond the current standard of care.

Acknowledgments

None.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Bown SG. Phototherapy in tumors. World J Surg 1983;7:700-9.
2. de Poorter J, de Wagter C, de Deene Y, Thomsen C, Ståhlberg F, Achten E. Noninvasive MRI thermometry with the proton resonance frequency (PRF) method: *In vivo* results in human muscle. Magn Reson Med 1995;33:74-81.
3. Ivan ME, Mohammadi AM, de Deugd N, Reyes J, Rodriguez G, Shah A, *et al*. Laser ablation of newly diagnosed malignant gliomas: A meta-analysis. Neurosurgery 2016;79 Suppl 1:S17-23.
4. Kamath AA, Friedman DD, Akbari SH, Kim AH, Tao Y, Luo J, *et al*. Glioblastoma treated with magnetic resonance imaging-guided laser interstitial thermal therapy: Safety, efficacy, and outcomes. Neurosurgery 2019;84:836-43.
5. Leuthardt EC, Duan C, Kim MJ, Campian JL, Kim AH, Miller-Thomas MM, *et al*. Hyperthermic laser ablation of recurrent glioblastoma leads to temporary disruption of the peritumoral blood brain barrier. PLoS One 2016;11:e0148613.
6. Li QJ, Cai JQ, Liu CY. Evolving molecular genetics of glioblastoma. Chin Med J (Engl) 2016;129:464-71.
7. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, *et al*. The 2016 World Health Organization classification of tumors of the central nervous system: A summary. Acta Neuropathol 2016;131:803-20.
8. Man J, Shoemake JD, Ma T, Rizzo AE, Godley AR, Wu Q, *et al*. Hyperthermia sensitizes glioma stem-like cells to radiation by inhibiting AKT signaling. Cancer Res 2015;75:1760-9.
9. Mensel B, Weigel C, Hosten N. Laser-induced thermotherapy. Recent Results Cancer Res 2006;167:69-75.
10. Meyronet D, Esteban-Mader M, Bonnet C, Joly MO, Uro-Coste E, Amiel-Benouaich A, *et al*. Characteristics of H3 K27M-mutant gliomas in adults. Neuro Oncol 2017;19:1127-34.
11. Missios S, Bekelis K, Barnett GH. Renaissance of laser interstitial thermal ablation. Neurosurg Focus 2015;38:E13.
12. Mohammadi AM, Sharma M, Beaumont TL, Juarez KO, Kemeny H, Dechant C, *et al*. Upfront magnetic resonance imaging-guided stereotactic laser-ablation in newly diagnosed glioblastoma: A multicenter review of survival outcomes compared to a matched cohort of biopsy-only patients. Neurosurgery 2019;85:762-72.
13. Montemurro N, Anania Y, Cagnazzo F, Perrini P. Survival outcomes in patients with recurrent glioblastoma treated with laser interstitial thermal therapy (LITT): A systematic review. Clin Neurol Neurosurg 2020;195:105942.
14. Ostrom QT, Cioffi G, Gittleman H, Patil N, Waite K, Kruchko C, *et al*. CBTRUS statistical report: Primary brain and other central nervous system tumors diagnosed in the United States in 2012-2016. Neuro Oncol 2019;21 Suppl 5:v1-100.
15. Sanai N, Polley MY, McDermott MW, Parsa AT, Berger MS. An extent of resection threshold for newly diagnosed glioblastomas. J Neurosurg 2011;115:3-8.
16. Stafford RJ, Fuentes D, Elliott AA, Weinberg JS, Ahrar K. Laser-induced thermal therapy for tumor ablation. Crit Rev Biomed Eng 2010;38:79-100.
17. Stupp R, Mason WP, van den Bent MJ, Weller M, Fisher B, Taphoorn MJ, *et al*. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med 2005;352:987-96.
18. Thomas JG, Rao G, Kew Y, Prabhu SS. Laser interstitial thermal therapy for newly diagnosed and recurrent glioblastoma. Neurosurg Focus 2016;41:E12.
19. Weller M, Stupp R, Reifenberger G, Brandes AA, van den Bent MJ, Wick W, *et al*. MGMT promoter methylation in malignant gliomas: Ready for personalized medicine? Nat Rev Neurol 2010;6:39-51.
20. Yan H, Parsons DW, Jin G, McLendon R, Rasheed BA, Yuan W, *et al*. IDH1 and IDH2 mutations in gliomas. N Engl J Med 2009;360:765-73.

How to cite this article: Khan AB, Matsuoka CK, Lee S, Rahman M, Rao G. Prolonged survival after laser interstitial thermal therapy in glioblastoma. Surg Neurol Int 2021;12:228.