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ORIGINAL ARTICLE

Stereotactic laser ablation for subependymal giant cell astrocytomas: personal experience and review of the literature

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Abstract

Purpose Subependymal giant cell astrocytomas (SEGAs) are rare tumors typically found in tuberous sclerosis patients. They typically grow in the region of the foramen of Monro and can occlude it, leading to hydrocephalus. Currently, gross total resection is the standard of care, with low rates of recurrence but high rates of complication, especially with larger lesions. Laser interstitial thermal therapy (LITT) is a newly emerging treatment modality for a variety of pathologies. Here, we present a case series of SEGAs managed via LITT and endoscopic, stereotactic septostomy.

Methods A retrospective chart review was performed to identify three cases in which SEGAs were treated via LITT and septostomy. Stereotactic ablation was performed via magnetic resonance (MR) thermometry with laser output set to 69% for 2.5 min, with post-ablation scans for visualization of treatment area.

Results Average age at surgery was 8.2 years. Pre-operative tumor volumes were 0.43, 1.51, and 3.88 cm^3. Post-operative tumor volumes were 0.25, 0.21, and 0.68 cm^3. Mean tumor volume reduction was 70%. No complications occurred.

Conclusion LITT with septostomy should be considered a viable primary or adjunct treatment modality for SEGAs.

Keywords Subependymal giant cell astrocytoma · Laser ablation · Septostomy

Abbreviations

cm	centimeters
CSF	cerebrospinal fluid
FFE	fast field echo
FoV	field of view
GKS	gamma knife surgery
Hz	hertz
LITT	laser interstitial thermal therapy
mm	millimeters
MR	magnetic resonance
MRI	magnetic resonance imaging
ms	milliseconds
mTOR	mammalian target of rapamycin
SEGAs	subependymal giant cell astrocytomas
TE	echo time
TR	repetition time

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Introduction

Subependymal giant cell astrocytoma (SEGA) is a rare tumor almost exclusively found in tuberous sclerosis patients [1]. These low-grade (WHO grade I) lesions typically develop in the first two decades of life, are slow-growing, arise from periventricular tissue, and can lead to cerebrospinal fluid (CSF) outflow obstruction at the foramen of Monro [2–5]. Given that SEGAs are low-grade, current management involves close monitoring for developing hydrocephalus and changes in tumor growth rate [5].

When intervention is indicated, surgical excision is the standard with excellent results in smaller lesions and considered curative with gross total resection [3, 6]. However, surgery-related complications can be as high as 67% with lesions greater than 3 cm in diameter and when adherent to surrounding critical structures [7, 8]. Thus, medical therapy and stereotactic radiosurgery represent alternative treatment modalities [6]. Mammalian target of rapamycin (mTOR) inhibitors such as everolimus has shown greater than 50% tumor volume reduction in clinical trials [9, 10]. However, further studies are warranted to evaluate the necessity of prolonged therapy to prevent tumor regrowth as well as the long-term sequelae of prolonged therapy [3, 4]. Gamma knife surgery (GKS) has been employed in SEGA treatment, but the efficacy has been variable and safety data is lacking [3, 8].

Laser interstitial thermal therapy (LITT) is a stereotactic, percutaneous procedure employed for thermal ablation of lesions. LITT produces light energy via a fiberoptic catheter with the recent incorporation of magnetic resonance (MR) thermometry in real time to visualize the thermal energy delivered to surrounding tissue. This modality is particularly effective when surgical excision is not a viable option secondary to deep-seated, inaccessible lesions or in patients who cannot tolerate general anesthesia for an extended time due to comorbidities. Various pathologies have been treated with MR-guided LITT, including deep-seated tumors, radiation necrosis, and epileptogenic lesions [11]. To date, only a handful of studies have evaluated the efficacy of LITT for SEGA [6, 12, 13].

In this study, we report three cases of SEGA treated with LITT and concurrent endoscopic, stereotactic septostomy.

Methods

Patient selection

A retrospective chart review from January 2016 to December 2017 found three patients with SEGAs treated via LITT. Of these patients, mean tumor volume was calculated via the formula $4/3*\pi*(a*b*c)$, where a, b, and c were radii measured on pre-operative magnetic resonance imaging (MRI), which was performed immediately prior to ablation after Leksell head frame placement [14]. All had tuberous sclerosis complex, demographics is as in Table 1, and intervention was decided secondary to rapidly enlarging lesions encroaching on the foramen of Monro.

Operative details

Frame-based stereotaxy

Leksell frame was placed under mild sedation and local anesthesia outside the intra-operative MRI suite.

Pre-ablation MRI

A 1.5 Tesla MRI scanner was used for all imaging. A stealth protocol MRI was performed after frame placement in preparation for laser fiber placement.

Laser fiber placement

Target and trajectory were determined via stealth imaging such that target was the center of the lesion and trajectory along the long axis of the tumor, avoiding vascular structures. Burr holes were then created, through which two of the three patients had a biopsy taken followed by fiber placement. All three patients had an additional burr hole created for septostomy.

Ablation settings

The Visualase Laser Ablation system was utilized (Medtronic Inc., Dublin, Ireland). Laser output was set to 15 W at 69% for 2.5 min, while MR thermometry was simultaneously performed.

MRI parameters

MR thermometry was performed with a fast field echo (FFE) sequence in single shot, long-term averaging mode. Field of view (FoV) was 28.0 cm, voxel size was $1.1 \times 1.1 \times 1.3$ mm with a slice thickness of 1.25 mm. Repetition time (TR) was 5.25 ms, echo time (TE) 2.50 ms, flip angle 15.0°, and bandwidth 400 Hz.

Post-ablation MRI

After the ablation, a T1 post-contrast MRI was performed to confirm no hemorrhage and to visualize treatment volume.

Table 1 Demographics

Patient	Age at surgery (years)	Pre-operative tumor volume (cm^3)	Immediate post-operative tumor volume (cm^3)	Long-term post-operative tumor volume (cm^3)	Percent decrease in size pre-operative to long-term post-operative	Timing of long-term post-operative MRI (months after surgery)	Adjuvant or neoadjuvant therapy	Clinical outcome	Length of clinical follow-up (months after surgery)
1	8.9	0.43	0.37	0.25	42%	15	None	No complication. At baseline at 6-week follow-up.	21
2	6.7	1.51	0.97	0.21	86%	21	None	No complication. Doing well at 2.5-week follow-up.	22
3	8.9	3.88	2.28	0.37	90%	16	None	No complication	16

Post-operative care

The laser fiber and frame were removed, and scalp sutured closed with monocryl. Each patient was monitored in recovery area and then the neurosurgical floor overnight.

Results

Demographics are as listed in Table 1 with selected MRIs shown in Fig. 1. All patients had tuberous sclerosis with rapidly enlarging lesions encroaching on the foramen of Monro. Two of the three had biopsies performed just prior to ablation, with pathology resulting as WHO grade 1 SEGA. All three had septostomies performed in addition to ablation. Mean tumor volume reduction at long-term post-operative MRI was 70 $\pm$ 27% across all three patients. Two patients were discharged home in good condition post-operative day 1, and one discharged in good condition on post-operative day 2. All were provided a 2–3-week taper of dexamethasone. None of the patients required extended hospitalization, none had any immediate or late post-operative complication, and none received adjuvant or neoadjuvant therapy (Figs. 2 and 3).

Discussion

In this study, we present three patients with SEGAs treated via LITT and concurrent endoscopic, stereotactic septostomy. Mean tumor volume reduction was 70 $\pm$ 27% across all three patients with no complications.

A limited number of studies to date have evaluated the efficacy of LITT for SEGA (Table 2) [6, 12, 13, 15]. In these studies, significant tumor volume reduction was noted in four

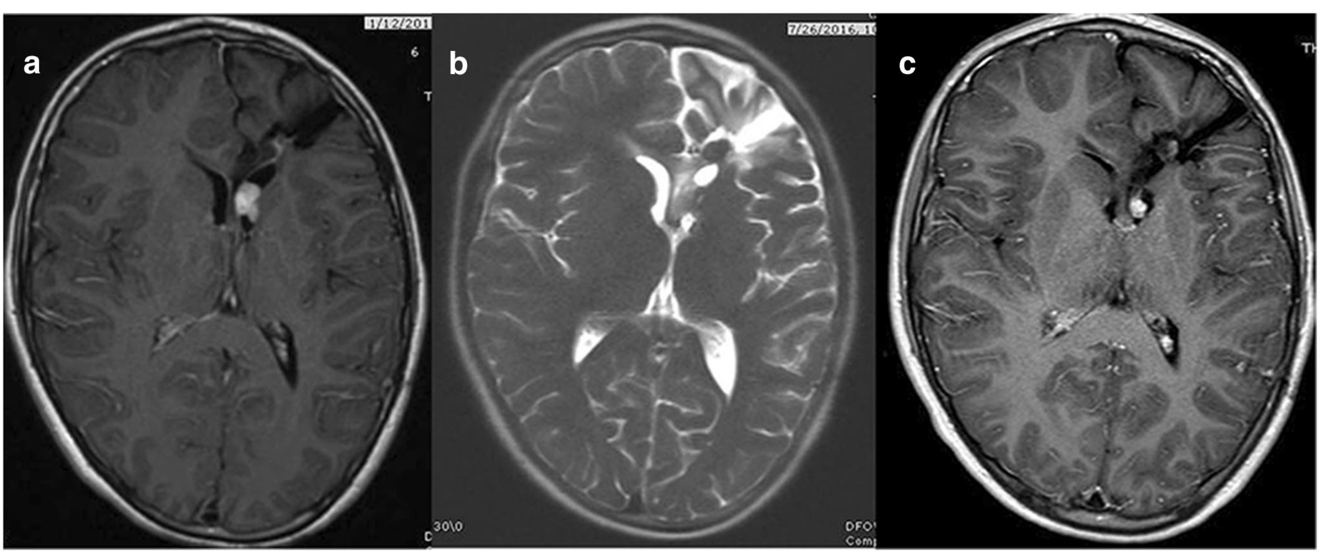

Fig. 1 Patient 1 underwent left frontal ablation and endoscopic, stereotactic septostomy. **a** Pre-operative axial T1 post-contrast image demonstrating SEGA in left frontal horn of lateral ventricle. **b** One month post-operative axial T2 image demonstrating decreased lesion size. **c** Fifteen-month post-operative axial T1 post-contrast image demonstrating continued decrease in lesion size

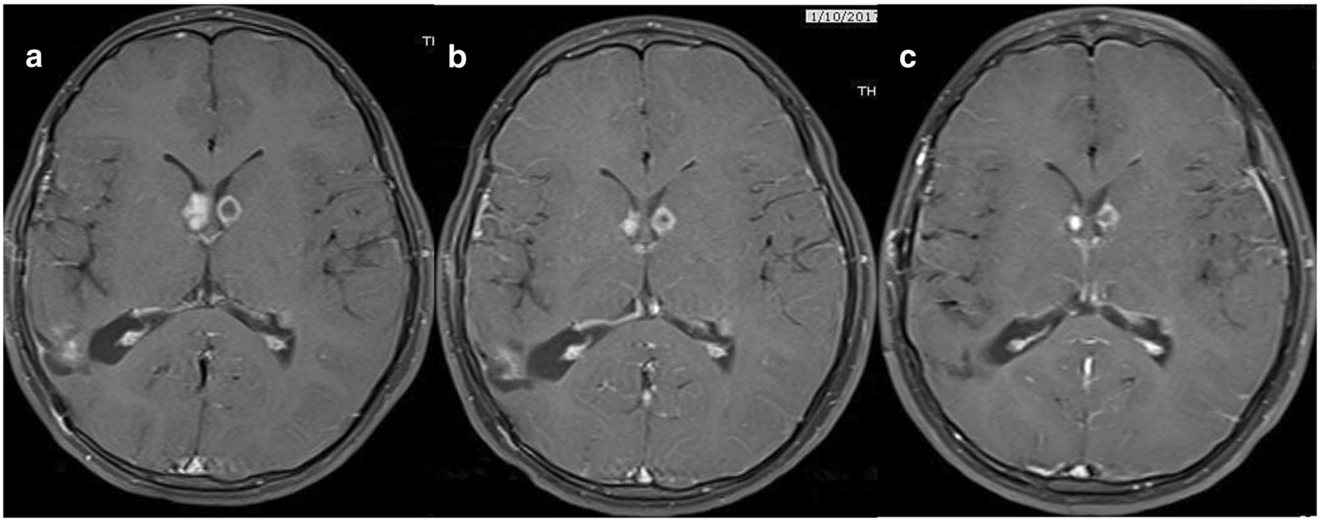

Fig. 2 Patient 2 underwent right frontal biopsy in addition to ablation in addition to a left frontal biopsy of cystic lesion with septostomy. **a** Pre-operative axial T1 post-contrast image demonstrating SEGA in right frontal horn of lateral ventricle as well as cystic lesion in left frontal horn. **b** Four-month post-operative axial T1 post-contrast image demonstrating decreased size in bilateral lesions. **c** Twenty-one-month post-operative axial T1 post-contrast image demonstrating continued decrease in bilateral lesions

out of seven patients (57%); two (29%) had no postoperative tumor volume reported while only one (14%) had tumor regrowth [6, 12, 13, 15]. Notably, three patients (43%) received concurrent or delayed everolimus therapy [12, 13]. Of the four patients responding to LITT therapy, mean tumor volume reduction was 68 ± 6.5%.

Only one patient suffered intraventricular gadolinium contrast extravasation perioperatively, while no other perioperative complications were noted [15]. Two patients (29%) developed obstructive hydrocephalus requiring temporary ventriculostomy or delayed septostomy. Due to the inherent risk of peritumoral edema post-ablation causing obstructive hydrocephalus, in our study, preemptive septostomy was performed, obviating the need for temporary ventriculostomy—which induces risk for infection and extends hospitalization—and obviating the risk of delayed hydrocephalus and its resultant symptoms.

Given the variability in these previous studies in terms of everolimus therapy and timing of long-term follow-up MRI, the data is difficult to analyze systematically. Nevertheless, an overall qualitative analysis suggests the safety and efficacy of LITT as a treatment modality for SEGA.

Alternative treatment options for SEGA, other than the standard treatment of surgical resection, are endoscopic-assisted resection, mTOR inhibitors such as everolimus or sirolimus, and radiotherapy [6, 8, 15, 16]. Endoscopic-assisted techniques can be useful only in select cases [17]. While mTOR inhibitors have shown up to 50% tumor volume

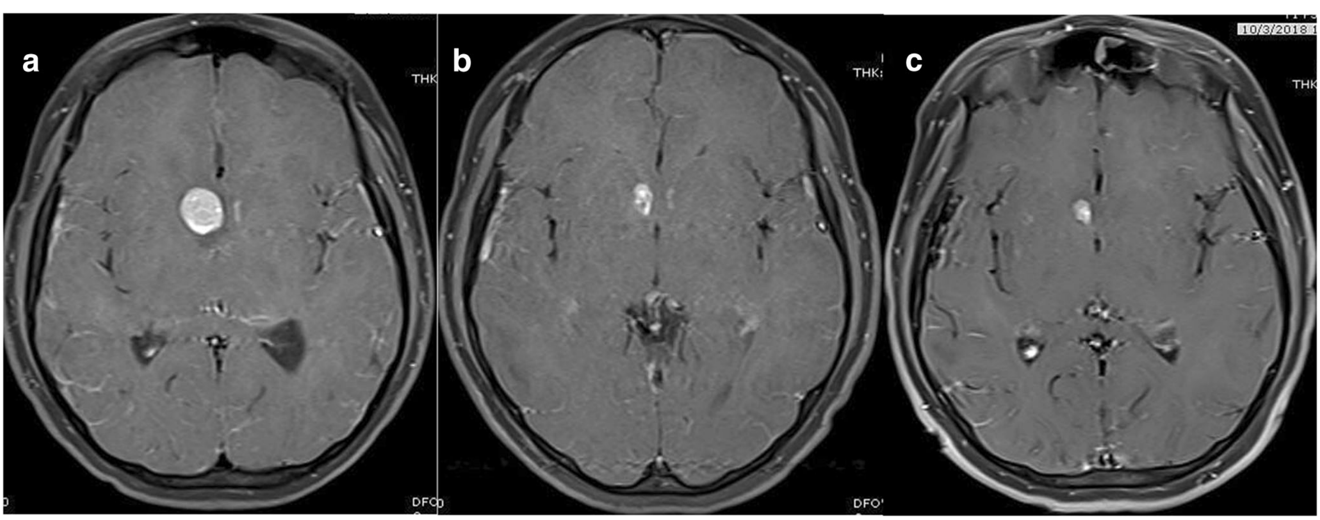

Fig. 3 Patient 3 underwent right frontal biopsy in addition to ablation and septostomy. **a** Pre-operative axial T1 post-contrast image demonstrating SEGA in right frontal horn of lateral ventricle. **b** Four-month post-operative axial T1 post-contrast image demonstrating decreased lesion size. **c** Sixteen-month post-operative axial T1 post-contrast image demonstrating continued decrease in lesion size

Table 2 Literature review

Study	Age at surgery (years)	Pre-operative tumor volume (cm^3)	Immediate post-operative tumor volume (cm^3)	Long-term post-operative tumor volume (cm^3)	Percent decrease in size pre-operative to long-term post-operative	Timing of long-term post-operative MRI (months after surgery)	Adjuvant or neoadjuvant therapy	Clinical outcome	Length of clinical follow-up (months after surgery)
Buckley et al. (2016)	18.4	4.1	1.4	1.6	61%	12–15 months[a]	Everolimus	No complication.	28.4
Buckley et al. (2016)	7.5	4.1	1.2	4.6	–		Everolimus	No perioperative complication. Postoperative tumor progression requiring everolimus therapy.	29.5
Buckley et al. (2016)	13	1.4	1	0.5	64%		None	No complication.	12.3
Dadey et al. (2016)	13	2.62	–	0.68	74%	3 months	None	No complication. Improved behavior and quality of life, reduced seizure frequency, and stable neurologic exam relative to pre-operation.	9
Dadey et al. (2016[b])	14	2.7	–	–	–	–	Concurrent ventriculostomy	No complication. Improved behavior and personality with no change in seizure frequency relative to pre-operation.	4
Tovar-Spinoza et al. (2016)	6	11.73	13	3.15	73%	27 months	Everolimus	No perioperative complication. Postoperative tumor progression requiring everolimus therapy starting 7 months after ablation.	27
Karsy M et al. (2018[c])	5	–	–	–	–	–	Repeat ablation and delayed septostomy	No perioperative complication during first ablation. After 18 months, tumor regrowth necessitated second ablation, during which time intraventricular gadolinium extravasation was noted. Delayed obstructive hydrocephalus developed 9 months after the second ablation, necessitating endoscopic septostomy for CSF diversion.	18 months after the first ablation. 9 months after the second ablation.

[a] Exact timing of long-term MRI not specified

[b] Post-operative exact tumor volume not reported, although shrinkage noted

[c] Tumor volume pre- and post-operative not reported

reduction, their expense, requirement for long-term administration, and regrowth after ceasing therapy make medical therapy a less desirable treatment modality [9, 10, 18]. Lastly, response rates to gamma knife radiosurgery have been highly variable [8, 15, 16].

LITT should be considered as a primary or adjunct treatment modality for SEGAs. In fact, early surgery for smaller lesions could be considered, as it has a lower complication rate; however, the difficulty lies in the fact that these lesions have an insidious onset with patients not presenting till seizures, behavioral changes, or hydrocephalus develop [3]. While the patients in this study were followed from 4 to 21 months post-ablation with no evidence of recurrence or regrowth, these patients should continue to be followed.

Gross total resection has a very low recurrence rate but very high complication rate, up to 49%, especially for lesions larger than 3 cm in diameter [3, 6–8, 19]. In these patients, LITT could be considered for shrinking the tumor prior to resection.

In our study, we performed concurrent septostomy to obviate development of hydrocephalus in the situation that the tumor swells post-ablation and occludes the foramen of Monro. Other authors have recommended concurrent external ventricular drain placement for CSF diversion [12].

Limitations of this study include small sample size and single surgeon experience. Further studies are warranted to determine optimal laser settings and use of LITT prior to surgical resection.

Conclusion

LITT with endoscopic, stereotactic septostomy should be considered a viable primary or adjunct treatment modality for SEGAs that are rapidly enlarging or encroaching on the foramen of Monro. Here, we present three SEGAs successfully treated with LITT with a mean tumor volume reduction of 70 ± 27%.

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Compliance with ethical standards

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