Original Article

Initial experience of the treatment of large glioma with microwave ablation-assisted surgical resection

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ABSTRACT

Aim: This study aimed to investigate the preliminary clinical outcomes of microwave ablation (MWA)-assisted surgical treatment for large glioma.

Materials and Methods: In total, six cases of large glioma (diameter >4 cm) were described. All cases were treated with MWA-assisted surgical resection, which was performed using ultrasound to guide the accurate placement of the antenna in the central region of the tumor. The MWA power was 40–45 W, and 6 min was applied. Changes in the ablation area were observed using intraoperative Doppler ultrasound and contrast-enhanced ultrasound (CEUS). Ten patients treated with surgical resection alone were included in the control group. Data on surgical times (i.e., the time from the incision of the dura to the removal of the tumor), intraoperative blood loss, and complications were recorded.

Results: The median patient age was 45 years (range: 36.5–60.3 years). The median lesion diameter was 4.9 cm (range: 4.3–5.8). The microwave power was 40–45 W, and the median ablation time was 240 s (range: 208–297 s). The intra-tumoral vascular flow was significantly reduced after MWA. The median surgical time was shorter (38.5 min [range: 34.3–42.8 min]) and the median intraoperative blood loss was less (400 mL, [range: 400–450 mL]) in the combination treatment group than in the surgery-alone group. During the ablation process, no obvious additional neurological deficits were detected; however, a tube-shaped carbonide was found after the operation.

Conclusion: MWA may be a useful complement to conventional techniques for the surgical resection of large glioma.

KEY WORDS: Large glioma, microwave ablation, ultrasound imaging guidance

INTRODUCTION

Gliomas are the most common and lethal primary intracranial tumors. There are a multitude of treatment options available for gliomas, such as surgical resection, radiation, and chemotherapy, with surgery generally being considered the intervention of choice. However, the prognosis and survival rates of gliomas are very poor and have not improved significantly over the last few decades. Overall survival is only 14–18 months after the initial diagnosis, and the mean progression-free survival is often <1 year.[1,2] Simultaneously, patients with tumors adjacent to important neuroanatomical structures or tumor recurrence present many difficulties in terms of surgical resection, which may lead to errors in surgery and permanent neurologic deficits.[3,4] Subtotal resection and partial resection are often attempted to optimize survival and minimize perioperative complications. However, studies have shown that extensive surgical resection is associated with substantial prolongation of overall and progression-free survival in patients with glioma.[5,6] Therefore, exploring a less-invasive therapy to reduce tumor burden is urgent for patients with

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glioma with poor anticipated outcomes, which could preserve neurological function and maintain optimal quality of life.

With the advent of modern imaging, minimally invasive thermal ablation treatment, such as radiofrequency, microwave, and laser ablation, has been used for the management of extracranial solid tumors, such as liver, kidney, and lung cancer.[7] At present, stereotactic laser ablation is widely applied in certain patients with primary and metastatic brain tumors.[8] Compared to open surgery, stereotactic laser ablation can offer a survival benefit with lower complication rates and a decreased hospital stay[9] Laser ablation as a single therapy also has limitations in its application, as it involves the following elements: Large tumors (>3 cm in diameter) may be unsuitable, there is a high risk of cerebral edema and intracranial hypertension, the procedure is complicated and time-consuming (typically requiring 5–6 hours), and treatment expenditure tends to be higher (approximately $30,000).[8-11] Recent research shows that the combination of laser ablation and surgical resection may provide an alternative that minimizes potential morbidities and the extent of residual tumors.[12]

Microwave ablation (MWA) has several theoretical advantages over radiofrequency and laser ablation, including larger ablation zones, shorter procedural times, more effective heating, and cheaper equipment.[13,14] The initial survey revealed that MWA can be a useful tool as a complement to conventional brain tumor microsurgery techniques, but not all types of brain tumors showed the same reaction to ablation.[15]

To the best of our current knowledge, evidence concerning the application of MWA in patients with large gliomas is lacking. In this study, we initiated the surgical treatment of large gliomas using MWA as an assistant measure. This is the first study, which explored the use of a combination of MWA and surgical resection as an alternative to subtotal resection for large gliomas.

MATERIAL AND METHODS

Ethics

Ethics approval for this research was obtained from the Institutional Review Board of the Research Institute (Number: DTYY2021021). The research was conducted in accordance with the principles outlined in the Helsinki Declaration. All participants provided written, voluntary informed consent for research participation.

Study design

We conducted an observational, prospective trial (Clinical Trial Registration Number: ChiCTR2000037774).

Selection and description of participants

Both the neurosurgeon and the interventional radiologist communicated with all patients in detail about their treatment options, including surgical resection, radiosurgery, conventional radiation, chemotherapy, and MWA, as an assistant method for surgical intervention. Another ten patients treated with surgical resection alone were included as part of the control group. The inclusion criteria were as follows: 1) patient >18 years old; 2) tumor first diagnosed as a single glioma by contrast-enhanced magnetic resonance imaging (MRI) before treatment and eventually confirmed by postoperative pathology; 3) tumor diameter >4 cm; (4) no history of other anticancer treatment; and 5) a Karnofsky performance scale (KPS) score ≥70. The exclusion criteria were as follows: 1) tumors diagnosed as non-glioma based on postoperative pathology; 2) tumor diameter <4 cm; 3) intervention of interest (MWA) not performed; 4) pregnancy in females; (5) patients with intracranial metal or electromagnetic devices; and (6) uncontrolled organ dysfunction syndrome (e.g., infection, dysfunction of the heart, kidney, or chronic obstructive pulmonary disease).

Technical information

In the operating room, the patient was positioned appropriately based on access to the tumor. The procedure was performed under general anesthesia with suitable monitoring of vital signs. First, craniectomy was performed to sufficiently expose the dural and operative access to the tumor area according to the preoperative planning derived from MRI and to allow simultaneous use of the ultrasound transducer on the dural surface. Second, intraoperative ultrasound and contrast-enhanced ultrasound (CEUS) were performed on all patients to evaluate the size, depth, tumor blood supply, and surrounding cerebral structures. Third, the MWA antenna was inserted precisely into the lesions under ultrasound guidance to avoid puncturing blood vessels and important cerebral structures. Fourth, microwave electrode placement was performed based on the expected ablation zone size, considering a sufficient safety margin (>10 mm) around the tumor. The device parameters were as follows: frequency, 2450 MHz; needle type, internal water cooling; antenna diameter, 16G; antenna length, 150 mm; power, 40–45 W; and distance from the aperture of the MW emission to the needle tip, 0.5 mm. Under real-time ultrasound and evoked cortical potential and electroencephalogram monitoring, treatment began from the deep to the shallow of tumor and was repeated on a section-by-section basis to cover most of the tumor. Ablation changes that manifested as a high echo on ultrasound images were observed in real time, when hyperechoic regions covered the targeted lesions, the therapy was stopped, and the MWA antenna was extracted. Fifth, repetitive intraoperative ultrasound and CEUS were used to evaluate the tumor blood supply, non-perfusion area of the tumor, and adjacent structures. Finally, under surgical microscope monitoring, standard radical resection of the entire tumor was performed. The control group underwent the same resection. Surgical time (i.e., the time from the incision of the dura to the removal of the tumor), intraoperative blood loss, KPS scores, and postoperative complications were recorded.

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The effect of treatment was evaluated clinically using MRI or computed tomography (CT) during the follow-up period.

Statistical analysis

The parameters were tested for normality using the Shapiro–Wilk test. The means and standard deviations (SD) of continuous, normally distributed parameters were determined and compared using a one-way analysis of variance or an independent-samples *t*-test. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (SPSS; IBM Corporation).

RESULTS

Six patients (four males and two females) were treated using a combination of MWA and conventional surgical resection. The median age of the patients was 45 years (range: 36.5–60.3 years). Preoperative KPS scores were 90–100. The median lesion diameter was 4.9 cm (range: 4.3–5.8 years). The microwave power was 40–45 W, and the median ablation time was 240 s (range: 208–297 s).

The intra-tumoral vascular flow was significantly reduced after MWA. The median surgical time was shorter in the combined group (38.5 min, range: 34.3–42.8 min) than in the control group (44.6 min, range: 40.4–54.8 min). Intraoperative blood loss was also less in the combined treatment group (400 ml, range: 400–450 mL) compared with the single surgery group (450 mL, range: 450–500 mL). During the ablation process, there were no markedly abnormal findings on intraoperative neuromonitoring. In all resected glioma specimens, except for obvious necrosis resulting from MWA, we found a tube-shaped carbonide with a length of approximately 15 mm and a width of nearly 3 mm.

A representative case of the utility of a combination of MWA and surgical resection is presented in this report. Table 1 provides the general details of the patients treated with a combination of MWA and single surgical resection and their pre- and postoperative conditions. A 58-year-old male patient who presented with headache accompanied by nausea and vomiting sought treatment at the neurosurgical clinic of the hospital with a KPS score of 100. On the preoperative MR images, a lesion with a diameter of 5.6 cm was located in the left temporal region [Figure 1a]. MWA treatment was performed through a supraorbital craniotomy under trans-operative ultrasound guidance [Figure 1b and c]. The preoperative color Doppler ultrasound and CEUS images showed abundant bloodstream signals branching into the tumor [Figure 1d and e]. The microwave power was set at 45 W, and the microwave time was 4 min. After MWA treatment, the intra-tumoral vascular flow was obviously reduced [Figure 1f], the appearance of the necrotic component of the tumor was variable on CEUS [Figure 1g], and the percentage of non-perfused volume (i.e., the non-perfused tumor volume compared with the whole tumor after treatment) was approximately 85%. A standard gross total resection was performed, and a postoperative specimen with a wide range of necrosis was observed, which was confirmed by pathology [Figure 1h and i], and a tube-shaped carbonide measures approximately 15 mm in length and nearly 3 mm in width [Figure 1j]. MRI showed total removal of the tumor and obvious edema in the surrounding tissues 24 h after the surgery [Figure 1k and l]. The KPS score of the patient was still 100, and he had no obvious additional neurological deficits.

DISCUSSION

Doctors face various challenges in the treatment of glioma, a common intracranial tumor associated with a high mortality risk. Although the survival benefits of surgical resection,

Table 1: Baseline data of patients and tumors in the two groups

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Sex (F/M)	F	F	M	M	M	M
Age (Y)	42	67	37	58	35	48
Tumor location	Left temporal	Left temporal	Right temporal	Left temporal	Left frontal	Left temporal
Tumor diameter (cm)	5.0	6.5	4.3	5.6	4.7	4.1
Preoperative symptoms	Mixed aphasia	Mixed aphasia	Physical examination	Headache, vomit	Headache	Epilepsy
Preoperative KPS	90	90	100	100	100	100
MW power(W)	40	40	40	45	45	45
MWA time(S)	240	182	216	240	287	326
Operative time(Min)	40	45	42	37	32	35
Blood(ml)	450	400	400	400	450	400
Postoperative complications	Motor aphasia	Muscle strength decrease (right lower limb grade 2; upper limb grade 0)	Fever	Psychiatric symptoms	No	Motor aphasia
Postoperative KPS	80	40	80	100	100	90
Postoperative pathology	GBM WHO IV	GBM WHO III	Anaplastic astrocytoma WHO III	GBM WHO III	Anaplastic astrocytoma WHO III	Anaplastic astrocytoma WHO III
Hospital stay(day)	14	18	13	12	18	16
Follow-up	10	7	7	7	7	2
Outcome	A	A	A	A	A	A

Note: F—female; M—male; Y—year; W—watt; S—second; KPS—Karnofsky performance status; ST—survival time; A—alive; GMB—glioblastoma multiforme; WHO—World Health Organization

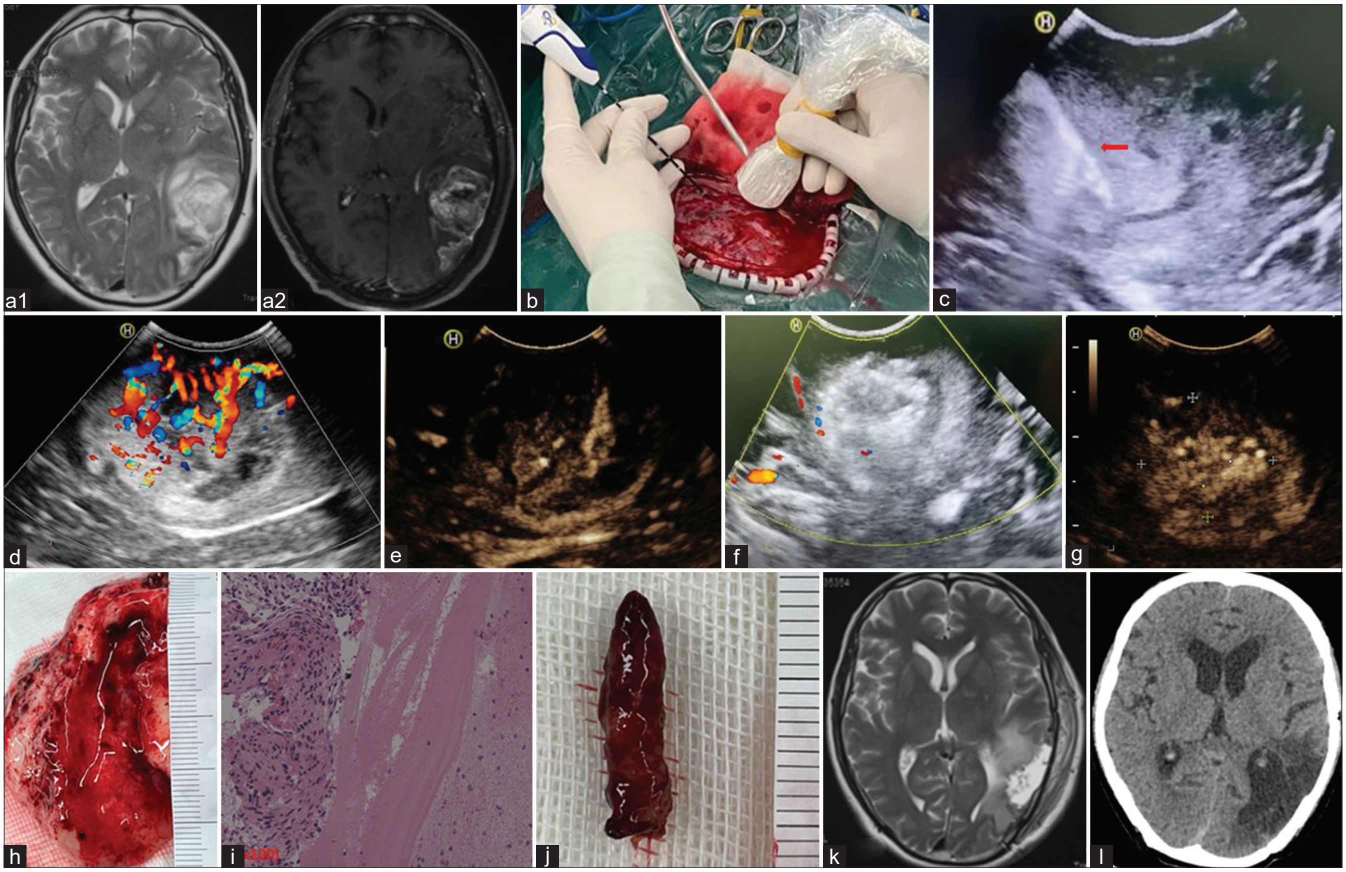

Figure 1: (a) A1 the axial T2-MRI indicated a lesion located in the left occipital–temporal regions, with a size of 4.8 cm × 5.2 cm; A2, the axial contrast-enhanced MRI showed abundant feeding artery, (b) the MWA treatment was carried out through a supraorbital craniotomy under the guidance of trans-operative ultrasound; (c) the MWA antenna (as indicated by red arrow) was inserted precisely into the lesions under the guidance of ultrasound, (d) abundant bloodstream signals branched into tumor on the color Doppler ultrasound; (e) CEUS images showed abundant bloodstream signals, (f) the color Doppler ultrasound showed blood flow signal was absent inside the tumor; (g) CEUS images showed an obvious non-perfusion area inside the tumor, (h) prominent central necrosis was observed in the postoperative glioma sample and was demarcated from surrounding tumor tissue; (i) a wide range of necrosis with distinct borders could be observed in the pathological section, (j) a tube-shaped carbonide was found in the postoperative glioma sample, (k) the axial T2-MRI showed that obvious edema in surrounding tissues of the operation area was observed 24h after the surgery; (l) the axial CT showed no local tumor recurrence at 7 months after the surgery

radiation, and chemotherapy in patients with incipient glioma are generally accepted, patients with recurrent rumors, unresectable tumors, or critical basic diseases are still difficult to treat. Therefore, a safe, effective, easy operation, and minimally invasive treatment approach is needed to prolong survival and optimize the quality of life.

Stereotactic laser ablation has been widely used as a minimally invasive thermal ablation technique in patients with brain tumors.[8] There are also some disadvantages, such as a small volume of coagulation, the complicated and timely nature of the operation, and the need for expensive equipment.[8-11]

To date, there has been very little research on the application of MWA in patients with large gliomas. The present paper sheds light on the safety and effectiveness of MWA as an assistant measure in the surgical treatment of large gliomas. Preliminary results suggested that the intra-tumoral vascular flow was reduced, and the necrotic component of the tumor was variable, after MWA was performed. After treatment with MWA, surgical resection became easier, bleeding volume decreased, and operation time was shorter. Although MWA took approximately 10–15 minutes, the overall treatment time was comparable in the combined group compared with the control group. However, MWA was performed while preserving dural integrity, which reduces the risk of infection and bleeding arising from exposure of the subdural brain tissue and might contribute to shortening hospitalization times and reducing hospitalization costs. Therefore, in the combined group, shortened surgical time was more likely to be beneficial for patients. These results are consistent with those of a previous study on laser ablation.[12] The MWA-assisted surgical resection procedure was also simple and easy to perform, reducing operating times. The reasons for these advantages might be that microwave energy produces faster heating and higher temperatures, resulting in a larger demarcated ablation zone.[13-16] Under real-time ultrasound

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guidance, microwave electrode placement can be performed, which has potential advantages over laser ablation guided by MRI.

This study also showed that tube-shaped carbonides were found in all postoperative specimens. We thought that the carbonide was formed during ablation and attached to the microwave electrode; when the antenna was extracted, the carbonide broke away from the antenna and was left in the tumor.

The mechanisms by which carbonide was formed were unclear. However, we speculate that this phenomenon can be attributed to two major reasons. First, MWA does not rely on electric currents and conduction through tissue; the temperature of tissues surrounding the microwave electrode could reach above 100°C in a short space of time.[7,17,18] Higher temperatures result in a larger ablation zone, but they also lead to the carbonization of tumor tissue. Second, lipids and proteins are the major solid elements for the composition of the brain,[19,20] which has a strong adhesive force at high temperature, and necrotic tissue after ablation easily attaches itself to the microwave electrode and is further heated to form carbide. The bicarbonate not only blocks heat conduction and reduces the effectiveness of MWA, but also increases the risk of damage to the surrounding normal brain tissue in the process of pulling out the electrode. Therefore, controlling the appropriate temperature caused by MWA and investigating new anti-adhesion materials used for fabricating microwave electrodes are problems that should be considered in future studies.

Our study had certain limitations, which significantly reduced the value of the study. These included a small sample size, limited follow-up period, and non-randomized controlled design, and tumors lying near important functional zones were not included. This study was also confined to a specific group, and our results therefore cannot be generalized to all patients with gliomas.

In conclusion, MWA may be a viable alternative to larger brain tumor resection surgery. It could decrease the bleeding amount, shorten the operation time, and facilitate surgical resection of the lesion. Prospective studies surveying the safety and efficacy of this combined operative approach in prolonging overall and progression-free survival compared with surgical resection are needed in the future.

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Conflicts of interest
There are no conflicts of interest.

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