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Original Article

Selective excision of cerebral metastases from the precentral gyrus

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Abstract

Background: The surgical management of cerebral metastases to the eloquent cortex is a controversial topic. Precentral gyrus lesions are often treated with whole brain radiation therapy (WBRT) or stereotactic radiosurgery (SRS) because of the concern for causing new or worsened postoperative neurological deficits. However, there is evidence in the literature that radiation therapy carries significant risk of complication. We present a series of patients who were symptomatic from a precentral gyrus metastasis and underwent surgical excision.

Methods: During a 2-year period from 2010 to 2012, 17 consecutive patients harboring a cerebral metastasis within the precentral gyrus underwent microsurgical resection. All patients were discussed at a multi-disciplinary tumor board. The prerequisite for neurosurgical treatment was stable systemic disease and life expectancy greater than 6 months as determined by the patient's oncologist. Patients also were required to harbor a symptomatic lesion within the motor cortex, defined as the precentral gyrus.

Results: We present the 3-month neurological outcome for this group of patients. Surgery was uneventful and without any severe perioperative complications in all 17 patients. At 3 month follow up, symptoms had improved or been stabilized in 94.1% of patients and were worsened in 5.9%.

Conclusion: Our results have shown that surgery for cerebral metastases in the precentral gyrus can be done safely and improve or stabilize the neurological function of most patients. Microsurgical resection of precentral gyrus metastases should be a treatment option for patients with single or multiple lesions who present a focal neurologic deficit. This can be performed safely and without intraoperative cortical mapping.

Key Words: Cerebral metastases, neurological outcome, operative treatment, precentral gyrus

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INTRODUCTION

Cerebral metastasis is the most common type of brain tumor in adults and a significant cause of morbidity and mortality in cancer patients.[23] The incidence of these tumors is increasing largely as a result of the enhanced ability to detect them on imaging and prolonged patient survival.[23] Currently, up to 40% of cancer patients will develop cerebral metastases during their disease course.[8] Surgical resection followed by whole brain radiation therapy (WBRT) has been used as the main treatment modality for limited intracranial metastasis, particularly for single lesions, and can provide excellent tumor control.[26] This is supported by randomized trials and also by the recommendations of treatment guideline committees.[4,11,26] In comparison, patients with cerebral metastases treated with WBRT alone is poor, with a median survival of approximately 7 months and significant quality of life concerns.[16] In patients with a single metastasis, several studies have demonstrated improved outcomes in patients treated with surgery, alone or in combination with postoperative WBRT.[26,27]

Stereotactic radiosurgery (SRS) has been advocated as a first line treatment for a single metastasis or in combination with surgical resection.[22,28,29] SRS has been readily accepted as a treatment alternative for cancer patients because, in theory, the risks of surgery and WBRT can be negated. The advantage of SRS is the ability to deliver focused radiation to a specified area of brain while avoiding the deleterious neurocognitive effects of WBRT.[5] This ability also makes SRS an attractive choice for the treatment of lesions within eloquent cortex, such as the precentral gyrus, as it removes the surgical risk of a new or worsened postoperative neurological deficit.

However, recent reports have associated this treatment modality with up to a 40% complication rate.[35] Common neurologic complications include new-onset seizures, visual and motor deficits, as well as worsening cerebral edema, steroid dependency, and radiation necrosis.[35] As such, SRS cannot necessarily be regarded as a benign alternative to performing microsurgical resection of cerebral metastases that lie within eloquent brain.

The treatment of tumors originating in eloquent cortex represents a special challenge for clinicians. Traditionally, lesions of this area have been approached with caution and less-invasive treatment modalities employed when possible.[6,8] For symptomatic lesions, the balance between providing timely relief of neurologic deficits caused by tumor mass effect, associated cerebral edema, and the risk of causing a new or worse focal motor deficit must be carefully considered. These issues are significant in any patient with a cerebral metastasis but are especially important in metastases to eloquent cortex. SRS as first-line therapy has been shown to be a reasonable treatment option for many patients, but the relief of mass effect and resultant clinical symptoms is delayed.[1,22] Therefore, a need exists for prompt treatment of those lesions that are the cause of a patient's deficit. Given that postoperative WBRT has been shown to reduce intracranial relapse rates and improve survival for patients with multiple metastases, there is a clear role for surgical resection of a 'symptomatic lesion' even in those patients with extensive cerebral disease and especially if that lesion is in an eloquent area.[26] Historically, these patients have been considered poor candidates for resection as they were not expected to live long enough to realize the benefit of surgical intervention.[14,25] The role of resection in these patients remains controversial and to date no prospective randomized controlled trials have been performed. However, as imaging and surgical technology has improved, more neurosurgeons are pursuing surgical treatment for these patients when coupled with standard postoperative radiation therapy. The goal is to alleviate the acute symptoms of cerebral edema and mass effect causing neurologic deficits even in patients who would not have previously been considered surgical candidates due to widespread intracranial disease.[12] Additionally, we propose that microsurgery for lesions in the precentral gyrus may be done safely in lieu of SRS given the reported complications of SRS for tumors in this part of the cerebrum.[7,35]

There are few reports in the literature that describe surgical removal of cerebral metastases located in eloquent cortex with an acceptable morbidity.[33,34] We present our experience after surgery for 17 consecutive patients suffering from a cerebral metastasis located within the precentral gyrus with the goal of illustrating the safety of microsurgical resection for this subset of patients and even for patients who harbor multiple metastases. Furthermore, we discuss our results compared with the current literature on this topic.

MATERIALS AND METHODS

During a 2-year period from 2010 to 2012, 17 consecutive patients harboring a cerebral metastasis within the precentral gyrus underwent microsurgical resection. This time period was selected because it represents the starting point of our surgical treatment of precentral gyrus metastases up to the current time period. Metastatic brain lesions are almost exclusively treated by the senior author (LM) at our institution and the patients in this study were selected by reviewing every case of cerebral metastasis and identifying those patients with a precentral gyrus lesion that was surgically removed. Precentral gyrus location was determined by review of all magnetic resonance imaging (MRI) scans by the junior author (RK) and correlation with the neuroradiology report and operative report by the senior author (LM). Patient characteristics and outcomes are summarized in Tables 1-3.

The prerequisite for neurosurgical treatment was stable systemic disease and life expectancy greater than 6 months as determined by the patient's oncologist. Patients also were required to harbor a symptomatic lesion within the precentral gyrus. The lesions were all classified as Grade III based on the classification system proposed by Sawaya *et al.*[31] Grade I lesions are located in noneloquent brain, Grade II lesions in near-eloquent brain, and Grade III lesions in eloquent brain. Eloquent locations in the Sawaya study are the motor/sensory cortices, visual center, speech center, internal capsule, basal ganglia, hypothalamus/thalamus, brainstem, and dentate nucleus.[31]

The tumors originated from different primary cancers [Table 2]. All patients were symptomatic at the time of presentation. In 9 out of 17 patients multiple metastases were identified.

A focal motor deficit was the most common presenting symptom (16 patients). Two patients also had seizures in addition to a hemiparesis and one patient developed arm numbness alone as the presenting symptom. Patients with multiple cerebral metastases were selected for surgery only if one lesion in particular was felt to be culpable for symptoms. Patient information was obtained from the hospital chart and outpatient records from the Departments of Neurosurgery, Oncology, and Radiation Oncology. This work was conducted as part of studies approved by the institutional review board at Rush University Medical Center (Chicago, IL).

Table 1: Preoperative data on 17 patients with cerebral metastases to the precentral gyrus

Ratio (male:female)	8:9
Age	Mean 62.5 years (range 46-80 years)
Preoperative symptoms	Hemiparesis (*n*=16, 94.1%)
	Seizure (*n*=2, 11.7%)
	Other (*n*=1, 5.9%)
Average tumor diameter	1.9 cm
RPA class	I (*n*=6, 35.2%)
	II (*n*=8, 47.1%)
	III (*n*=3, 17.6%)
KPS	>70 (*n*=14, 82.4%)
	50-70 (*n*=1, 5.9%)
	<50 (*n*=2, 11.8%)

RPA: Recursive partitioning analysis, KPS: Karnofsky performance status

Seventeen patients, 8 men and 9 women with a mean age of 62.5 years, underwent image-guided microsurgical resection of metastatic tumors originating within the precentral gyrus during a 2-year period. Tumor histology was as follows: 10 nonsmall cell lung carcinoma, 4 squamous cell lung carcinoma, 1 head/neck squamous cell carcinoma, 1 rectal adenocarcinoma, and 1 colon adenocarcinoma. The average tumor diameter was 1.9 cm with the largest being 4 cm and the smallest 0.8 cm.

The Eastern Cooperative Oncology Group (ECOG) Performance Status was assigned by the patient's oncologist preoperatively and at a 3 month follow up appointment after surgery.[24] The ECOG score was then converted to a Karnofsky Performance Status (KPS) score by a published method.[20]

An institutional interdisciplinary tumor board discussed all patients in this study. Consensus among the treating oncologist, radiation oncologist, and neurosurgeon (LM) was always obtained prior to proceeding with microsurgical resection.

Preoperative MRI images were used for frameless stereotactic guidance of craniotomy placement and tumor localization. Gadolinium-enhanced T1-weighted MRI scans were primarily used for this purpose [Figure 1]. Additional information was taken from

Table 2: Patient characteristics and outcomes

Patient	Age	Sex	Primary cancer	Preop strength/symptom	Postop strength
1	59	M	Lung adenosquamous carcinoma	R UE pronator drift	5/5 strength
2	64	M	Lung adenocarcinoma	R UE 4/5, word finding difficulty	5/5 strength, speech improved
3	52	F	Lung squamous cell	L hemiparesis 4/5, seizure	4/5 strength
4	72	M	Lung adenocarcinoma	L hand 4/5	5/5 strength
5	61	F	Head/neck squamous cell	L LE 3/5	5/5 strength
6	46	F	Lung adenocarcinoma	L UE pronator drift	5/5 strength
7	64	M	Rectal adenocarcinoma	R UE 4/5	5/5 strength
8	57	M	Lung adenocarcinoma	Strength 5/5, seizure	R UE 4/5
9	58	M	Lung adenocarcinoma	R UE 3/5, R LE 2/5	Strength 4/5
10	63	F	Lung adenocarcinoma	L UE numbness	Resolved, strength 5/5
11	57	M	Lung squamous cell	R UE and R LE 4/5	Strength 4/5
12	78	F	Lung adenocarcinoma	R hand 0/5	Strength 4/5
13	61	F	Lung squamous cell	L UE 2/5	Strength 4/5
14	56	F	Lung adenocarcinoma	L UE 4/5	Strength 5/5
15	80	F	Lung squamous cell	L UE 3/5	Strength 5/5
16	68	F	Colon adenocarcinoma	L LE 4-/5	Strength 4+/5
17	67	M	Lung adenocarcinoma	R hand 4/5	Strength 5/5

M: Male, F: Female, R: Right, L: Left, UE: Upper extremity, LE: Lower extremity

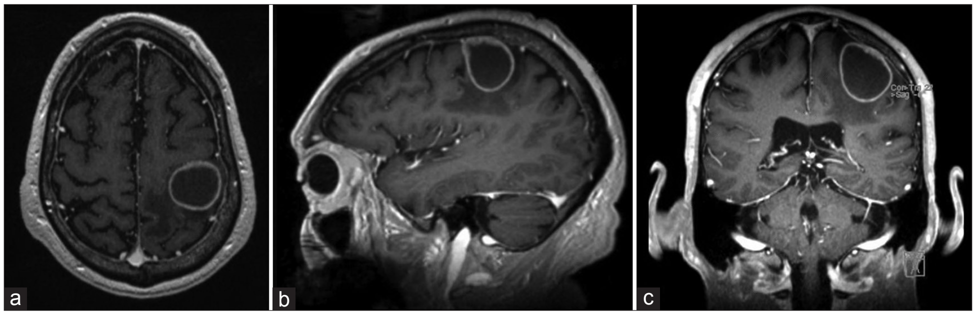

Figure 1: Contrast enhanced T1-weighted MRI images of a cystic cerebral metastasis in the precentral gyrus (a) axial view (b) coronal view (c) sagittal view

Table 3: Clinical symptoms of 17 patients at 3 month follow up compared with preoperative status

	3-month follow up
Hemiparesis	Improved (n=13, 76.4%)
	Stable (n=3, 17.6%)
	Worsened (n=1, 5.9%)

unenhanced T1, T2, and Fluid-Attenuated Inversion Recovery (FLAIR)-scans. The best surgical approach was determined by reviewing the pertinent images with respect to tumor location, sulcal anatomy, and position of cortical veins. A representative MRI can be found in Figure 1.

Surgical technique

All patients underwent craniotomy using general anesthesia with no cortical mapping or stimulation. Neuronavigation was employed for planning of the craniotomy and localization of the tumor. The regional anatomy was carefully assessed preoperatively on MRI and intraoperatively in all cases, especially with regard to the sulcal anatomy and cortical veins. The safest identifiable corridor was identified by, if possible, establishing a route to the lesion via noneloquent cortex, utilizing sulcal dissection to allow corticotomy to be as close to the lesion as possible, and by avoiding cortical veins when present. An ultrasound machine was always available to be used if the accuracy of the neuronavigation system was in doubt. Once the craniotomy had been completed and the dura incised, the tumor location was again confirmed with neuronavigation. An operating microscope was always utilized. Taking into consideration the above, we proceeded with *en-bloc* tumor removal via the safest identifiable corridor and with utilization of as little brain manipulation and retraction as possible.

Complications were surgical if they occurred within 30 days or, if later than 30 days, were a direct result of surgical intervention. Complications were transient if they resolved within 30 days of surgery or definitive management or prolonged if they persisted until last follow up or death.

Patients were generally mobilized on postoperative day #1 and were seen as outpatients between 2 and 4 weeks after surgery. After the first month, patients were seen every 3 months with repeat MRI studies at 3-month intervals. Additional or expedited neuroimaging was obtained if central nervous system-related signs or symptoms developed. The patient's oncologist provided all systemic cancer care.

RESULTS

We present the 3-month neurological outcome for this group of patients. Surgery was uneventful and without any severe perioperative complications in all 17 patients. Gadolinium-enhanced T1-weighted MRI scans obtained on postoperative day #1 revealed a gross total resection in all patients.

At 3-months follow up all patients remained alive. Each of the 17 patients received either SRS or WBRT at the discretion of the treating radiation oncologist. KPS scores remained unchanged in all patients. Thirteen out of the 16 patients who presented with a hemiparesis had improved strength at their 3-month follow up visit. The two patients who also presented with seizures were adequately controlled on a regimen of anticonvulsive drugs. The patient who presented with arm numbness also reported resolution of that symptom. Three patients who had a preoperative hemiparesis were found to have a stable deficit.

There was one complication of surgery [Patient 8 in Table 2] that resulted in a new postoperative hemiparesis. This patient had presented with seizures and was hemiparetic in his postictal state. However, his weakness would subsequently resolve after several hours; thus, preoperatively he was considered to have no focal neurologic deficit. His MRI scan revealed a tumor within the left precentral gyrus. In the immediate postoperative period he was found to have only 2/5 strength in his right upper extremity and 4/5 strength in his right lower extremity. He was maintained on steroids and completed a full course of physical therapy and rehabilitation. At his 3-month follow up appointment, his strength had improved to 4/5 in the right arm and 5/5 in the right leg.

DISCUSSION

The surgical management of metastatic tumors originating within eloquent cortex is an evolving area of cancer care. Due to the fact that life expectancy after the diagnosis of cerebral metastasis may be limited, surgical and radiation options are palliative in nature.[25] Our experience at this institution has been that patients are as likely to die from systemic disease as from cerebral disease. There have been many publications concerning the treatment of cerebral metastases, but few have discussed surgery for lesions in eloquent cortex.[25,33,34]

Weil *et al*. published a study on their series of patients who underwent surgical resection of metastases located in eloquent cortex in which they report that 94.1% of patients had improved motor strength at a 3-month follow up visit.[34] Walter *et al*. reported on a series of similar patients, and showed that 83.3% of patients had improved or unchanged motor deficits after surgery for lesions within the central area.[33] In both of the above series extensive preoperative functional mapping and intraoperative cortical mapping and stimulation were performed. Our series compares well with 94.1% of patients having an improved or stable deficit at 3-month follow up. Utilizing an awake craniotomy for surgery of lesions in eloquent cortex is a proven and valuable technique[6,9] that should always been considered when evaluating patients with these lesions, but is not without caveats.[15] Kamp *et al*. published their series of 19 patients with central area metastases and used awake craniotomy but encountered new postoperative deficits more frequently than in the present series.[13] Another tool to consider is intraoperative neurophysiologic monitoring with motor-evoked potentials, as this has been reported to be associated with better neurological outcomes.[19] Our experience shows that good surgical outcomes can be obtained for patients with metastatic lesions, which can be achieved without the use of neurophysiologic monitoring or intraoperative cortical stimulation, although larger series of patients with appropriate controls are needed to validate this point. We believe that the key to safely performing these procedures without the benefit of awake cortical mapping is careful review of preoperative imaging and evaluating the regional anatomy to select the best operative corridor. This is more apparent when the eloquence of the surrounding brain matter is declared based upon a presenting motor deficit concomitantly with a lesion seen in the precentral gyrus.

A tenet of surgery established by Halsted[11] holds that improved patients outcomes will be had through the use of careful tissue handling and this extends to the practice of neurosurgery as well. Minimization of brain manipulation can be achieved with thorough intrasulcal dissection and judicious use of retractors if they are required. This topic has been infrequently studied, but there is evidence that performing awake surgery with stimulation for eloquently located tumors does not necessarily confer a better neurological outcome than surgery performed for similarly located tumors under general anesthesia.[9] It follows that this should be also be true when operating on a cerebral metastasis given that these lesions are typically well encapsulated and have a readily identifiable plane between neoplasm and normal surrounding brain. This is a distinct characteristic of extra-axial brain lesions, especially metastases, which can be used to the surgeon's advantage as opposed to many intraaxial brain lesions in which there is no plane or the tumor infiltrates the surrounding brain tissue.

There has been a historical focus on treating those patients with multiple intracranial lesions with radiation only and forgoing surgery completely.[11] The thought behind this approach is that subjecting a patient with a significant intracranial disease burden, and, thus, a limited life expectancy, to the risk of surgery will not improve outcomes. However, there have been studies that have showed benefit of radiation for patients with multiple cerebral metastases.[17,30] Alternatively, there is some literature that suggests surgical intervention provides a better outcome as measured by KPS and quality of life surveys.[33] Additionally, lesions of the precentral gyrus may often be deemed unsafe for surgery given a perceived high risk of postoperative neurological complications.

SRS has proven to be an effective alternative to surgery for the treatment of cerebral metastases with studies showing comparable survival and, in some cases, superior local control rates.[2,3,18] This approach is not, however, without risk. Williams *et al*. published a comprehensive study reviewing their institution's complication rate with SRS for the treatment of cerebral metastases and found it to be 40%.[36] SRS for tumors located in an eloquent region in the same study had a complication rate of 64%.[35] For lesions located in the precentral gyrus, 26% of patients suffered a new neurological deficit after the procedure and this is not including worsening of preexisting deficits.[35] Additionally, new onset seizures were the most frequent complication overall, constituting 13% of all complications. A high number (32%) of patients in the Williams study were also considered to be steroid-dependent after SRS. In a separate study, Varlotto *et al*. reported a complication rate of 11.4% at 5 years for their series of patients.[32] A phase II trial conducted to evaluate the feasibility of performing SRS in lieu of WBRT found that 47.2% of study participants suffered from SRS toxicity.[21] It is clear from these studies and others that the morbidity of radiation is not negligible.

Our results have shown that surgery for cerebral metastases in the precentral gyrus can be done safely and improve the neurological function of most patients. Surgery also promptly addresses symptoms related to cerebral edema, mass effect, and midline shift. These are issues that cannot be alleviated by radiation in a timely manner and that contribute to loss of quality of life for the patient. Limitations of our treatment paradigm include our use of general anesthesia for all cases without neurophysiologic monitoring or awake cortical mapping. The potential to avoid new neurologic deficits with these tools should not be ignored although our results compare well to the published literature. Microsurgical resection of precentral gyrus metastases should be a treatment option for patients with single or multiple lesions, especially if they present with a focal neurologic deficit.

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