Acta Neurochir (Wien) (2000) 142: 527–537

Acta Neurochirurgica

Gamma Surgery for Hemangiopericytomas

B. R. Payne, D. Prasad, M. Steiner, and **L. Steiner**

Lars Leksell Center for Gamma Surgery, Department of Neurological Surgery, University of Virginia, Charlottesville, Virginia

Summary

A retrospective analysis of a consecutive series of 12 patients with 15 intracranial hemangiopericytomas treated at the University of Virginia using Gamma surgery is presented. Clinical and radiographic follow up of 3 to 56 months is available for 10 patients with 12 tumors. There was one tumor present at the time of initial Gamma surgery in each patient. Two new tumors occurred in patients previously treated. Nine of the tumors decreased in volume and three remained stable. Four of the nine tumors that shrank later progressed at an average of 22 months after treatment. Of the tumors that decreased in volume and have not progressed, the response has been for an average of 11 months. The follow-up for two tumors that remained unchanged was 10 and 34 months (average 22 months). A third tumor was unchanged at 42 months but the patient died of new disease adjacent to the treated area in the anterior skull base. There were no complications and the quality of life following the procedure was maintained or improved in every case. Gamma surgery is effective in palliating the patients by decreasing tumor volume and delaying recurrence.

Keywords: Gamma surgery; Gamma knife; hemangiopericytoma.

Introduction

Hemangiopericytomas are malignant tumors with sarcomatous characteristics. They were first described by Cushing and Eisenhardt in 1938 as a variety of angioblastic meningioma. The name hemangiopericytoma was used for the first time in 1942 by Stout and Murray to describe a soft tissue sarcoma of the thigh [22]. Begg and Garret recognized the similarity of the angioblastic meningioma described in 1938 to this soft tissue sarcoma in 1954 [2]. Although some authors have maintained that hemangiopericytomas are a form of meningioma [24], their clinical and biological behavior is dramatically more aggressive.

Grossly meningeal hemangiopericytomas are lobulated and of firm consistency with a pink-gray to red color. They usually have a broad meningeal base but do not spread en plaque or invade brain [10, 13]. They are highly vascular but at surgery are usually separated from surrounding brain without difficulty.

The histopathological identification of hemangiopericytomas can be difficult. They can resemble fibrous or meningotheliomatous meningiomas [12]. These tumors are very cellular and often contain stag horn shaped, thin walled capillaries. Mitoses are often seen and their number is variable between fields [11]. Calcium, whorls and psammoma bodies are not seen [10, 14].

On imaging studies they resemble meningiomas and this is often the preoperative diagnosis. Irregular borders and a mushrooming lobulated appearance may suggest the correct diagnosis. Bony change is uncommon but if present is erosion [17]. Angiography is sometimes helpful in making a preoperative diagnosis. Feeding arteries often have a corkscrew appearance and early filling veins are not uncommon. A sustained venous phase is frequently seen [15]. The location in which hemangiopericytomas are found is similar to meningiomas.

Hemangiopericytomas tend to metastasize outside the brain if the patient survives for an extended length of time. The incidence of metastasis increases with time and has been reported as 13%, 33% and 64% at 5, 10 and 15 years respectively. The presence of extracranial metastases significantly shortens survival [11].

Initial treatment of meningeal hemangiopericytomas is usually surgical. Preoperative embolization of the feeding vessels can be helpful in controlling bleeding during surgery. However this is often not as helpful as for meningiomas because of the propensity of hemangiopericytomas to parasitize cortical vessels. Approximately half will have a significant internal carotid vascular supply [11, 13, 15] and intra-operative hemorrhage can complicate surgery [3]. They typically re-

cur after gross total resection and their progression is relentless. The time to recurrence after resection tends to shorten after subsequent surgeries and clinical outcome tends to worsen with each operation [11]. Median recurrence intervals of 40 [11] to 50 [18] months have been reported. The interval to subsequent recurrences after surgery shortens and the morbidity and mortality of repeated surgery increases [11]. The use of palliative chemotherapy for metastatic lesions is of only marginal benefit [8] [1].

Hemangiopericytomas are radiosensitive tumors and are responsive in both intracranial and extracranial locations [7, 18]. Post operative radiation therapy for intracranial hemangiopericytomas prolongs survival significantly [5] and with a longer latency period before recurrence [10].

The goal of this report is to present the imaging and clinical response of intracranial hemangiopericytomas to Gamma surgery, and to try to determine if there is any role for this treatment in the management of these difficult tumors.

Patients and Methods

Patient Material

Twelve patients with 15 hemangiopericytomas were treated between 1991 and 1999. The average age at initial Gamma surgery was 45.9 years (range 31 to 69 years). All but one of the patients was male and all had previous neurosurgical procedures with recurrences. The average number of craniotomies was 2.9 (range 1 to 6). This includes one patient with two transsphenoidal procedures. The average interval from initial craniotomy to Gamma surgery was 10.7 years (range 2 to 24 years). Fractionated radiation was used for four of the ten patients prior to Gamma surgery. One patient was treated with chemotherapy and two with Ventriculo-peritoneal shunting. Two patients received endovascular embolization of the tumor's blood supply. One of these preoperatively (craniotomy) and another received three sessions of therapeutic embolization unrelated to other treatment.

Tumor Parameters

The mean volume of the tumors at the time of treatment was 7.6 cm^3 (range 0.3 to 33.6 cm^3). All patients had a single tumor at their initial Gamma surgery. Three tumors were treated twice. Two patients had a recurrence outside the initially treated area that were subsequently treated. One patient had two tumors at the time of treatment but one was not treated because of proximity to the optic chiasm. This tumor has not been treated in any way and is not included in the results section.

Treatment Parameters

The Gamma Knife model B (Elekta Corporation, Atlanta) was used in all treatments. The treatment parameters varied with tumor size and history of previous radiation therapy. The mean maximum dose was 37 Gy (range 8.0 to 51.4 Gy) and the mean periphery dose was 14 Gy (2.8 to 25.0 Gy). The mean number of isocenters used was 4 (range 2 to 6). The dose rate of the Gamma knife ranged from 174 to 351 cGy/min referenced to an 18 mm collimator at an 8 cm focus distance with a water equivalent phantom.

Volumetry

We have developed software at UVA that allows estimation of the tumor volume on the basis of MRI and CT performed without a stereotactic frame. The program evaluates the area of interest on each slice as drawn by the observer, using polygonal estimation techniques [21]. The area in each slice is then multiplied by the slice thickness and integrated over the relevant slices. On evaluation the margin of error of this method is $\pm 7\%$ for lesions smaller than 1 cc and $\pm 2\%$ for volumes larger than 1 cc. Changes in volume were rounded off to the nearest tenth.

Follow up

Ten patients with 12 tumors have imaging follow up available. Two additional patients have been treated recently, with imaging follow-up no longer than three months available. Clinical assessment was available for all cases (average 24.8 months).

Results

Imaging Outcome

Responsive Tumors. Five tumors (in five patients) regressed following Gamma surgery and have remained stable for an average eleven months (range 3–24 months) (Fig. 1). The degree of regression ranged from 30 to 80%. One of these patients developed abdominal metastases prior to Gamma surgery. One patient had a 60% reduction in the volume of the treated tumor at 12 months while a small untreated tumor had doubled in volume during the same interval.

Stable Tumors. Three tumors (in three patients) were unchanged in volume after an average of 29 months (range 10–42 months, patients 2, 5 and 7).

New or Progressive Tumors. Four patients had tumors that were initially stable (one) or regressing (three) and later progressed within the treatment field. The mean regression was 60% (range 20 to 90%) achieved from 3 to 14 months after treatment. Three of these progressive tumors were retreated with Gamma surgery and the fourth was operated. Of the three patients retreated with Gamma surgery all have imaging follow-up. One remained stable for ten months before progressing, another has shrunk 30% at three months follow-up.

The tumor in the first patient remained unchanged 12 months when there was a recurrence adjacent to the

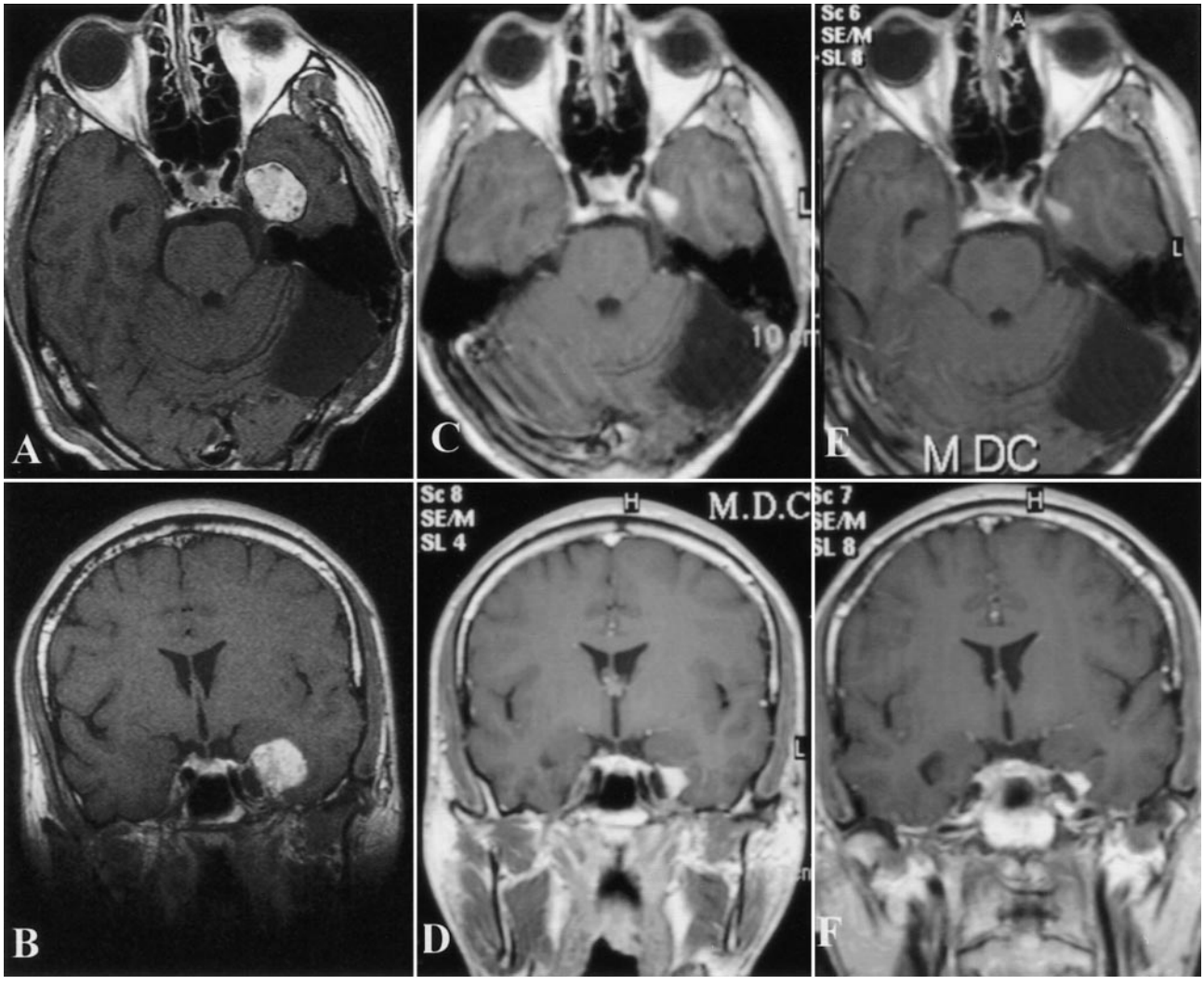

Fig. 1. A 31 year old man with a left medial temporal lobe hemangiopericytoma as shown on the treatment post contrast axial (A) and coronal (B) MRI. Five months later the tumor is 50% smaller as shown on axial (C) and coronal (D) images. One year after Gamma surgery the tumor had continued to regress as shown on axial (E) and coronal (F) scans. (Patient 8, Table 1.)

treated area. This new lesion was treated with Gamma surgery and the tumor volume decreased 40% within 6 months. At 12 months the treated volume was stable, however there was new growth outside the treatment field. This was treated again. At that time there was significant extracranial extension of the tumor but no evidence of metastases. The patient died of progression of his disease 42 months after his first Gamma surgery and 22 years following his initial diagnosis (patient 2, Table 1).

Another patient had two recurrences, both at, and outside the initially treated area. This case is described below:

Representative Case (Patient 3, Table 1)

A 47 year old man presented with right facial paresthesiae and on exam was found to have a mild left hemiparesis. A right CP angle tumor was found on imaging studies and resected through a sub occipital craniectomy. Histopathology was consistent with hemangiopericytoma. Follow up MRI two years later revealed a recurrence (Fig. 2A). This was treated with Gamma surgery using a 36 Gy maximum dose and an 18 Gy marginal dose. An MRI obtained 40 months after treatment (Fig. 2B) showed an 90% decrease in the volume of the treated tumor, but there was new tumors in the cavernous sinus. This was treated with a 40 Gy maximum dose and 16 Gy at the periphery of the tumor. An MRI obtained nine months after the second treatment showed that the tumor in the cavernous sinus had responded with an 80% decrease in volume but that the initially treated tumor in the CP angle had recurred. This tumor was retreated with a maximum dose of 45.7 Gy and a margin dose of 16

Table 1.

Patient	Age at Gamma surgery (years)	Previous therapy	Interval to Gamma surgery (years)	Volume at treatment in cubic centimeters (tumor)	Maximum and periphery dose in Gy (no. of isocenters)	Length of imaging follow-up (months)	Time to progression of tumor (months)	Clinical outcome since Gamma surgery	Imaging outcome
1	35	5 craniotomies	4	6.3 (1)	50/25 (3)	20	16	dead at 20 months of post-op complications	tumor regression (60%) then progression
2	46 47 48	3 craniotomies radiation therapy-60 Gy	18	8.1 (1) 9.3 (2) 33.6 (2)	34/10.2 (6) 35/10.5 (3) 30/9 (4)	42 29 15	15[4] 10 10	dead at 42 months of tumor progression	tumor stable then recurrence[1]
3	40 43 44	1 craniotomy	2	4.5 (1) 6.9 (2) 10.0 (1)	36/18 (5) 40/16 (5) 45.7/16 (5)	56 13 3	44§ N/A N/A	unchanged	initial regression (87%) then progression[2]
4	47 50	2 craniotomies 2 trans-phenoidal resections radiation therapy-54Gy	24	0.3 (1) 3.8 (1)	8/2.8 (3) 51.4/18 (3)	41 8	17 N/A	unchanged	initial regression (66%) then progression. 85% regression following 2nd treatment (compared to first treatment's volume)
5	39	4 craniotomies VP-shunt radiation therapy-50 Gy	12	4.8 (1)	10/3.3 (2)	34	N/A	unchanged	stable
6	69	1 craniotomy 1 embolization	2	5.5 (1)	40/20 (5)	24	N/A	unchanged	35% decrease
7	46	2 craniotomies 3 emboliza-tions	14	11.8 (1)	42.5/17 (6)	10	N/A	unchanged	stable
8	31	2 craniotomies radiation therapy-54 Gy	11	6.2 (1) 0.5[3]	40/20 (5) N/A	12 12	N/A N/A	diplopia resolved	60% decrease of treated tumor Untreated tumor has doubled in volume
9	59	6 craniotomies	16	1.5 (1)	41.7/16 (3)	6	N/A	decreased seizure activity	42% decrease
10	41	1 craniotomy V-P shunt	4	1.9 (1)	51.4/18 (3)	3	N/A	unchanged	26% decrease

[1] 1st treatment-4% decrease (stable). Tumor recurred outside of treated area and 2nd treatment controlled growth (shrank 20%) of second lesion for 10 months before progression. Third treatment controlled growth of second lesion for 10 months (unchanged) before progression. This patient's third treatment was suboptimal due to the large size of the tumor and the extracranial portion of the tumor was not treated.
[2] 1st treatment-tumor shrank 87% and was stable for 49 months before progressing and was recently retreated (shrank 15% at 3 mo. follow-up after second procedure). Tumor also recurred at an untreated area at 44 months and was treated. This portion has shrunk 84% with 9 months follow up.
[3] Patient has a second tumor not treated because of proximity to the optic chiasm.
[4] Recurred outside initially treated area.

Gy. At 9 months follow up this tumor had decreased in volume 40% and the tumor in the cavernous sinus remained unchanged from the prior study. Five years since his first Gamma surgery the patient is clinically stable and feels well.

The third patient with tumor progression was treated with a low dose at her first Gamma surgery. She had an initial 70% regression of her tumor which then started to grow 18 months after Gamma surgery. This lesion was retreated with a higher dose and has regressed 85% from the initial treatment volume (90% from the second treatment volume) after eight months. (patient 4, Table 1), (Fig. 3).

The fourth patient had a reduction of 60% of the volume of his tumor at 11 months. A control MRI

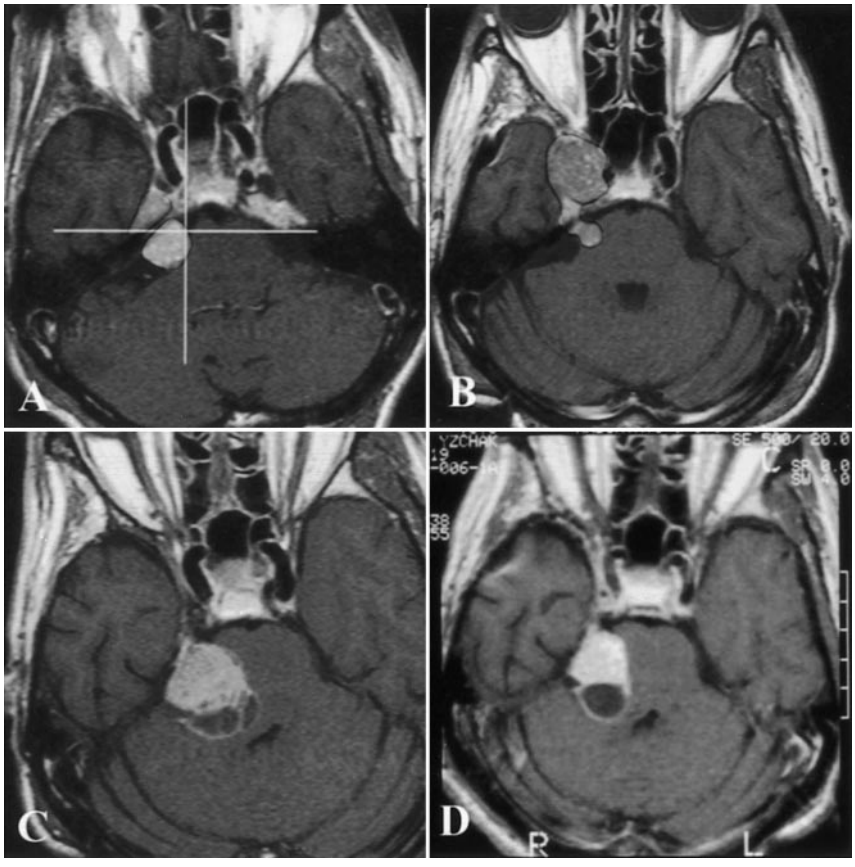

Fig. 2. A 47 year old man with a right cerebellopontine angle hemangiopericytoma shown in the post contrast T1 weighted axial MRI obtained at the time of initial Gamma surgery (A). Forty months later the CP angle lesion was 90% smaller but there was a new tumor in the right cavernous sinus which was treated (B). Nine months later the cavernous sinus lesion was 80% smaller but the CP angle tumor progressed and was retreated (C). Three months following the last Gamma surgery the cavernous sinus tumor was stable and the CP angle tumor shrank 15%. (Patient 3, Table 1.)

performed at 18 months showed the tumor was larger than prior to treatment with the Gamma Knife. He underwent a craniotomy (this was his sixth craniotomy since presentation) and succumbed to post operative complications (pneumonia) one month later. (patient 2, Table 1)

Other Changes on Imaging Follow Up

There was no new signal change identified within the brain on T2 weighted images of any patient following Gamma surgery that was not present prior to treatment.

In summary, of the 12 tumors treated with Gamma surgery nine responded with a decrease in volume and three remained stable. Of the nine that decreased in volume, maximum decrease in volume was generally seen within a year and as early as 3 to 6 months. The time to maximum decrease in volume for the six tumors with greater than one year follow up was 3 to 16 months (mean 9.7 months). The average decrease in volume was 50% (range 20 to 90%). There were four tumors that initially decreased in volume and then progressed. The average time to the MRI demonstrating progression was 23 months after treatment and 7.5 months after the last MRI that showed maximum decrease in volume. This is significant because in three of the four cases where the tumor progressed after initially responding with regression, the tumor became larger than it was prior to treatment.

Clinical Outcome

Two patients died. One died of post operative complications following a repeat craniotomy twenty months after Gamma surgery. The second patient died

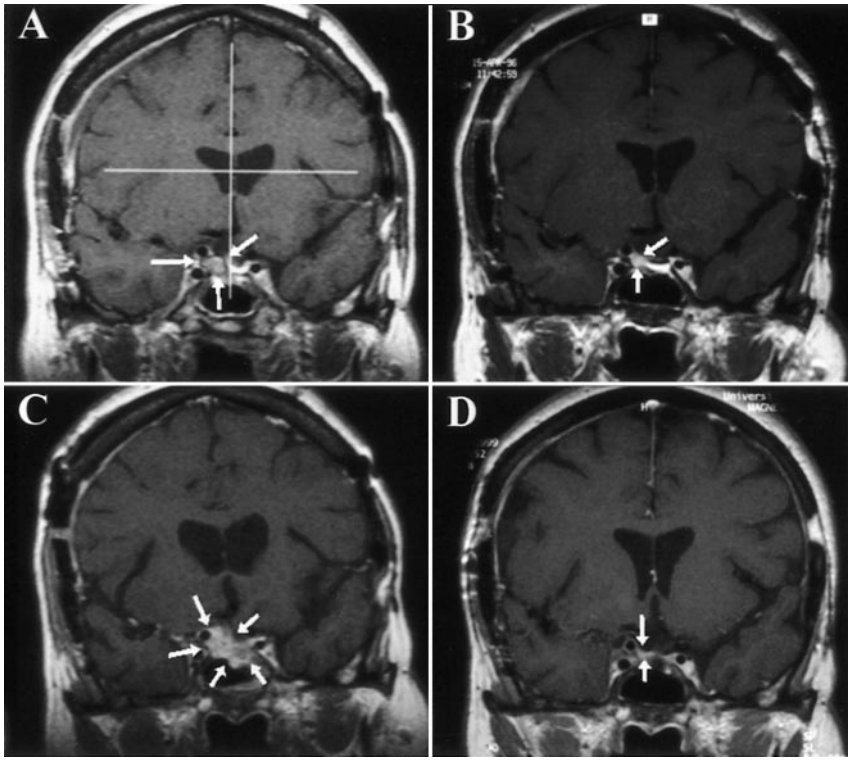

Fig. 3. A 47 year old woman with a right cavernous sinus hemangiopericytoma as shown on the treatment post contrast coronal T1 weighted MRI (A). Three months later the tumor shrank 70% (B). Thirty months after the initial Gamma surgery the tumor was larger than at the time of treatment and the procedure was repeated (C). Ten months after the second treatment the tumor again decreased 90% in volume. (Patient 4, Table 1.)

of local recurrent and distant disease (intracranial) following three procedures with the Gamma Knife. He had also undergone three craniotomies and 60 Gy of fractionated radiation therapy.

There were no complications attributable to Gamma surgery. One patient had improvement of his trigeminal paresthesiae and gait ataxia following Gamma surgery and tumor regression for a CP angle hemangiopericytoma, but symptoms recurred when the tumor began to grow again. This has recently been retreated with Gamma surgery and the tumor has regressed 15% at three months follow-up. Another patient has had a 75% decrease in the frequency of his seizures following Gamma surgery associated with a 40% decrease in the volume of his tumor at three months follow up. Another patient with suprasellar extension of his tumor had resolution of his oculomotor palsy several weeks following Gamma surgery. All other patients are clinically unchanged since Gamma surgery.

Discussion

The alternatives in the management of intracranial hemangiopericytomas include microsurgery, embolization, radiation therapy and Gamma surgery, either alone or in combination.

Microsurgical Management of Hemangiopericytomas

Hemangiopericytomas are malignant tumors that recur at or near the site of their excision and with time metastasize outside the skull. Treatment of these tumors should have multiple goals. Symptomatic lesions should be reduced in volume and asymptomatic tumors should be prevented from further growth. Ideally, gross total excision should be performed to provide immediate relief of symptoms and a meaningful interval to recurrence. Guthrie found that if microsurgery was the sole treatment for hemangiopericytoma, the tumor recurred after an average of

29 months. Subsequent recurrences following additional microsurgery occurred at progressively shorter intervals [11]. Because this tumor is associated with a prolonged clinical course, and recurrence is nearly inevitable making repeated procedures necessary, the accrual of iatrogenic neurological deficits in the pursuit of improved resection should be discouraged, and quality of life preservation should be the foremost goal.

Embolization

Preoperative embolization of intracranial hemangiopericytomas with the purpose of limiting blood loss during surgery has been reported [4, 9, 19] but because of the frequent parasitization of cortical arteries, complete devascularization is difficult. There is no report in the medical literature of therapeutic embolization without subsequent microsurgery for hemangiopericytomas. However, three patients were therapeutically embolized at the University of Virginia. One patient was embolized three times over the course of three years and the therapy was successful in postponing an additional craniotomy for three years after the last embolization. This patient's last embolization was associated with a persistent Horner's syndrome. Another patient had two simultaneous recurrences, both of which embolized but only one surgically extirpated. Neither tumor was visible at one year follow up imaging. A third patient was embolized but the therapy was not successful in preventing tumor growth and the lesion was treated with Gamma surgery nine months following embolization. Two years after Gamma surgery this tumor had decreased in volume by 35%.

Radiation Therapy

Several authors advocate fractionated radiation therapy in the treatment of hemangiopericytomas [10, 11, 16, 23]. Little has been reported on its use as a primary modality but used in the postoperative period it has been shown to significantly lengthen the time to tumor recurrence following surgical extirpation. It appears that a regional minimum of 50 Gy should be used to prevent early recurrence [11]. The purpose of radiation therapy is to delay recurrence of tumors. In a review of all the patients treated with microsurgery for intracranial hemangiopericytomas at the University of Virginia in the past ten years, three received 54 Gy regional fractionated radiation therapy following the first procedure and the remaining five did not receive any radiation therapy. Those that were not irradiated averaged 2.4 years between their 26 procedures while those that were irradiated post operatively averaged 7.5 years between their 9 procedures. No patient had died or developed systemic metastases. One patient underwent resection and radiation 1 year before Gamma surgery for a new lesion and has not recurred at the operative site to date (11 years since surgery). This is in concordance with Guthrie's finding that hemangiopericytomas irradiated post operatively recur an average of 74 months after their first operation, while those not irradiated recur at an average of 29 months [11]. The experience of Jaaskelainen suggests that the use of radiation therapy should be after the initial resection. Two patients irradiated after initial gross total resection were disease free at 167 and 263 months respectively. Three patients irradiated for recurrent non-resectable tumors had progression of their disease [13].

Gamma Surgery

Published reports of the results of Gamma surgery in the treatment of hemangiopericytomas are scarce. Coffey *et al.* reported on five patients treated with Gamma surgery for 11 hemangiopericytomas. The treated tumors all responded with a decrease in volume with an average follow-up of 14.8 months (range 10 to 17 months) However, there was recurrence of the tumor outside the treatment field in two of the patients during the follow-up period [6].

The patients in Coffey's group were included in a larger series reported by Galanis *et al.* In this series of ten patients with 20 tumors treated with Gamma surgery, all of their tumors responded to treatment either with a decrease in volume or were unchanged but the effect lasted less than a year in the majority of their patients. Most of the tumors had also received fractionated radiation therapy and averaged 32 mm in greatest dimension. A subgroup of three patients with solitary tumors less than 25 mm in greatest diameter that had not been treated with radiation therapy all showed complete imaging response that had persisted for a median of 36 months. Two of these patients received radiation therapy following Gamma surgery [8]. The marginal dose applied in this series was tumor volume dependent. Those less than 4.2 cm^3 received a dose of 20 Gy. Volumes between 4.2 and 14 cm^3 received 18 Gy and those larger 16 Gy. Doses were

Table 2.

	No. of patients	No. of tumors	mean F/U (months)	Mean dose (max/min)	Tumor diameter or volume range	Number of tumors without progression	mean F/U (months)	# patients that developed new intracranial tumors	Deaths from disease progression	Mean time to death (months) after Gamma surgery
Coffey	5	11	15			11	15	2	1	17
Jaques	3	6	42	75/37	1–30 cc	6	42	2	2	48
Kabayashi	5	5	31	33/16	2.8 cm	4	25	0	0	N/A
Larson	5	5	44	27/18	2–22 cc	4	45	0	0	N/A
Payne	10	12	25	37/14	0.3–33.6 cc	8	14	2	2[2]	28
Pendl	1	1	30	40/18	21 cc	0	N/A	0	1[2]	30
Total	29	40	30			35 (86%)	23	6 (15%)	6 (15%)	33

* Includes one post operative death following microsurgery and two other tumors greater than 20 cm^3
[2] These patients died of progression of disease in the treatment field.

decreased 2 to 4 Gy if the patient had received previous radiation therapy. These doses are similar to those used in our series but because they had more large tumors the average dose utilized was less.

Other Centers. We communicated with several centers performing Gamma surgery requesting information of their results in treating intracranial hemangiopericytomas. Five centers that had experience with this tumor type replied. One had treated five patients but had not analyzed the follow-up data (T. Hirai personal communication). The results and details of the other centers are summarized in Table 2.

Pendl *et al.* (personal communication) treated one patient with a large hemangiopericytoma that had been operated upon and irradiated post operatively. A 21 cm^3 recurrence was treated with Gamma surgery three years later. The patient was clinically stable for six months before developing a hemiparesis. The tumor was resected again and the patient treated with chemotherapy. He died two years later of apparent progression of his intracranial disease. Kobayashi (personal communication) treated five patients with intracranial hemangiopericytomas with Gamma surgery. Two patients with 13 month clinical and radiographic follow up have shown either complete or greater than 50% reduction in the size of the tumor. Another patient showed greater than 50% reduction in the volume of his tumor at 26 months but required another Gamma surgery for a second tumor remote from the original site. A fourth patient's tumor has remained stable at 26 months but also required a second Gamma surgery for a tumor remote from the treated area. The last patient, with the largest tumor, has had four staged Gamma surgeries of the same tumor. The tumor has progressed slowly but the patient is alive 57 months after his initial Gamma surgery.

At the University of California at San Francisco, Larson (personal communication) treated six patients, each of which had one hemangiopericytoma, with Gamma surgery. Follow up was available for five of them. Four of the five had received regional fractionated radiation and all had previous microsurgical resections. Three were less than 2 cm^3 in volume, one approximately 7 cm^3 and one 22 cm^3 in volume. The three smallest tumors have either decreased in volume (one) or remained stable (two) an average of 33 months (range 20 to 58 months) following Gamma surgery. Two of these patients developed seizures after treatment which were controlled with medication. One tumor approximately seven cm^3 in volume, increased in volume and then underwent necrosis resulting in a hemiparesis which has improved. The patient is alive at 80 months without recurrence of tumor. The largest tumor (22 cm^3) had a partial response and then began to grow after 33 months. He is alive at 38 months with bone metastases.

At Good Samaritan Hospital in Los Angeles, Jacques (personal communication) treated three patients with hemangiopericytomas. One patient's single tumor which measured less than 1 cm^3 in volume is unchanged at 31 months. Another patient with a large (>30 cm^3 volume) tumor was treated four times with Gamma surgery. The patient died of recurrent disease adjacent to the treated tumor 20 months after his first Gamma surgery. The third patient has been treated twice for the same tumor. After failing to decrease in volume after the initial Gamma surgery (although it did not increase in volume) the tumor was treated a

second time. This treatment was complicated by tumor necrosis and peritumoral edema. The patient died of recurrent adjacent disease 76 months after his first Gamma surgery.

The results of these other series are similar to our own. The only deaths attributable to treated tumors were in very large tumors (>20 cm^3) and a single death following microsurgery for a recurrence. All tumors treated responded with a decrease in volume or a cessation of growth. There was a 33% incidence of recurrence of growth of a treated tumor in our series but only 11% in the remaining series. This is difficult to explain except in the case of Coffey's report because of shorter follow up and Jacques' series because of higher doses used. Retreatment of local recurrent tumors in our series has been successful however with two of the three recurrences retreated showing reduction of volume following the second Gamma surgery. The occurrence of new tumors was similar in our series (2/10) to the remaining series (4/19).

The advantage of Gamma surgery in the treatment of hemangiopericytomas is the low risk of adverse effects and the effectiveness in local control of tumor growth, as demonstrated in this paper. The disadvantage of Gamma surgery is the delay of response to treatment and the theoretical limitation of repeated Gamma surgery treatments because of the increase in integral dose applied. In our series there were no radiation induced complications associated with retreatment of tumors or the treatment of large tumors, and this concern still remains to be substantiated. However, in order to minimize the chance of a radiation induced complication it is important to treat the tumors when they are small. This should reduce the risk of radiation associated complications and allows for higher marginal doses to be used [20]. It is important to note that while the majority of patients treated with conventional radiation were treated soon after a gross total resection , those in the Gamma surgery series are often only partially excised and undergo delayed gamma surgery on apparent failure of expectant management.

Combined Therapy

The integration of different therapeutic modalities in the management of a patient harboring an intracranial hemangiopericytoma requires identification of the goals of treatment. The initial preoperative diagnosis based on imaging is usually meningioma. The true diagnosis is not generally known until permanent histological and immunohistochemical analysis has been performed. When the nature of the disease is realized, prevention of recurrence, maintenance of neurological function and preservation of quality of life for as long as possible should have highest priority. High dose regional fractionated radiation therapy or Gamma surgery should be initiated immediately after the initial resection. This seems to delay recurrence significantly. When a recurrence does occur microsurgical extirpation should be repeated as many times as possible with low risk of significant morbidity or mortality. Pre operative embolization should be considered to lessen the blood loss during open surgery of these tumors. The endovascular treatment of these lesions as an isolated modality may be appropriate on occasion when the vascular supply is predominantly dural based, but because this is a largely untried approach, vigilant imaging follow up should be maintained. If recurrence occurs and the tumor can no longer be safely extirpated Gamma surgery should be done or repeated as the case may be. It is important to treat these tumors when they are small so Gamma surgery should be performed at the first sign of recurrence, or in the postoperative period if residual tumor is known to be present following microsurgery. We safely performed repeated Gamma surgery in the present series without complications. It is possible as experience grows and hemangiopericytomas are treated multiple times with Gamma surgery that radiation associated complications may occur. However, following the above stages of therapy the alternative is to declare the patient untreatable and allow the tumor to progress. If a recurrent tumor grows to a large size, subtotal debulking with preservation of neurological function, should be considered prior to Gamma surgery.

Because recurrence of these tumors, both at the treated site and distant to it, following Gamma surgery is common, the ability to treat multiple times becomes an issue. There is very little reported in the literature regarding repeated treatment of oncotic pathology with Gamma surgery. In our experience when retreating metastases, pituitary tumors and meningiomas, the incidence of radiation associated complication is no higher than usual. The importance of total integral dose received by the brain when multiple treatments are performed with the Gamma Knife still remains to be defined. However in cases with relatively limited life expectancy it is less relevant.

The maximum dose that can be applied to malig-

nant tumors (primary and metastatic) following radiation therapy has not been extensively reviewed. Shaw *et al.* have recently reported that this dose is dependent upon the size of the tumor. For malignant tumors with a maximum diameter of less than 20 mm, 24 Gy was the highest marginal dose that could be safely applied. For tumors 20 to 30 mm in maximum diameter the highest marginal dose safely applied was 18 Gy. For tumors greater than 40 mm in maximal diameter 15 Gy was the highest dose safely prescribed [20]. In the majority of cases treated by us and at other centers the doses used were lower than that. In the future availability of radiosensitizers and normal tissue protectants could all lead to the exploration of higher peripheral doses with the intention to lower the incidence of recurrence at the treated area. In the series of Galanis the peripheral dose was decreased 2 to 4 Gy if the patient had previously received radiation therapy.

Conclusion

Hemangiopericytomas are vexing tumors to treat due to their proclivity to recur and tendency to arise from the cranial base. Gamma surgery is effective in the treatment of intracranial hemangiopericytomas and is associated with a low risk of adverse effects. It allows for the treatment of tumors difficult to remove with microsurgical techniques, extended survival and maintenance of neurological function. Aggressive imaging surveillance of these patients is important.

References

1. Beadle GF, Hillcoat BL (1983) Treatment of advanced malignant hemangiopericytoma with combination adriamycin and DTIC: a report of four cases. J Surg Oncol 22: 167–170
2. Begg CF, Garret R (1954) Hemangiopericytoma occurring in the meninges. Cancer 7: 602–606
3. Brunori A, Delitala A, Oddi G, Chiappetta F (1997) Recent experience in the management of meningeal hemangiopericytomas. Tumori 83: 856–861
4. Casasco A, Herbreteau D, Houdart E, George B, Tran Ba Huy P, Deffresne D, Merland JJ (1994) Devascularization of craniofacial tumors by percutaneous tumor puncture. Ajnr: Am J Neuroradiol 15: 1233–1239
5. Chan RC, Thompson GB (1984) Morbidity, mortality, and quality of life following surgery for intracranial meningiomas. A retrospective study in 257 cases. J Neurosurg 60: 52–60
6. Coffey RJ, Cascino TL, Shaw EG (1993) Radiosurgical treatment of recurrent hemangiopericytomas of the meninges: preliminary results. J Neurosurg 78: 903–908
7. Friedman M, Egan JW (1960) Irradiation of hemangiopericytoma of Stout. Radiology 74: 721–729
8. Galanis E, Buckner JC, Scheithauer BW, Kimmel DW, Schomberg PJ, Piepgras DG (1998) Management of recurrent meningeal hemangiopericytoma. Cancer 82: 1915–1920
9. George B, Casasco A, Deffrennes D, Houdart E (1994) Intratumoral embolization of intracranial and extracranial tumors: technical note. Neurosurgery 35: 771–773; discussion 773–774
10. Guthrie BL (1995) Meningial Hemangiopericytomas. In: Kaye AH *et al* (eds) Brain tumors. Churchill Livingston, Edinburgh, pp 705–711
11. Guthrie BL, Ebersold MJ, Scheithauer BW, Shaw EG (1989) Meningeal hemangiopericytoma: histopathological features, treatment, and long-term follow-up of 44 cases. Neurosurgery 25: 514–522
12. Horten BC, Urich H, Rubinstein LJ, Montague SR (1977) The angioblastic meningioma: a reappraisal of the nosological problem. Light-, electron-microscopic, tissue, and organ culture observations. J Neurol Sci 31: 387–410
13. Jaaskelainen J, Servo A, Haltia M, Wahlstrom T, Valtonen S (1985) Intracranial hemangiopericytoma: radiology, surgery, radiotherapy, and outcome in 21 patients. Surg Neurol 23: 227–236
14. Kochanek S, Schroder R, Firsching R (1986) Hemangiopericytoma of meninges. I. Histopathological variability and differential diagnosis. Zentralbl Neurochir 47: 183–190
15. Marc JA, Takei Y, Schechter MM, Hoffman JC (1975) Intracranial hemangiopericytomas. Angiography, pathology and differential diagnosis. Am J Roentgenol Rad Ther Nucl Med 125: 823–832
16. Mena H, Ribas JL, Pezeshkpour GH, Cowan DN, Parisi JE (1991) Hemangiopericytoma of the central nervous system: a review of 94 cases. Hum Pathol 22: 84–91
17. Osborne DR, Dubois P, Drayer B, Sage M, Burger P, Heinz ER (1981) Primary intracranial meningeal and spinal hemangiopericytoma: radiologic manifestations. Ajnr: Am J Neuroradiol 2: 69–74
18. Schroder R, Firsching R, Kochanek S (1986) Hemangiopericytoma of meninges. II. General and clinical data. Zentralbl Neurochir 47: 191–199
19. Shaffrey ME, Persing JA, Ferguson RD, Shaffrey CI, Cantrell RW, Jane JA, Newman SA (1990) Vascular lesions involving the cranial base: combined surgical and interventional radiologic approach. J Craniofacial Surg 1: 106–111
20. Shaw E, Scott C, Souhami L, Dinapoli R, Kline R, Loeffler J, Farnan N (1998) Update of Radiation Therapy Oncology Group (RTOG) Protocol 9005: single dose radiosurgical treatment of recurrent brain tumors. Int J Radiat Oncol Biol Phys 42: 41(S)196
21. Stone M (1986) A mnemonic for areas of polygons. Am Maths Month 93: 479–480
22. Stout AP, Murray MR (1942) Hemangiopericytoma: a vascular tumor featuring Zimmerman's pericyte. Anns Surg 116: 26–33
23. Uemura S, Kuratsu J, Hamada J, Yoshioka S, Kochi M, Ushio Y, Nakahara T, Kishida K (1992) Effect of radiation therapy against intracranial hemangiopericytoma. Neurol Med Chir 32: 328–332
24. Zulch KJ (1979) Histological typing of tumors of the central nervous system. World Health Organization, Geneva

Comment

As could be expected from this very experienced expert group, this is an *excellent papter:* It does not only describe the 2nd largest number of patients with hemangiopericytomas ever treated by Gamma knife surgery; it does also include communicated reports from other

Gamma Knife Centers in order to achieve a representative ''state of the art'' – publication on this topic. In addition, all methods of treatment (alone or in combination) for Hemangiopericytomas are discussed in detail.

M. Gaab

Correspondence: Ladislau Steiner, M.D., Ph.D., Department of Neurosurgery, University of Virginia Hospital PCC Room G-512, Box 484 Lee Street, Charlottesville, VA 22908.