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Clinical Article

Gamma knife radiosurgical management of petroclival meningiomas results and indications

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Summary

Background. Surgical treatment of petroclival meningiomas remains challenging. In order to refine indications for the use of stereotactic radiosurgery in the treatment of these tumours, we retrospectively evaluated our experience in this field.

Methods. Thirty-two patients harboring a petroclival meningioma were treated consecutively using a Gamma knife between December 92 and June 1998. Eight patients underwent radiosurgery after one or more attempted surgical removals and 24 had radiosurgery as the primary treatment. The main symptoms before radiosurgery were cranial nerve palsies, including a sixth nerve deficit in 10 patients and a trigeminal nerve disturbance in 9. All patients underwent a conformal multi-isocentric treatment (mean isocenter's number 8.8) and the dose delivered at the tumour margin ranged from 10 to 15 Gy (mean dose 13 Gy).

Findings. The duration of follow-up varied from 24 to 118 months (mean clinical follow-up 56 months, mean radiological follow-up 52.6 months). All 32 patients survived. The tumour volume remained unchanged in 28 patients and decreased slightly in 4. Neurological status worsened permanently in 2 patients with a delayed hemiparesis due to focal pontine infarction. These complications were associated with large meningiomas with vascular involvement and ventral brainstem compression, and occurred at the very early stage of our experience. At last follow-up, preoperative fifth or sixth cranial nerve deficits had improved or recovered in 13 out of 19 patients and any delayed worsening or new cranial nerve deficits were not observed after radiosurgery.

Conclusions. Stereotactic radiosurgery with a Gamma knife provides effective management of small to middle sized petroclival meningiomas and is an alternative to microsurgery. Careful selection of patients and use of major technical refinements should improve the safety of this treatment.

Keywords: Cranial nerves; gamma knife; petroclival meningiomas; stereoractic radiosurgery.

Introduction

Management of petroclival meningiomas still represents a significant challenge for neurosurgeons, despite great advances of skull base surgical techniques, neuromonitoring and peri-operative care. Expert skull base neurosurgical teams report substantial peri-operative morbidity (around 50%) and mortality (2–10%) [1–3, 12]. Moreover, achievement of even gross total removal is obtained in less than 80% of patients, leaving many at risk of regrowth of residual tumour [5, 8], and a need for additional treatment.

Indication for and timing of surgery are also complicated by the clinical presentation often being with very mild features, even with a big tumour. Nevertheless, there is a considerable consensus about the use of primary microsurgery for large symptomatic petroclival meningiomas. In contrast, controversy exists about the management of small to middle sized lesions, especially because new treatments are emerging as alternatives to microsurgery.

In order to increase understanding of the indications for radiosurgery in the treatment of petroclival meningiomas, we reviewed retrospectively the results obtained by Gamma knife radiosurgery in the first 32 patients consecutively treated in our institution.

Methods and material

Patient population

Since July 1992, 1060 patients with a meningioma have been treated by Gamma knife in our center, out of a total of 4310 procedures. Seventy-two of these meningiomas were considered to be of petroclival origin. Due to the slow growing nature of meningiomas and in order to evaluate the effectiveness of radiosurgery and also its potential toxicity, we deliberately excluded from the field of this study the last 40 petroclival meningiomas that have been radiosurgically treated in the most recent period. The present study is focused on the group of 32 patients (5 men and 27 women) who have been treated consecutively between December 92 and June 1998. The patients ranged in age from 34 to 77 years (mean 53 years). When treatment was delivered after microsurgery, the benign nature of the meningioma was always confirmed by the pathologist. When radiosurgery was used as a first line procedure, so that histopathological confirmation of the diagnosis of a meningioma could not be made, the diagnosis was made on the basis of clinical characteristics and radiological findings, that is, iso- to hypo-intense on T1-weighted MR images and hypo- to hyperintense on T2-weighted MR images, and homogeneous enhancement.

Eight patients had undergone at least one craniotomy and attempted tumour resection. Gross total resection was thought to have been achieved in 2 cases, but radiosurgery was done after tumour recurrence. In 6 patients, resection was incomplete and radiosurgery was applied to the residual meningioma. Radiosurgery was performed as the primary treatment in another 24 patients, with evidence of symptoms due to the tumour or radiological features of tumor growth.

The patients presenting neurological signs were mainly cranial neuropathies. A sixth nerve deficit was observed in 10 patients, the fifth nerve in 9 (2 had facial numbness and 7 had trigeminal neuralgia), and the eight nerve was involved in 3 patients. Two patients mainly had gait ataxia. A lack of clinical symptoms and signs related to the tumor was noted in 11 patients who had an asymptomatic but growing tumour.

Tumour classification

The radiological characteristics of the meningiomas are described in Table 1. The treated tumours were small to middle sized, with a mean diameter never exceeding 3 centimeters. The tumour volume was 2282 cubic millimeters on average (250–6000). The volume of the tumour was calculated assuming the tumour to be an ellipsoid. The ellipsoid volume was then equated to a sphere of an equivalent volume, and a tumour equivalent diameter was computed as the diameter of the sphere, following the publication from Sekhar *et al.* [13]. When a Gamma Plan workstation was available for the treatment planning, the tumour volume was automatically provided by the computer. We also classified the tumours according to their main and accessory attachment. As shown in Table 1, 24 of the 32 patients had a focal origin. The relationships of the meningioma to the surrounding areas and to critical neurovascular structures are also shown.

Table 1. *Origin and extension of 32 petroclival meningiomas before radiosurgery*

Main insertion	Accessory insertion		
	clivus	petrous apex	petroclival junction
Clivus	4	1	2
Petrous apex		14	5
Petroclival junction			6

Extension to neighbouring areas					
Meckel cave	tentorium	cavernous sinus	cerebellopontine angle	brain stem mass effect	vascular engulfment
10	5	3	1	11	2

Radiosurgical treatment

Patients were admitted to hospital the day before treatment. On the day of treatment, a Leksell Model G stereotactic frame was fixed to the patient's head under local anesthesia. A stereotactic enhanced CT scan and/or MR imaging was performed to determine the stereotactic coordinates of the treatment target. Because the target was always the tumour and not its vascular supply, stereotactic angiography was not performed. Computarized dose-planning was performed initially on a Kula Micro-VAX workstation for the first 22 patients. A GammaPlan workstation was available for the 10 patients treated between September 1997 and June 1998. In all patients, radiosurgery was performed using the 201-source cobalt-60 Leksell gamma knife Model U (Elekta Instruments).

Multi-isocentric treatment was used in all patients, with the average number of isocenters 8.8 (4–20). The reference peripheral isodose was the 50% isodose in the majority of cases. The mean dose delivered to the tumour margin was 13 Gy (10–15 Gy), according to preliminary studies [4, 6, 7]. Parameters of the treatment, particularly selection of doses, were adjusted to the individual tumour volume and evidence of relationship to critical neural structures.

Follow-up evaluation

After treatment, patients were instructed to return for clinical evaluation (obtained by the referring physician or the treating neurosurgeon) and serial imaging at 6-months, 1, 2, 3, 5, 7, 9 years.

Results

All of the patients were discharged at 24 hours after the treatment and were able to return to their previous activity. The duration of follow-up varied from 24 to 118 months and the median patient follow-up time was 48 months. The mean clinical and radiological follow-up times were respectively 56 and 53 months. At the time of the last evaluation, the number of patients followed at 2, 3, 4, 5, 6, 4, 8 and 9 years after radiosurgery were respectively 6, 6, 4, 6, 1, 2, 3, 4.

Tumour control

Tumour control (assessed on serial imaging and defined by the absence of tumour growth) was observed in all cases. The 5-years progression free survival rate was 100%. In 28 patients, tumour volume remained unchanged while it decreased slightly in 4 cases. None of the patient required additional microsurgical or radiosurgical intervention.

Functional results

A cranial nerve complication was observed in two patients who complained of transient worsening of facial pain in the first 9 months after treatment. In each patient, this deficit recovered in a few weeks after steroid administration.

At the latest clinical follow-up, trigeminal neuralgia remained unchanged in 2 patients, had improved significantly in 3, and recovered in 2. Facial numbness remained unchanged in the 2 patients who had this sign before treatment. Among the 10 patients who had a sixth nerve deficit before treatment, 4 remained unchanged, 2 improved and 4 recovered. The duration and degree of sixth nerve deficit before radiosurgery were correlated to its outcome after treatment. No change of hearing was observed in the 3 patients with initial hearing impairment and tinnitus also remained unchanged.

Brain stem complications

Brain stem dysfunction was observed in 3 patients after the treatment (1 transient, 2 permanent) and deserves detailed analysis.

Patient 1. A 76-year-old woman was referred to our institution in October 1993 for the primary radiosurgical treatment of a left petrous apex meningioma. MR imaging showed a 22 millimeters-mean tumour diameter causing a slight mass effect upon the lateral aspect of the pons and middle cerebellar peduncle. Clinical examination showed a slight kinetic cerebellar disturbance and a left facial numbness. Gamma knife treatment was undertaken using 8 isocenters and delivering 15 Grays at the tumour margin (50% isodose). Three months after treatment, the gait ataxia and the left trigeminal disturbance worsened. The patient also complained of left-sided tinnitus. MR imaging did not show any brain stem abnormality and the volume of the tumour remained unchanged. Subsequent MR examinations remained unchanged. Recovery to the previous status gradually occurred over some months, except for the tinnitus.

Patient 2. A 57-year-old woman was referred to us in December 1992, and had a moderate gait ataxia on the left side. MR imaging showed a midclivus meningioma of 20 millimetre mean diameter. A mass effect on the anterior pons and engulfing of the basilar trunk were observed. Primary radiosurgery delivered 14 Grays at the tumour margin (50% isodose). The first clinical and radiological follow up assessments at 6 months showed no change but worsening of the gait ataxia and a right hemiplegia occurred at 11 months after radiosurgery. MR imaging showed a 5 millimeters paramedian mid pontine area of decreased signal on T1-weighted images and increased signal on T2 sequence, located 2 millimeters behind the posterior pole of the tumour. The signal and volume of the meningioma remained unchanged. This finding was considered to be a small infarction in the territory of one of the basilar trunk short perforators. Despite steroid therapy, the patient did not fully recover. At 3 years follow-up the patient was able to walk with assistance. MR image findings did not change.

Patient 3. A 41-year-old woman presented with facial numbness and reduced hearing in the right ear. Five years previously, the patient had undergone a gross total removal of a right petroclival meningioma but recent MR imaging had displayed a recurrent-en-plaque meningioma occupying the middle third of the clivus. The mean tumour diameter was 25 millimetres, the right vertebrobasilar junction was engulfed by the meningioma (Fig. 1), and there was a slight mass effect upon the pontomedullary junction on the right side, without features of brain stem oedema on T2-weighted MR

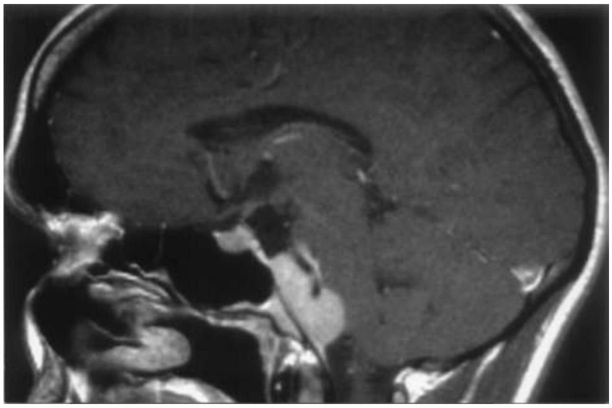

Fig. 1. Post Gadolinium T1-weighted MR image obtained at the time of radiosurgery. Note the close relationship of the midclivus meningioma with the ventral brainstem and involvement of the basilar artery

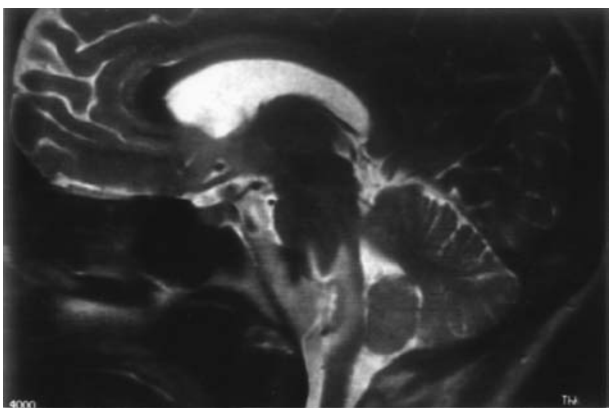

Fig. 2. T2-weighted image obtained at 14 months after the treatment, at the time of neurological impairment. Note the broad area of increased signal at the pontomedullary junction

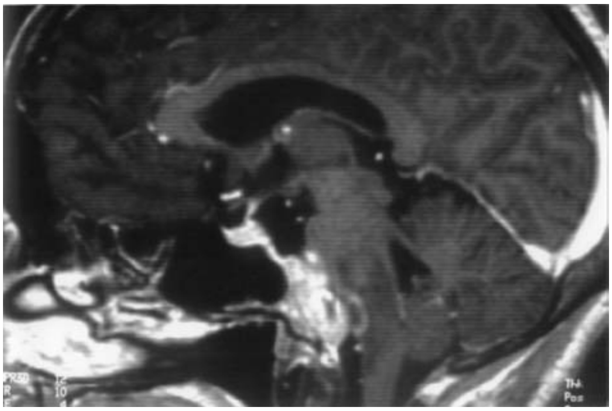

Fig. 3. Post Gadolinium T1-weighted MR image obtained at 7 years follow-up. The abnormal signal is still visible inside the brainstem whereas the tumour volume is unchanged

images. In May 1993, Gamma knife radiosurgery delivered 15 Grays dose at the tumour margin (50% isodose), using 6 isocenters. Forteen months after the treatment, left motor weakness appeared suddenly. MR imaging displayed a striking hyperintense signal at the pontomedullary junction on the T2 sequence (Fig. 2). Steroid administration promoted significant improvement and the brain stem hypersignal disappeared, nevertheless her functional status is still impaired at 7 years follow-up, while tumour volume remains stable (Fig. 3).

Discussion

Meningiomas are usually benign and slow growing neoplasms predominantly affecting women usually after the mid-forties. Several options of treatment can be offered but it is widely agreed that the best chance of cure is total surgical removal of the tumour and its nidus of origin. This is also our current practice for most patients, even for some with a skull base meningioma. We also consider that, despite the significant morbidity-mortality of microsurgery [1–3, 12], a large petroclival meningioma is causing brain stem compression and multiple cranial nerve deficits. Thus, surgical removal should be considered as a primary treatment, on the assumption that there is no effective alternative technique to treat such a life-threatening tumour.

Recent publications about radiosurgical treatment of selected small to middle sized skull base meningiomas have shown promising results in terms of functional preservation and tumour control at the short to intermediate term follow up [9, 14]. Such small to middle size petroclival meningiomas are usually responsible for only very mild symptoms and signs, and the risks of surgery may counterbalance the expected benefit. This was our reason for offering radiosurgery in this group of patients and results reported in the present study support this strategy.

Radiosurgical literature

Analysis of previous publications provides data about several kinds of skull base meningioma taken altogether but most papers do not clearly identify separately the results from the petroclival subgroup. This is illustrated by the study from Morita *et al.* [9] in which there were 16 petroclival meningiomas among 88 skull base meningiomas. However, a recent study from the Pittsburgh team reviewed retrospectively 62 patients with a petroclival meningioma and treated by Gamma knife radiosurgery [13]. During a median follow-up period of 37 months, tumour control was obtained in 92% of cases and the projected tumour control rate was 86.7% at 96 months, excluding the 2 patients who had malignant meningiomas. Neurological status improved in 21%, remained stable in 66% and worsened in 13%. Transient complications consisted of 2 abducens nerve palsies in the year following the treatment. In 3 cases (5%), worsening or new cranial nerve palsies occurred after radiosurgery and did not resolve. These deficits were unrelated to tumour growth. The short duration of follow-up in this study is sufficient to assess complications of radiosurgery but inadequate to arrive at conclusions about the long-term tumour control rate of these slow-growing tumours. Furthermore, the patients were poorly defined in terms of neuroradiological data (brainstem relationship, subtype of petroclival origin, extension to neighbour areas). Many patients in this cohort had previously received radiotherapy, and some malignant cases were included. Selection bias may have occurred and limits interpretation of results.

The issue of tumour control after radiosurgery

In our present study, we report a 100% ‘‘intermediate-term control rate’’. This clearly requires long lasting confirmation reflecting the biological behavior of a meningioma, but is in accord with previous series. However, as we previously reported with cavernous sinus meningiomas [11] and parasagittal meningiomas (unpublished data), we did not observe a marked change in tumour volume and only a small minority (13%) of the tumours displayed such shrinkage over time. Reports of other authors of a higher rate of ‘‘responding’’ skull base meningiomas [9, 15] are surprising. Features of these other cohorts may not be matched to our population, but the indications for radiosurgery and follow-up are quite similar. To the best of our knowledge, a marked decrease in volume of meningiomas cannot be expected after radiosurgery, and this information has to be given to patients, to referring physicians and to radiologists who will interpret the follow up MR. This is in sharp contrast with the shrinking that is well documented after radiosurgery of another extra-axial benign slow growing tumour, the acoustic schwannoma [10].

Limitations of radiosurgery

The precise definition of the target may be one limitation, particularly with en-plaque clivus meningiomas, or tentorium and tentorial edge extensions of the tumour. Sometimes, the main bulk of the meningioma is compatible with radiosurgical treatment but pathological contrast enhancement along the free edge of the tentorium cannot be totally included in the target and hence limits long term tumour control. Brain stem mass effect and encasement of basilar perforators are also important considerations. In the current series, we observed brain stem injuries. Theoretically, radiosurgery delivered at conventional doses, does not occlude normal vessels and it is possible to postulate that vessels encased in the meningioma were already affected before treatment. Nevertheless our experience demonstrates clearly that there is a risk of microvascular ischemia when treating skull base meningiomas by radiosurgery. These complications have occurred in the very early period of our experience and we believe that our personal learning curve and the availability of technical refinements with the use of the Gamma Plan workstation for dose planning and fused CT and MR imaging have contributed to avoiding such events subsequently. This finding is in keeping with the results which have been reported in the study from Subach *et al.* [14].

Indications of radiosurgery (Table 2)

Gamma knife radiosurgery after surgery. There is a lot of supportive evidence that large petroclival meningiomas should be resected using advanced skull base techniques. Less retraction of the brain, various angles of vision, early control of insertion and vascularization, and radical extirpation are the main advantages of these techniques [12, 13]. However, a most recent series [3] brings arguments to recommend adjunctive radiosurgery in cases of unextirpable residual tumours located in critical structures. We believe that close collaboration with the skull base surgeon in a situation of planned two staged strategy is an optimal way to treat difficult cases. Whether this radiosurgery has to be performed in the immediate postoperative period, or only with the proof of tumor growing after surgery remains a matter of debate.

Gamma knife radiosurgery as a primary treatment. Results from this and previous studies provide a strong argument for recommending Gamma knife radiosurgery as primary treatment for a small to medium sized petroclival meningioma. The patient can reasonably expect functional benefit, particularly when he initially presents with a cranial nerve deficit. Fifth and sixth nerve deficits can improve significantly after radiosurgery but

Table 2. *Current management of petroclival meningiomas: proposal for a general algorithm*

Age	Tumor size	Presentation	First therapeutic option	Following evaluation
Young	small tumour	no signs	conservative	growing tumour: GKS
		signs	GKS	
	large or brain stem compression		microsurgery (optimal radical resection or planned two-step strategy)	residual tumour – small: GKS – large: another surgery or radiotherapy (also if malignant)
Elderly	small		conservative	growing tumour: GKS
	large	no signs	conservative	growing tumour: Total suboptimal removal
		signs	microsurgery (total suboptimal removal)	residual tumour: – small: GKS – stereotactic radiotherapy if too large

GKS Gamma knife radiosurgery.

complete long lasting palsies are unlikely to benefit. We do not consider that a limit of 30-mm diameter, as stated by Subach *et al.* [14], is the only factor in deciding about radiosurgical treatment. In our experience, careful definition of the site of origin, and relationships to brainstem, vessels and perforators need to be taken into account. Thus, we observed axial injury in 2 patients after treatment of a mid-clivus meningioma which was displaying clear aggressiveness towards the pons and involving the basilar perforators.

Conclusion

Our observations indicate that radiosurgery is a safe and effective treatment for small to middle sized petroclival meningiomas. Therefore, it can be recommended as a primary treatment for these lesions, or as an adjuvant therapy for residual post-operative meningioma remaining after surgery of large tumours that require a combined strategy. Nevertheless, even when the tumour is less than 3 cm-diameter, and so "volume-compatible", stereotactic radiosurgery may not be suitable if the involvement of perforating arteries points to possible ischemic vascular complications.

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Comment

This paper presents a subset of the wide experience of the Marseille Gamma Knife unit. As they say, these petroclival meningiomas pose a great surgical challenge and, in the current climate of less aggressive neurosurgical management their results are going to be influential in the decision making process. It is reassuring that these, small and medium sized tumours can be controlled using a minimally invasive method. The authors are careful to point out that, in spite of this minimal invasion, the treatment carries risks both to the brain stem and to the eloquent vasculature of the region. I believe that their caution with those tumours where involvement of the perforating arteries raise the chance of late ischaemic complications is useful, even if radiological demonstration of such involvement may be very difficult in most cases.

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