Clinical Neurology and Neurosurgery 124 (2014) 123–126

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

# Surgery followed by radiosurgery: A deliberate valuable strategy in the treatment of intracranial meningioma

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ARTICLE INFO

*Article history:*
Received 19 March 2014
Received in revised form 23 June 2014
Accepted 29 June 2014
Available online 6 July 2014

*Keywords:*
Meningioma
Radiosurgery
Progression free survival
Combined treatment

ABSTRACT

*Objective:* The aim of our study is to show that surgery followed by Gamma Knife Radiosurgery is an effective and safe combined treatment for the control of intracranial meningiomas located close to critical structures.

*Materials and methods:* This retrospective study followed 31 patients with intracranial meningioma between 2005 and 2010. We included patients when initial therapeutic decision was deliberate subtotal surgical resection preparing a target for early postoperative GKR. Early MRI was performed to evaluate the tumor residual volume after surgical procedure. Annual MRI was performed to detect any tumor progression.

*Results:* The mean follow-up was 4.5 years. The mean margin dose was 14.5 Gy and the mean target volume was 2.4 $cm^3$. The mean progression free survival after combined treatment was 4.4 years in the irradiated target volume and 3.9 years on the limit or remotely of irradiated target volume. Of all patients, we recorded 5 tumor progressions after combined treatment, in-field in 1 case and out-of-field in 4 cases. All tumor progressions were high-grade meningiomas.

*Conclusion:* Surgery followed by radiosurgery is a safe and effective combined treatment for intracranial meningiomas. We recommend it in case of meningioma located close to critical structures for which it is safer to leave in place a tumor remnant to reduce morbidity.



## 1. Introduction

Intracranial meningiomas are usually benign tumors but sometimes they show histological aggressivity categorizing them into the grade 2 or 3 of WHO classification [1,2]. They may occur in various locations. Convexity meningiomas or parasagittal meningiomas are the most frequent [3]. Skull base meningiomas are rare but their treatment is more difficult because they frequently involve neurovascular structures, thus limiting the possibility of complete surgical complete resection [4]. However, the main treatment of meningiomas remains surgery but other therapeutic tools may have an adjuvant role to limit tumor progression. Radiotherapy is, for example, recommended after surgery for grade 2 or 3 meningiomas but the occurrence of cognitive disorders should be considered after this treatment, especially in elderly patients or patients with neurovascular diseases [5,6]. Gamma Knife Radiosurgery (GKR) is also an effective adjuvant treatment for meningiomas [7,8] associated with low morbidity [9]. The aim of our study is to show that surgery followed by GKR is an effective and safe combined treatment for intracranial meningiomas located close to critical structures in order to reduce the morbidity of surgical procedure.

## 2. Materials and methods

### 2.1. Population

This monocentric, retrospective and continuing series followed 31 patients with intracranial meningioma between 2005 and 2010 in Lille University Hospital. This study was approved by the local ethic committee and all patients gave their informed consent prior to their inclusion. We included patients in our series when initial therapeutic decision was a deliberate subtotal surgical resection preparing a target for early postoperative GKR. We excluded patients for whom a complete tumor resection was considered feasible by the surgeon. There were 8 men and 23 women. The mean

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http://dx.doi.org/10.1016/j.clineuro.2014.06.035
0303-8467/

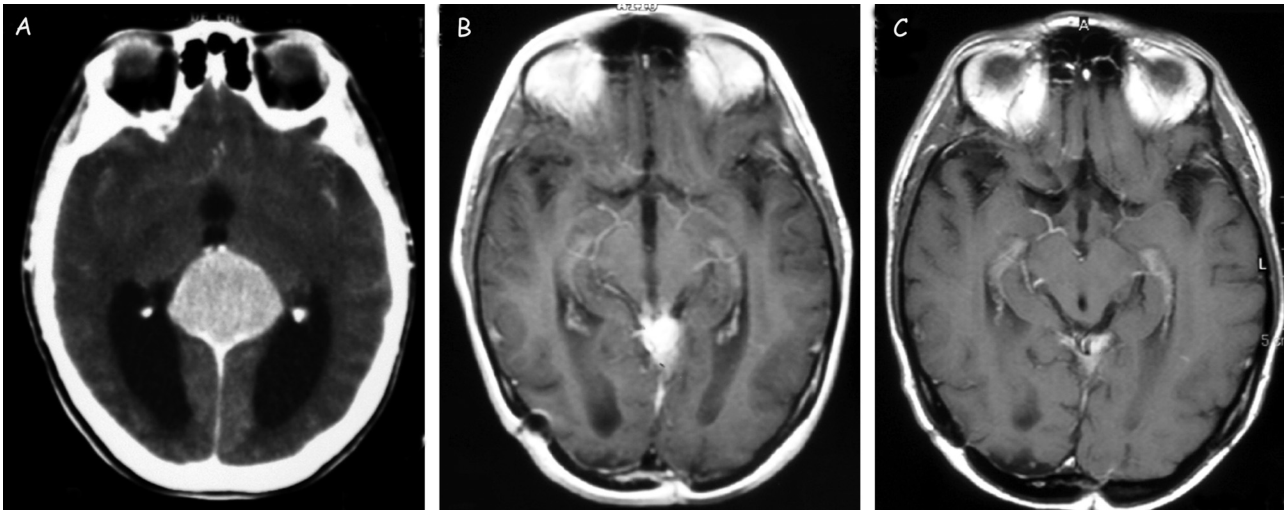


**Fig. 1.** Preoperative CT-scan (A) of a 45 year old woman who underwent the subtotal resection of a voluminous tentorial incisura meningioma. The postoperative MRI (B) confirmed residual tumor adherent to the Galen vein, which was treated by gamma knife radiosurgery. The MRI follow up (C) confirmed the tumor control at 8 years.

age at diagnosis was 51.7 years (range 30 to 78 years; SD: ±11) (Fig. 1, Table 1).

### 2.2. Surgical procedure

All patients underwent a deliberate subtotal resection (Simpson 4). The surgical procedure consisted on a retrosigmoid approach in 19 patients, a parasagittal craniotomy in 6 patients, a pterional craniotomy in 3 patients and a posterior fossa approach in 3 patients. No complication occurred during the procedure. The location of residual tumor was cavernous sinus in 10 cases, Meckel's cave in 9 cases, superior sagittal sinus in 6 cases, internal auditory canal in 3 cases, transverse sinus in 1 case, middle cerebral artery in 1 case and tentorial incisura in 1 case. The histology was grade 1 meningioma in 26 patients, grade 2 meningioma in 4 patients and grade 3 meningioma in 1 patient.

### 2.3. Radiosurgical procedure

As it was a deliberate strategy, radiosurgery was performed during the 3 postoperative months. All patients were treated under local anesthesia, with a unique dose using the Leksell-gamma knife.

**Table 1**
Main demographical data and summarize of treatment planning and follow-up (Rth: radiotherapy; Surg: surgery; GKR: radiosurgery).

| Patient | Sex | Age | Location | Grade | Dose (Gy) | Volume ($cm^3$) | Tumor control | Salvage therapy |
|---|---|---|---|---|---|---|---|---|
| 1 | 2 | 30 | CPA | 1 | 12 | 2.4 | 1 | |
| 2 | 2 | 69 | CPA | 1 | 15 | 3.3 | 1 | |
| 3 | 1 | 39 | SSS | 2 | 15 | 4.9 | 0 | GKR |
| 4 | 1 | 58 | SO | 3 | 21 | 1.1 | 0 | Surg + Rth |
| 5 | 1 | 39 | SSS | 1 | 15 | 1.1 | 1 | |
| 6 | 1 | 57 | SSS | 2 | 18 | 2.5 | 0* | Rth |
| 7 | 2 | 34 | CPA | 1 | 15 | 4.4 | 1 | |
| 8 | 2 | 59 | SSS | 1 | 15 | 1.5 | 1 | |
| 9 | 2 | 61 | CPA | 1 | 14 | 2.4 | 1 | |
| 10 | 1 | 58 | CPA | 1 | 14 | 1.4 | 1 | |
| 11 | 2 | 61 | CPA | 1 | 13 | 0.3 | 1 | |
| 12 | 1 | 54 | SSS | 1 | 14 | 7.4 | 1 | |
| 13 | 2 | 59 | CPA | 1 | 13 | 0.2 | 1 | |
| 14 | 1 | 40 | TI | 2 | 15 | 1.5 | 0 | GKR |
| 15 | 2 | 49 | CPA | 1 | 13 | 1.0 | 1 | |
| 16 | 2 | 65 | CPA | 1 | 15 | 0.2 | 1 | |
| 17 | 2 | 49 | CPA | 2 | 15 | 0.2 | 0 | Rth |
| 18 | 2 | 55 | CPA | 1 | 14 | 3.3 | 1 | |
| 19 | 2 | 65 | CPA | 1 | 14 | 2.5 | 1 | |
| 20 | 2 | 49 | CPA | 1 | 13 | 1.6 | 1 | |
| 21 | 2 | 37 | CPA | 1 | 15 | 0.3 | 1 | |
| 22 | 2 | 38 | CPA | 1 | 15 | 0.4 | 1 | |
| 23 | 2 | 70 | CS | 1 | 13 | 4.0 | 1 | |
| 24 | 2 | 63 | CPA | 1 | 15 | 0.2 | 1 | |
| 25 | 2 | 42 | TS | 1 | 15 | 2.5 | 1 | |
| 26 | 1 | 43 | CPA | 1 | 13 | 2.0 | 1 | |
| 27 | 2 | 43 | CPA | 1 | 14 | 1.7 | 1 | |
| 28 | 2 | 38 | SSS | 1 | 13 | 11.1 | 1 | |
| 29 | 2 | 51 | SF | 1 | 15 | 2.5 | 1 | |
| 30 | 2 | 50 | CPA | 1 | 14 | 3.5 | 1 | |
| 31 | 2 | 78 | TS | 1 | 15 | 1.6 | 1 | |

* Recurrence in the field of radiosurgery.
CPA: cerebello-pontine angle, SSS: superior sagittal sinus, SO: spheno-orbital, TI: tentorial incisura, CV: cavernous sinus, TS: transverse sinus, SF: sylvian fissure.

The dosimetry planning was based on multimodal imaging (MRI and CT-scan). The mean margin dose was 14.5 Grays (Gy) (range 12 to 21 Gy; SD: ±7.2). The mean target volume was 2.4 $cm^3$ (range 0.2 to 11.1 $cm^3$; SD: ±2.9). The mean dose was 13.9 Gy (range 12–15 Gy) for grade 1 meningioma, 15.75 Gy (range 15–18 Gy) for grade 2 meningioma and 21 Gy for the grade 3 meningioma.

### 2.4. Clinical and radiological follow-up

All patients had a clinical examination, before treatment, performed by a senior neurosurgeon in our institution. Clinical data were reported in the medical records. Early post operative MRI was performed to evaluate the tumor residual volume after surgical procedure. We recorded the age at diagnosis, the tumor location, the degree of surgical resection using Simpson classification [10] and the histology of all operated meningiomas using the WHO classification. For GKR procedure, we reported the residual tumor volume, the margin doses and all related complications.

The monitoring that consisted on a physical examination and a cranial MRI was scheduled at 3 months and then annually.

Tumor control was defined as a regression or stability in size over time. In contrary, tumor progression was defined as an increase of tumor size or regrowth after a transient regression.

## 3. Results

The mean follow-up was 4.5 years (range 2.1 to 9 years; SD: ±4.6) and all patients were still alive at the time of the study.

### 3.1. In-field tumor control

Concerning the irradiated target volume, a reduction in tumor size after radiosurgery was observed in 7 patients (22.5%), the tumor volume remained stable in 23 patients (74%) and a progression of the tumor volume was noted in only 1 patient. The mean period between this treatment and the tumor volume reduction was 3.6 years.

The mean progression free survival in the irradiated target volume was 4.4 years (range 2.1 to 9 years). Of all patients, we recorded only 1 tumor progression after combined treatment which histology was a grade 2 meningioma.

### 3.2. Out-of-field tumor control

Of all patients, we recorded 4 tumor progressions after combined treatment: 1 on the limit of irradiated target volume and 3 remotely. The histology was grade 2 meningioma in 3 cases and grade 3 meningioma in 1 case. No patient with grade 1 meningioma experienced recurrence at distance.

The mean progression free survival on the limit of irradiated target volume or remotely was 3.9 years (range 1.9 to 9 years).

### 3.3. Complications

After the surgical procedure, we reported 17 complications that occurred in 13 patients, 3 patients experienced 2 or 3 complications. These complications consisted on 3 trigeminal neuralgia, 5 diplopia (2 transient, 3 definitive), 6 facial nerve paralysis (4 transient, 2 definitive), 3 partial hearing loss. Thus, a total of 11 definitive complications were reported.

No fatal or life-threatening complication has been reported. No complication related to the Radiosurgical procedure has been noted.

### 3.4. Salvage therapy

The patient, who demonstrated a recurrence in the field of radiosurgery, underwent a conventional radiation therapy with a good tumor control at last follow-up.

Two patients with grade 2 meningioma harbored a delayed (17 and 24 months) and distant recurrence which was treated by a new radiosurgical procedure (15 Gy, 2.7 $cm^3$ and 15 Gy, 5.1 $cm^3$). One patient developed an early distant recurrence which required a conventional radiation therapy, with good tumor control. One patient with grade 3 meningioma developed a voluminous distant recurrence which required a new surgical resection followed by a conventional radiation therapy. Unfortunately, the tumor control was not efficient enough, and the patient died 29 months after the tumor recurrence.

## 4. Discussion

The strategy of deliberate incomplete surgical resection, leaving a small residual tumor involving critical structures, followed by GKR may reduce the morbidity of treatment without affecting tumor control.

Meningiomas are often histologically benign tumors [11] but their complete resection may be difficult because of their location. Incomplete resection increases the risk of tumor recurrence [12]. Nevertheless the goal of surgery is to remove as much of tumor as possible without taking vital or functional risk for the patient. The residual tumor can be controlled by other more appropriate therapeutic tools. In case of grade 2 or 3 meningiomas, adjuvant radiotherapy must be considered as a treatment option in oncological multidisciplinary discussion, regardless of the quality of resection [13,14]. Concerning grade 1 meningiomas, because of their slow growth, only radiological monitoring is often performed after incomplete resection, adjuvant radiotherapy is usually used when tumor recurrence is demonstrated [15,16]. Complete resection is, in most cases, performed for meningiomas of the convexity but rarely in case of parasagittal meningiomas or skull base meningioma [17]. The involvement of the superior sagittal sinus for parasagittal meningiomas and with the cavernous sinus, the Meckel's cave or the internal auditory canal for cerebellopontine angle meningiomas, makes complete resection dangerous. Our strategy is to perform a large resection of the tumor and then to perform GKR on the residual tumor located in the critical area. This surgical procedure is precisely defined for the neurosurgeon and for the patient in order to reduce morbidity.

GKR is a reliable technique, which has already demonstrated its effectiveness regarding tumor control of intracranial meningiomas. In Lee's series, the 10-year tumor control rate was 93% in patient with grade 1 meningioma and 72% in patient with high-grade meningioma [18]. The adverse effects of radiosurgery are rare according to data from the literature [19,20]. In our series, we noted only one case of transient increase of facial hypoesthesia after irradiation of residual tumor in the Meckel's cave. In our study, a long-term tumor control without tumor recurrence was recorded in all patients with grade 1 meningioma. The tumor recurrences were, in most cases, on the limit (1 case) or remotely (3 cases) of the irradiated target volume in patient with grade 2 or 3 meningiomas. These data has already been reported by others studies [21,22]. In Attias's study, among 24 patients with grade 2 meningioma who underwent radiosurgery, he found 4 tumor recurrences on the limit and 2 tumor recurrences remotely of the irradiated target volume [21]. In our series, we noted only 1 tumor recurrence in the irradiated target volume in a patient with grade 2 meningioma. In this case, the margin dose was only 15 Gy and we believe that this is an inadequate dose for the treatment of high-grade meningiomas. A higher dose, close to 20 Gy, is recommended for grade 2 meningiomas [21,23]. In our series, tumor recurrence remotely from the irradiated target volume could be explained by the absence at the time of adjuvant radiotherapy in patients with grade 2 meningiomas. Committees of Neuro-Oncology now propose to carry out external radiotherapy at an early stage in patients with grade 2 or 3 meningiomas [5]. We recommend performing an early postoperative GKR for patients with grade 1 meningioma when surgical resection is incomplete. Patients with high-grade meningioma should be treated with early postoperative radiotherapy. The combination of surgery with radiosurgery has been used by other neurosurgical teams for the treatment of intracranial meningiomas located on the skull base [17,24,25] but in our study we defined, as some other authors [26], this strategy before surgery. In our study, the tumor volume reduction was noted in 7 patients (22.5%) after surgery followed by GKR, while it was only noted in 13.9% of patients in Davidson's series [17]. This difference in results could be related to the longer follow-up and to the location of meningiomas only on the cranial base in his study. Moreover, in Davidson's series, the GKR was sometimes performed for tumor recurrence after numerous surgical procedures. In our series, the Gamma Knife surgery was performed early after the first surgical resection and only 19 patients out of 31 presented with cranial base meningiomas. The target volume of these meningiomas is more difficult to define because of their invasive nature and their proximity to the neurovascular structures. However, tumor recurrence appears to be related to histological grade and not to the location of the tumor in our study. Several studies have shown tumor progression regarding untreated meningiomas and remnants of meningiomas for which monitoring was decided. We believe it is better to perform an early GKR after surgical resection to prevent tumor progression in order to improve the effectiveness of postoperative radiosurgery. A larger tumor volume and a more diffuse tumor infiltration of eloquent structures reduce the effectiveness of radiosurgery on tumor control [22]. Moreover Girvigian demonstrated that large tumor volume in patients undergoing radiosurgery was associated with onset of post-treatment symptomatic peritumoral edema [19]. Our results should be carefully interpreted because of the low number of patients and the short mean follow-up.

## 5. Conclusion

Surgery followed by radiosurgery is a safe and effective combined treatment for intracranial meningiomas. We recommend it in case of grade 1 meningioma located close to critical structures for which it is safer to leave in place a tumor residual in order to reduce morbidity. For high-grade meningiomas, conventional radiotherapy should be discussed.

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