Surgical management of giant sphenoid wing meningiomas encasing major cerebral arteries

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OBJECTIVE Sphenoid wing meningiomas are a heterogeneous group of tumors with variable surgical risks and prognosis. Those that have grown to a very large size, encasing the major cerebral arteries, are associated with a high risk of stroke. In reviewing the authors’ series of giant sphenoid wing meningiomas, the goal was to evaluate how the extent of the tumor’s invasion of surrounding structures affected the ability to safely remove the tumor and restore function.

METHODS The authors conducted a retrospective study of a series of giant sphenoid wing meningiomas operated on between 1996 and 2016. Inclusion criteria were meningiomas with a globoid component ≥ 6 cm, encasing at least 1 major intradural cerebral artery. Extent of resection was measured according to Simpson grade.

RESULTS This series included 12 patients, with a mean age of 59 years. Visual symptoms were the most common clinical presentation. There was complete or partial encasement of all 3 major cerebral arteries except for 3 cases in which only the anterior cerebral artery was not involved. The lateral wall of the cavernous sinus was invaded in 8 cases (67%) and the optic canal in 6 (50%). Complete resection was achieved in 2 cases (Simpson grades 2 and 3). In the remaining 10 cases of partial resection (Simpson grade 4), radical removal (> 90%) was achieved in 7 cases (70%). In the immediate postoperative period, there were no deaths. Four of 9 patients with visual deficits improved, while the 5 others remained unchanged. Two patients experienced transient neurological deficits. Other than an asymptomatic lacuna of the internal capsule, there were no ischemic lesions following surgery. Tumor recurrence occurred in 5 patients, between 24 and 168 months (mean 61 months) following surgery.

CONCLUSIONS Although these giant lesions encasing major cerebral arteries are particularly treacherous for surgery, this series demonstrates that it is possible to safely achieve radical removal and at times even gross-total resection. However, the risk of recurrence remains high and larger studies are needed to see if and how improvement can be achieved, whether in surgical technique or technological advances, and by determining the timing and modality of adjuvant radiation therapy.

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KEYWORDS giant meningioma; vascular encasement; sphenoid wing; surgical management; cavernous sinus
widest diameter, arising along the sphenoid wing with
encasement of at least 1 major cerebral artery: the supra-
clinoïd internal carotid artery (ICA), the middle cerebral
artery (MCA), and/or the anterior cerebral artery (ACA).
We define encasement to be when at least a portion of the
length of the artery is surrounded by the tumor, either par-
tially, by at least 180° (50%) of its circumference, or com-
pletely, as noted on preoperative MRI using magnetiza-
tion-prepared rapid acquisition gradient-echo (MPRAGE)
and/or thin-slice T2-weighted sequences. The extent of
encasement was categorized into 3 approximations: 50%,
75%, and 100%. We excluded meningiomas arising from
the olfactory groove, petroclival meningiomas, and menin-
giomas arising from the cavernous sinus (CS).

Data Collection
Data were collected from the patient’s medical file, the
operative report, and the specimen’s pathology report.
Data collection focused on preoperative symptoms, imag-
ery, surgical technique, immediate postoperative clinical
neurological status, and time span before recurrence. Pre-
and postoperative imaging was reviewed and correlated
with intraoperative findings. We particularly looked for
invasion of the CS or of the optic canal (OC), brain tis-
sue edema, and encasement of the major cerebral arteries.
Extent of resection was determined according to Simpson
grade and postoperative images. Data were compiled in an
electronic database and cross-checked for accuracy mul-
tiple times during collection. Our study was approved by
our institution’s ethics committee.

Surgical Technique
The goal of the surgical management of any giant sphe-
noidal meningioma is its complete resection, while obvi-
ously preserving surrounding neurovascular structures
and their function. In cases in which complete resection
poses a great risk of injury to neurovascular structures, the
goal is the maximum safe removal of the tumor, which re-
quires constant intraoperative surgical analysis and judg-
ment. Because important structures are embedded within
these giant tumors and since the brain is compressed by
them, wide exposure is required. This minimizes brain re-
traction and allows early recognition of normal structures
before proceeding with tumor resection. In our series, all
patients were operated on via a pterional approach; an or-
bitozygomatic variant was not required. However, to push
the temporal muscle away from the line of sight, inter-
fascial muscular dissection was performed to expose the
lateral orbit and the horizontal segment of the zygomatic
bone, and to retract the temporal muscle posteroinferiorly.
The sphenoid wing is drilled to reach at least the superior
orbital fissure.

Upon opening the dura, to minimize brain retraction,
dissection begins with a wide opening of the sylvian fış-
sure. Dissection proceeds from the distal part of the fis-
sure to its proximal part, because proximal normal arterial
intradural blood vessels, hidden by the tumor, cannot be
seen. The goal at this point is to identify branches of the
MCA, just distal to the tumor. The tumor is resected little
by little, alternately debulking and pursuing extracapsu-
lar dissection to progressively expose the entire proximal
MCA and its perforators, then the ICA bifurcation, and
ultimately the entire intradural ICA and the optic nerves
(ONs), while preserving the arachnoid plane. Dissection
of the skull base meningiomas, when judged necessary, ex-
posure of the extradural ICA by removing the anterior clinoid process and the
opening of the OC were performed late in the surgery,
ultimately, to prevent the tumor from filling the empty space thus
created. In our series, despite some cases with a well-
vascularized tumor, preoperative embolization was not
necessary, nor was it necessary intraoperatively to initiate
with devascularization of these large tumors at the base
of the skull.

Results

Patient Population
From 1996 to 2016, a total of 680 various meningio-

mas, most of them skull base meningiomas, were surgically
removed by the senior author (M.W.B.). Among them,
12 patients qualified for the selection criteria of this study.
Of these 12 patients, 10 were women and 2 were men, with
a mean overall age of 59 years (Table 1). Visual symp-
toms were the most common at presentation, affecting 9
patients (75%). Of these 9 patients, 4 presented with visual
field defects and the other 5 with visual acuity disturbance.
Headache was a common symptom at presentation (6 pa-
tients, 50%). Cognitive impairment with memory deficit
was present in 6 patients (50%). Motor symptoms in the
form of contralateral hemiparesis were found in 4 patients
(33%). Extraocular movement disturbances were found in
2 patients (17%), one with third cranial nerve palsy and the
other with sixth cranial nerve palsy. One patient presented
with mixed aphasia (Table 2).

Tumor Characteristics
All 12 patients underwent MRI, which included
MPRAGE and/or thin-slice T2-weighted sequences, which in our experience offer images allowing for a bet-
ter assessment of vessel encasement than MR angiography
or CT angiography can provide. In our series, 3 patients
underwent digital subtraction angiography (DSA) preop-
eratively, only 1 patient underwent MR angiography, and
none of the 12 patients had a CT angiogram.

Mean tumor size at its widest diameter was 6.6 cm
(range 6–8 cm). The tumor was on the left side in 8 cases

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(67%) and on the right in 4 cases (33%). Because of their huge size, and based on preoperative MRI and intraoperative findings, all except 1 of the meningiomas were assumed to originate from the middle segment of the sphenoid wing, just lateral to the anterior clinoid process; the exceptional case originated from the more external part. Complete encasement of the ICA was present in all cases. Complete encasement (100%) of the MCA was present in 9 cases, 75% encasement in 1 case, and 50% encasement in 2 cases. Complete encasement of the ACA was present in 6 cases, 75% in 1 case, 50% in 2 cases, and the ACA was not encased at all by the tumor in 3 cases. No luminal narrowing was observed in our series. CS involvement was present in 8 cases (67%) and the tumor extended into the OC in 6 cases (50%). The ON was medially pushed by the meningioma most of the time (8 cases), and more rarely the tumor completely encased the ON (3 cases). In 1 case, the ON was pushed upward. Two tumors were highly calcified. Peritumoral edema assessed on preoperative MRI was severe in 4 cases, moderate in 2 cases, mild in 3 cases, and absent in 3 cases. Ten tumors were WHO grade I, and 2 were grade II (Tables 1 and 3).

Surgical Treatment

None of our cases underwent embolization prior to surgery. All tumors were approached via a pterional craniotomy; an orbitozygomatic variant was not necessary in this series. Three tumors were found to be very hemorrhagic during resection (Table 4). Tumor consistency was found to be fibrous in 5 cases and soft in 7. Complete macroscopic resection was achieved in 2 cases (1 Simpson grade 3 and 1 Simpson grade 2). The remaining 10 cases were left with residual tumor (Simpson grade 4): 90% or more of the tumor was resected in 7 of them (Figs. 2 and 3), 80% resected in 1 case, and 70% or less in 2 cases. Tumor rem-
nants were located on a main cerebral artery in 5 cases, in the CS in 3 cases, and along the lesser sphenoid wing in 1 case. In the 2 cases in which less than 70% of the tumor was resected, resection was limited by extensive calcification in 1 case and by the patient’s inability to undergo subsequent surgery in the other, due to a preexisting clinical condition. Two cases necessitated 2 surgical sessions (Table 4).

Postoperative Outcome
In the immediate postoperative period, 2 patients had a new deficit: mixed aphasia in 1 case (case 5) and hemiparesis in the other (case 2; Table 2), with both deficits being transient and due to postoperative edema. Another patient (case 1) became hemiparetic due to significant brain edema requiring bone flap removal. This patient recovered in 10 days. Four patients remained neurologically unchanged from their preoperative state, while 5 others improved: 4 patients who had had visual symptoms and 1 patient who had had hemiparesis. The mean follow-up duration after surgery was 61 months (range 3–252 months). At the last follow-up evaluation, 6 patients were in a stable unchanged neurological state, 2 had progressive deficits, 3 were continuing to improve, and 1 died 2 years later due to progression of residual tumor in which less than 70% of the tumor had been removed (Table 4).

Postoperative Imaging
Clinically significant edema occurred in 3 patients, and all completely recovered. None of the cases had a hemorrhagic complication, as noted on the CT scan obtained routinely on postoperative day 1. In 1 case, the CT scan revealed an ischemic lacuna in the posterior arm of the internal capsule, later confirmed on MRI. This lacunar infarct was fortunately asymptomatic. There was no other ischemic injury in our series (Table 4).

Tumor Recurrence
Five cases (42%) experienced either a recurrence or progression of the residual tumor, with a mean time for recurrence of 61 months. The 7 others were stable at a mean follow-up of 30 months. The origin of recurrence was the site of the residual tumor in all but 1 case, in which recurrence occurred on the MCA following gross-total removal. Of those 5 tumors that progressed or recurred, 1 was treated with radiotherapy alone, 1 was treated with surgery alone, 2 were treated with both surgery and radiotherapy, and 1 was closely observed with no further treatment (Table 4).

Discussion
Giant sphenoid wing meningiomas (≥ 6 cm) encasing major cerebral arteries pose a great technical challenge in their surgical management. Because of their size and their mass effect, there is no question as to whether to proceed with surgery; the real challenge is during surgery. Their huge size engulfs surrounding vital structures, obscuring them from view. Moreover, at times the tumor adheres to these structures, making it very risky to remove it.2,18,23

Although such meningiomas may originate anywhere along the sphenoidal wing, in our series most of them originated from its intermediate segment just lateral to the anterior clinoid process, extending predominantly superiorly and laterally. Had they extended medially, visual symptoms would have prompted earlier diagnosis prior to the tumor having grown to such a large size. In our series, in 8 cases the tumor had invaded the lateral wall of the CS, and in 6 of these 8 cases the OC was also invaded. It is interesting to note that whenever the tumor had infiltrated the OC, the CS was also involved, but not inversely. This would also suggest that to reach such a large size before diagnosis, these tumors originating from the lateral side of the clinoid process first reached the CS, spreading then to the OC as they grew. Another reason why these meningiomas may reach such a huge size before diagnosis—other than the fact that they are slow growing—is that there is often no associated brain edema. In fact, in our series, despite the size of the lesions, 6 of 12 cases had no significant preoperative brain swelling.

### TABLE 1. Demographic data, tumor size, localization, and relationship with intracranial arteries and other structures

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Tumor Size (cm)</th>
<th>Tumor Side</th>
<th>Involved Vessel (% encasement)</th>
<th>Other Involved Structures</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57, F</td>
<td>6</td>
<td>Lt</td>
<td>ICA 100, MCA 100, ACA 100</td>
<td>CS, OC</td>
</tr>
<tr>
<td>2</td>
<td>66, F</td>
<td>6.5</td>
<td>Rt</td>
<td>ICA 100, MCA 100, ACA 100</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>51, F</td>
<td>7.4</td>
<td>Lt</td>
<td>ICA 100, MCA 100, ACA 75</td>
<td>CS, OC, ON (encased)</td>
</tr>
<tr>
<td>4</td>
<td>66, F</td>
<td>6.6</td>
<td>Rt</td>
<td>ICA 100, MCA 0, ACA 0</td>
<td>CS, OC</td>
</tr>
<tr>
<td>5</td>
<td>69, F</td>
<td>6</td>
<td>Lt</td>
<td>ICA 100, MCA 100, ACA 100</td>
<td>CS</td>
</tr>
<tr>
<td>6</td>
<td>68, M</td>
<td>8</td>
<td>Rt</td>
<td>ICA 100, MCA 75, ACA 50</td>
<td>CS</td>
</tr>
<tr>
<td>7</td>
<td>61, F</td>
<td>7</td>
<td>Lt</td>
<td>ICA 100, MCA 50, ACA 0</td>
<td>—</td>
</tr>
<tr>
<td>8</td>
<td>79, F</td>
<td>6</td>
<td>Rt</td>
<td>ICA 100, MCA 50, ACA 0</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>68, F</td>
<td>6</td>
<td>Lt</td>
<td>ICA 100, MCA 100, ACA 100</td>
<td>CS, OC</td>
</tr>
<tr>
<td>10</td>
<td>45, M</td>
<td>6.5</td>
<td>Lt</td>
<td>ICA 100, MCA 100, ACA 100</td>
<td>CS, OC, ON (encased)</td>
</tr>
<tr>
<td>11</td>
<td>49, F</td>
<td>6.5</td>
<td>Lt</td>
<td>ICA 100, MCA 100, ACA 100</td>
<td>CS, OC, ON (encased)</td>
</tr>
<tr>
<td>12</td>
<td>26, F</td>
<td>6</td>
<td>Lt</td>
<td>ICA 100, MCA 100, ACA 100</td>
<td>—</td>
</tr>
</tbody>
</table>
Not surprisingly, the main clinical manifestation was visual deficit. This visual deficit was not only related to the invasion of the OC, but also due to the increased intracranial pressure caused by the size of the tumor and sometimes also due to brain edema. In addition, the mass effect and the elevated intracranial pressure produced cognitive dysfunction in half of our patients, symptoms seen more rarely in meningiomas from the middle segment of the sphenoid ridge, such as tuberculum sellae meningiomas.3,26 These symptoms may at times reach such a severe level that even following partial resection there is no improvement whatsoever, and consequently a second surgical session would be deemed ineffectual, as was the case in 2 of our patients (cases 2 and 3).

One worrisome aspect of the surgery in detaching the tumor from the main arteries is the extent to which they are encased.16,18,22,23,25,31 In all 12 of our cases, the ICA was completely encased. The MCA was also encased in all 12 cases, in 9 of them completely and in the 3 others partially. Only in 3 cases was the ACA not encased; thus, in 9 of 12 cases parts of all 3 main arteries were completely encased. It is interesting to note that whenever the ACA was encased, the MCA was always encased, if not completely, then partially. This information helps to anticipate technical difficulties in dissecting the tumor from these vessels and their perforators. However, as reported by other authors, and as noted in our series, no imaging criteria could predict which tumor is adherent enough to the major arteries precluding its safe complete resection.6,18 For the 3 patients who had had DSA, there was no correlation between preoperative imaging of the degree of tumor vascularization or the degree to which major cerebral vessels were stretched and the level of difficulty encountered intraoperatively. As is the case for smaller lesions engulfing the arteries, it is only during surgery, following maximal debulking of the tumor, that one can assess if the tumor can be safely detached from the artery. In our series, no luminal narrowing was observed; when present, this characteristic may be potentially associated with a higher surgical risk.

Despite the extent of tumor encasement of the vessels and the invasion of the lateral wall of the CS, radical removal was possible in 9 (75%) of the 12 cases, i.e., more than 90% of the tumor was removed; in 2 of these 9 cases, gross-total removal was achieved. Two cases required 2 surgical sessions, and in 1 gross-total removal was achieved. Table 4 lists the site of residual tumor in each case.
case. Of note, in 50% of the cases with a tumor remnant, the remnant was on a main artery; in our series, the main anatomical characteristic preventing gross-total removal of these giant meningiomas was the extent to which they adhered to the main cerebral blood vessels and their perforators. Yet, despite the extent of resection, there was no stroke in any of the 12 cases other than an asymptomatic lacuna involving the posterior limb of the internal capsule in 1 case, as revealed on postoperative MRI. This is likely because when a tumor is firmly attached to the vessels and difficult to remove, we do not hesitate to leave a remnant, although efforts are made to leave as little tumor as pos-

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Tumor Consistency</th>
<th>Extent of Resection (%)</th>
<th>Simpson Grade</th>
<th>Location of Tumor Remnant</th>
<th>Postop Ischemia or Hemorrhage</th>
<th>Time Before Recurrence (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fibrous</td>
<td>95</td>
<td>4</td>
<td>CS</td>
<td>Internal capsule lacuna</td>
<td>24</td>
</tr>
<tr>
<td>2</td>
<td>Soft, hemorrhagic</td>
<td>70</td>
<td>4</td>
<td>Sphenoid wing</td>
<td>None</td>
<td>24</td>
</tr>
<tr>
<td>3</td>
<td>Fibrous, calcified, hemorrhagic</td>
<td>&gt;50</td>
<td>4</td>
<td>Sphenoid wing</td>
<td>None</td>
<td>36 (stable)</td>
</tr>
<tr>
<td>4</td>
<td>Soft</td>
<td>&gt;90</td>
<td>4</td>
<td>MCA</td>
<td>None</td>
<td>3 (stable)</td>
</tr>
<tr>
<td>5</td>
<td>Soft, hemorrhagic</td>
<td>80</td>
<td>4</td>
<td>MCA</td>
<td>None</td>
<td>48 (stable)</td>
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<tr>
<td>6</td>
<td>Soft</td>
<td>&gt;90</td>
<td>4</td>
<td>MCA</td>
<td>None</td>
<td>4 (stable)</td>
</tr>
<tr>
<td>7</td>
<td>Fibrous</td>
<td>&gt;90</td>
<td>4</td>
<td>MCA</td>
<td>None</td>
<td>3 (stable)</td>
</tr>
<tr>
<td>8</td>
<td>Soft</td>
<td>&gt;95</td>
<td>4</td>
<td>Sphenoid wing</td>
<td>None</td>
<td>60 (stable)</td>
</tr>
<tr>
<td>9</td>
<td>Soft</td>
<td>&gt;90</td>
<td>4</td>
<td>MCA, CS</td>
<td>None</td>
<td>42</td>
</tr>
<tr>
<td>10</td>
<td>Fibrous, very calcified</td>
<td>GTR</td>
<td>2</td>
<td>—</td>
<td>None</td>
<td>60 (stable)</td>
</tr>
<tr>
<td>11</td>
<td>Fibrous</td>
<td>&gt;95</td>
<td>4</td>
<td>CS</td>
<td>None</td>
<td>48</td>
</tr>
<tr>
<td>12</td>
<td>Soft</td>
<td>GTR</td>
<td>3</td>
<td>—</td>
<td>None</td>
<td>168</td>
</tr>
</tbody>
</table>

GTR = gross-total resection.
All patients underwent a pterional approach.

**FIG. 2.** Case 9. **Upper row:** Preoperative T1-weighted MR images with Gd showing a left sphenoid wing meningioma completely encasing the ICA, MCA, and ACA. **Lower row:** Postoperative contrast-enhanced CT scan showing residual tumor along the left CS and left proximal MCA (arrows).
sible. A significant rate of surgical complications has been reported with meningioma encasing major cerebral vessels.\(^4,6,18\) However, with a prudent approach using modern surgical techniques, the risk of arterial injuries is reported to be low.\(^5,10,15,30\)

In our series, the second main anatomical characteristic preventing gross-total removal is CS invasion. Our tumoral resection was limited to outer-layer dura propria of the external wall of the lateral CS. Even today with modern microsurgical techniques, resection of meningio-

FIG. 3. Case 11. **A:** Preoperative angiogram of the left ICA showing a tumoral vascular blush and stretching of the left MCA. **B:** Preoperative T1-weighted MR image with Gd showing a meningioma of the left sphenoid wing completely encasing the ICA, MCA, and ACA. **C:** Postoperative contrast-enhanced CT scan showing residual tumor along the left CS (arrow).

FIG. 4. Case 2. **Upper row:** Preoperative T1-weighted MR images with Gd showing a right-sided sphenoid wing meningioma completely encasing the ICA, MCA, and ACA. **Lower row:** Postoperative T1-weighted MR images with Gd showing partial removal of the tumor with significant residual tumor.
mas involving the CS is associated with high morbidity regardless of the size of the entire tumor. When resection is contemplated, it is most often limited to the lateral compartment of the CS, followed by observation, or radiation therapy for symptomatic patients in order to reduce the rate of morbidity. 

Although theoretically certain physical characteristics of the tumors, such as their hard or soft texture, the extent of their calcification, and/or the degree to which they are vascularized, would not prevent gross-total removal, they are nonetheless factors in determining whether more than 1 surgical session would be required. Obviously, highly calcified lesions (such as in case 10) or highly vascularized ones require more time for resection, and sometimes may not be completed in 1 session. The patient’s clinical condition may determine whether he or she is suitable for multiple surgeries. In fact, this was so in 2 of our cases, resulting in only partial resection because a subsequent surgery was not recommended (cases 2 [Fig. 4] and 3).

During the immediate postoperative period, in all 12 cases there were no permanent neurological complications; 2 experienced a new neurological deficit in terms of mild transient aphasia and hemiparesis, which lasted less than 10 days. There was substantial improvement of vision within the first week in 4 patients, whereas in 4 other patients the neurological state remained unchanged. In addition, as previously noted, despite the encasement of the major cerebral arteries and the extent of resection, there was no stroke in any of the 12 cases other than an asymptomatic lacuna involving the posterior limb of the internal capsule in 1 case. Obviously, resection of these giant sphenoidal meningiomas encasing major cerebral arteries allows adjuvant radiation therapy, which would be otherwise inappropriate in most, if not all, cases.

In our series, despite the fact that 9 of 12 cases underwent radical tumor removal, the rate of recurrence was significant. This is mainly due to the extent to which the tumor adhered to the arteries. These results do not support the hypothesis that leaving small amounts of tumor has little impact, or that many of the tumor remnants undergo growth arrest and remain dormant.

Follow-up data of at least 2 years are available in only 9 of our 12 cases and revealed tumor recurrence in 5 of these 9 patients; in 4 of them, recurrence was at the site of the tumor remnant, and in 1 in whom gross-total removal had been achieved, recurrence was on the MCA. Because the degree of resection in most of our cases was Simpson grade 4, one would expect the rate of recurrence to be high, emphasizing the need for long follow-up durations.

Radiation therapy is indicated after partial resection and in cases of tumor recurrence. However, recent studies assessing volume rather than diameter of residual tumor have demonstrated a significant recurrence in a short time span following radiation therapy. We must insist on the importance of aiming to remove as much of the tumor as possible when complete resection is not possible. Freeing the optic pathways should be a main goal. Determining how much or how little of the tumor to resect in cases when complete resection is not suitable is certainly one of the main challenges in the surgical management of these giant meningiomas, and requires surgical judgment and experience. Intraoperatively assessing the amount of tumor that has been removed is not always obvious, and it can be frustrating to note on postoperative MRI how much more of the tumor could have been removed. The use of intraoperative MRI or CT can certainly improve discerning how much more of the tumor can be safely removed.

Conclusions

Long-term prognosis for these giant sphenoid wing meningiomas is obviously related to the amount of resection. Although these giant lesions encasing major cerebral arteries are particularly treacherous for surgery, our series, albeit small, demonstrates that it is indeed possible to safely achieve radical removal and at times even gross-total resection. However, the risk of recurrence remains high and constant surveillance is required. Larger studies are needed to see if and how improvement can be achieved in surgical technique or technological advances, and by determining the timing and modality of adjuvant radiation therapy.

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Author Contributions
Conception and design: Bojanowski. Acquisition of data: all authors. Analysis and interpretation of data: Bojanowski, Champagne. Drafting the article: all authors. Critically revising the article: Bojanowski. Reviewed submitted version of manuscript: Bojanowski. Approved the final version of the manuscript on behalf of all authors: Bojanowski. Administrative/technical/material support: Bojanowski. Study supervision: Bojanowski.

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