Hemangiopericytomas of the skull base

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Object. Intracranial hemangiopericytomas are frequently located along the dural sinuses along the skull base and represent rare, aggressive CNS neoplasms that are difficult to distinguish from meningiomas based on both imaging and gross characteristics. The authors of this study describe 3 patients with these lesions and review the pertinent literature.

Methods. Two men and 1 woman, whose median age at the time of the initial presentation was 37 years (range 20–53 years), constitute this series. They underwent multimodal treatment consisting of resection, embolization, radiation therapy, and in 1 case chemotherapy.

Results. Two of the 3 patients treated were alive after a mean follow-up of 93 months (range 4–217 months). One patient died 217 months after the initial diagnosis. The longest tumor progression–free interval after the initial or secondary resection was 43 months (range 4–84 months).

Conclusions. Hemangiopericytomas have been reclassified as mesenchymal nonmeningothelial tumors. They have an inevitable tendency to recur locally and metastasize distally. The mainstay of therapy remains an aggressive attempt to achieve gross-total resection at the initial surgery. Postoperative adjuvant radiotherapy should be offered to all patients, regardless of the degree of resection achieved. Diligent long-term follow-up is paramount as local recurrences and distal metastases can develop sometimes years after the initial treatment.

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KEY WORDS • hemangiopericytoma • skull base • stereotactic radiosurgery

Primary meningeal HPCs are rare, aggressive, dura-based tumors thought to originate from Zimmermann pericytes, which are contractile spindle cells surrounding capillaries and postcapillary venules. These tumors are composed of spindle cells with a rich vascular network, which apparently arises from pericytes, cells of smooth muscle origin that lie around small vessels. The clinical, radiographic, and gross characteristics of these lesions often render them indistinguishable from meningiomas. Such characteristics contributed to their early misclassification by Cushing and Eisenhardt as an angioblastic variant of meningioma. Benign and malignant HPCs exist, and the rarity of these lesions in general has led to considerable confusion in distinguishing between the benign and malignant variants.

In 1954 Begg and Garret reported on the first documented case of a primary intracranial HPC, but meningeal HPCs were not classified as a distinct entity by the WHO until 1993, despite their demonstration of a unique immunohistochemical profile. Observing that peripheral soft-tissue tumors share histopathological features identical with meningeal HPCs ultimately led to the latter’s more accurate classification as “mesenchymal nonmeningothelial tumors,” which can arise from multiple organ systems. Moreover, the long-term biological and/or clinical behavior of an HPC differs from that of a meningioma, with its local recurrence rates as high as 91% and a 15-year risk of distant metastasis approaching 70% after surgery alone.

We describe 3 patients with HPCs of the skull base. Neurosurgeons have treated these lesions as meningioma variants for a long time, and certain commonalities in their surgical management apply. Hemangiopericytomas have an aggressive nature, and a different philosophy is used in their optimal treatment. Thus, it is imperative that the surgeon include HPC as part of the differential diagnosis when evaluating patients with dura-based extraaxial lesions of the skull base.

Methods

From the senior author’s (C.B.H.) prospectively maintained database, we found 3 cases of skull base HPCs. The 2 men and 1 woman in these cases had a median age of 37 years (range 20–53 years) at the time of their initial presentations. None of these patients has been reported on previously.
Two patients had previously undergone resection and had neuropathological confirmation of the diagnosis, whereas 1 patient (Case 3) was a new presentation (Fig. 1). The average number of craniotomies per patient was 2 (range 1–3). Two additional craniotomies were performed for tumor recurrence. Endovascular embolization was used twice (Cases 1 and 3; Fig. 1C–E). In 1 patient (Case 2) a diagnostic angiogram did not reveal a suitable embolization target.

One patient (Case 1) received chemotherapy concurrent with fractionated radiotherapy, 1 patient underwent Gamma Knife surgery after a secondary resection, and 1 patient underwent fractionated radiotherapy after the initial resection. Two patients had intracranial recurrences adjacent to the initial resection site; the most recent recurrence in the patient in Case 1 was unresectable (Table 1). Variations in the presenting symptoms correlated with the location of the lesion in this series of cases.

On follow-up, patients were monitored for changes in their neurological condition and the development of recurrent tumors or metastases. Follow-up neurological assessments were performed at our institution by the senior author (C.B.H.). Follow-up imaging was typically performed 6 months after the initial treatment. After obtaining a number of unchanged scans in any patient, the interval between imaging studies was extended slightly, up to yearly intervals. Clinical evaluations were performed around the time of scheduled follow-up imaging assessments.

Results

Two of the 3 patients treated in this series remained alive after a mean follow-up of 93 months (range 4–181 months; Table 1). The patient in Case 1 was last seen by us 181 months after surgery, and then she was monitored by local physicians, for a total follow-up of 217 months before she ultimately succumbed to her disease. The follow-up interval was approximately 5 years in another patient (Case 2). Before presenting to us with a recurrence, 1 patient (Case 2) suffered from homonymous hemianopia after an initial resection (Fig. 2). A hemorrhage from residual tumor in the surrounding occipital lobe caused a clinical deterioration with complete loss of vision. After decompression and resection, the patient was able to recover some useful vision. In the patient in Case 1 right trigeminal neuropathy

![Fig. 1. Case 3. Preoperative axial (A) and sagittal (B) post-Gd T1-weighted MR images demonstrating a homogeneously enhancing lesion near the right transverse sinus, extending into the supratentorial space and the posterior fossa. Selective right vertebral artery injection angiogram (C), posterior-anterior projection, demonstrating tumor blush with feeders from the superior cerebellar artery and anterior inferior cerebellar artery enhancing the posterior fossa component of the tumor. External carotid artery injection angiogram (D), posterior-anterior projection, showing feeders and tumor blush from the occipital artery. External carotid artery angiogram (E), lateral projection, demonstrating the liquid embolic material used to embolize feeders arising from the occipital artery.](image-url)
Skull base hemangiopericytoma

TABLE 1: Summary of demographic and clinical data in 3 patients with HPCs*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (yrs)</td>
<td>20</td>
<td>53</td>
<td>39</td>
</tr>
<tr>
<td>sex</td>
<td>F</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>initial clinical presentation</td>
<td>headaches, nausea, vomiting, visual field defect, seizures (lt arm)</td>
<td>altered mental status, rt visual field defect</td>
<td>dizziness, disequilibrium</td>
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<tr>
<td>primary location of tumor</td>
<td>rt sphenoid wing, cavernous sinus &amp; middle fossa floor</td>
<td>lt occipital falcotentorial junction</td>
<td>rt tentorial posterior fossa &amp; supratentorial</td>
</tr>
<tr>
<td>follow-up (mos)</td>
<td>181</td>
<td>58</td>
<td>4</td>
</tr>
<tr>
<td>longest progression-free period (mos)</td>
<td>84</td>
<td>41</td>
<td>4</td>
</tr>
<tr>
<td>no. of resections (craniotomies)</td>
<td>3</td>
<td>2</td>
<td>1</td>
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<tr>
<td>reason for repeat craniotomy</td>
<td>2nd: residual tumor; 3rd: recurrence</td>
<td>2nd: recurrence</td>
<td>NA</td>
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<tr>
<td>endovascular embolization</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>chemotherapy</td>
<td>Adriamycin</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>radiotherapy treatment</td>
<td>fractionated intensity-modulated therapy; total dose 60 Gy</td>
<td>GKS; 16 Gy to 50% isodose line</td>
<td>fractionated intensity-modulated therapy; 33 fractions, total dose 180 Gy</td>
</tr>
</tbody>
</table>

* GKS = Gamma Knife surgery; NA = not applicable.

developed, with abnormal and dysesthetic sensation on the right side of the face due to involvement of the right cavernous sinus by recurring disease.

The longest mean tumor progression–free interval following the initial or secondary resection was 43 months (range 4–84 months).

**Discussion**

*Pathological Features and Presentation*

Hemangiopericytomas are rare, aggressive neoplasms that most often involve the musculoskeletal system and skin. Intracranial HPCs represent less than 1% of all intracranial tumors and approximately 2%–4% of all meningeal tumors. They almost always present as solitary, supratentorial (62%) dura-based lesions often arising from the falx, tentorium, dural sinuses, and skull base. Histopathologically, they are characterized by spindle cells with a rich vascular network, with large, dilated, “staghorn” vascular channels (Fig. 3). Their relative vascularity coupled with their frequent association with vital neural structures often makes GTR challenging.

In contrast to meningiomas, whose incidence in female patients predominates, HPCs tend to occur more often in males, with a male/female ratio approaching 2:1.

**Imaging Features**

Radiological differentiation of an HPC from a meningioma is important for preoperative planning and subsequent management. Knowing that the differential diagnosis favors HPC has significant influence on the surgical approach, mainly because of the greater risks of severe bleeding and local recurrence that are associated with this tumor as compared with those for a meningioma. Imaging similarities between the 2 tumor types are profound and distinguishing between the two can be difficult. Nevertheless, the combination of characteristic features, such as the presence of internal signal voids, heterogeneous enhancement, and adjacent bony erosion, suggest HPC as a likely diagnosis. Hemangiopericytoma margins are often lobulated, with frequent internal serpentine signal voids and absent calcifications, as compared with meningiomas, in which margins are usually smooth, flow voids are rare, and calcifications occur in 20%–25% of cases. Hemangiopericytomas display a relative paucity of peritumoral edema and have a common angioarchitectural pattern that can be used to distinguish them from meningiomas. The angioarchitecture includes a dual supply from the internal carotid or vertebral and external carotid arteries, with the dominant supply coming from the internal carotid artery branches rather than the primarily external carotid supply seen with meningiomas, numerous corkscrew vessels arising from a main feeder within the tumor, a dense, fluffy, long-lasting tumor stain rather than the sunburst pattern of meningiomas, and no early draining veins.

**Multimodal Management**

**Surgery.** Hemangiopericytomas are neoplasms with an aggressive natural history. The optimal method of treatment consists of GTR followed by postoperative radiotherapy. Surgery not only offers immediate relief of mass effect but also allows tissue confirmation of the histopathological diagnosis to differentiate HPCs from other meningiomas. Because of the high vascularity of the lesions, preoperative embolization can sometimes be advantageous. Soyuer et al. reported a superior 5-year local control rate in patients treated with GTR (84%) as compared with the rate in patients treated using subtotal resection (38%).
Radiotherapy. The propensity of HPCs to arise from the skull base or in close association with the dural sinuses can often preclude GTR. Consequently, postoperative radiotherapy has gained increasing acceptance in the initial management of these tumors. Two groups reported that radiotherapy after an initial resection extended the mean time to local recurrence from 34 to 75 months and extended overall survival from 62 to 92 months. Dufour et al. reported in their series that HPCs recurred after an average interval of 74 months if they were subjected to irradiation after the first surgical treatment, as compared with an average of 29 months if they were not treated with radiotherapy after initial resection.

Radiotherapy in addition to the quality of resection and the duration of follow-up affects local recurrence following the resection of HPCs. The response of HPCs to radiotherapy is dose dependent, with overall treatment doses of 45 Gy or higher resulting in superior local control. The current SRT treatment plan used in most centers delivers 46–52 Gy fractionated over 25–35 sessions. In recent years, SRT has emerged as a viable salvage strategy for the treatment of recurrent intracranial HPCs, ideally less than 3 cm in their greatest dimension. A focal fractionated radiation dose of 50 Gy is recommended as a standard to prevent recurrence.

Stereotactic Radiosurgery. Gamma knife radiation has occasionally been used as an upfront therapy for the treatment of HPC, and the literature supports a role for this treatment in recurrent lesions, as disease-free survival tends to be higher in cases of newly diagnosed HPCs treated with a combination of resection and adjuvant postoperative SRT. Sheehan et al. demonstrated in a series of 14 patients with 15 HPCs treated with radiosurgery, 7 of which had been subjected to radiotherapy, an 80% local control rate for recurrent intracranial HPCs using Gamma Knife surgery, with a median time to local recurrence of 21 months. Authors of this study also demonstrated Kaplan-Meier survival rates of 76% and 100% 5 years after Gamma Knife surgery but reported remote metastases in 29% of the patients, and thus concluded that local tumor control afforded by radiosurgery provided seemingly little protection from distant metastases. In a later paper the Virginia group reported on a series of patients with an 81% 5-year survival rate after radiosurgery.
but a tumor control rate of only 29% at the 5-year mark. Prior fractionated irradiation or a radiosurgical prescription dose did not correlate with tumor control. In 4 (19%) of 21 patients, extracranial metastases developed. Stereotactic radiosurgery is most effective for treating tumors < 8 cm (< 2 cm in diameter) in volume with radiation doses of 15 Gy or higher at the 50% isodose line. Recurrent lesions ≥ 3 cm in their greatest diameter are best treated by reresection followed by postoperative SRS, whereas recurrent lesions < 3 cm in their greatest diameter can be successfully controlled by SRS alone. Unfortunately, although the addition of either SRT or SRS seems to confer superior local control over surgery alone, these therapies do not appear to provide any significant protection against the development of distant metastases. In patients with advanced, symptomatic extracranial HPC, radiotherapy may also play an important palliative role. Based on the data summarized in Olson et al., it appears that a higher margin dose of at least 18–20 Gy should be recommended to avoid early recurrence.

Chemotherapy. The role of chemotherapy in the treatment of systemic HPC is unclear, and the collective experience documented in the literature is limited. Hemangiopericytoma can be considered a soft-tissue sarcoma, and progress in the chemotherapeutic treatment of this entity has been unexceptional. Anthracycline and ifosfamide have been established as the most active agents for metastatic sarcoma, with ongoing debate about the advantage of combination versus single-agent chemotherapy in the treatment of soft-tissue sarcoma. However, both a meta-analysis and a recent randomized phase III trial suggest that single-agent doxorubicin is the treatment of choice for advanced soft-tissue sarcomas. Other chemotherapeutic agents used include doxorubicin and dacarbazine, both with equally poor results. There have been some attempts to treat HPC with interferon immunomodulatory therapy, as α-interferon appears to have antiangiogenic activity by slowing endothelial proliferation and migration and by suppressing the production of 2 proangiogenic factors, interleukin-8 and basic fibroblast growth factor. The investigation of other antiangiogenic agents, for example, bevacizumab or sunitinib, could be considered as well. Another report describes monotherapy utilizing dasatinib as a molecular therapy targeting the Src gene–related tyrosine kinases, which led to a stable tumor after multiple recurrences in 1 case. Even most HPCs treated with GTR and adjuvant SRT tend to locally recur by years after treatment. However, cases of local recurrence and distal metastases have been reported more than 20 years out from the initial diagnosis. Therefore, long-term follow-up with annual serial imaging is suggested for optimal management. Screening should not be limited to the intracranial compartment, as extracranial metastases tend to represent a relatively common occurrence in the natural history of HPC.

Conclusions

Intracranial HPCs, frequently located along the dural sinuses along the skull base, are rare, aggressive CNS neoplasms that are difficult to distinguish from meningiomas based on both imaging and gross characteristics. Once thought to be histopathologically related to meningiomas, these lesions have been reclassified as mesenchymal nonmeningothelial tumors. Hemangiopericytomas seem to have an inevitable tendency to recur locally and metastasize distally. The mainstay of therapy remains aggressive GTR at the initial surgery. Postoperative adjuvant radiotherapy should be offered to all patients, regardless of the degree of resection achieved. Chemotherapy can be considered, but no clear data exist regarding its efficacy, and consensus about the appropriate agent or timing of therapy is lacking. Frequent imaging follow-up is necessary to discover recurrences early, and a follow-up interval of 6 months is recommended in most cases.

Recurrent intracranial disease management must be tailored to the size and location of the local recurrence and the overall systemic disease burden. Postoperative radiation treatment does not confer any significant protection against the development of distant metastases, making long-term clinical and radiographic follow-up in these patients necessary.

Local recurrences and distal metastases may develop long after the initial treatment, sometimes after several years, underlining the need for long-term follow-up.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: both authors. Acquisition of data: both authors. Analysis and interpretation of data: Schirmer. Drafting the article: Schirmer. Critically revising the article: both authors. Reviewed final version of the manuscript and approved it for submission: both authors. Study supervision: Heilman.

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C. M. Schirmer and C. B. Heilman

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