Meningeal Hemangiopericytoma

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Case Presentation

• **HPI:** 19-year-old male noted “the worst headache of his life” associated with left visual field abnormalities

• **PMHx:** None

• **PSHx:** None

• **FHx:** No first-degree relatives with cancer

• **Soc Hx:** College student, non-smoker

• **ROS:** No other pertinent symptoms
Pre-Treatment Imaging

- MRI brain with contrast showed right parieto-occipital dural-based lesion that was enhancing and solid/cystic in nature with significant peritumoral edema

June 21, 2021
Clinical Course

• Patient underwent craniotomy, and maximal safe resection of mass was attempted

• However, surgery was prematurely aborted due to significant intra-operative bleeding and edema requiring IV mannitol

• Pathology from surgery demonstrated WHO grade II hemangiopericytoma
Hemangiopericytoma (HPC)

- HPC: rare benign neoplasm derived from pericytes lining the endothelium of smaller vessels\(^1-2\)
  - 1% of intracranial tumors
  - 2.5% of meningeal tumors

- Following WHO 2016 classification, now considered type of solitary fibrous tumor (SFT)\(^3\)
  - SFT and meningeal HPC share a defining molecular characteristic: NAB2/STAT6 gene fusion\(^4\)

- Meningeal HPC: dural-based, intracranial SFT
HPC: Classic & Unique Features

• **Imaging:**
  – “Corkscrew” vascularization, extensive associated edema, and irregular/lobulated borders\(^5\)

• **Clinical features:**
  – Prone to bleeding
    • Illustrated by patient in our case - intra-op bleeding
  – Predilection for:
    • Local recurrence, even for lower grade (I-II) tumors\(^6\)
    • Distant metastases (DM rate as high as 65% at 15 years)\(^2\)
      – Sites: lungs, bone, liver, subcutaneous tissue, pleura\(^7\)
    • Late development of DMs (mean time to DM: 7.5 years)\(^7\)
# HPC: Clinical Features and DDx

<table>
<thead>
<tr>
<th>Feature</th>
<th>Meningeal HPC</th>
<th>Meningioma</th>
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<tbody>
<tr>
<td><strong>Location</strong></td>
<td>Supratentorial &gt; infratentorial</td>
<td>Supratentorial &gt; infratentorial</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>&lt;1% of intracranial tumors</td>
<td>15-20% of intracranial tumors</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>4&lt;sup&gt;th&lt;/sup&gt; decade of life</td>
<td>5&lt;sup&gt;th&lt;/sup&gt; decade of life</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>Male &gt; female</td>
<td>Female &gt; male</td>
</tr>
<tr>
<td><strong>Recurrence Risk</strong></td>
<td>Very high/expected</td>
<td>Lower risk</td>
</tr>
<tr>
<td><strong>Metastatic potential</strong></td>
<td>Very high</td>
<td>Minimal</td>
</tr>
<tr>
<td><strong>outside CNS?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Enhancement on imaging?</strong></td>
<td>Yes</td>
<td>Homogenous</td>
</tr>
<tr>
<td><strong>Calcification</strong></td>
<td>Rarely</td>
<td>Commonly</td>
</tr>
<tr>
<td><strong>Effect on adjacent bone</strong></td>
<td>Bony erosion</td>
<td>Hyperostosis</td>
</tr>
<tr>
<td><strong>Primary treatment</strong></td>
<td>Surgery +/- adjuvant RT</td>
<td>Surgery +/- adjuvant RT</td>
</tr>
<tr>
<td><strong>Bleeding risk?</strong></td>
<td>High</td>
<td>Rare except for skull base</td>
</tr>
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HPC: WHO Grading

<table>
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<tr>
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<tbody>
<tr>
<td>I</td>
<td>Highly collagenous, relatively low cellularity, spindle cell lesion</td>
<td>Solitary fibrous tumor</td>
</tr>
<tr>
<td>II</td>
<td>More cellular, less collagenous tumor with plump cells and “staghorn” vasculature</td>
<td>Hemangiopericytoma</td>
</tr>
<tr>
<td>III</td>
<td>Five or more mitoses per 10 high-power fields</td>
<td>Anaplastic hemangiopericytoma</td>
</tr>
</tbody>
</table>

- By older WHO grading, grades II-III were classically regarded as HPCs (and stage I as SFT)
Back to our patient...

• Following initial attempt at surgery, a second effort was made at completing gross total resection (GTR). However, this was complicated by cerebral edema.

• The patient was subsequently seen for initial consultation in radiation oncology clinic in April 2012 following full staging work-up with CT C/A/P.

• Recommendation was made for adjuvant radiotherapy with conventional fractionation.
Target Volumes
(Conventional Fractionation)

• Gross tumor volume (GTV)
  – Tumor bed with any residual nodular enhancement noted on post-op T1 post-contrast MRI

• Clinical target volume (CTV)
  – GTV + areas at risk for microscopic spread. Often incorporates a 1-2 cm margin (e.g. dura) while respecting anatomic boundaries.

• Planning target volume (PTV)
  – 3-5 mm depending on institutional practice, IGRT
Treatment

- May 2012 – July 2012: Patient received adjuvant radiotherapy with 50.4 Gy in 28 fractions with IMRT to the post-op tumor bed and gross residual disease
- Boost to gross disease: 10.8 Gy in 6 fractions
- Cumulative dose: 61.2 Gy in 34 fractions
Treatment Paradigm for HPC: GTR

- For all SFTs, 1\textsuperscript{st} step: upfront surgical resection\textsuperscript{10}
- First step for all HPC cases: Gross total resection (figure: Simpson grading)\textsuperscript{11}
  - Based on high vascularity, even with pre-op embolization, estimated GTR rate about 33-66\%\textsuperscript{12}
  - Extent of resection associated with recurrence-free survival\textsuperscript{13}

<table>
<thead>
<tr>
<th>SIMPSON GRADE</th>
<th>DEGREE OF RESECTION</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Macroscopic complete removal with excision of dural attachment &amp; abnormal bone</td>
</tr>
<tr>
<td>II</td>
<td>Macroscopically complete with endothermy coagulation of dural attachment</td>
</tr>
<tr>
<td>III</td>
<td>Macroscopically complete without resection or coagulation of dural attachment or of its extradural extensions</td>
</tr>
<tr>
<td>IV</td>
<td>Partial removal leaving tumor in situ</td>
</tr>
<tr>
<td>V</td>
<td>Simple decompression ± biopsy</td>
</tr>
</tbody>
</table>
Treatment Paradigm for HPC: Adjuvant RT

• No existing randomized data; limited retrospective/population-based analyses only

• However, adjuvant radiotherapy following GTR has a well-established role due to notoriously high risk for locoregional recurrence

• Adjuvant RT improves:
  – Local control
    • Study by Rutkowski et al. (n=35) found that adjuvant RT increased time to recurrence from 3.9 years to 6.6 years, independent of extent of resection\textsuperscript{14}
  
  – Overall survival (see Table on next slide*)\textsuperscript{12-20}

<table>
<thead>
<tr>
<th>Study Year</th>
<th># of Patients</th>
<th>Median FU (mo, range)</th>
<th>Median tumor volume (cm³)</th>
<th>Median marginal dose or mean dose (Gy, range)</th>
<th>New lesions (% of patients)</th>
<th>Extra-cranial metastasis (%)</th>
<th>Median OS</th>
<th>Summary of Study Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rutkowski et al., 2010</td>
<td>277</td>
<td>78</td>
<td>5.36</td>
<td>N/A</td>
<td>43</td>
<td>27</td>
<td>156</td>
<td>OS benefit demonstrated with gross total resection (GTR)</td>
</tr>
<tr>
<td>Rutkowski et al., 2012</td>
<td>35</td>
<td>2-408</td>
<td>4.4</td>
<td>N/A</td>
<td>46</td>
<td>20</td>
<td>194.4</td>
<td>Trend towards statistical significance for improved recurrence-free survival with post-op radiation</td>
</tr>
<tr>
<td>Ghia et al., 2013</td>
<td>88</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>111</td>
<td>Both GTR and post-op radiation associated with improved OS</td>
</tr>
<tr>
<td>Ghia et al., 2013</td>
<td>63</td>
<td>N/A</td>
<td>N/A</td>
<td>60 (35-66.4)</td>
<td>51</td>
<td>N/A</td>
<td>154</td>
<td>Post-op radiation associated with better local control, especially at doses &gt; 60 Gy</td>
</tr>
<tr>
<td>Sonabend et al., 2014</td>
<td>227</td>
<td>34</td>
<td>5</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Statistically significant improvement in OS with GTR and radiation vs GTR alone</td>
</tr>
<tr>
<td>Chen et al., 2015</td>
<td>38</td>
<td>61 (15-133)</td>
<td>4.6</td>
<td>N/A</td>
<td>66</td>
<td>13</td>
<td>N/A</td>
<td>GTR with adjuvant radiation associated with improved OS and recurrence-free survival</td>
</tr>
<tr>
<td>Cohen - Inbar et al., 2016</td>
<td>90</td>
<td>59 (6-183)</td>
<td>4.9</td>
<td>14 (12-16)</td>
<td>55</td>
<td>24.4</td>
<td>N/A</td>
<td>Margin dose &gt;16 Gy associated with better local control</td>
</tr>
<tr>
<td>Kim et al., 2017</td>
<td>18</td>
<td>71.8 (3.3-153.3)</td>
<td>1.2</td>
<td>20 (13-30)</td>
<td>80</td>
<td>38.9</td>
<td>225.7</td>
<td>GK SRS may be used repeatedly for intracranial recurrence or progression</td>
</tr>
</tbody>
</table>
Adjuvant RT: Modality & Dose

• Adjuvant RT following maximal safe resection may be administered using IMRT or SRS (if candidate)

• **Dose escalation is important!**
  – For IMRT: Improved local control with >60 Gy versus 50 Gy\textsuperscript{13,16}
  – For SRS: While recommendations for marginal dose range from 14-22 Gy, ≥16-17 Gy advised\textsuperscript{19}
    • Kim et al. (2010, n=17) found improved local control with marginal doses ≥17 Gy without significantly worse radionecrosis or peritumoral edema\textsuperscript{21}
  – Regardless of modality: push dose when feasible
What about protons?!

• Proton therapy is an emerging area of study
• Ongoing phase II feasibility study by PTCOG (NCT01117844): Proton Radiation for Meningiomas and Hemangiopericytomas
  – Eligibility: Age 18 or older with WHO grade I-III meningiomas and hemangiopericytomas
  – “Standard dose” (non-dose escalation study)
  – Primary objectives: feasibility and safety
  – Secondary objectives: side effects, QOL, late complications, dose distribution/DVH, and local control/survival outcomes

June 21, 2021
Our Patient: Toxicity

• Our patient completed his prescribed course of treatment and tolerated it well overall with mild fatigue and alopecia

Anticipated side effects (conventional fx):

• Acute: fatigue, dermatitis, alopecia, headache, n/v

• Late: Location-dependent
  – Neurocognitive/audiovisual deficits
  – Hypopituitarism if treating close to sella turcica with doses exceeding 50 Gy
Our Patient: Surveillance

- Completed adjuvant RT in July 2012
- Underwent surveillance (clinical exam/imaging)

Surveillance Recommendations:

- MRI brain with contrast at 3 months and 6 months following completion of RT, then every 6 months
- Patients undergo lifetime surveillance (at least up to 20 years) due to risk of late recurrence
- Based on index of suspicion, consider imaging of common sites of DM (lungs, liver) with CT C/A/P
Treatment Response/Tumor Kinetics

• For SFTs, tumor response following RT reflects the kinetics associated with tumor growth\textsuperscript{23}

• While HPCs may respond more quickly than other SFTs, tumor response time exhibits a wide range of variability
  
  – Some intracranial HPCs may take as long as 2 years to demonstrate even a partial response\textsuperscript{24}
Our Patient: Response

- July 2012-May 2020: No evidence of recurrence
- May 2020: Surveillance MRI brain demonstrated radiographic progression of enhancing nodule at the anteromedial aspect of the resection cavity, now measuring about 2 cm in widest diameter.
HPC: Salvage Treatment

• Options:
  – Repeat surgical resection
  – Salvage radiotherapy

• Considerations:
  – Neurologic functioning
  – Extracranial disease status
  – Timing of prior radiotherapy
  – Intracranial tumor volume
HPC: Salvage Treatment

- Most studied treatment option for salvage reirradiation is SRS

- Limited existing data in reirradiation setting
  - Olson et al. (2010): Repeat SRS (n=13)\(^{25}\)
    - Mean Rx dose: 17 Gy; maximum dose: 40.3 Gy
    - Found SRS to be safe and effective for treating new or recurrent HPCs over long follow-up period
  - Kim et al. (2017):\(^ {20}\)
    - Mean marginal dose 20 Gy (range: 13-30 Gy)
    - Used GK SRS – found it may safely be used repeatedly for recurrence
Our Patient: Salvage Treatment

- Patient decided against surgery
- Our patient received salvage reirradiation with Gamma Knife (GK) SRS
- 24 Gy prescribed to the 50% isodose line was delivered to the right parieto-occipital/parafalcine mass
Our Patient: Treatment Technique

• 33 shots were placed
• Elegant solution:
  – Preferential dose spill into surgical cavity to preserve adjacent normal tissue (delineated in orange)
  – Allowed for ability to push prescription dose to 24 Gy to maximize local control
    • Especially important in salvage setting
Our Patient: Follow-Up

- Most recent follow-up: March 2021
- Patient doing well without clinical or radiographic evidence of progression
- Most recent MRI brain with contrast shown on the right
Summary

• HPCs are highly vascular and carry significant bleeding risk, making GTR challenging and further increasing importance of adjuvant radiotherapy
• They are likely to recur as well as spread distantly & up to many years following initial therapy
• When feasible, escalating RT dose improves outcomes
• SRS is an excellent salvage option

*Figure extrapolated from: Bajaj A, Saeed H. Solitary fibrous tumors/hemangiopericytoma. Sarcomas and Skin Cancers: A Practical Guide on Radiation Treatment Techniques. Publisher: Springer; Editors: Edward Kim MD, Upendra Parvathaneni MBBS, Meng Welliver, MD. In process.
References


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