Case Report

Sellar-parasellar epithelioid hemangioendothelioma

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Abstract

Epithelioid hemangioendothelioma is a rare vascular tumor that presents histological features and biological behavior of low-grade malignancy. The authors report a case of a malignant sellar-parasellar tumor. A 36-year-old female, who had a history of head trauma 16 years before, presented with mild headache, and diplopia, 10 months later she presented rapidly progressive ophthalmologic, ptosis and right amaurosis. CT-scan reveals an intra- or suprasellar mass with non-specific features, with calcifications and bone destruction. She underwent transcraeal partial resection of a suprasellar tumor. This lesion was histological diagnosed as epithelioid hemangioendothelioma that showed papillary endothelial hyperplasia. Immunohistochemically the neoplasm displayed striking positivity for CD31, CD34, EVGF, EVGF-RII and vimentin. The pathogenesis, correlation of histopathologic, radiology, and management of epithelioid hemagioepithelioma are reviewed. EVGF and its receptor can be useful of predictor behavior.

Keywords: Epithelioid hemangioendothelioma; immunohistochemistry, sellar-parasellar tumors, vascular tumors

Özet


Anahtar Kelimeler: Epitelioid hemangioendotelyoma; imünohistokimya, sellar-parasellar tümör, vasküler tümör

INTRODUCTION

The term epithelioid hemangioendothelioma (EHE) was coined by Weiss and Enzinger to nominate a unique vascular tumor with an epithelioid appearance (1), is the prototype of a group of vascular tumors, is a borderline or intermediate type characterized by epithelioid or histiocytoid endothelial cells (2). This neoplasm commonly occurs as a soft tissue mass but can be located in other organs, such as: lungs, liver, bones, penis (2), etc. Epithelioid hemangioendothelioma of bone is a rare lesion that constitutes less than 1% of primary malignant skeletal neoplasm. Only rare cases arising in the skull have been published (1).
Intra-axial involvement of the brain by an epithelioid hemangioendothelioma is rare, and biological properties of the tumor are uncertain. Most of the primary brain manifestations are confined to the cerebral hemispheres. Its intracranial occurrence is rare, and the literature review revealed only 23 cases (14 adults and 9 children). Radiographic images showed a well-demarcated, osteolytic lesion in the skull bone, had sclerotic edges and another had specks of calcification.

Some authors consider that the male-to-female ratio varies with the tumor location. In adults the age range was between 20 and 74 year. EHE may cause symptoms due to space-occupying effects.

The prognosis of intracranial location has not yet been well defined, despite the favorable outcome noted in the majority of cases; rapid recurrence is possible due to incomplete removal.

Herein we report a 36-year-old female with destructive sellar and parasellar epithelioid hemangioendothelioma.

**CASE REPORT**

The patient, a 36-year-old woman, reported history of heat trauma 16 year before. She had a two years history of mild headache, reduced vision and diplopia in the right eye. She presented ptosis and progressive right amaurosis developed 10 month before she sought treatment.

The patient was admitted in our Institution with intense headache, nausea and vomiting. On initial examination, she exhibited bilateral sixth cranial nerve paralysis, ptosis on the right eyelid, and decreased visual acuity (4/10 on the right, 7/10 on the left). Fundoscopic examination showed blurring of the left optic disc and papilla stasis on the right. Preoperative endocrine evaluation was normal.

CT-scan and/or MRI revealed a sellar and suprasellar expanding, initial radiological impression was of cordoma (figure 1A).

![Figure 1a](image1a) Lateral cranial plain X-ray showed destructive lesion of the sellar region accompanied by osteolysis. 1b) MRI-imaging revealed an enlargement of sellar and clivus tumor, it affects the sphenoidal sinus. 1c) Close-up of the tumor. 1d) Lateral angiography’s showed complete obstruction of the internal right carotid artery with an adequate flux from the right arterial system to the right through the communicants.
A magnetic resonance imaging (MRI) scan revealed 43 x 42 x 50 mm enhancing homogeneous intra and suprasellar mass with extension into the sphenoid and cavernous sinuses bilaterally; the optic chiasm was not displaced (figure 1b and 1c). Angiography’s showed obstruction of the internal right carotid (fig. 1d).

2.1. Surgery

She underwent fronto-temporal craniotomy of the sellar lesion A vascular mass containing necrotic fragments, which involved the sphenoidal sinus, dura, and destroyed clivus interiorly. There was substantial intraoperative bleeding, and autologous blood transfusion was required, and she died 12 hours after.

2.2. Histological findings

Histological examination of the tumor demonstrated short strands and solid nests of rounded to slightly spindled, eosinophilic endothelial cells. Variable proportion of cells showed striking cytoplasmic vacuolation. The stroma was myxoid-hyalinised with focal mixed inflammatory infiltrate, and numerous elongated vessels lined by a single layer of hobnail endothelial cells, and papillary hyperplasia with hyaline collagenous cores (figure 2c, and 2d), necrosis was observed. Immunohistochemistry revealed neoplastic cells positive for CD31, DC34, EVGF and EVGF-RII. The results of immunohistochemistry and the characteristics of the primary antibodies that we used are listed on Table 1(figures 3).

![Figure 2a](image)

Figure 2a) Histological findings showed a tumor formed short strands and solid nests of rounded to slightly spindled, eosinophilic endothelial cells (H&E original magnification x200). 2b) The stroma was myxoid-hyalinised with numerous elongated vessels lined by a single layer of hobnail endothelial cells. Variable proportion of cells showed striking cytoplasmic vacuolation (H&E original magnification x 400). 2c and 2d) Papillary endothelial hyperplasia with hyaline collagenous cores (H&E original magnification x 400).
Table I. Immunohistochemistry and primary antibodies used.

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Results</th>
<th>Source</th>
<th>Clone</th>
<th>Dilution</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD34</td>
<td>Positive</td>
<td>DAKO</td>
<td>Qtend10</td>
<td>1:100</td>
</tr>
<tr>
<td>CD31</td>
<td>Positive</td>
<td>DAKO</td>
<td>JC70A</td>
<td>1:100</td>
</tr>
<tr>
<td>EVGF</td>
<td>Positive</td>
<td>BioGenex</td>
<td>AbNo350P</td>
<td>1:100</td>
</tr>
<tr>
<td>EVGF-R.II</td>
<td>Positive</td>
<td>BioGenex</td>
<td>Flt-1</td>
<td>1:150</td>
</tr>
<tr>
<td>GFAP</td>
<td>Negative</td>
<td>DAKO</td>
<td>6F2</td>
<td>1:50</td>
</tr>
<tr>
<td>EMA</td>
<td>Negative</td>
<td>DAKO</td>
<td>E29</td>
<td>1:100</td>
</tr>
<tr>
<td>Cytokeratin</td>
<td>Negative</td>
<td>DAKO</td>
<td>MNF116</td>
<td>1:150</td>
</tr>
<tr>
<td>Vimentin</td>
<td>Weak</td>
<td>DAKO</td>
<td>V9</td>
<td>1:50</td>
</tr>
<tr>
<td>S-100 protein</td>
<td>Negative</td>
<td>DAKO</td>
<td>S100</td>
<td>1:100</td>
</tr>
<tr>
<td>Desmin</td>
<td>Negative</td>
<td>DAKO</td>
<td>D33</td>
<td>1:100</td>
</tr>
<tr>
<td>Synaptophysin</td>
<td>Negative</td>
<td>DAKO</td>
<td>A0010</td>
<td>1:100</td>
</tr>
<tr>
<td>NEE</td>
<td>Negative</td>
<td>DAKO</td>
<td>RN4</td>
<td>1:100</td>
</tr>
</tbody>
</table>


Figure 3a) Immunohistochemistry revealed neoplastic cells and lumina positive for DC34 (original magnification 40x), EVGF positive cell (original magnification x 400).
2.3. Postmortem study

Autopsy findings include; Brain coronal section showed edema, without intraparenchymatous neoplasm (fig. 4a), gross examination of the skull base revealed a tumor affecting sellar-parasellar area and cavernous sinus and thrombosis in right carotid artery (Fig. 4b).

DISCUSSION

The heterogeneity of tissue types in the cranium base gives rise to a diverse group of benign and malignant neoplasms with vastly different prognoses, the distinct clinic pathologic features of some of the unique and problematic neoplasms of this region.

Intraoperative observations cannot easily distinguished carcinoma, metastasis carcinoma vs other malignant tumor from epithelial hemangioendothelioma. However, in our case the tumor had completely eroded to the bony sellar floor with marked enlargement, which was rater atypical adenoma. Profuse bleeding from metastatic carcinoma, pituitary carcinoma or vascular adenoma is well known may occur.

Vascular tumors represent one of the largest groups among soft tissue tumors. They are histological and clinically heterogeneous and, considering their ubiquity, are not all well understood (12).

It was not until the 1880s to use of the term hemangioendothelioma was introduced, Enzinger and Weiss utilized the term to describe the small subset of vascular tumor, which did not fit neatly into either the benign or malignant categories at that time (1). By the time of the second edition of Enzinger and Weiss published in 1988 the term “hemangioendothelioma” had become more firmly established to describe this intermediate group of vascular lesion and them entities of epithelioid hemangioendothelioma, spindle cell hemangioendothelioma and malignant endovascular papillary angioendothelioma were included under this heading (2). In the most recent revision of WHO classification (2002) the term of “hemangioendothelioma” is no longer regarded as strictly defining a specific group of lesions with intermediate behavior but, instead, is now used to describe lesion which would fall into the locally aggressive, rarely metastasizing and frankly malignant categories (12) which help to reflect the spectrum of behavior in this group of lesion. Many of the tumor types in this category are very uncommon. Although well known to occur also in lung, liver, bone, and
less often in other organs, almost any anatomic location may be affected. Involvement of the cranium is very rare. We have found less than twenty-three cases involving the skull and cranium bone in the English literature (4-8,10,12), (see table II), it may occur at any age, but it occurs most common between the second and third decades of life (3-9).

**Table II**: Cases reported of epithelioid hemangioendothelioma in base of cranium.

<table>
<thead>
<tr>
<th>Authors/Reference</th>
<th>Localization</th>
<th>Age/gender</th>
<th>Excision</th>
<th>Bleeding</th>
<th>Follow-up</th>
<th>Radiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peal et al (8)</td>
<td>Sellar/parasellar</td>
<td>73/males</td>
<td>Subtotal</td>
<td>Yes</td>
<td>Tumor</td>
<td>Yes</td>
</tr>
<tr>
<td>Phooyan et al (10)</td>
<td>Cavernous sinus</td>
<td>36/males</td>
<td>Total</td>
<td>non</td>
<td>4 months</td>
<td>Non</td>
</tr>
<tr>
<td>Rushing et al. (5)</td>
<td>Cilus</td>
<td>38/females</td>
<td>Total</td>
<td>yes</td>
<td>Tumor</td>
<td>Yes</td>
</tr>
<tr>
<td>Joo et al. (9)</td>
<td>Sphenoid bone</td>
<td>29/females</td>
<td>Total</td>
<td>non</td>
<td>Dead 6 months</td>
<td>Non</td>
</tr>
<tr>
<td>Aditya et al. (7)</td>
<td>Sellar/parasellar</td>
<td>4 cases (4-48)</td>
<td>Total</td>
<td>yes</td>
<td>Variable</td>
<td>Non</td>
</tr>
<tr>
<td>Hamlal et al. (6)</td>
<td>Infundibular</td>
<td>53/male</td>
<td>Total</td>
<td>yes</td>
<td>Stable, cyst tumor</td>
<td>Yes</td>
</tr>
<tr>
<td>Baehring et al. (4)</td>
<td>Sellar/parasellar</td>
<td>36/male</td>
<td>Subtotal</td>
<td>non</td>
<td>Dead 6 months</td>
<td>Non</td>
</tr>
<tr>
<td>Watanabe T. (14)</td>
<td>Petroclival</td>
<td>45/female</td>
<td>Subtotal</td>
<td>yes</td>
<td>Non</td>
<td>Yes</td>
</tr>
<tr>
<td>Adler et al. (13)</td>
<td>Skull base/spinal</td>
<td>16/male</td>
<td>Subtotal</td>
<td>yes</td>
<td>Dead</td>
<td>---</td>
</tr>
</tbody>
</table>

Immunohistochemical study is helpful in confirming the diagnosis by identifying factor VIII-related antigen, CD34 and CD31, which are a marker for vascular endothelial cell (1,12). Also, ultrastructural studies confirm the endothelial origin of the tumor (1).

EHE is distinguished from hemangioma by the more primitive vasoformative appearance and infiltrative growth (12). Angiosarcoma is separated from this tumor by nuclear anaplasia, conspicuous anastomosing vascular channels and brisk mitotic activity (12).

The epithelioid endothelial cells have minimal reactivity for CD34, small number of epithelioid endothelial cells expressed; cytokeratins, least focal muscle-specific actin-positive myopericytic cells were present bordering the endothelial cells (2).

The endothelial cells were immunoreactive to EVGF and EVFR-II. The most important responses, to EVGF and its receptors; is keeping with its role as an angiogenic factor, inducted by hypoxia, and may be, we can use as predictor of poor prognosis in vascular tumors. However the most primary EHEs of the brain appear to carry rather favorable prognosis (2-4).

The differential diagnosis of intracranial EHE is distinguished by its well-formed, canaliculated vessels and often lobular architecture includes; angiosarcoma, metastasis carcinoma, chordoid meningioma, and various sarcomas which an epithelioid appearance (2). Intracellular vacuoles indicate primitive lumen formation, this appearance is frequently confused with the mucin vacuoles of Adenocarcinoma (1), but the vacuolar contents of EHE do not stain epithelial mucin. The stroma of EHE varies from highly myxoid myxofibromatous, and hyaline (1,12). EHE should be differentiated from myxoid chondrosarcoma; characteristic histological features of cartilaginous tumor cells are often seen in myxomatous chondrosarcoma (1,12). Other common intracranial vascular tumors, such as hemangioblastoma, hemangiopericytoma, meningiomas with significant vascular component are included in the differential diagnosis of EHE (1,12).

High grade mixoid liposarcoma is sometimes mistaken for EHE, but differs by the presence of thin-walled arborising vessels, the usual presence of convincing lipoblast and negative for endothelial markers (1,12).

Papillary endothelial hyperplasia is a morphologic feature; is similarly and consist primarily of small papillae with hyaline cores associated with adjacent thrombus and often show eosinophilic fibrin in their core (1,12). Angiosarcoma, hemangioma may have papillary structures (1,12).
Recent data highlight the importance of distinguishing chordoma and chondrosarcoma of the skull. Among the less common, aggressive tumor entities in this anatomical region, infiltrating pituitary adenoma/pituitary carcinoma, pituitary sarcomas, superficial malignant gliomas, rhabdomyosarcoma etc.

The clinical and radiographic findings are similar to those seen in other cerebral tumors, often delaying diagnosis and treatment and subsequently jeopardizing prognosis.

The appearance of surrounding bony structure and rich vascularity are important findings for the differential diagnosis. Neuroimaging revealed an expansile, homogeneously enhanced intraosseous mass with bony shell and honeycomb configuration. Epithelioid hemangioendothelioma should be added to the differential diagnosis for lytic lesions of bone that are clustered in the same anatomic region and that might also present with visceral involvement.

CONCLUSION

A case of epithelioid hemangioendothelioma is presented with histological features of papillary endothelial hyperplasia of the sellar-parasellar tumor in a 36-year-old female, with history of head trauma. Immunohistochemistry was reactive to CD34, EVGF and EVFG-R1. To our knowledge those findings has been not noted in this type of vascular tumor previously. Involvement of the cranium is very rare.

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