Hemangiopericytomas (HPCs) were first described by Stout and Murray in 1942. Originally thought to arise from Zimmerman pericytes (contractile cells that ensheathe capillaries and postcapillary venules), their histopathogenesis is an area of ongoing discussion. The World Health Organization currently classifies extracranial HPCs as a soft-tissue tumor included in the fibroblastic/myofibroblastic tumor group, as a member of the subgroup called extrapleural HPC and solitary fibrous tumor (SFT). Indeed, many sarcoma pathologists recognize separate “fibrous” and “cellular” variants of SFT, and note that an HPC is essentially indistinguishable from a cellular SFT. Intracranial HPCs, on the other hand, are still regarded as a distinct entity and are not included in either the meningioma or fibrous tumor groups, although it has been suggested that this distinction is not warranted and intracranial lesions also belong in the SFT family.

Intracranial infantile hemangiopericytomas (HPCs) are exceedingly rare lesions. Only 11 cases have been previously reported in the literature. As such, little is known about the etiology, long-term prognosis, and optimal treatment paradigm. Clinically, they are consistently less aggressive than those in adults. The authors present the case of a 2-month-old boy with an intracranial HPC, review the available literature, discuss the evolving concepts of what defines an HPC, and offer a potential explanation to how HPC histology might relate to the clinical behavior of these lesions.

Key Words • hemangiopericytoma • intracranial • infantile • pediatric • oncology

The pediatric peripheral form is less common and accounts for 5%–10% of HPCs. As with the adult form, the majority of these lesions are found in the lower limbs, followed by the head/neck, pelvis, and visceral organs. Additionally, the pediatric form can be subdivided clinically according to the age of onset. Lesions occurring after an individual is 1 year of age behave more aggressively, similar to the adult form, and are often classified as such. In contrast, those that present within the 1st year of life have a tendency to be less aggressive and are more easily managed with chemotherapy, relative to the adult form. This subgroup has been termed “infantile” or “congenital” HPC.

Intracranial HPCs are much rarer than their peripheral counterparts and account for less than 1% of CNS tumors. As with peripheral lesions, the adult form is more prevalent and the pediatric form is again subdivided into “adult-like” and “infantile” based on age at presentation (< 1 or > 1 year). As such, the literature can routinely refer to any of the six current categories for HPCs (adult: peripheral vs intracranial; pediatric [adult-like]: peripheral vs intracranial; and infantile/congenital: peripheral vs intracranial), which can be confusing when making comparisons.

Adult intracranial HPCs have been reasonably well described in the literature. First identified by Begg and Garret in 1954, intracranial adult HPCs are aggressive, dural-based tumors that can be radiographically indistinguishable from meningiomas. A recent review has identified numerous cases with identical radiographic and clinical features, but the histologic diagnosis of HPC has been challenging. Despite this, the distinction between HPC and meningioma is important, as HPCs are considered malignant neurosarcomas with the potential for local recurrence and distant dissemination.

Clinically, both peripheral and intracranial HPCs have been separated into adult and pediatric forms. The adult peripheral form is the most common and typically occurs in the soft tissues of the lower extremities and pelvis. Outcome is typically favorable following gross-total resection, with a 10-year overall survival rate ranging from 54% to 89%, although more aggressive behavior with local recurrence and distant metastasis is seen in 15%–20% of cases.
able from meningiomas, often resulting in misdiagnosis. However, adult intracranial HPCs are significantly more aggressive than meningiomas and have a greater propensity for local recurrence and extraneural metastases.

Intracranial infantile HPCs, on the other hand, are exceedingly rare and little is known about their prognosis or course. Our literature review found only 11 documented cases of intracranial infantile HPCs. Here, we report the case of a 2-month-old boy diagnosed with a primary infantile intracranial HPC and review the available literature.

**Case Report**

**History and Physical Examination Findings.** A previously well, 2-month-old boy was brought to our pediatric clinic with increasing head circumference (44.25 cm; > 95th percentile). The boy was born full-term by a repeat C-section following an uncomplicated pregnancy. He was normal size in utero and at birth. There were no difficulties with extraction and no history of seizures was noted. His neurological examination showed intact status. A diagnosis of macrocephaly was made and imaging studies were ordered.

**Imaging.** Magnetic resonance imaging showed a left frontal extraaxial mass (2.8 × 2.2 × 3.0 cm), which was mildly hypointense on T1-weighted images and heterogeneously mildly hyperintense on T2-weighted images (Fig. 1A and B). After the administration of contrast, there was marked but mildly heterogeneous enhancement, with mild spiculation of the outer surface of the tumor (Fig. 1C). There was mass effect with midline shift to the right. Additionally, the mass appeared to be fed by an enlarged left middle meningeal artery (Fig. 1D). There was no restricted diffusion or acute hemorrhage appreciated.

**Operation and Postoperative Imaging.** After discussing options with the boy’s family, the parents elected to proceed with surgery. A left frontal craniotomy was performed directly over the tumor. Exposure of the lesion revealed it to be firmly adherent to the dura but separate from the arachnoid, with a thick arachnoid band at the level of the dura. The dura itself appeared to have increased vascularization. The larger vessels of the sylvian fissure that surrounded the tumor were successfully separated from the mass and remained intact. The tumor itself was removed en bloc and portions of it were sent for frozen section staining. Following resection, the dura was closed and the bone flap was replaced. Brainlab navigation software was used throughout the procedure to ensure safe and adequate resection and localization. Postoperative MRI confirmed gross-total resection of the mass (Fig. 2 left).

**Pathological Analysis.** On histological examination the tumor was found to be highly vascularized. Between vascular structures were intermediate-sized round and spindle-shaped neoplastic cells with polymorphic nuclei and relatively small amounts of cytoplasm (Fig. 3A). A small subset of tumor cells was shown to be positive for CD34 by immunohistochemistry, and numerous tumor cells were shown to be positive for both muscle-specific actin (Fig. 3C) and smooth-muscle actin (Fig. 3D), which was suggestive of myofibromatous differentiation. The tumor tissue contained abundant extramedullary hematopoiesis that was interpreted as being reactive (Fig. 3B). Immunohistochemistry for CD31 exclusively stained reactive vascular cells, but not tumor cells. Similarly, immunohistochemistry for CD45, CD99, epithelial membrane antigen, glial fibrillary acidic protein, glut-1, keratin AE1/AE3, Mak-6, neuron-specific enolase, and footnotes.
S100 were negative. Immunohistochemistry for vimentin showed very weak staining of a subset of cells. This immunohistochemical profile was consistent with HPC.

Follow-Up. At last follow-up, the patient was doing well, though he exhibited developmental delay. No new neurological symptoms or postoperative complications emerged. At 28 months postresection, MRI imaging revealed no evidence of recurrence (Fig. 2 right).

Discussion

Hemangiopericytomas are rare, highly vascularized neoplasms that typically occur in the skin and musculoskeletal systems. They are most commonly seen in adults (on average the diagnosis is made when people are in their 5th decade of life), and fewer than 10% of cases are reported in children. Intracranial HPCs are rarer still and account for less than 1% of all intracranial tumors. Infantile types of HPC, both peripheral and intracranial, have been noted to follow a less aggressive course than adult types of HPC. However, this clinical consistency lacks the appropriate histological associations. In other words, some infantile lesions appear histologically aggressive, yet are clinically quite benign. Many authors have argued that this phenomenon can be explained by reexaming the histopathogenesis of HPCs, an area of active debate.

In a recent review by Gengler and Guillou, the very concept of HPC is challenged. The authors argued that, as experience with HPCs has increased, it has become clearer that the characteristics used to define these lesions are not entirely specific and instead represent a growth pattern shared by a number of heterogeneous lesions. As such, many lesions have been misclassified over the years. In examining the initial report by Stout and Murray, Gengler and Guillou noted that indeed the original 9 tumors were divided into 4 distinct groups, which, based on the descriptions, according to a more modern understanding, can be reclassified as follows: 1) epithelioid glomus cell tumors; 2) myofibroma/myofibromatosis and myopericytoma; 3 and 4) solitary fibrous tumors. Additionally, the diagnosis of HPC has always been a diagnosis of exclusion. Gengler and Guillou suggest that no more than 30% of HPCs reported in the literature actually have evidence of pericyte differentiation. They argue that if you remove the misclassified non-HPC lesions (with HPC-type growth patterns), the majority of the remaining lesions are more readily understood as solitary fibrous tumors or SFTs.

Solitary fibrous tumors are themselves a relatively heterogeneous group of tumors. Initially described as a lesion of the pleura, an SFT has since been reported in almost every location in the body. Many pathologists typically distinguish between a fibrous and cellular variant. The heart of the HPC debate is that a cellular SFT is essentially indistinguishable from an HPC. Many have argued that the adult and pediatric “adult-like” peripheral HPC lesions are indeed cellular SFTs, a typically aggressive lesion. The clinically more benign peripheral infantile HPCs, on the other hand, remain in the category known as HPC. These lesions show ultrastructural and immunohistochemical evidence of pericyte differentiation and may represent “true” HPCs.

Adult intracranial HPCs have long been classified as unique entities, but there is evidence that they too belong in the category of cellular SFT. This begs the question of...
<table>
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<tr>
<th>Authors &amp; Year</th>
<th>Age at Op, Sex</th>
<th>Location</th>
<th>Presenting Signs/Symptoms</th>
<th>Intervention</th>
<th>Histopathological Findings</th>
<th>Follow-Up</th>
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<tr>
<td>present case</td>
<td>2 mos, M</td>
<td>lt frontal region, extraxial</td>
<td>macrocephaly</td>
<td>GTR</td>
<td>round &amp; spindle-shaped cells; highly vascularized tissue; abundant reactive extramedullary hematopoiesis; CD31 neg; CD34 pos; CD45; CD99 neg; EMA neg; GFAP neg; keratin neg; MSA pos; NSE neg; S100 neg; SMA pos</td>
<td>NED at 28 mos</td>
</tr>
<tr>
<td>Aouad et al., 1991</td>
<td>5 days, M</td>
<td>rt cerebrum</td>
<td>lethargy; tense fontanels; bilat papilledema</td>
<td>GTR</td>
<td>spindle-shaped cell; numerous thin-walled vascular channels w/ single layer of endothelial cells; areas of necrosis; few mitotic figures; EMA neg; GFAP neg; S100 neg; NSE neg; reticulin pos; vimentin pos</td>
<td>NED at 5 mos</td>
</tr>
<tr>
<td>Blank et al., 1988</td>
<td>9 mos &amp; 31 mos, F</td>
<td>lt sylvian fissure</td>
<td>rt VII nerve palsy &amp; monoparesis of rt arm</td>
<td>initial op: STR; repeat op: GTR</td>
<td>“hemangiopericytoma”</td>
<td>recurrence at 20 mos after 1st op &amp; 2 mos after 2nd</td>
</tr>
<tr>
<td>Cavalheiro et al., 2002</td>
<td>34 wks gest, M</td>
<td>lt frontoparietal region</td>
<td>mother was in motor vehicle accident</td>
<td>GTR</td>
<td>highly cellular lesion w/ extensive vascular network; CD34 pos; EMA neg; reticulin pos; Ki 67/MIB-1 = 7%</td>
<td>NED at 2 yrs</td>
</tr>
<tr>
<td>Cole &amp; Naul, 2000</td>
<td>6 wks, M</td>
<td>rt parietooccipital region</td>
<td>seizures</td>
<td>GTR</td>
<td>EMA neg; GFAP neg; keratin neg; reticulin pos; vimentin pos</td>
<td>NED at 1 mos</td>
</tr>
<tr>
<td>Herzog et al., 1995</td>
<td>2.5 mos, M</td>
<td>rt parasagittal region</td>
<td>seizures</td>
<td>GTR</td>
<td>highly proliferative ovoid cells surrounding thin-walled capillaries; areas of necrosis; numerous mitotic figures</td>
<td>alive at 5 yrs</td>
</tr>
<tr>
<td></td>
<td>19 days, M</td>
<td>lt anterior temporal region</td>
<td>lt ophthalmoplegia &amp; ptosis</td>
<td>STR</td>
<td>highly proliferative ovoid cells surrounding thin-walled capillaries; extensive necrosis; numerous mitotic figures; EMA neg; GFAP neg; reticulin pos; S100 neg; vimentin pos</td>
<td>NED at 27 mos</td>
</tr>
<tr>
<td>Kerl et al., 2011</td>
<td>18 mos, F</td>
<td>lt occipitomental region</td>
<td>presented at 5 days w/ dehiscence of sagittal fissure; received chemo prior to resection</td>
<td>8 cycles of chemo; GTR</td>
<td>highly vascularized, cellular lesion w/ necrosis; low mitotic index; CD34 pos; Ki 67/MIB-1 = 4%</td>
<td>NED</td>
</tr>
<tr>
<td>Peace, 1954</td>
<td>3.5 days,† M</td>
<td>rt cerebrum</td>
<td>flaccid; seizures; bulging fontanel; fixed pupils</td>
<td>none</td>
<td>proliferation of ovoid cells &amp; associated hemorrhage; dense capillary networks; no mitosis; reticulin pos</td>
<td>DOD</td>
</tr>
<tr>
<td>Sobel et al., 2006</td>
<td>33 wks gest,† M</td>
<td>posterior fossa</td>
<td>diagnosed via neonatal ultrasound at 33 wks gest when mother presented w/ abdominal discomfort</td>
<td>none</td>
<td>hypercellular (ovoid) &amp; hypervascular lesion; extensive necrosis; many mitotic figures; CD34 pos; desmin neg; EMA neg; GFAP neg; NSE neg; S100 neg; synaptophysin neg; vimentin pos; Ki 67/MIB-1 = 40–50%</td>
<td>DOD at 11th day of life</td>
</tr>
<tr>
<td>Solitare &amp; Krigman, 1964</td>
<td>32 wks gest,† F</td>
<td>rt middle fossa</td>
<td>stillborn</td>
<td>none</td>
<td>3.5 × 2 × 4–cm mass; fusiform cells w/ reticulin fibers; “mixed HPC &amp; meningeal fibroma”</td>
<td>DOD</td>
</tr>
<tr>
<td>Wyler et al., 1973</td>
<td>6 mos, F</td>
<td>lt parietooccipital region</td>
<td>lethargic; tense fontanels</td>
<td>GTR &amp; cobalt radiotherapy</td>
<td>cellular lesion w/ abundant capillaries; noted necrosis; occasional mitotic figures; reticulin pos</td>
<td>NED at 14 mos</td>
</tr>
<tr>
<td>Fernandez-Pineda et al., 2011‡</td>
<td>7 yrs, NA</td>
<td>posterior fossa</td>
<td>NA</td>
<td>op (unknown result), chemo, &amp; radiotherapy</td>
<td>NA</td>
<td>DOD at 3 yrs</td>
</tr>
<tr>
<td></td>
<td>14 yrs, NA</td>
<td>pineal gland</td>
<td>NA</td>
<td>op (unknown result), chemo, &amp; radiotherapy</td>
<td>NA</td>
<td>DOD at 7 yrs</td>
</tr>
</tbody>
</table>

* chemo = chemotherapy; DOD = dead of disease; EMA = epithelial membrane antigen; gest = gestation; GFAP = glial fibrillary acidic protein; GTR = gross-total resection; MSA = muscle-specific actin; NA = not available; NED = no evidence of disease; neg = negative staining; NSE = neuron-specific enolase; pos = positive staining; SMA = smooth-muscle actin; STR = subtotal resection.† No surgery was performed.‡ Non-infantile cases; age at diagnosis and surgery significantly greater than the other reported cases.
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whether the less aggressive course of intracranial infantile HPCs is not explained by the same issue identified for their soft-tissue counterparts—namely, that infantile intracranial HPCs represent a unique pathology distinct from adult intracranial HPCs (which may be more accurately described as cellular SFTs) and, in fact, represent “true” HPCs.

Indeed, infantile HPCs share many clinicopathological characteristics with infantile myofibromatosis, a generally less aggressive pathology described in 1981 as a unique type of fibromatosis present in infancy.1,5,11 Mentzel et al. have suggested that infantile HPC is virtually indistinguishable from infantile myofibromatosis and, in fact, represents an immature stage of a single group of myofibroblastic/pericytic lesions of infancy.13

As mentioned, reports of intracranial infantile HPCs are exceedingly rare, with only 11 currently in the literature (Table 1).1,3,4,5,6,11,12,16,18,19,23 Age at initial surgery ranges from 2 days to 18 months. In terms of treatment and prognosis, complete excision following initial intervention was reported in 6 of the cases, and those patients had no evidence of disease at follow-up, which ranged from 1 month to 5 years.1,4,6,11,12,23 One of the patients with complete resection also underwent whole-brain cobalt radiotherapy.23 Another patient with complete resection was treated with neoadjuvant chemotherapy because the initial tumor was considered too large for attempted resection, and complete resection was performed 18 months later.12

There are 2 reported cases of partial resection, in one of which spontaneous regression of the residual tumor was demonstrated,11 and in the other of which the lesion was completely resected 20 months later;1 the first patient had no evidence of disease at follow-up at 27 months; the second had recurrence at 2 months. Interestingly, our literature review also identified 2 patients who were diagnosed with the disease and treated at significantly older ages than other reported cases (7 and 14 years).7 These patients received surgery (results not reported), chemotherapy, and radiation therapy; one died at 3 years and the other at 7 years after treatment. No histological workup was described for these cases. Finally, 3 patients died after diagnosis, before treatment had been initiated.15,18,19 The patient reported on here represents the seventh reported case of complete resection, and, as with the others, our patient shows no evidence of disease at current follow-up.

Histological descriptions are available for 10 of the previously reported cases.1,4,6,11,12,15,18,19,23 The growth patterns described are indeed consistent with what has traditionally been termed HPC, and most exhibit aggressive features such as hemorrhage and necrosis, despite their relatively benign clinical courses. Unfortunately, we found no definitive ultrastructural or immunohistochemical evidence of pericyte differentiation. Reviewing the case we have presented here reveals a growth pattern characteristic of HPCs. Additionally, a predominance of tumor cells are positive for smooth-muscle actin and muscle-specific actin, suggesting myofibromatous differentiation.

Our findings are consistent with the description suggested by Mentzel et al.13—a histological description best classified as an immature form of infantile myofibromatosis. Perivascular cells (myofibroblasts and pericytes) share a common progenitor, which in the case of tumor growth is neoplastic. We argue that when tumors of perivascular origin arise in younger patients, they have a predominance of myofibroblastic cells, stain accordingly, and exhibit characteristically benign clinical behavior.

Finally, the case presented here had the unique feature of intralesional extramedullary hematopoiiesis. Initially identified radiographically as areas of necrosis, histological examination later demonstrated pronounced regions of defined hematopoiiesis. In our review of the existing case discussions we did not find any description of reactive extramedullary hematopoiiesis.

Conclusions

When compared with their adult counterparts, infantile HPCs have long been associated with a relatively benign clinical course despite typically aggressive-appearing histology. The current explanation for peripheral lesions is that infantile HPCs represent an immature form along a spectrum of myofibroblastic/pericytic lesions of infancy, a so-called true HPC or, perhaps, immature infantile myofibromatosis, whereas adult HPCs are in fact cellular SFTs that exhibit HPC-like growth characteristics and have been misclassified over the years. Cellular SFTs are, by nature, a more aggressive pathology than the myofibroblastic/pericytic lesions of infancy. As an immature form of this myofibroblastic/pericytic pathology, infantile HPCs appear histologically aggressive. We propose the same is true in the case of intracranial HPCs.

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: Duncan, McHugh, Baranoski. Acquisition of data: McHugh, Baranoski. Analysis and interpretation of data: all authors. Drafting the article: McHugh, Baranoski. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Duncan. Study supervision: Duncan.

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