• BRIEF REPORT •

Central Nervous System Hemangiopericytoma, Retrospective Four Year Pathology Case Series

Mario E. Quintero-Aguiló, MD

Hemangiopericytomas (HPC) are uncommon, aggressive, difficult to diagnose tumors mostly found in the extremities and pelvis and very rarely within the Central Nervous System(CNS). CNS HPC closely mimics meningioma, which is a much more frequent benign tumor, while HPC is potentially lethal, thus correct diagnosis of HPC is vital. Due to the very low frequency of CNS HPC, local experience with this tumor is very limited. For this reason a retrospective four year review of CNS pathology cases was performed to observe the frequency of CNS HPC, histopathology, immunohistochemistry, correlate the proportion of HPC to meningiomas and compare these with the literature. Results showed that our past pathologic assessment of HPC as well as the incidence is consistent with the literature, while the ratio of HPC to meningioma was above expected. This is the first local study dealing with the pathology of CNS HPC, which discloses an adequate clinic-pathologic assessment within the UPR premises as reflected by pathologic-epidemiologic findings coincident with the literature. A discrepancy of the HPC to meningioma ratio was found.Further studies are warranted to delve into the etiologies of this discrepancy as the issue has major implications due to the benign and malignant behavior respectively of meningioma and HPC. [*P R Health Sci J 2012;3:145-147*]

Key words: Hemangiopericytoma, CNS, Pathology, Immunohistochemistry

Hemangiopericytomas (HPC) are rare tumors thought to be derived from Zimmermann pericytes (1-3), pericapillary cells regulating caliber and blood flow. HPC is not organ restricted as pericytes are ubiquitous in mesenchyme derived tissue, however most HPC afflict the musculoskeletal system and skin (4, 5). Central nervous system (CNS) HPC are uncommon, aggressive dural-based tumors comprising under 1% of all CNS tumors (6, 7) with approximate 5-year recurrence and metastasis rates of 65% and 33%, respectively (8). The histogenesis of CNS HPC is controversial, thought to be either soft tissue tumors or an aggressive variant of angioblastic meningioma (9). The current World Health Organization (WHO) classification of CNS tumors, places HPC within the mesenchymal, non-meningothelial tumor group (10). Though HPC exhibits different clinical behavior, immunohistochemical characteristics, and ultrastructural features from meningioma (10), they are similar on imaging, and this leads to frequent misdiagnosis. Because HPC are more aggressive than meningiomas with a propensity for both recurrence and metastases, correct diagnosis and treatment are critical.

Due to the rarity of this tumor, with only approximately 300 cases documented in the worldwide literature since it was first described in 1942 (2) and no local studies found, this study sought to report and discuss the pathology and epidemiology of the entity at the UPR.

Materials and Methods

With IRB authorization, a retrospective review of the surgical pathology electronic files of the UPR Department of Pathology was done from January 1, 2005 to December 31, 2008. Query terms were for all surgical cases coded as brain. Every resulting case was checked for diagnosis, only cases with a final diagnosis of HPC were included in the study. Data obtained from HPC cases was: age, sex, tumor location and results from any additional pathologic studies (special stains and/or immunohistochemistry). Representative tissue slides from every case were obtained for confirmation of original diagnoses and photomicrograph annotation. Statistical methods employed were descriptive, including for patients and tumors : yearly totals, incidence,range (from minimum to maximum), calculation of the mean age for patients afflicted with HPC and ratio of HPC to meningioma.

University of Puerto Rico Comprehensive Cancer Center, San Juan, Puerto Rico; Department of Pathology and Laboratory Medicine, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico; Surgical Oncology, University of Texas M.D. Anderson Cancer Center, Texas, United States of America.

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Address correspondence to: Mario E. Quintero-Aguiló, MD, PMB 371 PO Box 70344, San Juan, PR 00936-8344. Email: mquintero@cccupr.org; marugenio@yahoo.com

Results

From 2005 to 2008 eight hundred eighty-eight brain surgical pathology cases were identified, yearly totals ranging from 158 to 277 cases (Table 1). Excluding metastases, hematopoietic neoplasms and miscellaneous lesions there were a total of 871 primary CNS neoplasms ranging from 140 to 252 cases per year. A total of 5 hemangiopericytomas were identified, with numbers ranging from 0 to 2 cases per year. The HPC incidence for the study period (as a percentage of the total number of primary CNS neoplasms) was 0.57%. Meningiomas totalled 103 (range: 14 to 40 cases per year). The HPC to meningiomas ratio was from 1:15.5 to 1:20. Sex distribution for HPC was 3 females and 2 males. The patients age range was from 36 to 62 years old (mean 46). Immunohistochemistry (IHC) was performed on three cases (Table 2), generally the results were vimentin (VIM) and CD34 positive with negative S-100 (s100 protein), KER (Keratin), EMA (epithelial membrane antigen), DES (Desmin), BCL-2 (b-cell lymphoma kinase 2) and CD99 (CD99 antigen). Most tumors were either extra axial and/or associated to the falx. Histopathologically (Figure 1), tumors were moderate to highly cellular comprised of spindle cells with plump nuclei, scant cytoplasm arranged in short fascicles. Some, showed few hypocellular areas with dense acellular hyalinised(collagenised) foci. No whorling, pseudonucleoli, or calcifications were identified. Mitotic figures were sparse varying from 0 to 2 per 10 high power fields. There was no necrosis in any of the tumors. Dilated thin vasculature was noted, some with characteristic staghorn pattern. No mention of reticulin stain was made on any of the reports, but slides were found for one case, which disclosed a rich pericellular reticulin pattern within the tumor.

Table 1. Brain surgical cases UPR Department of Pathology 2005-2008.

Year	Hemangiopericytoma	Meningioma	Total brain tumors	Mets	Hematopoietic	Non-tumor	Total lesions
2005	0	14	140	13	-	5(cysts)	158
2006	2	31	201	13	3(1HD,2MM)	-	217
2007	2	40	252	21	3(2MZL,1GS)	S.mansoni	277
2008	1	18	228	7	1(HD)	-	236
Total	**5**	**103**	**821**	**54**	**7**	**6**	**888**

HD-Hodgkin Disease, MM-Multiple Myeloma, MZL-Marginal Zone Lymphoma, GS-Granulocytic Sarcoma, Mets-metastases

Table 2. Hemangiopericytoma cases demographics and immunohistochemistry results.

Case	Year	Age	Sex	Location	IHC pos(+)	neg (-)
1	2006	47	M	Falx/parietal	N/A	N/A
2	2006	43	M	Extra-axial	VIM	EMA,S-100,KER,CD34,DES
3	2007	42	F	Extra-axial/falx	VIM,CD34	EMA,S-100,KER,CD99
4	2007	36	F	Frontal/para-sagittal	CD34	EMA,S-100,BCL-2
5	2008	62	F	N/A	N/A	N/A

N/A-not available, VIM-vimentin, EMA-epithelial membrane antigen, S-100- s 100 protein, KER-keratin, DES-desmin, CD 99-, BCL-2-

Discussion

Most commonly HPC are in the extremities, pelvis, head and neck, and very rarely within the CNS. Begg and Garret reported the first CNS HPC (11). Among vascular tumors, the diagnosis of HPC is one of the most controversial, doubt has even been raised as to its existence as a specific tumor type. HPC, described by Stout and Murray in 1942, does not lend itself readily to histologic classification. Enzinger and Smith's 1976 paper on hemangiopericytoma warned of several tumors with which it may be confused due to similar staghorn shaped vessels. Classic HPC histology is of high cellularity and numerous blood vessels with "stag-horn" or slit-like, appearance. The cytoplasm is often sparse with variable nuclear hyperchromasia. Sometimes a "jumbled-up" pattern is described whithout specific architecture, but cells organizing in haphazard, loose clusters. Epithelioid features, whorls, and psammomatous calcifications (typical of meningioma) are distinctly absent. Many tumors harbor focal paucicellularity, giving a vague biphasic appearance. A striking feature of HPC is an abundant and elaborate reticulin network around individual or small groups of cells. Immunohistochemically (12) HPC is diverse and several antibodies : EMA, CD34, GFAP (glial fibrillary acidic protein), VIM, factor XIIIa (coagulation factor XIII A subunit), Leu 7 (Leu-7 antigen) and S-100, are sometimes positive. In this series two tumors had no immunostains results, this is rather unusual as IHC is usually essential when faced with this lesions, so these two cases might have been recurrent/residual (already immunostained previously), immunostained and IHC results not incorporated on the final report, or have been signed out by an experienced "old school" neuropathologist who was used to evaluating this sort of lesion before the advent of IHC relying solely on H&E morphology and reticulin stain. The most commonly used antibodies were VIM, EMA, CD34 and S-100. Both EMA and S-100 were negative in all patients. Two tumors were CD34 positive. Although no single marker is 100% sensitive or specific, the immunoprofile of HPC is sufficiently distinct (13) to differentiate it from meningioma (positive for EMA and VIM and variable positivity for S-100), whereas HPC are usually negative for EMA and S-100 and positive for VIM. CD34 is positive in solitary fibrous tumor (SFT) whereas only 25% to 30% of CNS HPC show CD34 positivity, thus leading some to ponder whether CNS HPC might represent the cellular form of SFT (less frequent CD34 expression). Two cases were CD34 positive, one with VIM co-positivity, thus favoring a

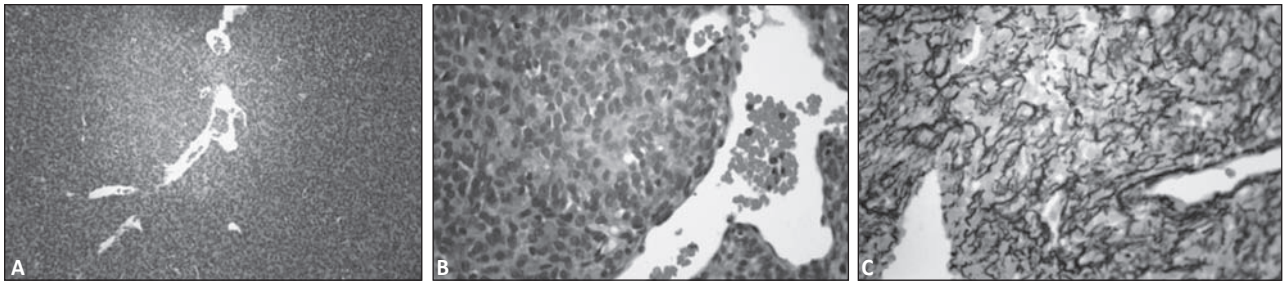

Figure 1. A) Low power photomicrograph showing moderate to highly cellular lesion with short fascicular arrangement and abundant dilated thin vasculature, some with characteristic staghorn pattern. B) High power photomicrograph reveals spindle - ovoid cells with plump nuclei, scant cytoplasm arranged in short fascicles. No evidence of whorling, pseudonucleoli, calcifications or necrosis. C) Reticulin stain showing a rich and intricate pericellular pattern within the tumor.

diagnosis of HPC over SFT. The other CD34 positive case was BCL-2 negative, which also favors HPC over SFT. Case 2, had classic expected immunoprofile (VIM positive and negative for SFT, meningioma and carcinoma markers).

The 0.57% HPC incidence (during the study period) is very close to the globally reported 0.4% incidence (10). The patients age range (36 to 62 y/o[mean 46]) matched the reported (mean 43 y/o), while sex distribution of 2 males and 3 females did not(reported 1.4:1). Regarding the sex distribution no inferences can be made due to the small sample size. The HPC to meningiomas ratio was from 1:15.5 to 1:20 (reported ratios 1:40 to 1:60) (14). As the found HPC incidence corresponds with the reported figures, it can be deducted that the altered HPC to meningioma ratio is due to a smaller number of meningiomas in this series as compared with the reported numbers. As this study deals with HPC and not meningiomas, additional studies would be worthwhile to ascertain the causes and significance of the reflected deviation of the found HPC to meningioma ratio along with imaging findings and clinical correlation for recurrence, response to treatment and survival data.

Resumen

Los hemangiopericitomas (HPC) en el sistema nervioso central (SNC) son muy raros, este tumor se presenta más bien en las extremidades y pelvis. Es un tumor infrecuente, recurrente y cuyo diagnóstico es retante. El diagnóstico certero de HPC es sumamente importante, particularmente dada su semejanza a los meningiomas, que son tumores benignos, mientras que los HPC son potencialmente mortales. Este estudio surge para analizar los casos diagnosticados como HPC del SNC en el departamento de patología del Recinto de Ciencias Médicas(RCM) en San Juan y ver si en base a los hallazgos el diagnóstico de esta lesión es comparable a lo descrito en la literatura. Se evaluó la histopatología e immunohistoquímica de HPC de SNC en los archivos de casos patológicos de entre 2005 y 2008. Además se obtuvo el número total de casos de SNC y de meningiomas para determinar la frecuencia e incidencia de HPC y determinar la proporción deHPC a meningiomas. La evaluación patológica e incidencia de los HPC de SNC durante el intervalo 2005-2008 coincide con lo publicado, hallándose una desproporción de HPC a meningioma. Este es el primer estudio descriptivo de la patología de HPC de SNC en Puerto Rico. Sería beneficioso realizar estudios postreros que tratasen de explicar la etiología de las discrepancias entre lo hallado en el RCM y la literatura publicada, en cuanto a la desproporción de HPC a meningiomas.

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