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Clinical metric for differentiating intracranial hemangiopericytomas from meningiomas using diffusion weighted MRI

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ABSTRACT

Purpose: Intracranial Hemangiopericytomas (IHP) are dural based tumors that frequently recur/metastasize. Unfortunately, their imaging appearance overlaps significantly with more benign meningiomas. We evaluated the use of diffusion weighted imaging (DWI) to differentiate IHP from meningioma.
Methods: We compared MRI of IHP tumors (WHO Grades II/III) ($n = 20$) to meningioma ($n = 48$, WHO Grade I/II).
Findings: ADC values differed between IHP (1.05 × 10–3 mm2/s) and meningiomas (0.89 × 10–3 mm2/s) ($p = 0.05$). Normalized ADC ratios (nADC), differed between IHP and meningiomas (1.30 vs 1.07, $p = 0.03$).
Conclusion: Importantly, a nADC cutoff of > 1.3 was specific (96%) but not sensitive (35%) for identifying IHP.

1. Introduction

First described in 1942, hemangiopericytomas are rare tumors that arise from the pericytes of Zimmerman, which surround capillaries [1]. Unfortunately, the early literature on mesenchymal tumors of the central nervous system was highly variable, leading to much confusion. In the most recent iteration of the World Health Organization (WHO) tumor classification, hemangiopericytomas are placed in a spectrum termed *solitary fibrous tumor/hemangiopericytoma* [2]. The current WHO Grade I, II, and III tumors correlate with the previously termed solitary fibrous tumor, hemangiopericytoma, and anaplastic hemangiopericytoma, respectively. In other words, solitary fibrous tumor (Grade I) are low grade tumors and hemangiopericytomas (Grade II)/anaplastic hemangiopericytomas (Grade III) represent higher grade tumors in the WHO 2016 classification.

WHO Grade II and III tumors, herein collectively termed intracranial hemangiopericytoma (IHP), are aggressive tumors that commonly recur after surgical resection (60%) and metastasize (20%) to distant organs such as lung, bone and liver [3]. Unfortunately, they are notoriously difficult to distinguish from benign dural based masses such as meningiomas using standard MRI sequences. Suggesting the diagnosis of IHP on preoperative imaging may alter surgical management as gross total resection has been shown to independently improve survival and IHPs may require preoperative embolization and/or radiation for adequate treatment [4].

Typical MR imaging features include the following: a heterogeneous dural-based mass, isointensity on T1, mild hyperintensity on T2, contrast enhancement, and prominent signal voids (i.e. 'flow voids') [5]. Multiple recent small series have suggested that diffusion-weighted imaging can be useful in differentiating IHP from other dural-based tumors. Liu et al. demonstrated that IHPs had significantly higher absolute ADC and ADC ratios [6]. Meng et al. demonstrated that ADC values were the sole independent predictor of HPC in their series [7].

Here, we present the findings from the largest retrospective MRI series of 20 patients with pathologically proven IHP (WHO Grade II and III) from two institutions. MRI findings, including diffusion weighted imaging (DWI) findings were compared with a control cohort of patients with WHO Grade I and II meningiomas. We hypothesize that IHPs in our series would demonstrate elevated ADC values.

2. Materials and methods

An IRB approved, retrospective review of pathology databases from two separate institutions for cases of IHP and meningioma from 2005 to 2016 was performed. Results were referenced with the PACS for preoperative MR imaging. Imaging required for inclusion consisted of the

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following sequences: axial fluid attenuated inversion recovery (FLAIR), pre-contrast T1-weighted image (T1WI), axial fast spin echo (FSE) T2-weighted image (T2WI), axial isotropic DWI, coronal FLAIR T2WI, sagittal FLAIR T1WI, and post contrast axial FLAIR T1WI with fat saturation.

At institution #1, a 3.0T clinical MR scanner (GE Medical Systems, Milwaukee, Wis) using standard head coil was used. The DWI sequence included a single shot spin-echo echo-planar sequence (TR 7000/TE 73) with b-values of 0 and 1000 s/mm2 (Matrix: 128 × 128 matrix; Slice Thickness: 5 mm with 0 mm gap; FOV: 220 × 220 mm). At institution #2, a 1.5 T clinical MR scanner (GE Medical Systems, Milwaukee, Wis) using a standard head coil was used. The DWI sequence included a single shot spin-echo echo-planar sequence (TR 10000/TE min) with b-values of 0 and 1000 s/mm2 (Matrix: 128 × 128 matrix; Slice Thickness: 5 mm, 1 mm gap; FOV: 260 × 260 mm).

Studies were reviewed by a CAQ trained Neuroradiologist and a radiology resident at each site. Imaging was evaluated specifically with regard to volume, diffusion characteristics, T1 and T2 signal characteristics, contrast enhancement and the presence of flow voids. As meningiomas are significantly more common, a subset of cases (both WHO Grade I and II) were selected from the pathology database utilizing a random number generator method in R (Vienna, Austria). Imaging examples from our series can be found in Fig. 1.

Quantitative ADC value measurements were then obtained using region-of-interest (ROI) analysis (GE FuncTool, AW workstation, GE Medical Systems, Milwaukee, WI). ROIs (ranging 0.3–1.0 cm in diameter) were placed in the homogeneous, most representative, portions of the tumors. Examples can be found in Fig. 2. Special attention was paid to avoiding signal voids (i.e. flow voids), areas of hemorrhage, mineralization, or artifact. In cases of larger tumors, up to two ROIs were placed in separate parts of the tumor and then averaged. ROI markers were also placed in normal-appearing contralateral white matter. A normalized ADC (nADC) ratio was then calculated by dividing tumor ADC values by the normal-appearing contralateral white matter ADC values.

Comparisons between different groups of IHP were performed using unpaired two-tailed student's *t*-test, one-way ANOVA and Fisher's exact test for categorical data. Receiver operating characteristics (ROC) were evaluated using an area under the curve (AUC) method. All statistical methods were performed using the R statistical software package (Vienna, Austria).

3. Results

3.1. Demographics

Of the 26 patients identified with histology confirmed IHP, 20 had relevant preoperative MR imaging available for review. The IHP study population was 70% male (age range: 22–78) and 30% female (age range: 22–75). The average IHP patient was 53.0 years old.

321 cases of WHO Grade I meningioma and 51 cases of WHO Grade II meningioma were identified in the above time period. 30 cases from each group were selected for inclusion in our series using a random number generator in the R software package. Of the 30 patients with histologically proven meningioma, 25 WHO Grade I and 23 WHO Grade II meningioma had adequate preoperative MRI imaging, respectively. While age did not significantly differ between IHP and meningioma populations ($p = 0.42$), there were significant difference in gender between the IHP (70% Male) and meningioma (33% Male) groups ($p = 0.01$). A summary of patient demographics can be found in Table 1.

3.2. Final pathology and conventional imaging characteristics

Final pathology of IHP cases revealed 15 WHO Grade II tumors (75%) and 5 WHO Grade III tumors (25%). While T1 and T2 characteristics of the tumors were variable, all IHP tumors demonstrated gadolinium enhancement (100%). Most were found to have flow voids (60%). The presence of flow voids was not significantly different between the different tumor grade (WHO Grade II vs III) ($p = 0.51$). Size was also found to be highly variable, however most tumors (90%) were < 90 cm^3. Notably, two tumors measured > 200 cm^3 (see Table 2).

All meningiomas demonstrated gadolinium enhancement (100%). 20 meningiomas (Grade I, $n = 7$, and Grade II, $n = 13$) demonstrated (42%) intratumoral flow voids which was a lower, but not significantly

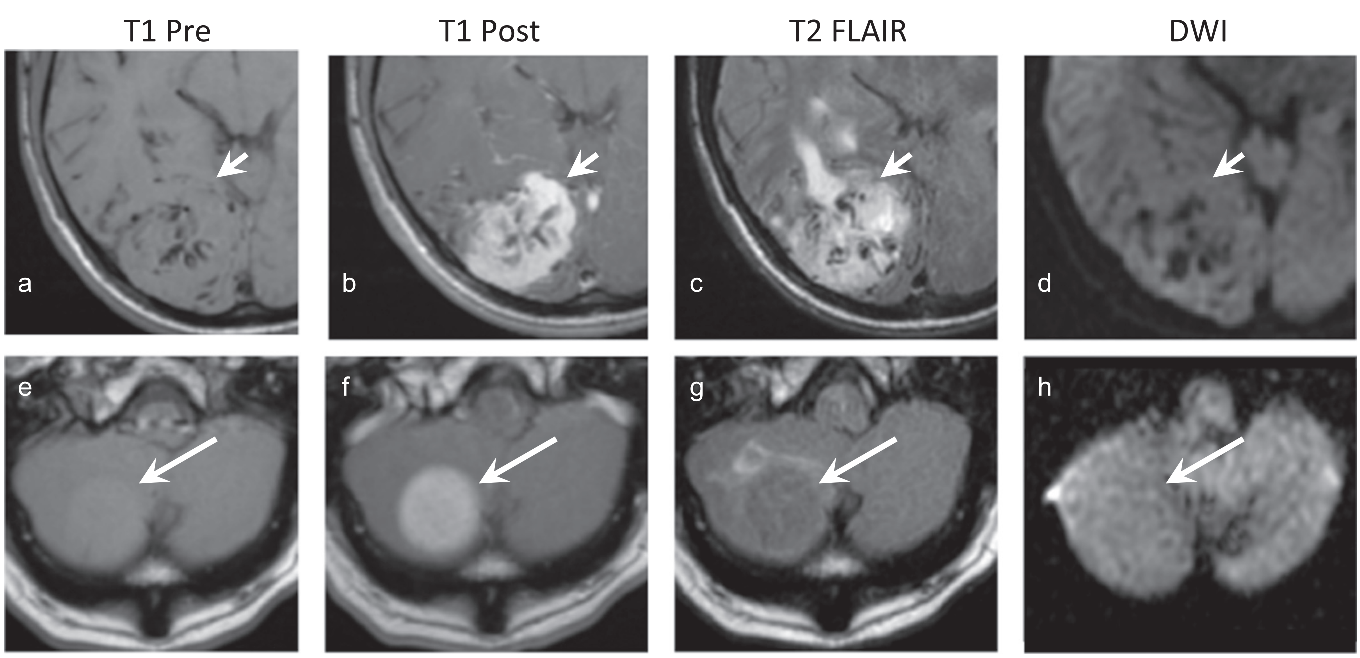

Fig. 1. (**a–d**) 50 year old man with IHP demonstrates T1 iso- and T2 hyperintensity. The tumor avidly enhances with contrast and contains several signal ("flow") voids. It demonstrates subjective isointensity on DWI. (**e–f**) 38 year old woman with IHP demonstrates slight T1 hyper- and T2 hypointensity. The tumor avidly enhances with contrast demonstrates isointensity on DWI.

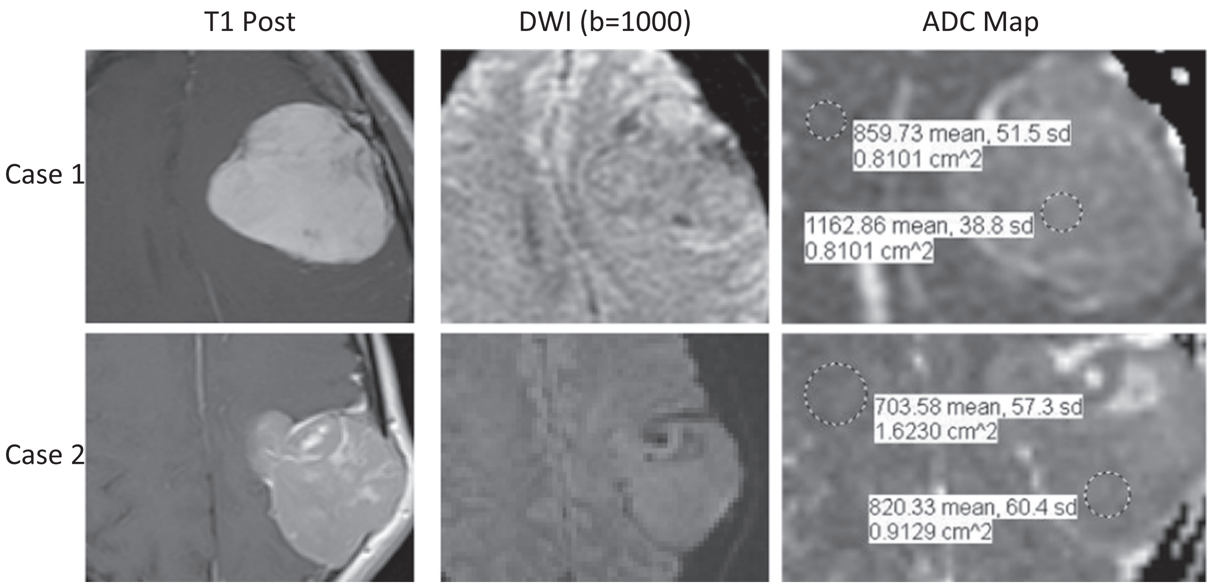

Fig. 2. Examples of ROI placement in two separate cases of IHP.

Table 1
Patient demographics.

Patient age IHP, median (range)	53.0 (22–78)
IHP gender (male/female)	14 (70%)/6 (30%)
Final IHP pathology (WHO grade II vs III)	15 (75%), 5 (25%)
Patient age meningioma, median (G1) (median)	60.6 (19–82)
Meningioma (G1) gender (male/female)	7 (28%)/18 (72%)
Patient age meningioma (G2), median (range)	57.4 (31–88)
Meningioma (G2) gender (male/female)	9 (39%)/14 (61%)
Final meningioma pathology (WHO grade I vs II)	25 (52%)/23 (48%)

Table 2
MR imaging findings.

IHP volume, range	2.4–210.0 cm^3
IHP volume, mean/median (cm^3)	5.5/62.0
IHP lesions with flow voids (%)	12 (60%)
IHP contrast enhancement	100%
IHP ADC to normal white matter ratio, mean/SD	1.30/0.40
IHP ADC, mean/SD ($\times 10^{-3}$ mm^2/s)	1.05/0.31
Meningioma (G1) ADC to normal white matter ratio, mean/SD	1.05/0.18
Meningioma (G1) ADC, mean/SD ($\times 10^{-3}$ mm^2/s)	0.90/0.17
Meningioma (G2) ADC to normal white matter ratio, mean/SD	1.11/0.19
Meningioma (G2) ADC, mean/SD ($\times 10^{-3}$ mm^2/s)	0.88/0.12

different, proportion than found in IHP ($p = 0.19$).

3.3. Diffusion-weighted imaging

Reduced diffusivity, measured as a nADC ratio < 1, was found in 6/20 (30%) of IHP cases. Of those that demonstrated nADC ratio < 1, only a minority 2/20 (10%) demonstrated substantially restricted diffusion ratio, nADC ratio < 0.90.

Increased diffusivity, nADC ratio > 1, was found in 14/20 (70%) of our cases. Among the cases with nADC ratio > 1, 12/14 (86%) cases demonstrated substantially elevated diffusion ration, defined by nADC ratio > 1.1.

ADC values differed between IHP (1.05×10^{-3} mm^2/s) and meningiomas (0.89×10^{-3} mm^2/s) ($p = 0.04$), and on subgroup analysis between IHP and WHO-G1 (0.88×10^{-3} mm(2)/s) and WHO-G2 meningiomas (0.90×10^{-3} mm^2/s) ($p = 0.03$ and $p = 0.05$ respectively) (Fig. 3A). Significant differences between IHP nADC Ratios (1.30) and all Meningiomas (1.07) were apparent ($p = 0.03$). Additionally, the difference between the nADC ratio for IHPs (1.30) and WHO grade II meningiomas (1.10) approached significance ($p = 0.08$) (Fig. 3B).

Receiver operating characteristic curves were analyzed using ADC values and nADC ratios as predictors for the IHP diagnosis as opposed to WHO Grade I meningiomas (Fig. 4). AUC were 0.64 and 0.68 respectively. An nADC ratio cutoff of > 1.3 for the diagnosis of IHP was highly specific, but not sensitive (Sens: 96%, Spec: 35%) (see Fig. 5).

4. Discussion

Generally speaking, restricted diffusion has been shown to correlate with tumor grade in numerous intracranial neoplasms. Previous work by Filippi et al. showed that DWI could differentiate low and high grade meningiomas, with higher grade meningiomas demonstrating more diffusion restriction than lower grade meningiomas [8]. While there is not a consensus on the biophysical basis of this phenomenon, it is generally thought to be the result of a combination of higher cellularity, tissue disorganization, and increased extracellular space tortuosity, all contributing to reduced motion of water [9]. While IHPs are characterized by high cellularity on histopathology, the presence of arborizing "staghorn" vessels are also common. The increased blood content of these tumors may, in part, account for their diffusion characteristics [3].

Our study demonstrates that IHPs have significantly higher ADC values compared to meningiomas. Even though no significant differences between 1.5T and 3.0T nADC ratios were identified, nADC ratios were calculated to mitigate this confounding factor. IHPs had higher nADC ratios than meningiomas ($p = 0.03$) and WHO grade II meningiomas ($p = 0.08$). When differentiating IHP from grade I meningiomas, our data suggest that ADC ratios > 1.3 is a specific (specificity: 96%) finding for IHP.

Multiple recent small series evaluating DWI characteristics of IHPs have shown that IHP tumor pathology demonstrated increased diffusivity. In a series of 7 patients, Mama et al., found that IHPs commonly demonstrated higher ADC values than normal appearing contralateral white matter [10]. In comparing imaging characteristics of 12 IHP cases with 17 cases of angiomatous meningioma, Meng et al. demonstrated that preoperative ADC values were the sole independent predictor of histologic outcome [11]. L. Liu et al. reviewed the MR imaging of 12 IHP patients, with diffusion imaging and found that IHPs had significantly higher mean ADC values $1.17 \pm 0.30 \times 10^{-3}$ mm^2/s

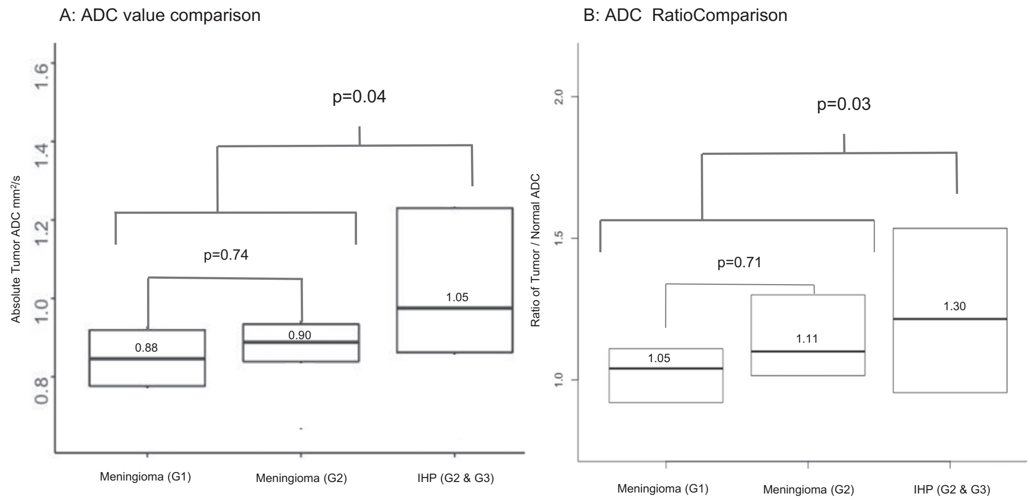

Fig. 3. Box plot diagram demonstrating the median values of (a) ADC and (b) ADC ratios for IHP. *p*-Values presented for student's *t*-test.

compared to anaplastic meningiomas $0.75 \pm 0.11 \times 10^{-3}\,mm^2/s$ [6]. Interestingly, their average IHP ADC value was slightly higher but not significantly different from our average ADC value of $(1.05 \pm 0.31) \times 10^{-3}\,mm^2/s$. In their series of 15 IHP patients, G. Liu et al. described the DWI characteristics of 10 IHP patients and found that mean MinADC value of HPC $(1.116 \pm 0.127) \times 10–3\,mm^2/s$ was significantly higher than that of meningioma $(0.875 \pm 0.104) \times 10–3\,mm^2/s$ [12].

Our series builds on this work by demonstrating that ADC values differ between IHP and meningiomas of varying grades in the largest series of IHP to date. Furthermore, our series is the first to incorporate several grades of IHP in concordance with the 2016 WHO tumor classification update and compare these tumors to a cohort of WHO grade 1 and 2 meningiomas, the primary differential consideration in clinical practice. Finally, we have derived the first clinically relevant DWI metric for suggesting the diagnosis of IHP when evaluating a dural based mass, i.e. nADC ratio > 1.3. In the future, comparing the diffusion characteristics with WHO Grade I tumors (previously termed *solitary fibrous tumors*) would help elucidate the potential physiological basis for the finding of increased diffusion given the biological similarity between these tumors.

A multi-institutional approach allowed for more statistical power in analyzing this rare tumor, however this method resulted in slight differences in imaging technique and protocol. For instance, while all imaging was performed on equipment from the same manufacturer, magnet strength did vary slightly. Most imaging was performed at 1.5 T (n = 13) with fewer cases at 3.0T (n = 7). Although this may have affected our results it is reassuring that ADC values did not significantly differ between magnet strength (p = 0.40). Using an nADC ratio methodology to internally correct for scanner differences served to

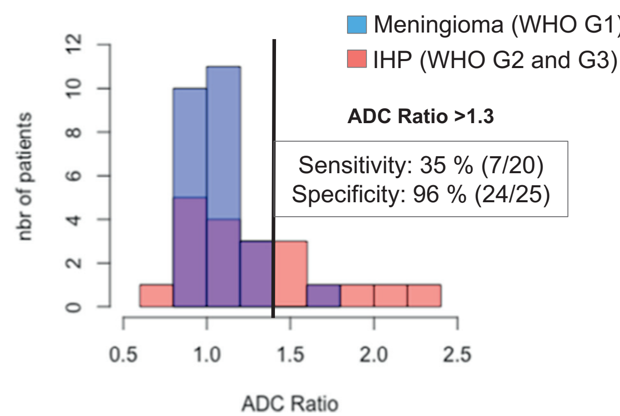

Fig. 5. Histogram comparing IHP (red) with WHO G1 meningiomas (blue). Only a single case of WHO G1 meningioma demonstrated a markedly elevated ADC ratio of 1.6. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

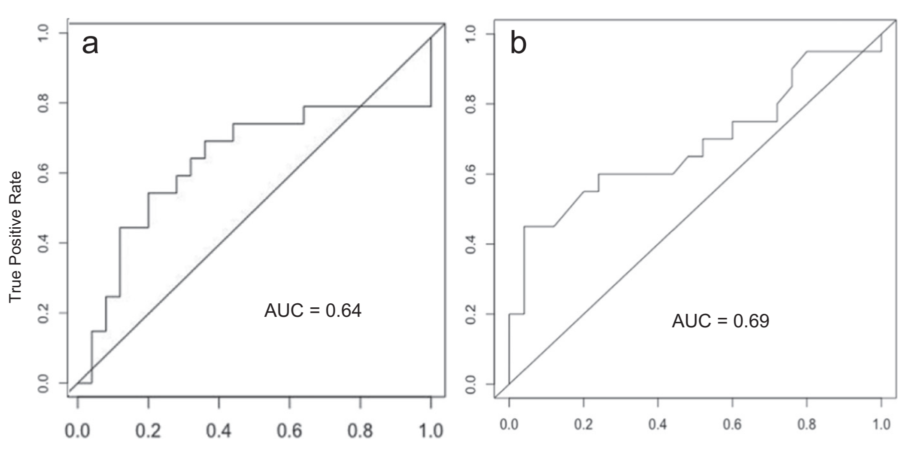

Fig. 4. Receiver operating curve (ROC) with area under the curve (AUC) values for the diagnostic performance of (a) ADC and (b) ADC ratios in predicting the diagnosis of IHP.

minimize the effect of scanner and protocol heterogeneity. Unfortunately, this method is not perfect and the heterogeneity in scanners and minor differences in sequence parameters could explain why our atypical meningioma cohort (WHO Grade II) demonstrated similar diffusivity to typical meningiomas unlike what has been demonstrated in the literature. Finally, gender differences between groups reached statistical significance ($p = 0.01$). The female predominance in the meningioma group is similar to established epidemiology of this tumor. However, IHP demonstrated a significantly higher rate of male gender, 70%, compared to the largest literature review of 523 patients where, essentially, no gender predominance was noted [13].

5. Conclusions

IHPs are rare extra-axial neoplasms which can have a similar appearance to the more common meningiomas on conventional MR imaging. As has been described in the literature, the presence flow voids and contrast enhancement were common. Our series, the largest MRI series of IHPs to date, suggests that elevated ADC values on DWI are also a common imaging feature, 70% in our series. In fact, this finding may be distinctive enough to differentiate it from meningiomas of varying grades with high specificity (96%) when using a nADC ratio cutoff of > 1.3. Although the finding of elevated ADC values requires further characterization, it may represent a useful clue for the Neuroradiologist to suggest the diagnosis of intracranial hemangiopericytoma.

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