Intracranial Cystic Tumors with a Mural Nodule: Conventional, Diffusion Tensor and Perfusion Magnetic Resonance Imaging Findings

Mboka Jacob^{1,2}, Seung-Koo Lee²

¹Department of Radiology, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania, ²Department of Radiology, Severance Hospital, Yonsei University College of Medicine, Yonsei University Heath System, Seoul, Korea

Correspondence: Dr. Mboka Jacob, Department of Radiology, Muhimbili University of Health and Allied Sciences, P.O. Box 65001, Dar es Salaam, Tanzania. E-mail: mbokajacob@gmail.com

ABSTRACT

Introduction: Intracranial cystic tumors with mural nodule have been extensively studied. None of these studies have established the role of conventional, fractional anisotropy diffusion tensor imaging (FADTI) and dynamic susceptibility contrast magnetic resonance imaging (MRI) in the assessment of grade and type of cystic brain tumors with a mural nodule. Materials and Methods: This was a retrospective cross-sectional study, which was conducted at Severance Hospital. Brain MRI of 15 consecutive patients with a cystic brain tumor with a mural nodule was analyzed. Results: Among the 15 studied patients 11 were females. The age ranged from 12 to 54 years. Six of the patients had high-grade tumors. Most five of the high-grade tumors showed cystic wall contrast enhancement while none was found among the low-grade group. All high-grade tumors showed increased regional cerebral blood volume (rCBV) compared to three of low-grade tumors. Hemangioblastomas, glioblastoma multiforme (GBM) and the primitive neuroectodermal tumor showed increased rCBV while pilocytic astrocytoma, ependymoma, and ganglioglioma showed decreased rCBV. There were no difference in fractional anisotropy (FA) values between tumor grades and types. Conclusion: Postcontrast T1-weighted image and perfusion MRI showed in this study to be very useful in differentiating high- and low-grade cystic tumors with the mural nodule. FA values added no benefit to tumor differentiation. Hemangioblastoma was the only tumor with increased rCBV among low-grade tumors. GBM, which is a malignant tumor, can present as a cystic lesion with a mural nodule.

Key words: Glioblastoma multiforme; hemangioblastoma; magnetic resonance imaging; pilocytic astrocytoma

Introduction

Magnetic resonance imaging (MRI) advanced techniques provide physiologic information that complements the anatomic information available from conventional MRI. Diffusion tensor imaging (DTI) measures the directionality (anisotropy) and the magnitude of water diffusion *in vivo*. Practional anisotropy (FA) and mean diffusivity reflect microstructural changes of tissue caused by damage from degenerative disease, brain ischemia, and brain tumors.

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Dynamic susceptibility contrast (DSC) MRI provides region cerebral blood volume (rCBV) and therefore, is one of the most reliable methods to evaluate tumor vasculature *in vivo*. rCBV is a commonly used perfusion MRI technique for the evaluation of tumor grade. [6,7] Region cerebral blood volume values are greater in high-grade than in low-grade tumors. [6,8-10] Hemangioblastoma is a low-grade tumor with greater rCBV values. [11] Pilocytic astrocytoma, hemangioblastoma,

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pleomorphic xanthoastrocytoma, ganglioglioma, meningioma and glioblastoma multiforme (GBM) can morphologically present as cystic masses with a mural nodule. [12-14] Prevalence of these tumors varies from 1% to 7% of all intracranial brain tumors and are common in children and young adults.[15-17] The common location of these tumors is the posterior fossa. [13,16] Most of the cystic tumors with mural nodule are benign and are classified by WHO as grade I or II.[16,18] These tumors present with the same morphological characteristics on conventional MRI sequences though the age at onset and tumor location might give a clue to tumor type. [11] Furthermore, some tumors have similar surgical and pathological characteristics like Hemangioblastoma and clear cell ependymoma of the cerebellum. Though most of the cystic tumors with mural nodules are benign, some of them have recurrence tendency, metastasize (rare) and have a malignant potential.[12,19,20] By knowing the exact characteristic of the cystic tumors with mural nodules will help in making accurate presurgical diagnosis hence proper patient management.

Therefore, the purpose of this study was to evaluate the role of conventional, diffusion tensor and DSC perfusion MRI in characterizing and differentiating intracranial cystic tumors with the mural nodule.

Materials and Methods

This was a hospital-based retrospective cross-sectional study whereby preoperative brain MRI of 600 patients were reviewed on picture archiving and communication system, at Severance Hospital from August to October 2012 whereby only 15 consecutive patients fulfilled the inclusion criteria. This is a university hospital for Yonsei University College of Medicine. All ethical issues were adhered to as per Institutional Review Board criterion. Only patients who underwent conventional, DTI and DSC enhanced perfusion MRI, with a cystic brain tumor with a mural nodule, and histopathologically confirmed were included in this study. Patients who had solid tumors, necrotic tumors with thick rind tumor wall, purely cystic tumors, and with no DTI and perfusion images were excluded.

Magnetic resonance imaging acquisition parameters

The MRI protocol for patients with brain tumors at this institution is T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR) T1-weighted with contrast, diffusion weighted imaging, DTI and perfusion studies. The reviewed brain MRI were done by using 3 Tesla MRI system (Philips Medical system, Achieva) with a standard head coil. For DTI, the protocol is repetition time (TR)-111,234, echo time (TE) 46,042, matrix 128×125 , field of view 23 cm.

Image assessment

The assessment was performed independently by a principal investigator PI and Neuroradiologist. In case of disagreement, the final judgment was reached by consensus. MRI findings

of all cystic tumors with mural nodule were retrospectively reviewed. Any mass with a cystic component which is more than 50% of the tumor volume was evaluated.^[21]

FA values of the mural nodule, immediate peritumoral region and white matter of contralateral normal brain on the FA maps were measured. The FA of a tumor was measured by placing regions of interest (ROI) on the FA maps. Uniform ovoid ROI of approximately 10 mm² was used carefully comparing the FA maps with conventional T2-weighted and pre- and post-contrast T1-weighted images of the identical section. [22]

Relative cerebral blood volume (relative CBV) of tumors was evaluated by using CBV color maps by visual grading. Tumor color was compared to that of a normal brain. A tumor with high rCBV was assigned to a high rCBV group if rCBV maps depicted any intratumoral area with signal intensity higher than that of gray matter. Similarly, if visual grading showed that the signal intensity of all intratumoral areas is similar to or lower than that of gray matter, the tumor was assigned to the low rCBV group.

MRI findings included:

- Location, size and evaluation of tumor margin
- Signal intensity on T1-weighted and T2-weighted images and FLAIR
- Contrast enhancement pattern on postcontrast T1-weighted image
- Perfusion characteristics on rCBV color maps
- Measurement of fractional anisotropy diffusion tensor imaging (FADTI) values of a solid portion of the tumor.

Data analysis and statistics

The patients' sex, age group, tumor signal intensity on T1-weighted image with/without contrast, T2-weighted image, FLAIR, FADTI, rCBV color maps, size cyst and mural nodule, nodule margin, location of the tumor, and pathological type of tumor were analyzed. Fishers' exact test was used to compare between demographic data, tumor signal intensity, rCBV and tumor grade histological type. Receiver operating characteristics (ROCs) curve was used to assess the accuracy of FADTI in differentiating high- and low-grade tumors. A P < 0.05 was chosen to indicate statistical significant difference. The following area under the ROC curve guide for classifying the accuracy of FA values in differentiating low- and high-grade tumors was used. 0.90-1 = excellent, 0.80-0.90 = good, 0.70-0.80 = fair, 0.60-0.70 = poor, 0.50-0.60 = fail. The area under the ROC curve of 1 was used to represent a perfect test; an area of 0.5 represented worthless test.[22]

Results

A total of 15 histologically confirmed patients with cystic brain tumors with a mural nodule were analyzed. The age range was 6–54 years of which 10 were females. Each patient had a single brain mass. Nine and six patients had low-grade and high-grade tumors, respectively. Among the low-grade group, three had pilocytic astrocytoma, one diffuse astrocytoma, one ependymoma, one ganglioglioma and three hemangioblastomas. Among patients with high-grade tumors, five had GBM, and one had a primitive neuroectodermal tumor (PNET) [Table 1]. Images are seen in Figures 1 and 2 for patients with hemangioblastoma and GMB, respectively.

Most of the tumors in young patients (≤ 30 years) were low-grade while high-grade tumors were more common among individuals above 30 years though the difference observed was not statistically significant (P = 0.089). There was also no statistical difference in the distribution of tumor grades by sex (P = 0.580) [Table 2]. The size of the largest tumor was an 8 cm, a ganglioglioma in a temporal lobe in a 27-year-old female, and the smallest was 2 cm hemangioblastoma in a 51-year-old female located in the cerebellum. There was no statistical significant difference in tumor size among high- and low-grade tumors (P = 0.174).

Tumor location was evaluated, commonly located in the cerebellum (33.3%), and this was observed more among individuals below 30 years of age [Table 3].

Relative cerebral blood volume

Hemangioblastomas [Figure 1], GBM [Figure 2] and PNET showed high rCBV color values while pilocytic astrocytoma, diffuse astrocytomas, ependymomas and gangliogliomas showed low rCBV color values and the difference was statistically significant (P = 0.026, and 0.020, respectively).

All high-grade tumors showed high color values (increased rCBV) [Table 4].

Fractional anisotropy diffusion tensor imaging values

The mean FA values of tumors (solid portion) were lower than those of white matter (0.14 and 0.5, respectively). FADTI values did not vary between low- and high-grade tumors. The area under the FA for Tumor solid portions curve was 0.472. Since this area is below 0.70, it is considered that by using FA values it is not possible to differentiate low- and high-grade tumors [Figure 3].

Discussion

Tumor size could not determine the type and grade of the tumor in this study. GBM was the most common tumor. Almost all patients with GBM, the tumor was located in cerebral hemispheres which are the common location for GBM. All pilocytic astrocytomas and hemangioblastomas were located in the cerebellum which is a typical location for these tumors. [23] The ganglioglioma in this study was located in the temporal lobe which is also the commonest location for this tumor. [23] Most 5 (83.3%) of high-grade tumors showed cystic wall contrast enhancement while only one tumor in the low-grade group did which was a diffuse astrocytoma (P = 0.002). It has been reported that occasionally some low-grade tumors show cystic wall enhancement [23] which is similar to the findings of our study.

In this study, all high-grade tumors showed high rCBV color values on rCBV color maps and 5 (83.3%) of the high-grade tumors were GBM. This correlate well with the findings reported by other studies elsewhere. [1,6,8,9,24] Among the

Table	1: Summary	of sociodem	ographic and	tumor	MRI findings
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Sex	Age	Tumor location	Tumor type (histopathology)	Cystic wall contrast enhancement	FADTI values (solid portion)	rCBV
			Lo	w-grade tumors		
Male	6	Parietal	Diffuse astrocytoma	Yes	0.10	Low
Female	12	Cerebellum	Pilocytic astrocytoma	No	0.10	Low
Female	15	Parietal	Ependymoma	No	0.14	Low
Male	26	Cerebellum	Pilocytic astrocytoma	No	0.09	Low
Female	26	Temporal	Pilocytic astrocytoma	No	0.13	Low
Female	27	Temporal	Ganglioglioma	No	0.29	Low
Male	48	Cerebellum	Hemangioblastoma	No	0.13	High
Female	51	Cerebellum	Hemangioblastoma	No	0.09	High
Female	54	Cerebellum	Hemangioblastoma	No	0.10	High
			Hig	gh-grade tumors		
Female	13	Frontal	PNET	No	0.08	High
Male	19	Parietal	GBM	Yes	0.09	High
Female	39	Basal ganglia	GBM	Yes	0.25	High
Female	45	Frontal	GBM	Yes	0.10	High
Female	53	Parietal	GBM	Yes	0.11	High
Female	54	Frontal	GBM	Yes	0.21	High

MRI – Magnetic resonance imaging; FADTI – Fractional anisotropy diffusion tensor imaging; rCBV – Regional cerebral blood volume; PNET – Primitive neuroectodermal tumor; GBM – Glioblastoma multiforme

Table 2: Distribution of tumor grade by age group and sex

Tumor grade	Age group (years)		Total	P
	6-30	31-55		
Low	8	1	9	0.089
High	2	4	6	
Total	10	5	15	
	Female	Male		
Low	5	4	9	0.580
High	5	1	6	
Total	10	5	15	

P value was calculated from Fishers' exact test

Table 3: Distribution of tumor location by age group

Tumor location	Age group (years)		Total	
	6-30	31-55		
Frontal lobe	1	2	3	
Parietal lobe	3	1	4	
Temporal lobe	2	0	2	
Cerebellum	4	1	5	
Basal ganglia	0	1	1	
Total	10	5	15	

Table 4: Distribution of tumor histological types and grade by rCBV

Tumor type	rCBV color value		Total	Р
(histopathology)	Low	High		
Pilocytic astrocytoma	3	0	3	0.020
Diffuse astrocytoma	1	0	1	
Ependymoma	1	0	1	
Hemangioblastoma	0	3	3	
Ganglioglioma	1	0	1	
GBM	0	5	5	
PNET	1	0	1	
Total	7	8	15	
Tumor grade	rCBV co	lor value		
	Low	High		
Low	6	3	9	0.028
High	0	6	6	
Total	7	8	15	

 $\it P$ value was calculated from Fishers' exact test. GBM – Glioblastoma multiforme; PNET – Primitive neuroectodermal tumor; rCBV – Regional cerebral blood volume

low-grade tumors all hemangioblastomas showed increased rCBV, none of the pilocytic astrocytoma, ependymoma, diffuse astrocytoma and ganglioglioma showed areas of increased rCBV. This finding also correlate well with what has been reported by Bing et al. [11] and Métellus et al. [25] The differences observed among the low- and high-grade tumors could be due to the differences in tumor vascularity. In high-grade tumors, there is neoangiogenesis, and these vessels are permeable to contrast contributing to high rCBV. The differences observed between hemangioblastoma and

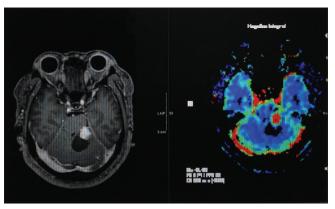


Figure 1: Hemangioblastoma in a 48-year-old male. Brain magnetic resonance imaging at the level of orbits. Axial postcontrast T1-weighted image (on the left shows intense contrast enhancement of the solid portion with no cystic wall enhancement) and dynamic susceptibility contrast perfusion magnetic resonance rCBV) color map (on the right) shows increased rCBV (red color) on the solid portion, respectively

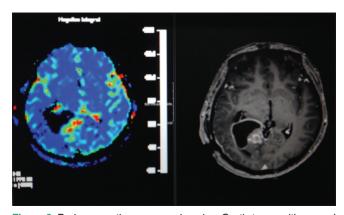


Figure 2: Brain magnetic resonance imaging. Cystic tumor with a mural nodule in the right temporo-occipital area in a 53-year-old female. Dynamic susceptibility contrast perfusion magnetic resonance imaging rCBV color map (on the left) shows high rCBV color value (in red) on the solid tumor portion and postcontrast T1-weighted image (on the right) shows cystic wall contrast enhancement and heterogenous strong enhancement of the solid portion. Histologically was proven to be a glioblastoma multiforme

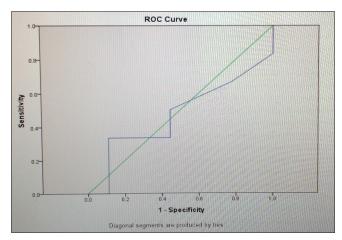


Figure 3: Receiver operating characteristic curve: Fractional anisotropy values (solid tumor portion). Area = 0.472

pilocytic astrocytoma, and other low-grade tumors are also due to differences in tumor vascularity. Hemangioblastomas are highly vascular tumors. [23]

The FA value is an indicator of the tissue damage of white matter. [4,5,26,27] The molecular movement of water is restricted by membranes in the brain [28] hence damaged tissue in myelinated fibers may have reduced FA values. Anisotropy is always reduced in brain tumors. [29] In the present study, the mean FA values of tumors (solid portion) were lower than those of white matter (0.14 and 0.5, respectively), which corresponded with previous findings. [29,30]

In this study, the FADTI values did not vary between low- and high-grade tumors. The area under the FA for Tumor solid portions curve was 0.472, and that of FA for IPTR was 0.620. As These areas are below 0.70, it is considered that by using FA values it is not possible to differentiate low- and high-grade tumors. This finding is similar to what was reported by Sinha *et al.* in 2002. [19] Also several studies have shown no significant difference for mean FA between low- and high-grade gliomas. [31-33] This finding is contrary to the findings reported by White *et al.* [34] in 2010, Inoue *et al.* [30] in 2005 Liu *et al.* [35] in 2012 whereby high-grade tumors had high FA values. This difference in findings could be due to smaller ROI of 10 mm² used for measurement of FA values in this study while other studies used ROI of 30 mm².

There were limitations to our study. The results were obtained on the basis of a small number of patients. Accurate FA measurement is also likely limited in small solid portions of tumors because the FA values of these tumors would likely be markedly affected by adjacent or infiltrating white matter fiber and the cystic tumor portion.

Dynamic, susceptibility-weighted, contrast-enhanced MRI showed in this study to be very useful in differentiating high- and low-grade tumors. Hemangioblastoma is the only tumor with increased rCBV among low-grade tumors which present as cystic mass with a mural nodule. GBM as a malignant tumor can also present as a cystic lesion with a mural nodule. In this study diffusion, anisotropic data added no benefit to tumor differentiation. The small number of patients and small solid portions of the tumors might have contributed to this finding.

Combined with postcontrast T1-weighted image, dynamic, susceptibility-weighted, contrast-enhanced (DSC) MR imaging MRI is useful in the preoperative diagnosis and differentiation of intracranial cystic tumors with a mural nodule.

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Conflicts of interest

There are no conflicts of interest.

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