Original Article:

Differentiation of typical from atypical and malignant meningiomas using diffusion weighted magnetic resonance imaging

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ABSTRACT

Background: Atypical and malignant meningiomas are associated with less favourable clinical outcome as they are more prone to recurrence and aggressive growth. Conventional magnetic resonance imaging (MRI) can reliably differentiate meningiomas from other extra-axial neoplasms, but grading of meningiomas as typical or atypical/malignant is not possible. Diffusion weighted MRI (DWMRI) has been used reliably for grading of gliomas. There are only few studies to investigate utility of DWMRI in grading of meningiomas. So we have planned in this study to investigate the utility of DWMRI parameters such as apparent diffusion coefficients (ADC) and normalized ADC (NADC) ratios in the preoperative characterization of meningiomas.

Methods: Thirty patients with pathologically proven meningiomas [typical (n=25) atypical/malignant (n=5)] underwent MRI at 1.5 T. The signal intensity of lesions on DWI was evaluated. ADC values of lesion and NADC ratios from lesion and contralateral normal white matter were calculated.

Results: The mean apparent diffusion constant (ADC) values ($\times 10^{-3}$ mm^2/ s) were 0.92±0.2 and 0.66±0.08 in typical and atypical/malignant meningiomas respectively. The mean NADC ratios were 1.24±0.28 and 0.86±0.08 for typical and atypical/malignant meningiomas respectively.

Conclusions: Atypical and malignant meningiomas have significantly lower ADC and NADC ratios compared to typical meningiomas.

Key words: *Meningioma, Differentiation, Diffusion magnetic resonance imaging, Apparent diffusion coefficients, Normalized apparent diffusion coefficients*

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INTRODUCTION

Meningiomas are the commonest primary, non-glial, intracranial, extra-axial tumours. Meningiomas constitute 14%-20% of all intracranial tumours and up to 10% are atypical or malignant variants. Recurrence rate for atypical/malignant meningiomas is high, 29%-41% as compared to typical meningiomas between 7%-20%.[1] Although meningiomas have readily identifiable features, conventional MRI techniques have not always been reliable in predicting the grade or natural history of tumours.[2-5] DWMRI has been used to study the histologic grading of gliomas.[6-13] Correlation between ADC values, tumour cellularity and tumour grades have been made. DWI along with calculation of ADC and NADC ratio is a reliable, noninvasive technique for the preoperative assessment and for the treatment planning of different types of brain tumours.[14-17] The objective of our study is to evaluate the benefits of DWMRI technique and in differentiation of typical from atypical malignant meningiomas using ADC and NADC ratios.

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MATERIAL AND METHODS

This prospective study was conducted in the Department of Radiodiagnosis, at our tertiary care teaching hospital at Tirupati during the period January 2014 to June 2015, and included 30 patients referred from Neuro-surgery Department. All of them were suspec-ted to have intracranial meningioma based on CT findings. This study was conducted after obtaining institutional research and ethics committee approval. Written informed consent was obtained from all patients.

All MRI studies were done using 1.5 Tesla (Siemens Magnetom Aera 1.5T, Germany) with phased array coil. All patients were asked to get rid of any metallic objects as well as they were asked about any contraindication to MRI examination (artificial heart valve, cardiac pacemaker, metallic stents or joint prosthesis except that made of titanium). The patients were informed about the duration of the examination, the position of the patient and the importance of being motionless.

MRI study was done with the patients in the supine position using the standard head coil. The examination was done before contrast administration, a scout sagittal T1-weighted view was obtained to verify the precise position of the patient and to act as a localizer for subsequent slices. Then multiple pulse sequences were used to obtain axial images followed by coronal and sagittal images.

The contrast media used was gadobenate dimeglumine administered intravenously in a dose of 0.1 mmol/kg body weight.

All cases were examined using the following protocol: Sagittal (T1-WI as a localizer with TE = 10-12 m/s, TR = 400-600 m/s), Axial and sagittal spin-echo sequences(short TR/TE (T1-weighted images): TE = 10–12 m/s, TR = 400-600 m/s), Axial, coronal fast spin-echo long TR/TE (T2-weighted images): TE = 70–90 m/s, TR = 2800-3500 m/s, Post-contrast axial, sagittal and coronal spin-echo sequence, short TR/TE (T1-weighted images) (TE = 10–12 m/s,TR = 400-600 m/s FOV = 24-18 cm in axial images and 30-22 cm in coronal images). Matrix was (frequency × phase) = 192 × 160, Slice thickness 6 mm with 2 mm interval in all sequences.

The imaging sequence for DWI was a multi-section single shot spin echo EPI sequence (TR/TE/NEX: 4200/140 ms/I) with diffusion sensitivities of b values = 0, 500 and 1000 mm^2/S. The diffusion gradients were applied sequentially in three orthogonal directions (X, Y and Z directions). Sections of 5 mm thickness, inter slice gap of 1 mm, FOV 240 mm and a matrix of 128 × 256 were used for all images. The total acquisition time was 80 sec.

Isotropic (trace, i.e., the summation of 3 orthogonal directions) DW images were visually inspected and classified as hyperintense, isointense, or hypointense compared with normal white matter. The intratumoural ADC values were measured using the manufacturer's software. To minimize variability, the regions of interest (ROIs), is kept a constant value of 40 mm^2, was placed manually in the solid part of the tumour, avoiding any cystic or calcified areas.

Control ADC values were obtained from normal-appearing white matter on the contralateral normal brain tissue unaffected by tumour *(centrum semiovale)*. The NADC ratios were calculated using the formula NADC = ADC of the tumour/ADC of the normal white matter, with NADC lower than 1.00 representing relatively restricted diffusion.

Statistical analyses were carried out using SPSS version 17.0 for Windows (SPSS Inc, Chicago, IL USA). Student's t-test was used for calculating the differences in the mean ADC values and the mean ADC ratios between each pair. A p-value < 0.05 was considered statistically significant.

RESULTS

Out of 30 patients, 12 patients were males, 18 patients were females, and age was in between 26-65 years with mean age of 46.9 years.

In our study most common location was cerebral convexity, followed by falcine, parasagittal, sphenoid wing, petroclival, CP angle. Rare locations being cribriform, tentorial, intraventricular locations were observed one case in each location (Table 1).

Twenty nine out of 30 cases included in our study showed typical conventional MR features of meningioma as they display iso to hypointense signal intensity on T1WI, iso to hyperintense on T2WI. Two cases were predominantly hypointense on T1W1 and T2WI because of presence of dense calcifications. Rest of the cases showed iso to hypointensity on T1WI, iso to hyperintense signal on T2WI. Intense enhancement was noted in all 30 cases after contrast administration. Four out of five atypical meningiomas were observed to having be heterogeneous enhancement; probably because of presence of necrosis in three cases and vascular channels in another case. Seven out of 25 typical meningiomas observed to be heterogeneous enhancement; five of them were due to necrosis, and two were due to excessive calcifications. Only one case out of 30, showed atypical features such as irregular margins, heterogeneous enhancement, adjacent bone involvement, disproportionate peritumoural edema (Table 2).

All cases of typical meningiomas (n = 25) appeared isointense or slightly hyperintense on DWIs, and iso to mildly hyperintense on ADC, the ADC values ranged from 0.8 to 1.78×10^{-3} mm^2/s, mean±SD – 0.92±0.21 (Figure-1).

All cases of atypical and malignant meningiomas (n = 5) appeared hyperintense on DWI and hypointense on ADC, the ADC values ranged from 0.58 to 0.78×10^{-3} mm^2/s, mean±SD – 0.66±0.08 (Figure-2) which were lower than normal brain (0.75×10^{-3} mm^2/s for white matter, 0.77×10^{-3} mm^2/s for grey matter). The normalized ADC (NADC) values ranged from 0.96 to 2.3 and 0.76 to 0.96 for typical and atypical meningiomas respectively. Mean NADC values were 1.24±0.28 and 0.86±0.08 for typical and atypical meningiomas respectively (Table 3). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of conventional MRI and diffusion weighted MRI in differentiation of typical from atypical malignant meningiomas in shown in Table 4. ADC values and NADC ratios of typical and atypicall malignant meningiomas reported in literature and the present study are shown in Table 5.

Table 1: Anatomical and pathological classification of 30 meningioma cases by its location and grading WHO

Location	Number of cases	WHO grade I	WHO grade II	WHO grade III
Falcine	6			1
Parasagittal	5		1	
Convexity	7		2	
Petroclival	3			
Sphenoid wing	4	4		
Tentorial	1		1	
Cribriform	1			
CP angle	2			
Intraventricular	1			
Total	30		4	1

CP angle = cerebellopontine angle; WHO = World Health Organization

Table 2: Conventional MRI findings in typical and atypical mangiomas

Meningiomas	Signal intensity on T1			Signal intensity on T2			Enhancement		Perilesional oedema		Calcifications		Irregular margins		Bone infiltration	
	Hypo	Iso	Hyper	Hypo	Iso	Hyper	Homo-geneous	Hetero-geneous	Present	Absent	Present	Absent	Present	Absent	Present	Absent
Typical (n = 25)	7	18	0	2	1	22	18	7	20	5	4	21	0	25	0	25
Atypical (n = 5)	4	1	0	0	0	5	1	4	5	0	0	5	1	4	1	4
Total	11	19	0	2	1	27	19	11	25	5	4	26	1	29	1	29

MRI = Magnitic resonance imaging

Table 3: DWI findings in typical and atypical meningiomas

Meningioma	SI on DWI	SI on ADC	ADC range	($\times 10^{-3}$ mm^2/s) mean	NADC ratio range	Mean
Typical (n=25)	Iso/hyper	Iso/hyperintense	0.8 - 1.78	0.92 ± 0.21	0.96 - 2.3	1.24 ± 0.28
Atypical (n=5)	Iso/hyper	Hypointense	0.58 - 0.78	0.66 ± 0.08	0.76 - 0.96	0.86 ± 0.08

DWE = diffusion weighted images; SI = signal intensity; ADC = apparent diffusion coefficient; NADC = normalized ADC

Table 4: Predictive value of conventional MRI and advanced MR imaging of typical meningioma versus atypical and malignant meningiomas

Modality	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Conventional MRI	20	100	100	86.2
DWI and ADC	100	100	100	100

MRI = magnetic resonance imaging; DWI = diffusion weighted images; ADL = apparent diffusion coefficient

Table 5: ADC values and NADC ratios of typical and atypical/malignant meningiomas reported in literature and the present study

Study	D_{av} values ($\times 10^{-3}$ mm^2/s)		NADC ratios	
	Typical	Atypical/malignant	Typical	Atypical/malignant
Filippi et al[17]	1.03±0.29	0.52±0.12	-	-
Nagar et al[18]	0.88±0.08	0.66±0.18	1.28±0.11	0.91±0.18
Bo Yin et al[19]	0.97±0.21	0.85±0.17	1.24±0.25	1.09±0.23
Toh et al[20]	0.96±0.17	0.79±0.23	1.27±0.24	1.05±0.17
Gupta et al[21]	0.83±0.11	0.70±0.09	1.08±0.17	0.85±0.15
Present study	0.92±0.21	0.66±0.08	1.24±0.28	0.86±0.08

ADC = apparent diffusion coefficient; NADC = normalized ADC

DISCUSSION

Intracranial brain space occupying lesions cause a significant health problem and present several imaging challenges. The role of imaging is no longer limited to merely providing anatomic details. The sophisticated MRI technique like DWI allows insight into the freedom of water molecule movement within the tumour and thus helpful for better characterization of lesion.[22]

Limitations of conventional MRI techniques include its inability to reliably differentiate between brain abscess and cystic or necrotic brain tumours, inability to distinguish high-grade from low-grade tumours. It cannot determine the exact limits of tumour extension and is unable to discriminate between typical from atypical and malignant meningiomas.[23]

Meninigomas are commonly occurring benign tumours that constitute approximately 20% of all intracranial tumours and are easily diagnosed during routine MR imaging. On the other hand, atypical and malignant meningiomas, although relatively uncommon, accounting for approximately 7.2% and 2.4% respectively are associated with less favorable clinical outcome because they are more prone to recurrence and aggressive growth. To date

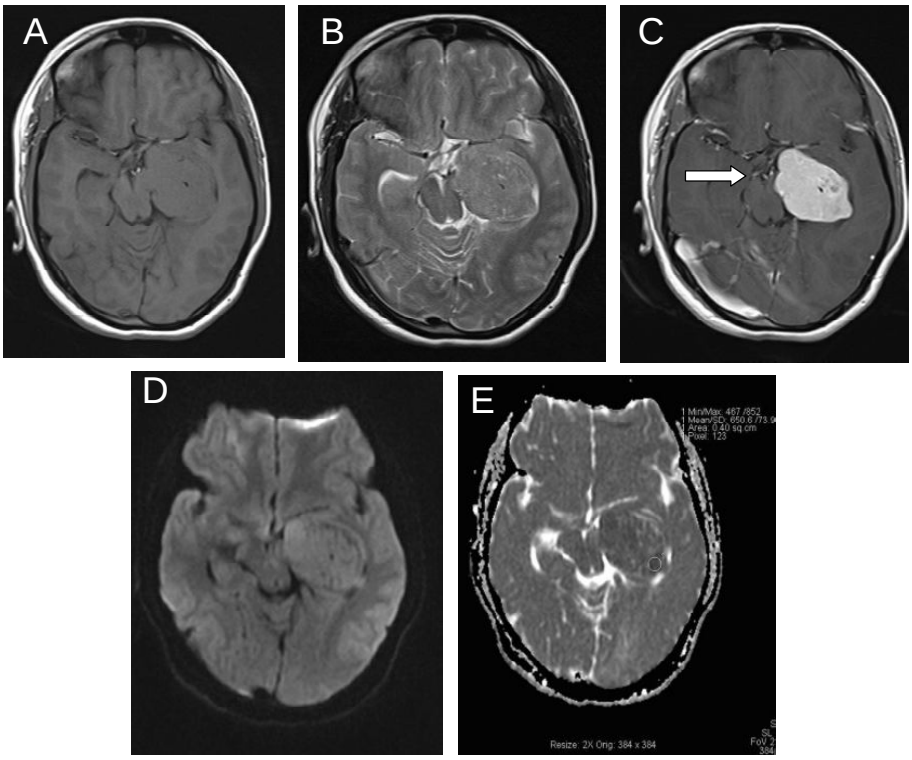

Figure 1: MRI brain images of a patient with typical meningioma in left middle cranial fossa (→). Lesion is isotense on T1W1 (A), hyperintense on T2W1 (B), showing heterogeneous enhancement on post contrast T1W1 (C), hyperintense on blood (D) and hypointense on ADC maps (E) with ADC values 0.65 and NADC values 0.89×10^{-3} mm^2/s.

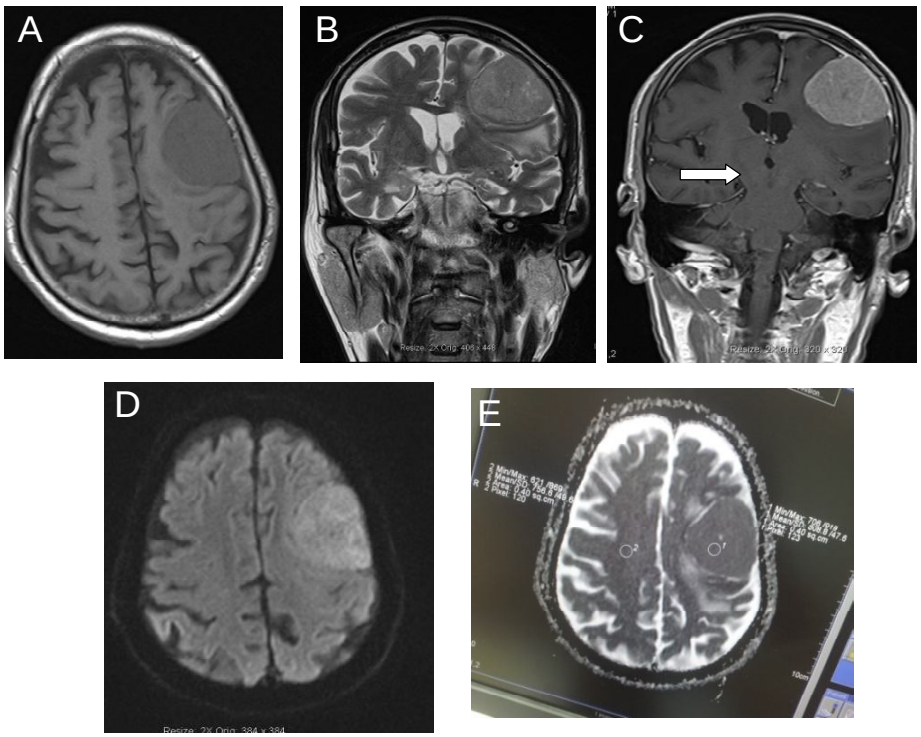

Figure 2: MRI brain images of a patient with atypical meningioma in left convexity (→). Lesion is isointense on T1W1 (A), hyper intense on T2W1 (B), showing enhancement on post contrast T1W1 (C), hypointense on blood (D) ad hypointense on ADC maps (E) with ADC values 0.81 and NADC value 1.06×10^{-3} mm^2/s
ADC = apparent diffusion constant; NADC = normalized ADC

investigators have been unsuccessful when attempting to predict the histologic types of meningiomas and to distinguish benign from atypical or malignant meningiomas on routine MR images.[24]

In our study out of 30 patients only one patient was diagnosed as atypical meningiomas based on conventional MR findings such as presence of irregular margins, bone erosion, heterogeneous enhancement, presence of disproportionate peritumoural oedema. Sensitivity, Specificity, PPV, NPV of conventional MRI in differentiation of typical from atypical and malignant meningioamas were 20%, 100%, 100%, 86.2% respectively.

Several studies showed that the findings of atypical/malignant meningiomas and benign meningiomas were not significantly different on DWI.[17] In contrast, the ADC maps of atypical/malignant meningiomas showed isointensity or hypointensity compared with those of normal brain parenchyma.[18,19] The lesions on DWMRI exhibit high signal intensity on DW images, as a result of the "T2 shine through" effects. There may be subjectivity and absence of quantitative analysis when investigators visually inspect DWMR images and ADC maps.

In our study, Atypical and malignant meningiomas (n = 5), classified as WHO Grade-II and Grade-III, respectively, all had markedly increased signal on DWIs, and extremely low ADC values, indicative of marked restriction to water diffusion, which is in consistence with Pavlisa et al,[25] who stated that high-grade tumours with increased cellularity have lower ADC values than low-grade tumours or normal brain.

Certain studies have revealed that the mean ADC values of benign meningiomas were higher than the mean ADC values of atypical/malignant meningiomas.[17, 18-21] In our study the mean and SD of intratumoural ADC in benign meningiomas were 0.92+/-0.20 x 10^{-3} mm^2/s and in atypical/malignant meningiomas were 0.66+/-0.0 x $10^{-3}mm^2/s$. In our study, when cutoff ADC value is taken as 0.80 x 10^{-3} mm^2/s, the sensitivity, specificity, PPV reached 100% in differentiating benign from the atypical and malignant meningiomas. Studies by Filippi et al,[17] Bo Yin et al[19] and Toh et al.[20] also showed results similar to our study.

The measurement of ADC values may vary across different scanners, DW imaging sequences and hardware configurations. The NADC ratio minimises the differences in ADC values caused by different diffusion techniques or sequences used for the evaluation.This normalization process should be preferred to more reliably demonstrate the changes in water diffusivity of human brain tumours and to eliminate inter image variability.[1] In our study, the mean NADC values were 1.24±0.28 and 0.86±0.08 for typical and atypical meningiomas respectively. Nager et al[18] showed that the mean NADC ratio were significantly lower in the atypical/malignant group (0.91±0.18) than in the benign group (1.28±0.11).

CONCLUSIONS

With advent of MRI, the quality of pre-operative diagnostic imaging has been improved dramatically and information about subtypes, vascularity and tumour consistency are possible. DWI and ADC maps are reliable in preoperative discrimination between typical, atypical and malignant meningiomas. The calculation of ADC value, NADC ratios are considered as a predictor of the grade of meninigioma.

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