Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(6D):2111-2119 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i06.049

Original Research Article

Role of Diffusion Weighted MRI in Intra-Axial Brain Tumours

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Abstract: The major aim of the present study was to measure the ADC values of low grade and high grade tumors using diffusion weighted MRI, to determine their contribution to differential diagnosis and also to propose a cut off ADC value. A retrospective study was done in which the magnetic resonance imaging findings of 50 patients diagnosed as having intra-axial brain tumors on histopathology were studied co-relate the ADC values with the World Health Organization grade of the tumor. Higher grade tumors had lower ADC values (<1.0 x 10^{-3} mm^2/s) than lower grade tumors (>1.0 x 10^{-3} mm^2/s). Conventional MR was 100% accurate in differentiating grade I from higher grade tumors. Cut-off ADC of >1.4 X10^{-3} mm^2/s was 100% specific for grade I tumors though differentiation among the various grade I tumors was not possible on DWI. Using a cut-off ADC value of 1.0 X10^{-3} mm^2/s, the sensitivity of MRI to differentiate low grade from high grade tumors was increased from 91% to 100%, specificity from 84.6 to 96% and accuracy from 86.4 to 97.3%. Diffusion weighted imaging and the accompanying ADC values can add useful information to the morphological details provided by contrast enhanced magnetic resonance imaging.. It can increase the PPV, NPV and accuracy of MRI to distinguish low grade from high grade neoplasm's as well as to differentiate lymphomas from other malignant lesions.
Keywords: Magnetic resonance imaging, Diffusion , Brain tumours , Diffusion MRI

INTRODUCTION

Primary brain tumors occur in people of all ages, but they are statistically more frequent in children and older adults. Metastatic brain tumors are more common in adults than in children. Although statistics for brain metastases are not readily available, it is estimated that more than 150,000 cancer patients per year will have symptoms due to a metastatic brain tumor or a metastatic brain tumor in the spinal cord[1].

Incidence rates are higher for men, in particular, malignant brain tumors occur more frequently in males while the benign meningiomas occur predominantly in females[2]. [10]Gliomas are the most common primary brain tumors, of which glioblastoma is the most common*"Brain Tumor Primer"*[1].Incidence of metastasis has increased considerably over the last few decades, possibly owing to better survival rates & now contribute to about half the cases of newly diagnosed brain tumors[3].Pediatric brain tumors and on histopathology found the commonest cerebellar brain tumors to be Pilocytic astrocytoma (48.2%) followed by medulloblastoma(22.2%)[4]. Diffuse intrinsic brainstem glioma constitute about 15-20% of all pediatric age tumors, which in our study were as common as medulloblastoma[5].In adults only 15-20% tumors arise below the tentorium[6]. In children, majority of the tumors are infratentorial(60%)[7].

MATERIALS & METHODS

Using a 1.5-T MR unit,three plane localizer is obtained for planning of the various sequences. We obtained axial T1-weighted images withTR/TE of 500/14–15, a slice thickness of 5 mm, an interslice gap of 1.5 mm, a field of view of240, and a matrix of 256 × 256; T2W spin-echo with TR/TE of 4500/97 ms and flip angle of 150º with 5 mm slice thickness, with a FOV of 240 mm ,with a 256x256 matrix in the axial plane. Followed by DWI obtained through a multisection spin-echo singleshot echoplanar sequence in the transverse planethat combined the motion-probing gradient (MPG) before and after the 180º pulse with EPI readout, and fat was suppressed by placing a frequency-selective RF pulse before the pulse sequence., using b values of 0, 500 and 1000 sec/mm^2, a TR/TE of 3700/102 ms, flip angle of 90º and slice thickness of 5 mm a, using matrix of 128 × 128,

bandwidth of 79 kHz, gradient strength of 22 mT, duration of diffusion gradients of 31 ms, and gradient separation of 42 ms, in three orthogonal directions.FLAIR sequence obtained in the axial plane using TR/TE of 9000/110 & TI of 2500. 5mm slice thickness is used.Additional sequences like susceptibility weighted imaging, T2 coronal, T1 axial. We then obtained contrast-enhanced, axial T1-weighted images from each patient. The ADC maps and values were calculated on a workstation. The ADC values from the solid portion of the tumor and from peritumoral, hyperintense areas on T2-weighted images wererecorded. The ADC values in our study represent averaged ADCs of two to five regions of interest (ROIs); each ROI was about 10 to 20 mm^2 . We also recorded signal intensities on DWIs of the tumor and of the peritumoral, hyperintense areas on T2-weighted images for possible contribution to tumor grading and quantification of neoplastic cell infiltration.

RESULTS

There were 13 cases of grade I tumors on histopathology- 6 pilocyticastrocytomas (PA), 3 hemangioblastomas (HGBL) and 2 cases each of DNET &ganglioglioma. The ADC values ranged from 1.4 to 2.8 (mean 1.9) $X10^{-3}$ mm^2/s.The commonest grade I tumor in our study was pilocytic astrocytoma with a mean ADC of 1.72 (range 1.4-1.9) $X10^{-3}$ mm^2/s (Fig. 1a-e). The mean ADC of DNET in our study was 1.99 $X10^{-3}$ mm^2/s. The mean ADC of hemangioblastoma in our study was 1.9 $X10^{-3}$ mm^2/s (Table. 1) . In our study, a cut-off of >1.4 $X10^{-3}$ mm^2/s showed 100% sensitivity, specificity and accuracy for grade I tumors, though differentiation among the various grade I tumors was not possible on DWI.

There were 11 cases of grade II tumors on histopathology. MR was thus 86% accurate, 91% sensitive and 84% specific in diagnosing low grade tumors.The ADCs of grade II tumors ranged from 0.88 to 1.4 (mean 1.16) $X10^{-3}$ mm^2/s. This was significantly higher than the mean ADC of high grade tumors- 0.96 $X10^{-3}$ mm^2/s for grade III and 0.78 $X10^{-3}$ mm^2/s for grade IV (Table.2). Using a cut-off ADC value of 1.0 $X10^{-3}$ mm^2/s, one low grade glioma that couldn't be differentiated from high grade tumour was correctly indentified when both morphology and ADC were considered together. The sensitivity was thus increased from 91 to 100%, specificity from 84.6 to 96% and accuracy from 86.4 to 97.3%.

Three cases of anaplastic astrocytoma were found on histopathology.Of these, only one was correctly identified on conventional MRI. The ADC value of these ranged from 0.78-1.02 (mean 0.96) $X10^{-3}$ mm^2/s (Table.1). Using the cut off ADC of <1.0 $X10^{-3}$ mm^2/s, one more case of anaplastic astrocytoma could be correctly identified. This improved the accuracy of distinguishing low grade gliomas from high grade gliomas from 86.4% to 97.3%. The PPV and NPV improved from 71.4% to 91.6% and from 95.6% to 100% respectively.

There were 14 cases of grade IV tumors on histopathology, of which 10 were glioblastoma. On MRI, 8 cases of GBM were correctly identified Of the three cases of medulloblastoma (now known as PNET-MB), two were correctly diagnosed on MRI. A case of supratentorial PNET was given the differential of ependymoma/subependymoma as it appeared to be an intraventricular tumor.MRI was thus 80% specific and 82% accurate in differentiating grade III from grade IV tumors.The mean ADC value of GBM was found to be 0.82 (range 0.5-1.2) $X10^{-3}$ mm^2/s. This was significantly lower than low grade gliomas and the ADC cut off of 1.0 $X10^{-3}$ mm^2/s improved the accuracy of conventional MR from 84% to 97% in distinguishing low grade from high grade tumors(Table.4).However, the ADC values of anaplastic astrocytoma overlapped greatly with those of GBM and no clear advantage of DWI could be seen in distinguishing the two in our study. Using the same cut off ADC value of 1.0 X 10^{-3} mm^2 /sec, the misdiagnosed case of ependymoma could be classified as a high grade tumor.

Of the 7 cases of metastatic tumor on histopathology, 6 were correctly identified on MR. The mean ADC of metastatic lesions in our study was found to be 0.79(0.62 to 0.88) X 10^{-3} mm^2 /sec. This was seen to overlap with the ADC values of GBM(Figure. 2,3),(Table.1).

Two cases of lymphoma were found on histopathology, out of which one had been correctly diagnosed on MRI. Both the cases however revealed restriction of diffusion on DWI with very low ADC values (mean 0.59 X 10^{-3} mm^2 /sec; range 0.55-0.62 X 10^{-3} mm^2 /sec)(Figure.4), (Table. 1).

Peritumoral T2/FLAIR hyperintensities were found in 27 patients. The ADCs in the surrounding T2/FLAIR hyperintense in high grade tumors was found to be between 0.9 to 1.9 X 10^{-3} mm^2 /sec and in metastases was between 1.1 to 2 X 10^{-3} mm^2 /sec (Table. 3)**.** No significant difference was found between the ADC values of peritumoural edema and infiltration.(Figure.2)

Table-1: ADC Values of All Tumors

S.No	WHO GRADING	TUMOURS	ADC RANGE ($X10^{-3}mm^2/s$)	MEAN ADC ($X10^{-3}mm^2/s$)
1.	I	Pilocytic Astrocytoma (PA)	1.4-1.9	1.72
		Hemangioblastoma (HGBL)	1.7-2.2	1.9
		DysembryonicNeuroepithilial Tumor (DNET)	1.8-2.1	1.99
		Ganglioglioma (GG)	2.0-2.8	2.4
2.	II	Low Grade Glioma (LGG)	0.88-1.38	1.2
		Oligodendroglioma (ODG)	0.9-1.3	1.1
		Ependymoma (EPM)	0.9-1.4	1.2
3.	III	Anaplastic Astrocytoma(AA)	0.88-1.02	0.96
4.	IV	GlioblastomaMultiforme(GBM)	0.5-1.2	0.82
		Medulloblastoma (MB)	0.62-0.88	0.72
		Primitive Neuroectodermaltumour (PNET)	-	0.7
5.		Metastasis	0.62-0.88	0.79
6.		Lymphoma	0.55-0.62	0.59

Table-2: Mean ADC of different tumour grades

S.NO.	TUMOUR GRADE	MEAN ADC ($X10^{-3}mm^2/s$)	ADC RANGE ($X10^{-3}mm^2/s$)
1	GRADE I	1.9	1.4-2.8
2	GRADE II	1.16	0.88-1.4
3	GRADE III	0.96	0.78-1.02
4	GRADE IV	0.78	0.5-1.2
5	METASTASIS	0.79	0.62-0.88
6	LYMPHOMA	0.59	0.55-0.63

Table-3: Comparision of ADC values of peritumoral edema

S.NO.	PERITUMORAL EDEMA	MEAN ADC ($X 10^{-3} mm^2/s$)	ADC RANGE ($X 10^{-3} mm^2/s$)
1	LOW GRADE	1.7	1.4-2.1
2	HIGH GRADE	1.5	0.9-1.9
3	METASTASIS	1.7	1.1- 2.0

Table-4: Overall distribution of tumours according to diagnosis on CE MR, MRI with ADC and HPE

S. NO	TUMOURS	MRI	MRI +ADC	HPE	ACCURACY of MRI	ACCURACY of MRI+ADC
1	GRADE I	13	13	13	100%	100%
2	LOW GRADE GLIOMA	7	6	6	83.3%	100%
3	EPENDYMOMA	5	3	3	80%	100%
4	OLIGODENDROGLIOMA	2	2	2	100%	100%
5	ANAPLASTIC ASTROCYTOMAS	6	4	3	50%	67%
6	GLIOBLASTOMA MULTIFORME	8	9	10	80%	90%
7	MEDULLOBLASTOMA	2	3	3	66%	100%
8	PNET	0	1	1	0%	100%
9	METASTASIS	6	6	7	85.7%	85.7. %
10	LYMPHOMA	1	2	2	50%	100%
	TOTAL	50	50	50	76%	94%(overall)

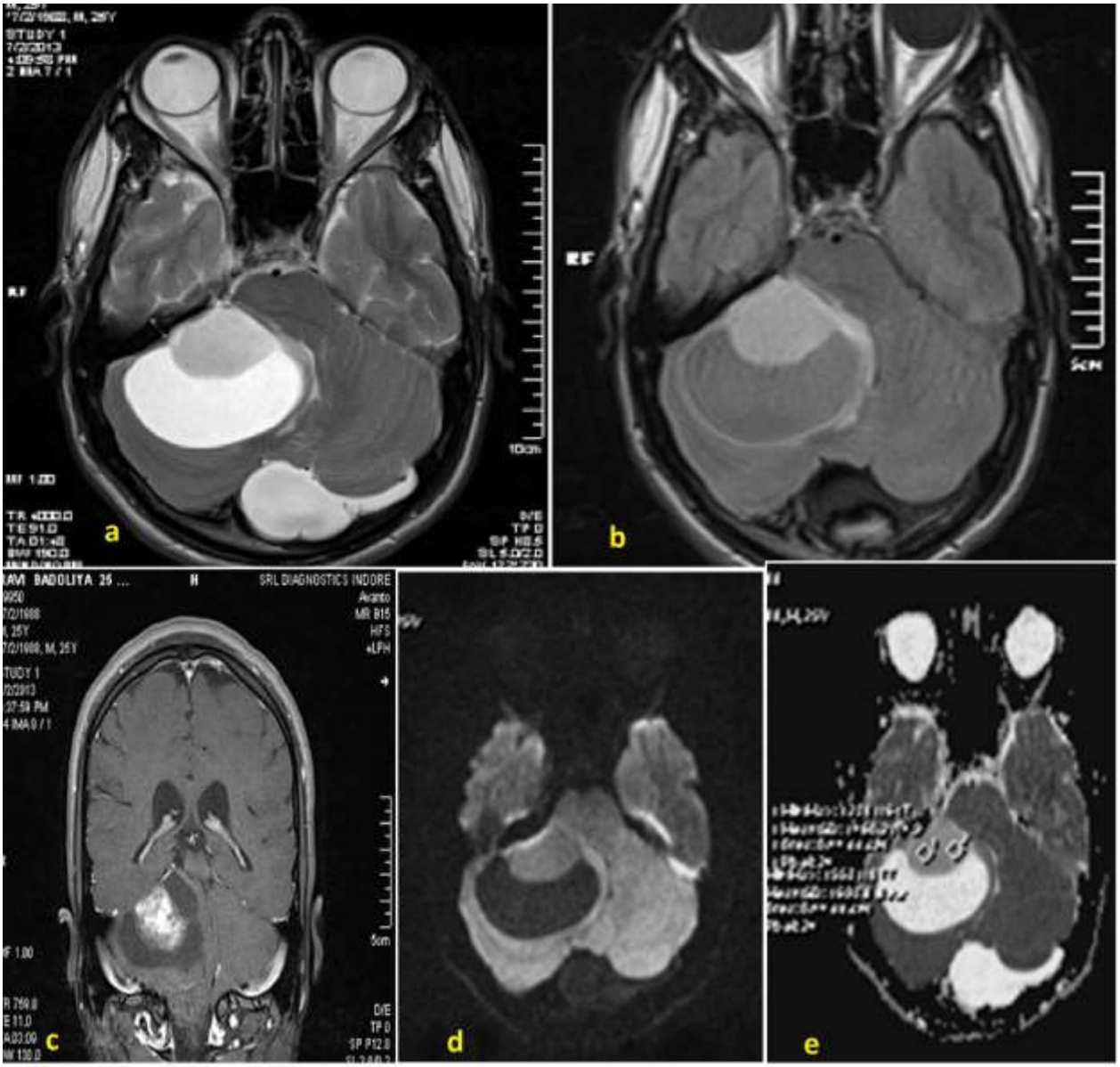

Figure1. a. Axial-T2 weighted image showing well defined cyst with a mural nodule in right cerebellar hemisphere. (b).Axial -FLAIR image: the fluid in the cyst is not supressed completely. (c).T1-weighted post contrast coeonal image shows intense enhancement of solid component. (d). Axial diffusion weighted image showing no restricted diffusion by the tumour. (e).ADC map showing calculation of the mean ADC from the solid component of the tumour. Mean ADC value : 1.72 (range 1.4-1.9) $X10^{-3}$ mm^2/s. Diagnosis :Pilocytic astrocytoma.

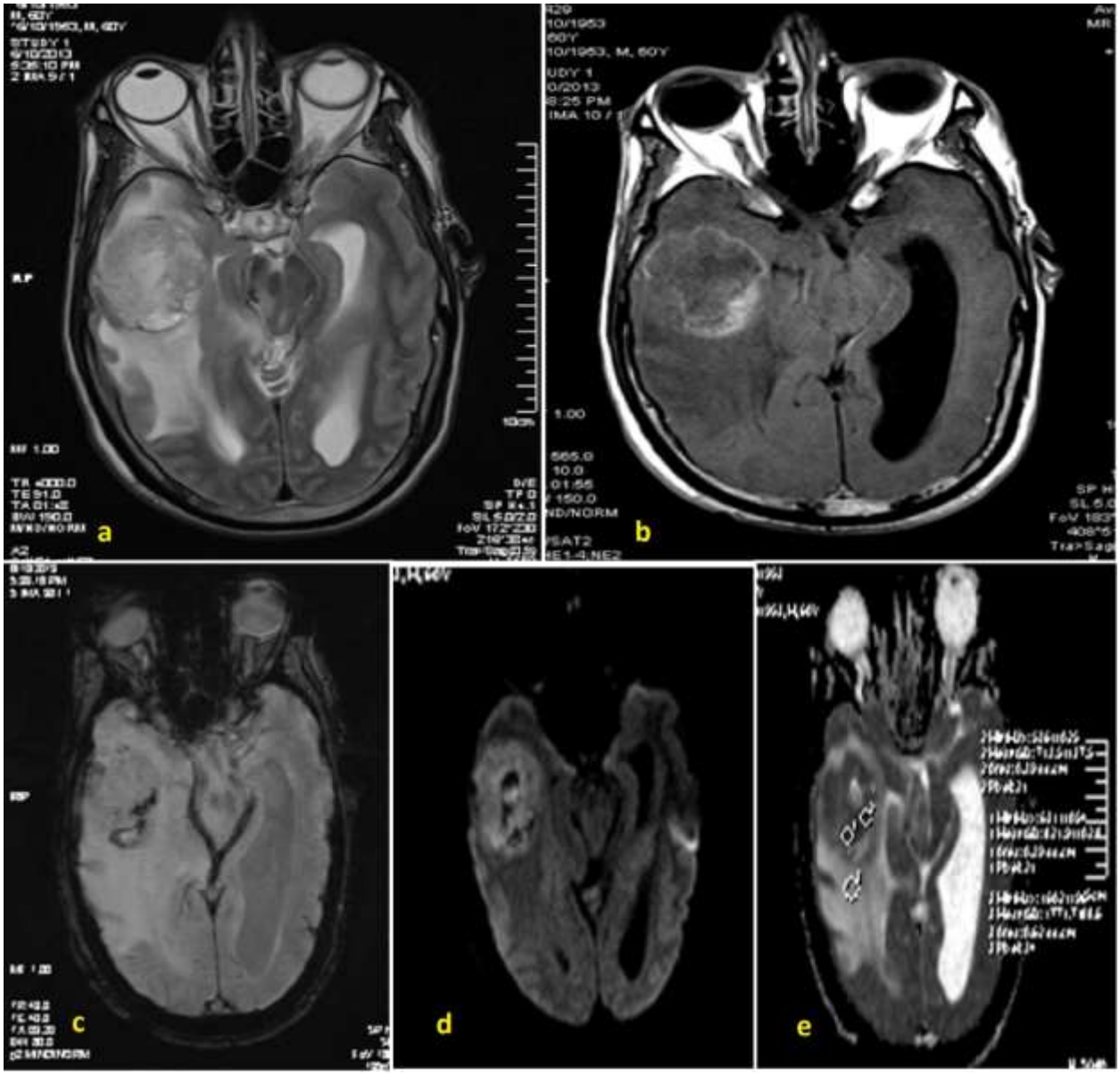

Figure.2.(a). Axial T2-weightedimage showing a well-defined hyperintense mass lesion in the right temporal lobe with moderate edema and mass effect. (b) Axial T1-post contrast image: lesion shows rim enhancement. (c) Axial Susceptibility Weighted Image showing areas of heamorrhage with the lesion.(d) Axial diffusion weighted image showing restricted diffusion. (e) ADC map showing calculation of ADC values from tumour as well as peritumoural edema with a Mean ADC of $0.82X10^{-3}$ mm^2/s and that of peritumoral edema is between 1.1 to 2 X 10^{-3} mm^2 /sec. Diagnosis : High Grade glioma. On histopathology : solitary metastasis.

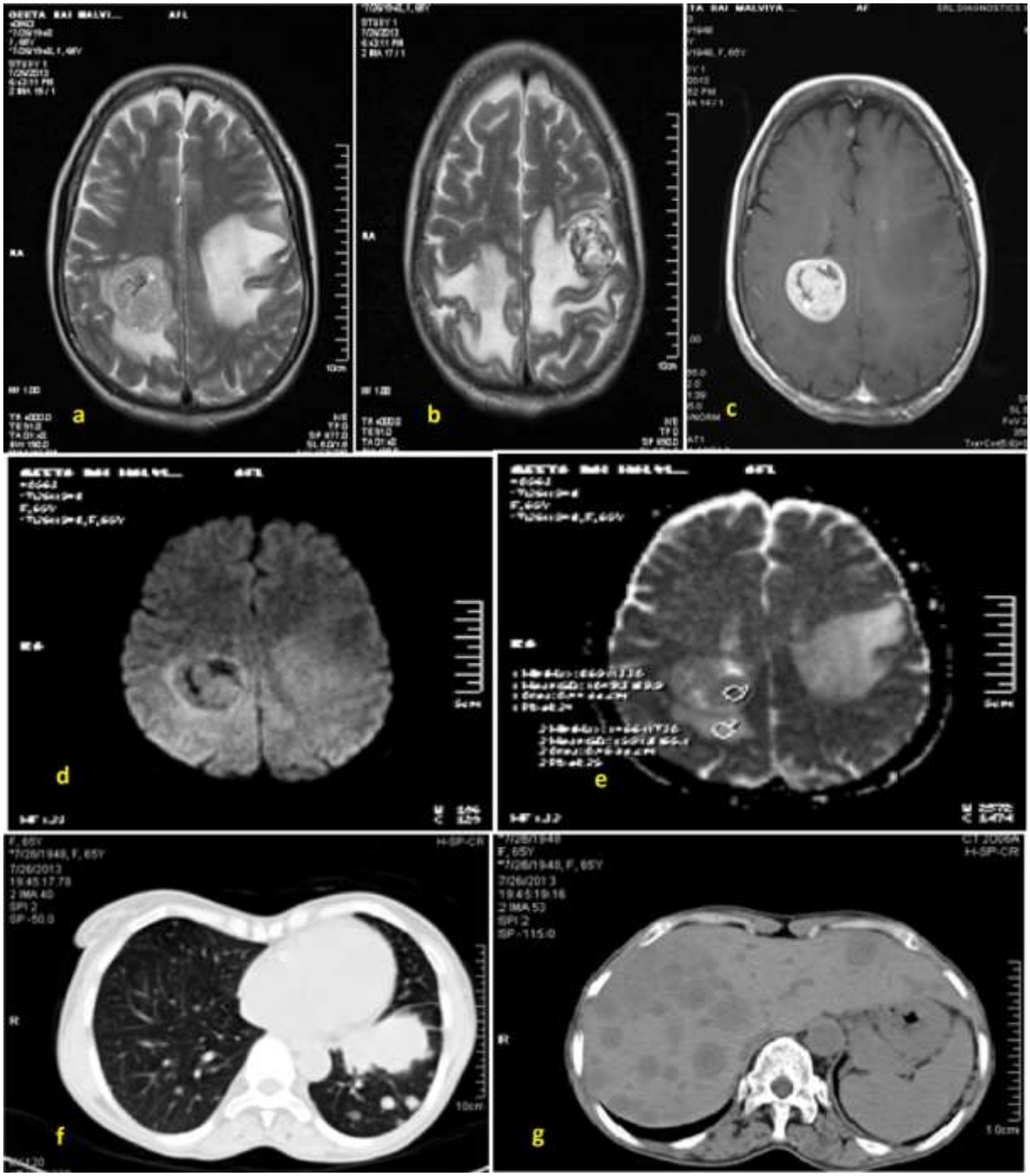

Figure.3.(a,b). Axial T2 weigted image Multiple well-defined space occupying lesions in both cerebral hemispheres with moderate surrounding edema. (c)Axial T1-post contrast shows intense solid enhancement.(d)Axial diffusion weigted image shows restriction of diffusion by the lesion. (e)ADC map : Shows calculation of ADC values from the solid component and the peritumoral hyperintensity. The Mean ADC values are 0.79(0.62 to 0.88) X 10^{-3} mm^2 and those of peritumoral hyperintensity could not differentiate it from infiltration.(f,g).Axial CT sections showing the primary lung mass with metastatic lesions in lung and liver.Diagnosis : Multiple metastasis.

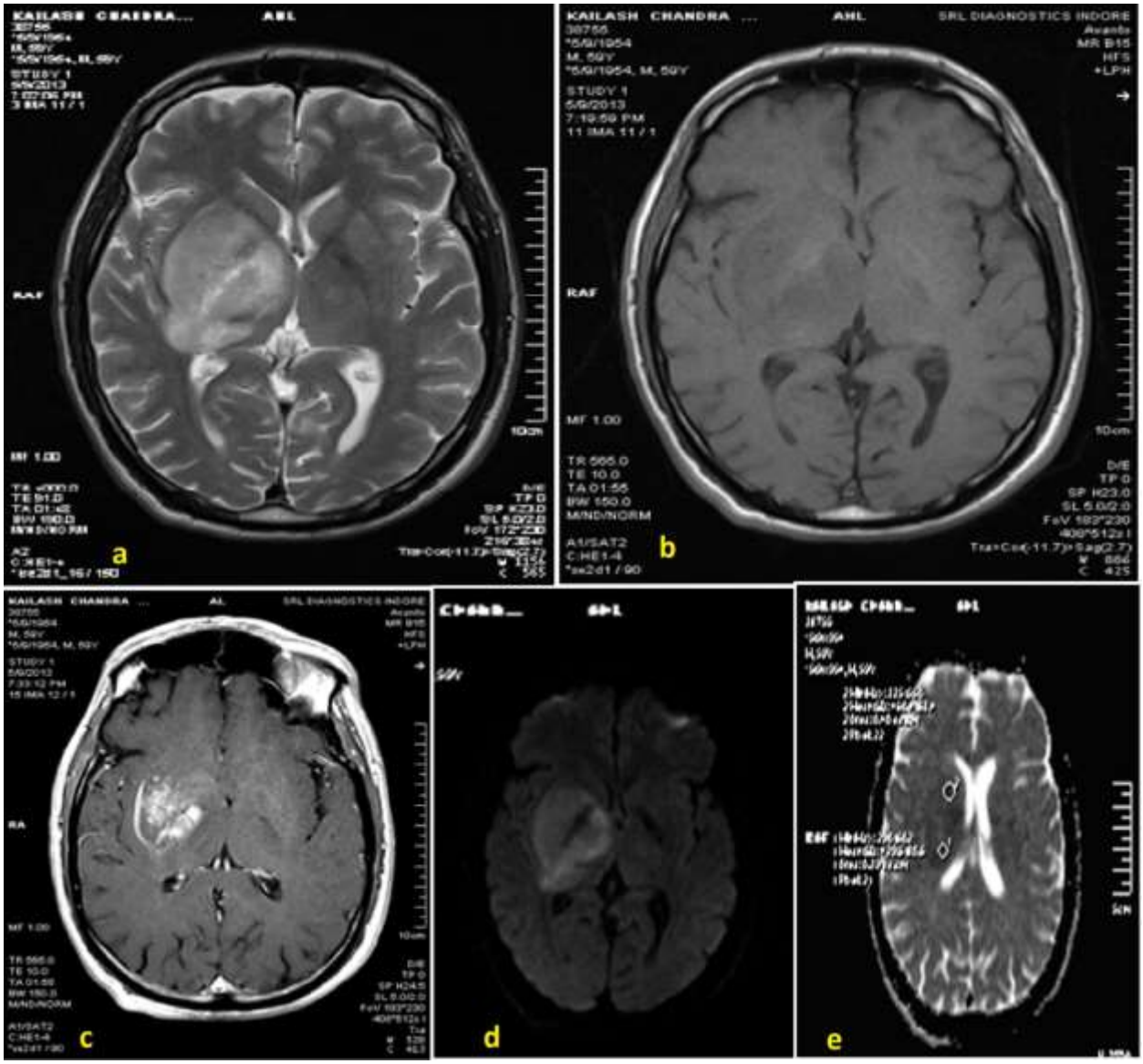

Figure. 4.(a). Axial T2 weighted image showing Expansile T2-hyperintense SOL in the right basal ganglia.(b)Axial T1 weighted image The mass is mostly iso to hypointense on T1.(c) Axial T1 post contrast image shows moderate enhancement in the lesion. (d) Axial Diffusion weigted image shows a very bright lesion showing severely restricted diffusion. (e) ADC map shows very low ADC values(mean ADC=0.63x10^{-3} mm^2/s).Diagnosis: Lymphoma

DISCUSSION

MR diffusion imaging has been used to study water mobility in normal brain tissue [8,9].In recent times the use of diffussion imaging has been widespread and gained immense importance in imaging of brain tumours. It has been found that the accuracy, sensitivity, and specificity, respectively, of ADC with conventional MRI is 90%, 88%, and 100% for discrimination of high-grade from low-grade neoplasms[10].

It is to be noted that due to overlapping characteristics, the ADCs are effective for grading but not for distinguishing different tumor types within the same grade[11]

We found thatenhancement is not a specific finding for discriminating low grade from high grade astrocytomas , about one third non enhancing gliomas are malignant , while upto 40% of anaplastic tumors may show no enhancement as reported by many workers[12,13,14]. Hence ADC can help overcome this problem of conventional MR in differentiation of low grade and high grade malignancies not showing enhancement .

There is no significant differences between the ADC values of glioblastomas& anaplastic astrocytomasand no clear advantage of DWI could be seen in distinguishing the two[15].ADC is 100% accurate in differentiating PNETs from ependymoma as all primitive neuroectodermal tumors show diffusion

restriction in contrast to ependymomas[16,17] . Certain tumors including medulloblastoma, malignant lymphomas and germinomas show high signal on DWI[18] .

Lymphomas have lower mean ADC values than high-grade gliomas and metastases[15]. The ADC is accurate in differentiating malignant lymphomas from glioblastomas and metastatic tumors and proves instrumental in diagnosis of lymphomas[16].

As there is overlap in the ADC values of GBM and metastasis therefore diffusion weighted imaging plays no role in differentiating high grade primary brain tumors from metastases[11,15,19].

The ADCs in the surrounding T2/FLAIR hyperintense in high grade tumors was found to be overlapping with that of metastasis , therefore differentiation of peritumoral edema and infiltration wasn't possible. As seen in the study by G G Fan *et al* [23] and Server A *et al.* but contrary to Tien *et al*[21] and K Krabbe *et al*[22].

Summary

MR diffusion imaging with ADC values add very important information to conventional MR which add to its sensitivity , specificity , negative and positive predictive values. While its very useful in detection of brain tumors and distinguishing between low and high grade malignancies , it has limited ability to differentiate between tumors of same class. It proves excellent in diagnosis of lymphomas , high grade malignancies and metastasis , but cannot differentiate between peritumoral edema and infiltration. To conclude diffusion MR with ADC must be a an important part of tumor imaging protocol.

REFERENCES

1. Brain Tumor Primer A comprehensive introduction to brain tumors, 9th edition American Brain Tumor Association, 2006.
2. Yeole BB. Trends in the brain cancer incidence in India. Asian Pac J Cancer Prev. 2008;9(2):267-70.
3. Osborn AG; Osborn's brain: imaging, pathology, and anatomy. Salt Lake City: Amirsys; 2013, ch 16 Introduction to Neoplasms, cysts, and tumor-like lesions: 443-452
4. Akay KM, Izci Y, Baysefer A, Atabey C, Kısmet E, Timurkaynak E; Surgical outcomes of cerebellar tumors in children. Pediatric neurosurgery. 2005;40(5):220-5.
5. Hargrave D, Bartels U, Bouffet E; Diffuse brainstem glioma in children: critical review of clinical trials. Lancet Oncol. 2006; 7(3):241-8.
6. Tobias JS, Hayward RD; Brain and spinal cord tumors in children. Thomas DGT. Neuro-oncology: primary malignant brain tumours. Baltimore. 1990;777:164-92.
7. Nasir S, Jamila B, Khaleeq S; A retrospective study of primary brain tumors in children under 14 years of age at PIMS, Islamabad. Asian Pac J Cancer Prev. 2010;11(5):1225-7.
8. Chenevert TL, Brunberg JA, Pipe JG; Anisotropic diffusion in human white matter: demonstration with MR techniques in vivo. Radiology 1990;177:401–405
9. Chien D, Buxton BR, Kwong KK, Brady JT, Rosen RB; MR Diffusion imaging of the human brain. J Comput Assist Tomogr 1990;14:514–520
10. Al-Okaili RN, Krejza J, Wang S, Woo JH, Melhem ER; Advanced MR Imaging Techniques in the Diagnosis of Intraaxial Brain Tumors in Adults 1. Radiographics. 2006;26(suppl_1):S173-89.
11. Bulakbasi N, Guvenc I, Onguru O, Erdogan E, Tayfun C, Ucoz T; The added value of the apparent diffusion coefficient calculation to magnetic resonance imaging in the differentiation and grading of malignant brain tumors.J Comput Assist Tomogr. 2004;28(6):735-46.
12. Fan G G, Deng Q L, Wu Z H; Usefulness of diffusion/perfusion-weighted MRI in patients with non-enhancing supratentorial brain gliomas: a valuable tool to predict tumour grading? The British Journal of Radiology, 2006;79: 652–658
13. Scott JN, Brasher PM, Sevick RJ, Rewcastle NB, Forsyth PA; How often are nonenhancing supratentorial gliomas malignant? A population study. Neurology. 2002;59(6):947-9.
14. White ML, Zhang Y, Kirby P, Ryken TC; Can tumor contrast enhancement be used as a criterion for differentiating tumor grades of oligodendrogliomas?. American journal of neuroradiology. 2005;26(4):784-90.
15. Kitis O, Altay H, Calli C, Yunten N, Akalin T, Yurtseven T; Minimum apparent diffusion coefficients in the evaluation of brain tumors. European journal of radiology. 2005;55(3):393-400.
16. Yamasaki F, Kurisu K, Satoh K, Arita K, Sugiyama K, Ohtaki M, Takaba J, Tominaga A, Hanaya R, Yoshioka H, Hama S; Apparent Diffusion Coefficient of Human Brain Tumors at MR Imaging 1. Radiology. 2005;235(3):985-91.
17. Kan P, Liu JK, Hedlund G, Brockmeyer DL, Walker ML, Kestle JR; The role of diffusion-weighted magnetic resonance imaging in pediatric brain tumors.Childs Nerv Syst. 2006;22(11):1435-9.
18. Okamoto K, Ito J, Ishikawa K, Sakai K, Tokiguchi S; Diffusion-weighted echo-planar MR imaging in differential diagnosis of brain tumors and tumor-like conditions.EurRadiol. 2000;10(8):1342-50.
19. Kono K, Inoue Y, Nakayama K, Shakudo M, Morino M, Ohata K, Wakasa K, Yamada R; The role of diffusion-weighted imaging in patients with

brain tumors. American Journal of Neuroradiology. 2001;22(6):1081-8.

20. Pauleit D, Langen KJ, Floeth F, Hautzel H, Riemenschneider MJ, Reifenberger G, Shah NJ, Müller HW;Can the apparent diffusion coefficient be used as a noninvasive parameter to distinguish tumor tissue from peritumoral tissue in cerebral gliomas?J MagnReson Imaging. 2004;20(5):758-64.
21. Tien RD, Felsberg GJ, Friedman H, Brown M, MacFall J; MR imaging of high-grade cerebral gliomas: value of diffusion-weighted echo planar pulse sequences. AJR Am J Radiol, 1994; 162:671-677.
22. Krabbe K, Gideon P, Wagn P, Hansen U, Thomsen C, Madsen F; MR diffusion imaging of human intracranial tumours. Neuroradiology. 1997;39(7):483-9.