DIFFUSION WEIGHTED IMAGE (DWI) AND MAGNETIC RESONANCE SPECTROSCOPY (MRS) OF MASS LIKE LESIONS IN THE BRAIN AS CORRELATED TO HISTOPATHOLOGY.

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ABSTRACT

Bachground and purpose:

DWI and MRS have been used for the differentiation and grading of the brain tumors for more than 10 yrs. We attempted to study the diagnostic efficacy of these two techniques in MR imaging as correlated to the histopathology.

METHODS

Seventy patients with mass like lesions diagnosed by conventional MRI and pathologically or clinically proved (11 low grade astrocytomas and 10 high grade astrocytomas, 7 metastases,3 lymphomas, 2 germinomas,1 medulloblastoma, and 1 neuroblastoma, as well as 17 meningiomas, 5 schwannomas and 13 non tumors) and 20 normal controls were prospectively evaluated with conventional MRI, MRS (Press TR1500 and TE135) and DWI(b=0,500and 1000 s/mm2)

RESULTS

MRS shows diagnostic efficacy in differentiate tumor from non-tumor($p<0.5$), benign from malignant ($p<0.5$) and intraaxial from extraaxial tumor. Cho/CR more than 1.3 is the key value for differentiate of tumor from non-tumor and increase frequency in lactate or lipid may be used for differentiate of malignant from benign tumor. The Cho mono peak is the characteristic of extraaxial tumor.The present of the alanin is the feature of meningioma. ADC values were not effective for grading tumor or to differentiate malignant from benign and tumor from non-tumor. Only restricted diffusion (low ADC value) were noticed in 2 brain abscesses but the number of case is too small.

INTRODUCTION

Conventional MRI is the most useful technique in the diagnosis and evaluation of mass like lesion in the brain. For some instances, it is ineffective. MRS have been used for detection of brain abnormality with nearly 100% sensitivity and differentiate of tumor types by characterization of metabolic changes.[2-24] DWI and ADC (apparent diffusion coefficients) have been used to distinguish normal white matter from necrosis, cyst formation, edema and solid enhancing tumor.[24-33] DWI were also very effective in grading

ADC = Apparent Diffusion Coefficient, **DWI** = Diffusion Weighted Image, **MRS** = Magnetic Resonance Spectoscopy, **CHO** = Choline, **CR** = Creatine, **b** = diffusion Strength, **s** = second

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tumor and in the demarcation of tumor by directional dependence of molecular diffusion.[25,28,29,34-38] In this study we attempted to evaluate the effectiveness of MRS and DWI for the differential diagnosis of mass like lesion in the brain. The main purposes were as follows: 1) to differentiate tumor from non-tumor. 2) to differentiate malignant from benign. 3) to do the grading of the tumor and 4) to distinguish pathologic subtypes by correlation of the MRS and ADC parameters with histopathologic findings.

METHODS

Study population:

70 patients comprising 40 men and 30 women ranging from 15 to 75 years of age (means age 45 yrs) with mass like lesion of the brain on conventional MRI were prospectively evaluated with DWI and MRS. 57 cases were pathological proved to be tumor and 13 were non-tumor. 20 normal control study were also done.

MRI evaluation:

All patients were examined by 1.5-Tesla MR imager (Magnetom vision plus, Seimens, Erlangen, Germany) with a standard head coil and protocol axial T1W(TR/TE=650/14 ms), T2WFSE(2000/80 ms) and Flair (TR/TE/TI=9000/2500/110 ms), 5 mms slice thickness, 210 mms FOV and 160x256 matrix size. DWI were done at tumor and peritumoral area and MRS at only tumor area (solid part) as well as other normal looking part.

MRS evaluation:

MRS were obtained by single voxel, PRESS sequence (TR/TE=1500/135 ms) with one-pulse water suppression and avoiding contamination from scalp fat, 256 acquisitions and automatic shimming. Spectroscopic data is from cubic volumes of 1.5x1.5x1.5 cms and acquisition time about 6.30 minutes.

MR diffusion imaging:

DWI were obtained by using axial echo-planar SE sequence (TR/TE=5700/139 ms), 5 mms slice thickness, 96x128 matrix size, FOV 240 mms in 22 seconds. The DWI were acquired by using b values of 0, 500, 1000 s/mm^2 applied in the X,Y, Z directions. Post processing of the ADC maps was performed by using software on a workstation and standard mean ADC values calculated automatically and expressed in 103 mm^2/s.

Histopathologic classification:

Total resection or multiple biopsy specimens were obtained from each patient. The tumor type and grading was according to WHO classification of nervous system tumors. For statistic analysis, lesions were classified as tumor or non-tumor, benign or malignant and high or low grade tumor.

Statistic analysis:

The mean and standard deviation (SD) of all MRS and ADC values were calculated with SPSS. Data were analyzed with independent sample T-test to compare mean of tumor versus non-tumor, benign versus malignant and high versus low grade tumor. The mean different was significant at the level of $p<.05$.

RESULTS

Seventy patients were screwed to the inclusion criteria comprising of 40 men and 30 women,age ranging from 15 to 75 yrs (mean age 45

ADC = Apparent Diffusion Coefficient, **DWI** = Diffusion Weighted Image, **MRS** = Magnetic Resonance Spectoscopy, **FOV** = Field of view, **b values** = Diffusion Strength, **PRESS** = Point Resolved Spectroscopy, **NAA** = N- Acitylaspartate **shimming** = Processes to make the magnetic field not variable, **SPSS** = Computer program for calculating different parameters in statistics such as, means, standard deviations, etc.

years). Fifty seven patients (81%) were tumors and thirteen patients(19%) non-tumors. Base on the histopathologic classification, 24/57(42%) were malignant (10 high grade astrocytomas, 7 metastases, 3 lymphomas, 1 medulloblastoma, 1 neuroblastoma and 2 germinomas) and 33/57 (58%) were benign (11 low grade astrocytomas, 17 menigiomas, 5 schwannomas). The 13 non-tumors were cerebral infarct 6, cysticercosis 3, abscess 2 and multiple sclerosis 2. The MRS showed that it is beneficial for differentiating tumor from non-tumor, malignant from benign, and extraaxial from intraaxial tumor. The most significant parameters were the Cho/Cr value with cut point at 1.3 and the presence of lactate or lipid, Cho/Cr more than 1.3 favored tumor and less than 1.3 favored non-tumor. Malignant tumor showed more frequent lactate and lipid. The character of choline mono peak was found only in extraaxial tumor which helped to differentiate from intraaxial tumor.The Alanin was present only in meningioma. The ADC values were not useful in the differentiating tumor from non-tumor, malignant from benign, or in the grading of the tumor. However, restricted diffusion with low ADC value was noted in both of the brain abscesses and MS.(Table 1)

MR spectroscopic findings:

MRS shows benefit to differentiate the tumor from non-tumor, malignant from benign tumor ($p<.05$). (Table 3&4). The most significant parameter to differentiate tumor from non-tumor is the Cho/Cr value with cut point at 1.3. Malignant tumor shows more Cho/Cr value but less NAA/Cr ratio. In grading of the tumor in the same type such as glioma, the MRS parameter shows no efficacy to differentiate(Table 5). The more frequency of lactate or lipid in malignant tumor (Table 7) is the parameter to differentiate malignant from benign tumor. The present of Alanin in only meningioma can used to be the character of this tumor (Table 6) as well as the Cho mono peak which was seen in other extraaxial tumnor such as Schwannoma as well.

Table 1: Summary of histopathologic diagnosis

Tumor group	Histodiagnosis	No of patients (n=70)
Malignant or high grade(n=24)	Astrocytoma grade 3,4 or GBM	10
	Germinoma	2
	Lymphoma	3
	Medulloblastoma	1
	Metastasis	7
	Neuroblstoma	1
Low grade(n=11)	Low grade astrocytoma	11
Benign(n=22)	Meningioma	17
	Schwannoma	5
Non-tumor(n=13)	Abscess	2
	Cysticercosis	3
	MS	2
	Cerebral infarct	6

Table 2: Normal control subjects

	N=20	N=20
Parameter	Mean	SD
NAA/Cr	1.90	0.46
Cho/Cr	0.85	0.13
ADC/Cr	88.00	5.00

Table 3: Differentiattion of tumor versus non tumor

	Tumors(n-57)		Non-tumor(n=13)			
Parameter	**Mean**	**SD**	**Mean**	**SD**	***P* value**	
NAA/Cr	0.91	0.59	1.35	0.56	0.02	Significant
Cho/Cr	2.03	1.16	1.00	0.21	0.002	Significant
Lactate/Cr	0.88	0.45	2.08	3.28		
Lipid/Cr	1.00	2.31	3.50	-		
Alanin/Cr	0.51	0.15	-	-		
ADCT	130.0	49.0	141.0	37.0	0.44	NS
ADCPT	157.0	38.0	158.0	46.0	0.97	NS

Note: ADCT indicates calculated ADC values from tumoral area. ADCPT, calculated ADC values from peritumoral area. NS = no significant different. P values were obtained by using independent Sample T-Test.

Table 4 :Differentiation of tumor as benign versus malignant

	Malignant(n=24)		Benign(n=33)			
Parameter	**Mean**	**SD**	**Mean**	**SD**	***P* values**	
NAA/Cr	1.16	0.65	1.15	0.47	0.41	NS
Cho/Cr	2.35	1.47	1.76	0.78	0.05	Significant
Lactate/Cr	1.01	0.49	-			
Lipid/Cr	1.71	2.62	0.93	0.30		
Alanin/Cr	-		0.51	0.15		
ADCT	126.0	41.0	135.0	53.0	0.51	NS
ADCPT	147.0	30.0	164.0	41.0	0.07	NS

Note: ADCT indicates calculated ADC values from tumoral area. ADCPT, calculated ADC values from peritumoral area. **NS** = no significant different. P values were obtained by using independent Sample T-Test.

Table 5: Differentation of tumor as low versus high grade

	High grade(n=10)		Low grade(n=11)			
Parameter	**Mean**	**SD**	**Mean**	**SD**	***P* values**	
NAA/Cr	1.35	0.78	0.93	0.49	0.15	NS
Cho/Cr	2.80	1.91	2.10	1.05	0.30	NS
Lactate/Cr	1.24	0.50	0.49	0.30		
Lipid/Cr	1.05	0.69	0.53	0.53		
Alanin/Cr	-		-			
ADCT	145.0	45.0	178.0	46.0	0.12	NS
ADCPT	147.0	27.0	151.0	31.0	0.79	NS

Note: ADCT indicates calculated ADC values from tumoral area. ADCPT is calculated ADC values from peritumoral area. **NS** = no significant different. P values were obtained by using independent Sample T-Test.

Table 6: Differentiation of histopathologic tumor types

	HGA (n=10)		Metastasis (n=7)		LGA (N=11)		Schwannoma (n=5)		MNG (N=17)	
Parameter	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
NAA/Cr	1.35	0.78	1.39	0.46	0.93	0.49	0.84	0.60	0.61	0.40
Cho/CR	2.89	1.91	2.07	1.33	2.10	1.05	1.47	0.19	1.63	0.64
Lactate/Cr	1.24	0.50	0.99	0.47	0.40	0.30	-		1.00	-
Lipid/Cr	1.05	0.69	2.60	0.43	0.53	0.10	0.90	0.42	-	
Alanin/Cr	-		-		-		-		0.51	0.15
ADCT	145.0	45.0	126.0	25.0	176.0	46.0	153.0	74.0	103.0	25.0
ADCPT	147.0	27.0	153.0	32.0	154.0	31.0	213.0	63.0	157.0	31.0

Note: ADCT indicates calculated ADC values from tumoral area. ADCPT is calculated ADC values from peritumoral area. **NS** = no significant different. P values were obtained by using independent Sample T-Test.

Table 7: Frequency of lactate or lipid in malignant and benign tumor

	Malignant tumor(N=24)	Benign tumor(N=33)
Frequency	n (%)	n (%)
Lactate	5 (20%)	3 (9%)
Lipid	10 (41%)	3 (9%)

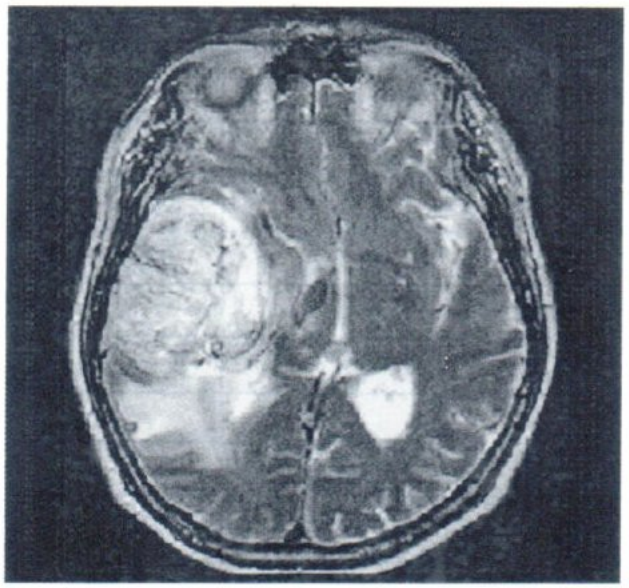

Fig. 1A

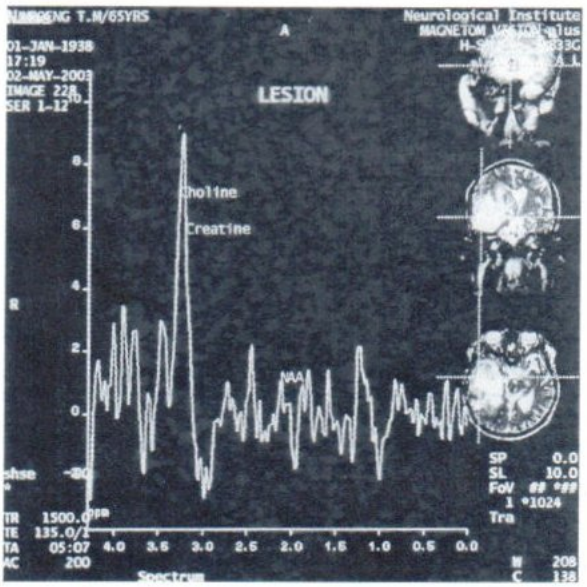

Fig. 1B

Fig.1 65-year-old man with meningioma at right sphenoid wing.

A: T2-weighted image shows a well demarcated slightly hyper SI with mild perifocal edema and mass effect.

B: MR spectrum reveals Cho mono peak with marked decrease of the NAA and presenting of the alanin(arrow).

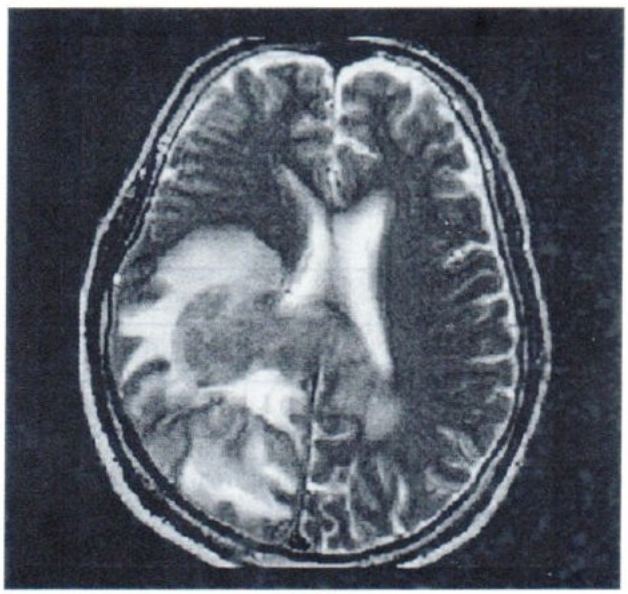

Fig. 2A

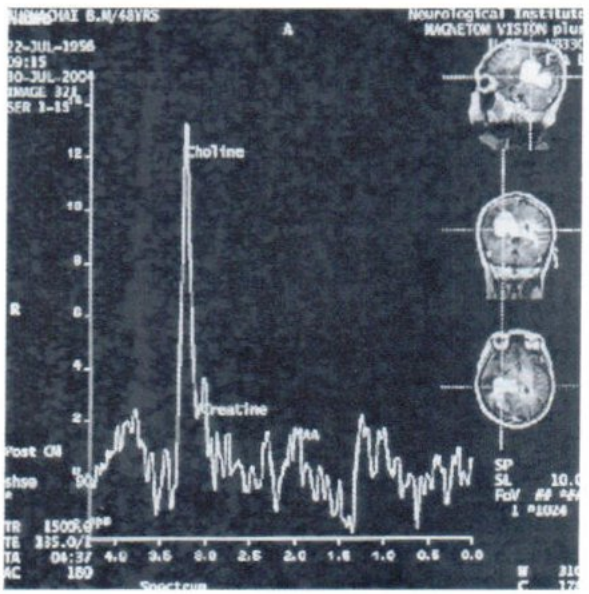

Fig. 2B

Fig 2 48-year-man with brain lymphoma at the splenium of right corpus callosum.

A: T2-weighted image shows slightly hyper SI mass at the splenium of right corpus callosum with moderated perifocal edema and mass effect.

B: MR spectrum of the tumor reveals marked increase level of Cho(CHO/Cr=2.6) and decrease NAA (NAA/Cr=0.6)

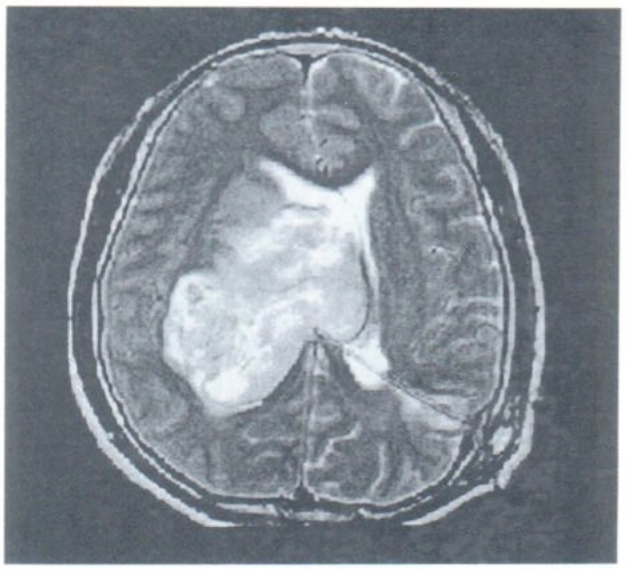

Fig. 3A

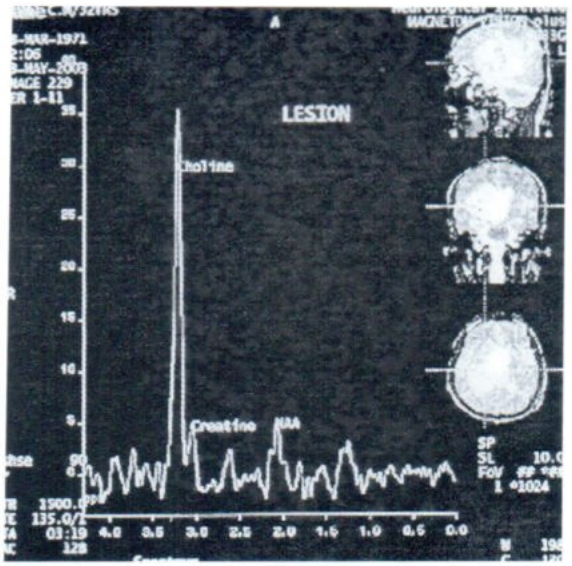

Fig. 3B

Fig. 3 32-year-man with Glioblastoma multiforme at right corona radiata

A: T2-weighted image shows a hyper SI mass at right corona radiata with moderated perifocal edema and mass effect.

B: MR spectrum reveals marked increase level of the Cho (Cho/Cr =4.00) and decrease NAA (NAA/Cr =1.00)

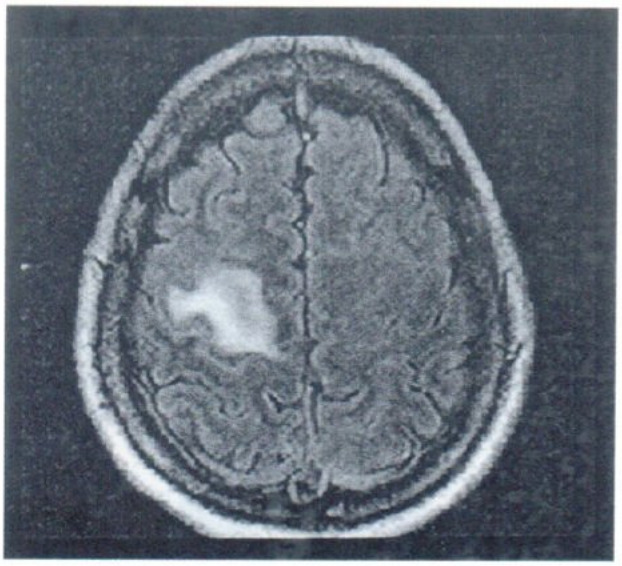

Fig. 4A

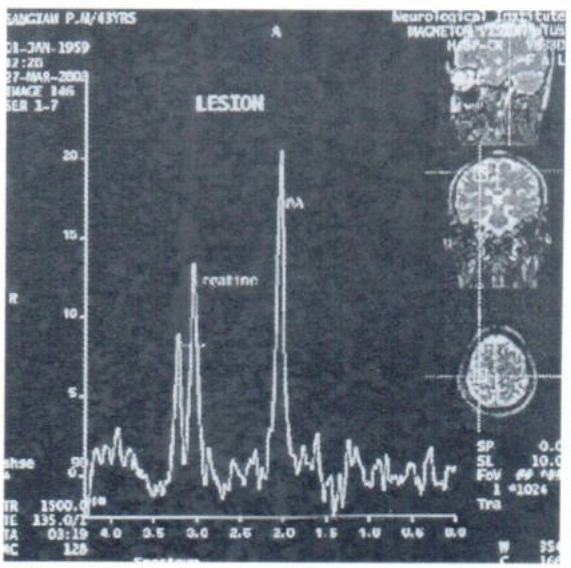

Fig. 4B

Fig. 4 43 year-man with brain cysticercosis in the right frontal lobe.

A; Flair image shows hyper SI lesion at right frontal lobe with mild perifocal edema and mass effect.

B: MR spectrum reveals mild decrease level of the NAA(NAA/Cr =1.4), unremarkable otherwise.

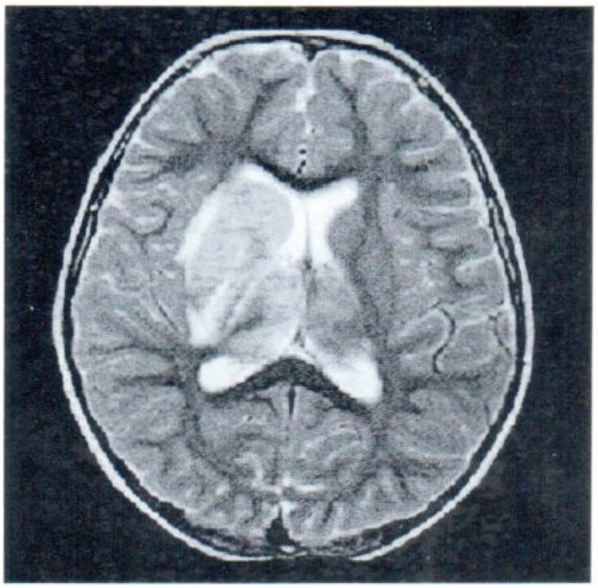

Fig. 5A

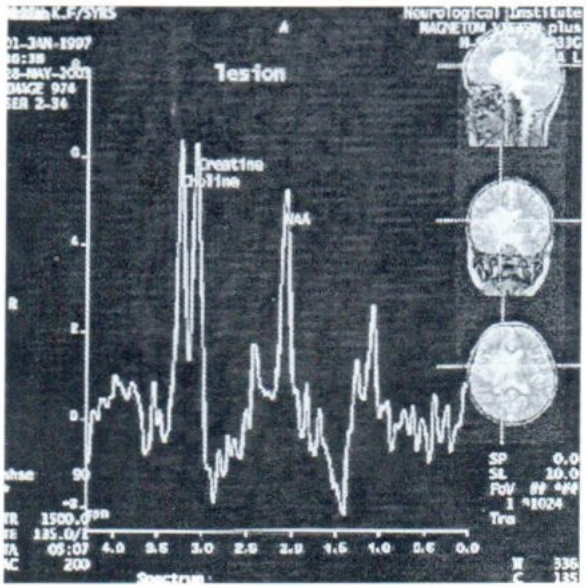

Fig. 5B

Fig. 5 5-year-female with cerebral infarct at right BSG and caudate neucleus.

A; T2-weighted image shows slightly hyper SI lesion at right BSG and caudate neucleus with mild perifocal edema and mass effect.

B: MR spectrum reveals decrease level of NAA(NAA/Cr=0.8) and presenting of lactate.

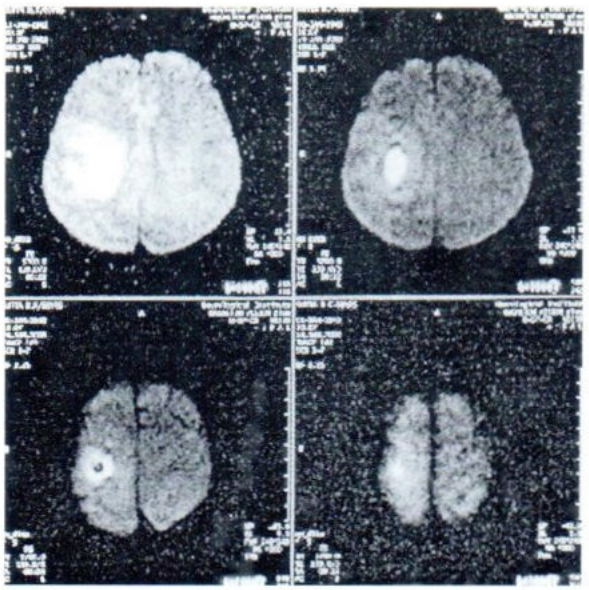

Fig. 6A

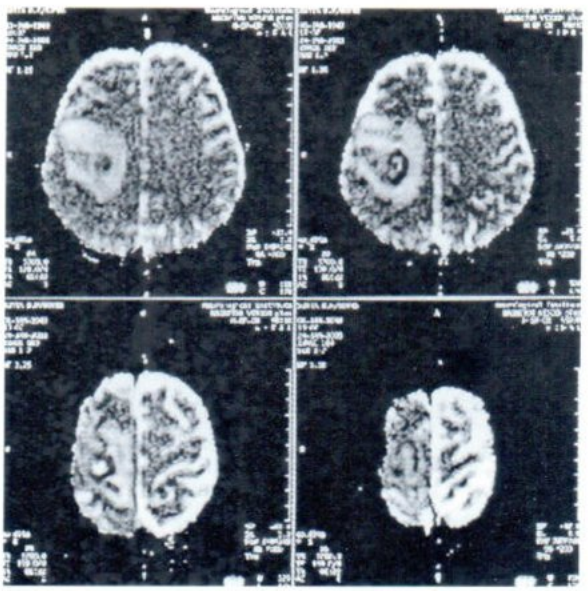

Fig. 6B

Fig. 6 60-year-female with brain abscess at centrum semioavale of right frontal lobe.

A: Diffusion weighted image (b=1000s/mm2) shows hyper SI lesion at right frontal lobe with moderated perifocal edema .

B: ADC map reveals the hyper SI lesion on DWI to be marked hypo SI and the calculated ADC value is 73 (Mean of ADC value of normal control= 88 ,SD=5 from table 2) ,consistent with restricted diffusion.

DWI and calculated ADC values

The ADC values in both tumor and peri tumor area were not useful in the differentiation tumor from non tumor, malignant from benign or in grading of the tumor(Table 2,3,4). Between subtypes of the tumor they also shows no efficacy, as shown in table 5. Only 2 restricted diffusion were noted in the brain abscesses, but the number of cases are too small.

DISCUSSION

DWI and MRS have been used in the evaluation of brain tumor for more than 10 years. Lower ADC values were accepted as a marker of high tumor grades.[24-39] NAA as marker of neuronal integrity, increase in Cho involved in increased cell membrane and myelin turn over as well as Cr represent cellular energetic and osmotic balance were reported. [2,3,6,8,12,17,18,22,40] Presence of the lactate and lipid were compatible with aggressiveness of the tumor, reflecting increase anaerobic metabolism and cellular necrosis, respectively. [2,3,6,7,9,12,17,18,22,40] The diagnostic accuracy of MRS in differentiate patients from control subjects was 0.96, and neoplasm from non-neoplasm was 0.96 and 0.83 in non blinded and blinded study, respectively.[41]

In our study ,the MRS could differentiate tumor from non-tumor and malignant from benign tumor but not effective in grading tumor. This is along with study by Nail et al.[1] The Decrease in NAA/Cr and incresse Cho/CR is the parameter for differentiate tumor from non-tumor. More malignant tumor shows more increase in Cho/Cr consistent with previous reports.[2,4,10,18,20,23] The increase Cho/Cr was mainly due to increase membrane turn over and liberation of unbound Cho-containing compound caused by destruction of neurons during malignant process, rather than decrease of the Cr level, which is rather constant in many conditions.[2,3,7,12] We also noticed more frequency of lactate or lipid in malignant tumor than benign tumor. This is also consistent with many reports.[7,10,12,23] Presence of lactate the indicator of non functional normal oxidative respiratory and increase anaerobic glycolysis[18] and it represented a loss of normal brain parenchyma and necrosis on MR image.[3] An increase in lipid level has been reported as the indicator of necrosis and usually prominent in non astrocytic tumors and metastasis.[7-9,13,22,23] We detected alanin in 12 of 17 meningioma close to the findings of Nail et al.[1] This could be the specific findings of meningioma. The alanin /Cr ratio in meningeal cells were three to four time higher in that found in astrocytes, neuron and oligodendrocytes.[12]

Krabbe et al[25] found that ADC of contrast enhancing areas and edema surrounding cerebral metastasis were significant higher than those of high grade astrocytoma and Kono et al[32] demonstrated a good correlation between ADC and cellularity in glioma, but in our study shows no different of the ADC in the tumor or peri tumor between malignant and benign as well as high and low grade tumor. Only restricted diffusion with marked low ADC was noticed in two brain abscesses compatible with the study by Noguchi et al.[30] Cho mono peak were found in nearly all extra axial tumor (Meningioma and Schwannoma) and this feature could be used to differentiate extraaxial from intraaxial tumor.

CONCLUSION

MRS showed diagnostic efficacy in differentiating tumor from non-tumor ($p<0.5$), benign from malignant tumors ($p<0.5$) and intraaxial from extraaxial tumors. Cho/CR more than 1.3 was the key value for the differentiation of tumor from non-tumor. The increased frequency in lactate or lipid might be used for differentiation of malignant from benign tumors. The Choline mono peak was the characteristic of extraaxial tumor. The presence of the alanin was the feature of meningioma. ADC values were not effective for grading tumor or differentiating malignant from benign tumor, and tumor from non-tumor, but restricted

diffusion (low ADC value) was noticed in brain abscess.

REFERENCES

1. Nail B, Murat K, Fatih O, Cem T , Taner U. Combination of single-voxel proton MR spectroscopy and apparent diffusion coefficient calculation in the evaluation of common brain tumors. AJNR Am J Neuroradiol 2003; 24: 225-233(Abstract/Free Full Text)
2. Bruhn H,Frahm J,Gyngell ML,et al. Noninvasive differentiation of tumors with use of localized H-1 MR spectroscopy in vivo:initial experience in patients with cerebral tumor. Radiology1989;172:541-548(Abstract)
3. Segebarth CM,Baleriaux DF,Luyten PR,den Hollander JA.Detection of metabolic heterogeneity of human intracranial tumor in vivo by H-1 NMR spectroscopic imaging.Magn Reson Medl 1991;62-76(Medline)
4. Fulham MJ,Bizzi A,Dietz MJ,et al. Mapping of brain tumor metabolites with proton MR spectroscopic imaging: clinical revevance. Radiology1992;185:675-686(Abstract)
5. Baker PB,Glikson JD,Brayn RN.In vivo magnetic resonance spectroscopcy of human brain tumorsTop Magn Reson Imaging 1993; 5:32-45(Medline)
6. Poptani H,Gupta RK,Roy R,Pandey R, Jain VK,Chhabra DK.Chracterization of intracranial mass lesions with in vivo proton MR spectroscopy.AJNR AM J Neuroradiol 1995;16:1593-1603(Abstract)
7. Castillo M,Kwock L,.Clinical application of MR spectroscopy.AJNR AM J neuroradiol 1996;17:1-15(Free full text)
8. Krouwer HGJ,Kim TA,Rand SD,et al .,Single -voxel proton MR spectroscopy of nonenoplastic brain lesions suggestive of a neoplasm. AJNR Am J Neuroradiol1998;19:1695-1703(Abstract)
9. Castillo M,Kwock L.Proton MR spectroscopy of common brain tumors.Neuroimaging Cli North Am1998;8:733-752
10. Meyeland ME, Pipas JM, Mamourian A, Tosteson TD, Dunn JF.Classification of biopsy-confirmed brain tumors using single -voxel MR spectroscopy.AJNR Am J Neuroradiol1999;20:117-123(Abstract/Free Full Text)
11. Nelson SJ,Vignerron DB,Dillon WP.Serial evaluation of patients with brain tumors using volume MRI and 3D 1-H MRSI. NMR Biomed1999;12:123-128 (Medline)
12. Castillo M,Kwock L.Clinical applications of proton magnetic resonance spectroscopy in the evaluation of common intracranial tumors.Top magn Reson Imaging 1999; 10: 104-113(Medline)
13. Grand S,Passaro G,Ziegler A,et al. Necrotic tumor versus brain abscess : importance of amino acids detected at 1-H MR spectroscopy-initial results.Radiology1999;213:785-793(Abstract/Free Full Text)
14. Burtscher IM, Skagerberg G, Geijer B, Englund E,StahbergF,Holtas S.Proton MR spectroscopy and preoperative diagnostic accuracy: an evulation of intracranial mass lesions characterized by stereotactic biopsy findings.AJNR Am J Neuradiol2000;21:84-93(Abstract/FreeFull Text)
15. Shimizu H,Kumbe T,Shirane R,Yoshimoto T. Correlation between choline level measured by proton MR spectroscopy and Ki-67 labeling index in gliomas.AJNR Am J Neuroradiol2000;21:659-665(Abstract/Free Full Text)
16. Bendszus M, Warmuth-Metz M, Klein R, et al. MR spectroscopy in gliomatosis cerebri. AJNR Am J Neuroradiol2000;21:375-28 -380(Abstract/Free Full Text)
17. Butzen J, Prost R, Chetty V, et al. Discrimination between neoplastic and nonneoplastic brain lesions by use of proton MR spectroscopy: the limits of accuracy with logical regression model. AJNR Am J Neuroradiol 2000; 21: 1213-1219 (Abstract/Free Full Text)

18. Kimura T, Sako K, Gotoh T, Tanaka K, Tanaka T, Invivo single-voxel proton MR spectroscopy in brain lesions with ring-like enhancement.NMR Biomed 2001; 14: 339 349 (Medline)
19. Dowling C, Bollen AW, Noworolski SM, et al. Preoperative proton MR spectroscopic imaging of brain tumors: correlate to histopathologic analysis and resection. AJNR Am J Neuroradiol; 22: 604-612 (Abstract/Free Full Text)
20. Schlmmer HP, Bachert P, Herfarth KK, Zunna I, Debus J, van Kaick G. Proton MR spectroscopic evaluation of suspicious brain lesions after stereotactic radiotherapy.AJNR Am J Neuroradiol;22:1316-1324(Abstract/ Free Full Text)
21. Tzika aa, Cheng, LL, Goumnerova L, et al. Biochemical characterization of pediatric brain tumors by using ex vivo magnetic resonance spectroscopy. J Neurosurg 2002; 96: 1023-1031(Abstract/Free Full Text)
22. Tzika AA, Zarifi MK, Goumnerova L, et al. Neiroimaging in pediatric brain tumors: Gd-DTPA-enhanced,hemodynamic,and diffusion MR imaging compared with MR spectroscopic imaging. AJNR Am J Neuroradiol 2002; 23: 322-333 (Abstract/Free Full Text)
23. Moller-Hartmann W, Herminghaus S, Krings T, et al. Clinial application of proton magnetic resonance spectroscopy in dianosis of intracranial mass lesions. Neuroradiology 2002; 44: 371-381(Medline)
24. Sener RN. Longstanding tectal tumor: proton MR spectroscopy and diffusion MRI findings. Comput Med Imaging Graph 2002; 26: 25-31(Medline)
25. Krabbe K, Gideon P, Wang P, Hansen U, Thomsen C, Madsen F. MR diffusion imaging ofhuman intracranial tumors.Neuroradiology 1997; 39: 483-489
26. Le Bihan D, Breton E, Lallemand D, Grenier P, Cabanis E, Laval-Jeantet M. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. Radilogy 1986; 161: 401-407(Abstract)
27. Remy C, Grand S, Lai ES, et al.1H MRS of human brain abscess in vivo and in vitro.Magn Reson Med1995;34:508-514
28. Tien RD, Felberg GJ, Frieman H, Brown M, MacFall J. MR imaging of high-grade cerebral gliomas: value of diffusion-weighted echoplanar pulse sequence AJR Am J Roentgenol1994;162: 671-677(Abstract)
29. Brunberg JA, Chenevert TL, McKeever PE, et al. In vivo MR determination of water diffusion coefficients and diffusion anisotropy: correlation with structural alteration in gliomas of the cerebral hemispheres. AJNR Am J Neuroradiol1995;16:361-371(Abstrat)
30. Noguchi K, Watanabe N, Nagayoshi T,et al. Role of diffusion-weighted echo planar MRI in distinguishing between brain abscess and tumor: a primary report. Neuroradiology 1999; 41:171-174(Medline)
31. Stadnik TW, Chakis C, Michotte A, et al. Diffusion-weighted imaging of intracerebral masses: comparison with conventional MR imaging and histologic findings. AJNR Am J Neuroradiol2001;22969-976(Abstract/Free full Text)
32. Kono K, Inoue Y, Nakayama K, et al. The role of diffusion-weighted image in patients with brain tumors. AJNR Am J Neuroradiol 2001;221081-1088(Abstract/Free Full Text)
33. Filippi CG, Edgar MA, Ulu AM, Prowda JC, Heir LA, Zimmerman RD. Appearance of meningioma on diffusion-weighted images: Correlating diffusion constants with histopathologic findings. AJNR Am J Neuroradiol 2001; 22: 65-72 (Abstract/Free Full Text)

34. Le Bihan D, Douek P, Argyropoulou M, Turner R, Patronas N, Fulham M. Diffusion and perfusion magnetic resonance imaging in brain tumors. Top Magn Reson Imaging 1993; 5:25-31(Medline)
35. Eis M, Els T, Hoehn-BerlageM, Hossman KA. Quantitative diffusion MR imaging of cerebral tumor and edema. ActaNeurochirSuppl (Wien) 1994; 60: 344-346 (Medline)
36. Castillo M, Smith JK, Kwock L, Wilber K. Apparent diffusion coefficients in the evaluation of high-grade cerebral gliomas. AJNR Am J Neuradiol2001;22:60-64(Abstract/ Free Full Text)
37. Maier SE, Bogner P, Bajzik G, et al. Normal brain and brain tumor: multi component apparent diffusion coefficient line scan imaging Radiology 2001;219: 842-849 (Abstract/Free Full Text)
38. Sinha S, Bastin ME, Whittle IR, Wardlaw JM. Diffusion tensor MR imaging of high-grade cerebral gliomas. AJNR Am J Neuroradiol 2002; 23: 520-527(Abstract/Free Full Text)
39. Law M, Cha S, Knopp EA, Johnson G, Arnett J, Litt AW. High-grade gliomas and solitary metastases: differentiation by using perfusion and proton spectroscopic MR imaging. Radiology 2002; 222: 715-72 (Abstract /Free Full Text)
40. Tedeschi G, Lundbom N, Raman R, et al. Increased choline signal coinciding with malignant degeneration of cerebral gliomas: a serial proton magnetic resonance spectroscopy imaging study. J Neurosurg 1997; 87: 516-527(Medline)
41. Rand SD, Prost R, Haughton V, et al. Accuracy of single-voxel proton MR spectroscopy in distinguishing neoplastic from non -neoplastic brain lesions. AJNR Am J Neuroradiol 1997; 18: 1695-1704 (Abstract)