ORIGINAL ARTICLE

MR SPECTROSCOPY IN THE EVALUATION OF SPACE OCCUPYING LESIONS IN BRAIN

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ABSTRACT

AIM: To evaluate the role of MR Spectroscopy (MRS) in the differential diagnosis of space occupying lesions of brain, to characterize and to grade focal brain lesions depending on features of MR Spectroscopy and to correlate the imaging findings with histopathological examination. **MATERIALS AND METHODS:** The study was performed on a whole body system at 1.5 Tesla, using a dedicated head coil. Multiplanar T1- and T2-weighted, diffusion, gradient images, using spin echo sequences, post contrast study and proton MR spectroscopy was performed in all cases. Single(STEAM AND PRESS) and multivoxels (CSI) with variable sized ROI according to size and location of lesion were used. **RESULT:** In case of gliomas, MRS by using choline/creatine (Cho/Cr) ratio and N-acetyl-L-aspartate/choline (NAA/Cho) ratio proved helpful in characterization and differentiating low grade from high grade gliomas. All high-grade gliomas (n= 37) showed high choline and low or absent N-acetyl-L-aspartate,creatine along with lipid and / lactate. N-acetylaspartate/choline ratio was significantly lower and choline/creatine ratio was significantly higher in high-grade gliomas. Alanine peak was increased in meningioma aiding in differentiating the extra axial lesions. **CONCLUSION:** MR spectroscopy (MRS) is highly sensitive in characterizing low grade from high grade gliomas, peri lesional infiltration and more specific in characterizing abscess with lipid / lactate peaks. It provides additional information over conventional study for extra axial tumors and non-neoplastic lesions. It also plays a vital role in pre-operative assessment and management in cerebral mass lesions thus may help in avoiding intervention innon-neoplastic lesions.

Key words: MR spectroscopy, cholin- creatinine ratio, alanine peak, brain space occupying lesions.

Introduction

Intracranial mass lesions comprise a diverse group of lesions. The high morbidity and mortality associated with them necessitates their early and accurate diagnosis to plan an effective therapeutic regimen. Despite the excellent soft tissue contrast provided by MRI, the sensitivity and specificity with which this modality differentiates the intracranial mass lesions is limited due to various factors. Proton1H MR Spectroscopy (MRS), by evaluation of central nervous system (CNS) metabolites in vivo, is used to grade tumors[1,2,3] and distinguish primary CNS neoplasms from metastases, abscess and demyelinating lesions. Spatially resolved metabolic data obtained from 1H MRS provides information which increases the diagnostic accuracy of imaging sequences in predicting the histology of intracranial mass lesions. Single voxel proton MRS is a relatively rapid method for obtaining information about the metabolism in 4-8 cc region within the lesion, however, it does not address spatial heterogeneity and is unable to con-tribute todefining the spatial extent of the lesion.[4,5] These factors are particularly important for planning focal treatments such as radiation and surgical resection

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and for following the response to therapy. To address these issues, it is necessary to consider multivoxel proton MRS imaging.

(Fig. 1) shows a typical proton MR spectrum from the white matter of the centrum semiovale of a human brain acquired at a short echo time (TE) of 35 ms at 3T. Metabolite signals from mobile lipids (Lip), lactate (Lac), N-acetylaspartate (NAA), creatine (Cr), alanine and choline-containing compounds (Cho), centered, respectively, at 0.9 and 1.5, 1.3, 2.02, 3.03, 1.48 and 3.2 ppm, were obtained . Differentiation of Lipid and Lactate peaks, which have the same positions, was based on the assumption of their different directions on 1H-MRS with TE 144 ms, therefore any upward directed peak located at 1.3 ppm was considered as predominantly Lipid, whereas any downward directed one was defined as Lactate. Myoinositol peak occurs at 3.56 ppm while Alanine occurs 1.3 and 1.4 ppm and therefore may be overshadowed by the presence of lactate.[6,7]

Major differentials of enhancing cerebral lesions are primary neoplastic lesion versus inflammatory and infective lesions. Brain abscess usually show reduced level of all major metabolites, including Cho, Cr and NAA, while neoplastic lesions show increased Cho peak with reduced NAA levels.[7,8] Lipid/lactate peak can be observed in both types of lesions, but more commonly in necrotic lesions and abscess cavities. Hence we aim is to evaluate the role of MR Spectroscopy in the differentialdiagnosis of space occupying lesions of brain,to characterize and to grade focal brain lesions depending on features of MR Spectroscopy and to correlate the imaging findings with histopathological examination.

Materials & Methods

The present study consisting of 50 cases of intracranial mass lesions was done in the period from May 2011 to April 2014. This was a prospective study and we used a whole body MR system with 1.5 Tesla strength. A lesion size of more than 1 cc (on MR) was the inclusion criterion for selection of patients for proton MR spectroscopy. The lesions were classified as intraaxial or extraaxial using conventional MR findings. Diagnosis of intracranial mass was confirmed by stereotactic biopsy or postoperative histopathological examination. The diagnosis of infective lesions was based on histopathological findings or MR features, clinical presentation, cerebrospinal fluid findings,response to specific treatment and supplemented by follow up MRI study. Gliomas of different histologic types were graded I to IV, according to the degree of malignancy. Grade I and II gliomas were taken together as low-grade and grade III and IV were considered high-grade gliomas. MR imaging-multiplanar T1- and T2-weighted, diffusion, gradient images, using spin echo sequences, were obtained in all patients. Post contrast study was performed in all cases. Proton MRS by Single (STEAM AND PRESS) and multivoxels (CSI) 31, 144, 270 MR spectroscopy was performed on 1.5 Tesla scanner (SIEMENS MAGNETOM) using 8 channel head coil with TR 2000, TE 31/144/288 with flip angle 90 degree before or after contrast study with variable sized ROIs according to size and location of lesion. Multi-voxel spectroscopic examinations were guided by T1-weighted or T2-weighted images and where needed post gadolinium T1-weighted MRI was used. Under three dimensional control the rectangular 1H-MRS voxel wasplaced on the lesion with avoidance from subcutaneous fat, skull, and cerebral ventricles. The size of the voxel used was 20. 9X 20.9X 20 mm (volume: 8cc). Spatial suppression pulses were applied to the outsides of the voxel to reduce spectral contamination, global and localized shimming on the water proton and optimization of the water suppression was done. In each case the reference spectrum with identical size of the voxel was obtained from the normal appearing white matter of the cerebral hemisphere.

INCLUSION CRITERIA FOR STUDY

Patients of all ages with clinical suspected diagnosis of space occupying lesions of brain with a focal brain lesion on CT examination were included.A lesion size of more than 1 cc (on MR) was the inclusion criterion for selection of patients for proton MR spectroscopy.

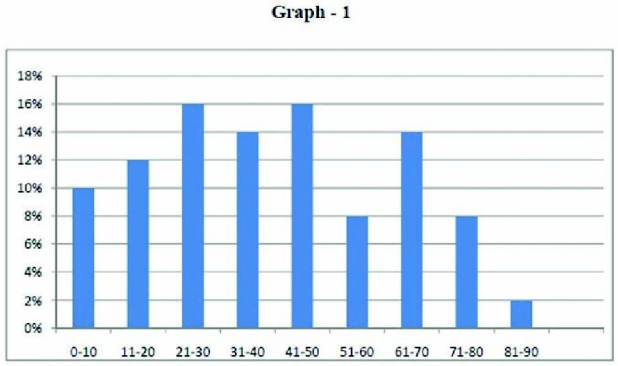
EXCLUSION CRITERIA FOR STUDY

1. Patients lost /died over follow up period without diagnosis.

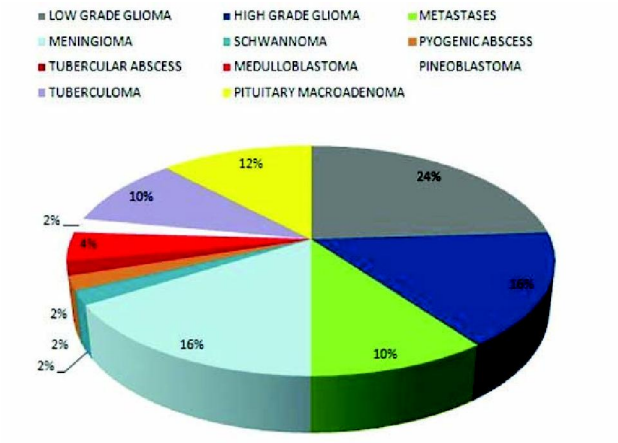
2. Patients without histopathological/ biochemical/ serological diagnosis.
3. Patients who had metallic implants/cardiac pacemakers.

Result

Highest incidence of patients in present study was found in 21-30 & 41-50years group (16 %) (Graph 1 and (Graph 2) illustrates the types of intracranial mass lesions with highest incidence of low grade



Graph 1



Graph 2

gliomas was noted (24%). Regarding grading of glioma, out of 20 patients with glioma, 12 had low grade gliomas and 8 had high grade gliomas. Spectroscopy findings are enumerated in (Tab. 3 A,B). In case of gliomas, MRS by using Cho/Cr ratio and NAA/Cho ratio proved helpful in differentiating low grade from high grade gliomas. Mean value of NAA/Cho ratio in high grade glioma is 0.26 and low grade

	Necrotic/ cystic areas (no. of cases)	Lipid peak (no. of cases)	Lactate peak (no of cases)	Cho/Cr ratio in lesion	Destectable NAA peak in necrotic/ systic area (no of cases)	NAA/ Cho ratio in lesion	NAA/ Cr ratio in lesion
Low grade glioma (n=12)	4	1	10	Mean 2.42	1	Mean 0.67	Mean 1.48
High grade glioma (n=8)	6	6	7	Mean 4.82	3	Mean 0.26	Mean 1.24

Table 3A: Characterization of Gliomas by Spectroscopy

Ratio	High grade (n=8)			Low grade (n=12)			P value (Two tailed)
	Mean	SD	SEM	Mean	SD	SEM	
NAA/Cho	0.26	0.13	0.0021	0.67	0.19	0.0030	0.000000
Cho/Cr	4.82	1.71	0.3655	2.42	0.88	0.0645	0.000236
NAA/Cr	1.24	0.82	0.0841	1.48	0.73	0.0444	0.561394

Table 3B: Metabolite signal intensity ratio in Glioma patients by spectroscopy

glioma 0.67 suggest significant decrease in NAA which is normal metabolite and significant increase in choline which is a marker of cell proliferation and its level depends upon grade of glioma. Mean value of Cho/Cr ratio in high grade gliomas was 5.40 and low grade glioma was 2.42 suggest value depend upon cellular growth of tumor. In the present study, NAA/Cr ratio did not provide any significant correlation with the degree of malignancy. All high-grade gliomas (n= 37) showed high choline and low or absent N-acetyl-L-aspartate, creatine along with lipid and/or lactate, whereas low-grade gliomas (n = 23) were characterized by low NAA and creatine and high choline and presence of only lactate. NAA / ch ratio was significantly lower and ch/cr ratio was significantly higher in high-grade gliomas.

Discussion

Magnetic Resonance Spectroscopy (MRS) is an analytical method enables the identification and quantification of metabolites in samples.It provide physiological and chemical information instead of anatomy which is given by the later. Protons (1H) are the most used nuclei for clinical applications in

the human brain mainly because of its high sensitivity and abundance.1H MR Spectroscopy, by evaluation of CNS metabolites in vivo, is used to grade tumors and distinguish primary CNS neoplasms from metastases, abscess and demyelinating lesions. The Cho signal from a neoplasm is frequently elevated relative to the Cr signal (or the NAA signal) (Fig. 2). Cho signal is also typically elevated relative to that

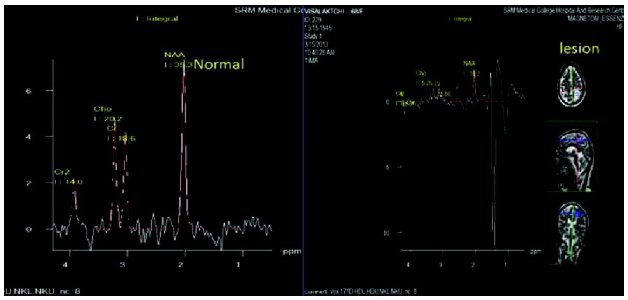


Figure 1: MRS showing normal spectra. On contralateral side spectra shows increased lipid & lactate peaks with reduction in Naa. Cho is within normal limits in a case of Tuberculous abscess.

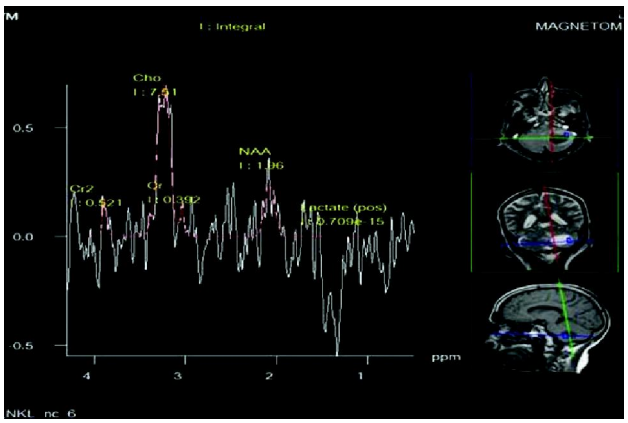


Figure 2: An ill defined heterogenously enhancing lesion in the left cerebellum appearingpredominently hypo on T1 hyper on T2, with no e/o diffusion restriction. MRS shows raise in Cho & Lactate peaks, reduction in NAA. NAA /cho-0.57, cho/cr - 3.20, NAA /cr-1.58 s/o Low grade glioma.

produced by adjacent normal tissues. In many instances, a Lactate signal is also detected. In our study NAA/Cho ratio for low grade gliomas was found to be 0.67 ± 0.19 (Fig. 3) and for high grade glioma 0.26 ± 0.13 with p value 0.00000 matches with Poptani et al study.[8] Cho/Cr and NAA /Cr ratio of our study also matches with Poptani study in grading gliomas as enumerated in (Tab. 3A, B). Presence of lipid in high grade gliomasin all 6 cases and absence in 11 case of low grade gliomas suggest presence of mobile lipid in necroticpart, which is helpful to differentiate high grade gliomas from low grade type.

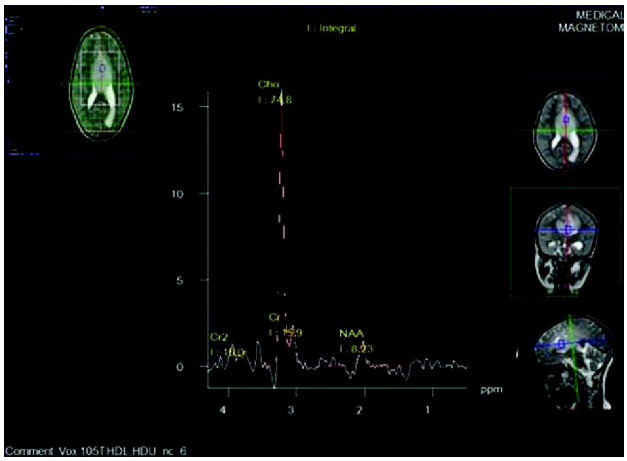


Figure 3: An ill defined heterogenously enhancing altered signal intensity mass lesion in left frontal periventricular region appearing with surrounding minimal edema & mass effect involving the corpus callosum and extension to opposite frontal lobe s/o Glioma. MRS shows raised CHO peak, with reduced NAA. NAA /cho 0.67, cho/cr 2.42, NAA /cr 1.48. HPE report-atypical Pleomorphic xanthoastrocytoma

Cho elevation is present at a two-fold greater level in high grade gliomas (Fig. 4) compared to lower grades of gliomas and to normal tissue as noted in

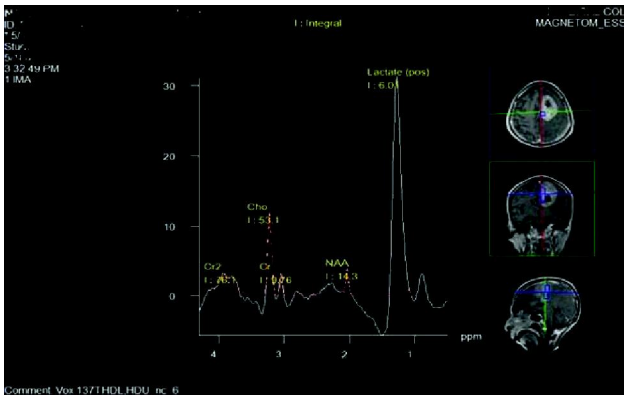


Figure 4: Well defined heterogenously enhancing altered signal intensity mass lesion showing both solid & necrotic components, blooming on GRE, no e/o diffusion restriction & surrounding moderate edema s/o Glioblastomamultiforme. MRS shows raised Cho &lactate peaks with reduced NAA. NAA /cho - 0.26, cho/cr-5.4, NAA /Cr - 1.46. HPE report - high grade glioma.

other studies.[7,8,9] At least some of the spectroscopic characteristics of neoplasia, particularly Cho signal elevation, have been attributed to cellular proliferation and may occur in non-neoplastic lesions also. Hence the extent of Cho signal elevation may be important. Neoplastic lesions would be expected to show substantially more elevated Cho levels compared to more benign processes.[9] However, there is no clear defi-

nition of what level of Cho signal elevation unequivocally represents tumor, could be established by our study. In our cases of high grade gliomas Cho peak was extremely high and gradually increases from low to high grade of as noted by Randeetal.[10] The second best discriminator between low-grade glial tumors and malignant gliomas was the amount of lipids and lipid lactate peak as it is present in all glioblastomamultiforme (GBM) and 15 of 19 grade 2-3 gliomas and absent in low grade gliomas.[10,11]

The differential diagnosis of intracranial infections from neoplastic disease with 1H-MRS has been significant as neoplastic lesions produce prominent Cho signals, while abscesses usually do not.[12,13,14] Furthermore, abscesses tend to produce prominent 1H-MRS signals from a variety of amino acids as observed by Grand et al., that are not typically seen in neoplasms, most likely the products of bacterial metabolism.[15]

Regarding cystic component of lesion Ping at el[16] studied pyogenic abscess and patient of necrotic cystic tumor and found 1H-MRS and diffusion weighted imaging (DWI) are useful for differentiating brain abscess from brain tumor, but the latter requires less time and is more accurate than is 1H-MRS. 1H-MRS is probably more limited in cases of smaller peripheral lesions, skull base lesions,and treated abscesses. As by previous studies[8,18] of tuberculoma and tuberculous brain abscesses show only Lac and lipid signals (at 0.9 and 1.3 ppm), without any evidence of amino acids. Amino acid signals therefore appear to discriminate pyogenic from tuberculous abscess (Fig. 5), correlated with our study results in (Tab. 4).

Type	Lipid	Lactate	Amino Acids, Acetate	Reduced NAA
Pyogenic abscess (n = 1)	1	1	1	1
Tubercular abscess (n=1)	1	1	0	1
Tuberculoma (n=5)	5	1	0	5

Table 4: Characterization of infective lesions by Spectroscopy

Shamile et al[17] evaluated the use of 1H-MRS for distinguishing tumefactive demyelinating lesions (TDL) from neoplastic lesions. They found the spectra from

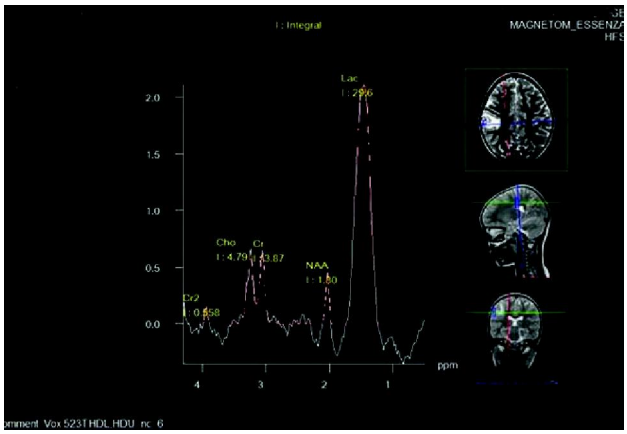


Figure 5: Well defined altered signal intensity lesion in the right parietal lobe appearing predominantly hypointense on T1 isointense on T2 with peripheral ring enhancement & mild perilesional edema s/o tuberculoma. MRS shows raised Lipid & Lactate peaks with reduction of Naa.

these two lesion types to be quite similar in appearance. Quantitatively no significant difference in Cho/Cr ratio between the two lesion types was found. However, NAA/Cr signal ratio (although lower than normal brain) was significantly higher in the demyelinating lesions.[17] Overall, however, the difference between the two groups declines.

Regarding contrast enhancement and peri lesional spectral analysis which aids in management of cases, all 8 cases of high grade gliomas (100%) and 8 cases of low grade gliomas (66.66%) showed pathological spectra not limited to contrast enhancing area suggesting infiltrative nature of lesions, with 4 cases of low grade gliomas (33.33 %) showing limited to contrast enhancing area. These 4 lesions however, showed no perilesional edema. Presence of pathological spectra limited to contrast enhancing area was noted in all case of metastases, meningioma, schwannoma and abscess like lesions suggesting non infiltrative nature of lesion (Tab. 5 A,B).

Burtscher et al[18] demonstrated that gliomas and lymphomas showed abnormal spectra outside the area of contrast enhancement while non-astrocytic circumscribed tumors (meningioma, pineocytoma, metastasis and germinoma) showed nopathological spectra outside the region of enhancementas noted in our study.

In metastasis Cho/Cr ratio was found raised in all lesions of study series (Mean - 4.20), with presence of lipid peak in 4 patients and lactate peak in 4 patients suggesting necrosis with raised cellular metabolism[19]

Type	Number of cases with pathological spectra (NAA/Cho < 1) limited to the area showing contrast enhancement		Number of cases with pathological spectra (NAA/Cho < 1) not limited to the area showing contrast enhancement	
	No. of cases	Percentage	No. of cases	Percentage
High grade glioma(n=8)	0	0%	8	100%
Low grade glioma(n=12)	4	33.33%	8	66.66%
Metastases (n=5)	4	100%	0	0%
Meningioma (n=8)	8	100%	0	0%
Schwannoma (n=1)	1	100%	0	0%
Abscess and tuberculoma (n=7)	7	100%	0	0%
Others (n=9)	9	100%	0	0%
Total	34		16	

Table 5 A, B

(Tab. 6). All cases of metastases showed pathological spectra limited to contrastenhancing area (Fig. 6).

	Raised Cho/Cr Ratio	Lactate	Lipid	NAA/Cho > 1 in peritumoral edema
Metastasis (n=5)	5 (Mean - 4.20)	4	4	5

Table 6: Characterization of metastases by Spectroscopy

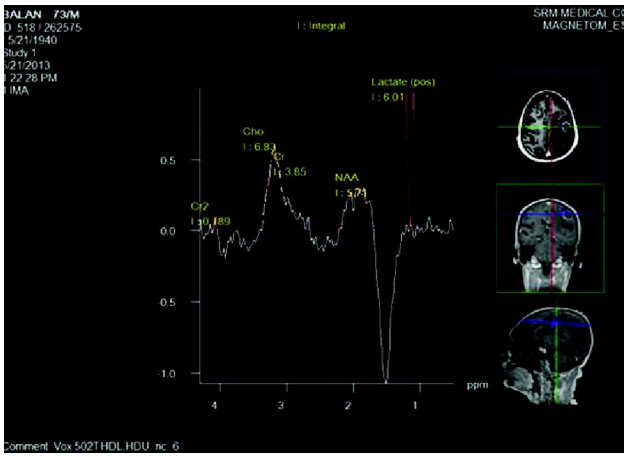


Figure 6: A case of bronchogenic Carcinoma with Multiple peipherally enhancing cystic lesions in both cerebral hemispheres with disproportionate edema appearing hypo in T1, hyper on T2, no e/o diffusion restriction s/o cystic metastasis. MRS shows raised cho & lipid, lactate peaks with Naa/Cho within the lesion was 0.52 & Naa/cho in the peri tumoral edema is >1. Thus MRS differentiates metastasis from primary tumours.

(Tab. 7) shows the spectral analysis in extra axial lesions.In present study alanine is detected in 50% cases of meningiomas. (Fig. 7A) compared to 92.3%

	Raised Choline	Detectable NAA peak	Alanine peak	Lipid peak	Lactate peak
Meningioma (n = 8)	8	5	4	1	1
Schwannoma (n = 1)	1	1	0	0	1
Pituitary macro-denoama (n = 6)	6	0	0	6	6
Pineoblastoma	1	0	0	0	0

Table 7: Characterization of extra axial intracranial mass lesions by Spectroscopy

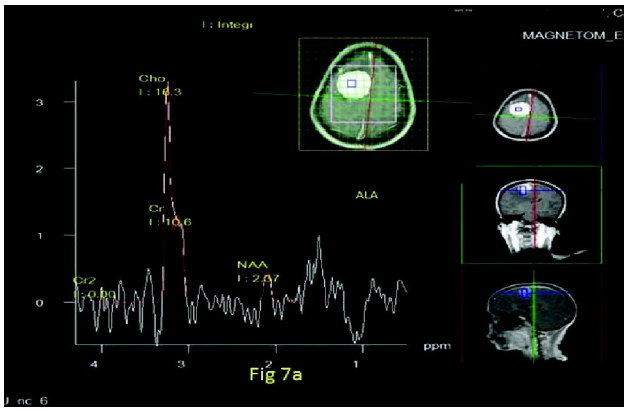


Figure 7A: Well defined extraxial mass lesion in right t frontal region with dural tail sign appearing hypo on T1, iso-hyper on T2 with homogenous intense contrast enhancement & moderate diffusion restriction s/o Meningioma. MRS shows raised Cho, NAA at the base line, Alanine peak at 1.4 ppm & inverted double lipid lactate peak. HPE report-meningioma

observed by Poptani et al.[8] Present study and Poptani et al[8] results showed absence of alanine peak in all cases of schwannomas as noted in our study (Fig. 7 B). In more malignant tumors as in PNET mass

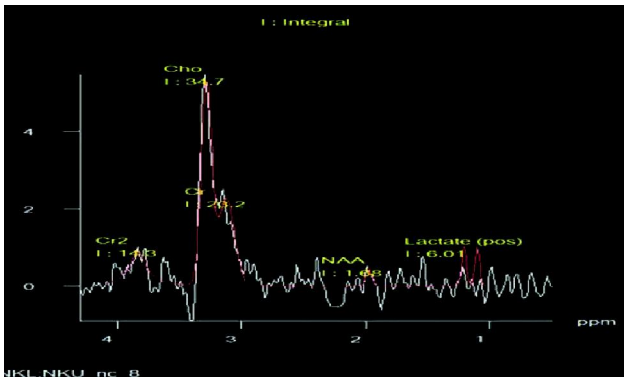


Figure 7B: A well defined heterogenous enhancing extraxial mass lesion in the CP angle cistern with widening of the internal auditory meatus appearing predominantly iso on T1, hyper on T2 &FLAIR with both solid & cystic components s/o acoustic schwannoma. MRS shows raise in Cho peak and mild raise in lactatate with NAA in the base line. No e/o alanine peak thus differentiating it from meningioma.

lesions, (Fig. 8A, 8B)cho peak was increased, Naa decreased or no significant changeand elevated lactate or lipid peaks were noted as by Sheron et al.[20]

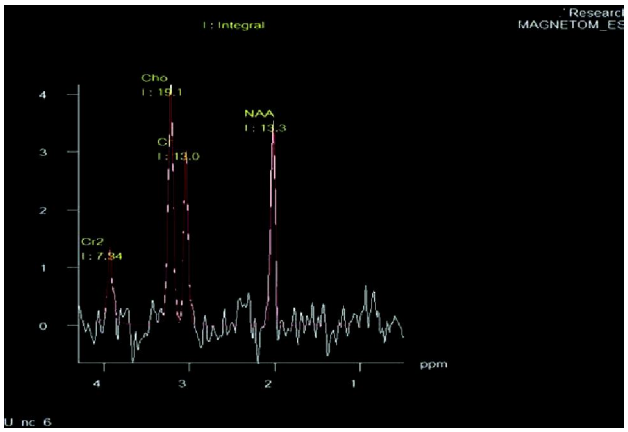


Figure 8A: MRS shows raised Cho with no significant change in Naa peak in a case of pineoblastoma.

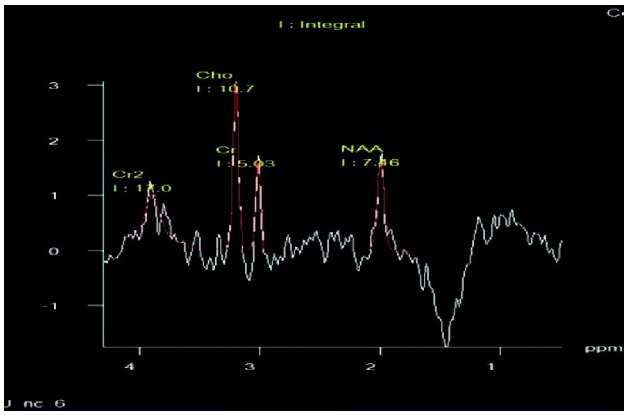


Figure 8B: MRS shows raised cho peak, inverted doublet lactate peak with reducion in Naa, Naa/cho ratio is reduced, Cho/crraised. HPE report medulloblastoma

MRS limitations: However, in vivo MRS has coarse spatial resolution due to low signal to noise ratio (SNR) and is not helpful in smaller size lesions and lesions near bones/air spaces. It has been difficult to distinguish brain neoplasia from other lesions using 1H-MRS alone accordingly, even if 1H-MRS proves to provide an accurate non-invasive diagnosis, caution should be exercised in its routine application in excluding neoplasm.

Conclusion

MRS by using Cho/Cr ratio and NAA/Choratio proved helpful in differentiating low from high grade gliomas with high significance of NAA/Cho, Cho/Cr ratio and poor correlation of NAA/Cr ratio. MRS helped in differentiation solitary metastasis from glioma, peri lesional tumor invasion which is helpful in differentiating as well for management. In case of multiple ring enhancing lesions MRS helped in differentiation of metastasis and abscess by showing presence of amino acids, lipid, lactate. MRS showed borderline results in few patients of low grade glioma and benign lesions showing border line increase in Cho/Cr ratio. MRS being a non-invasive tool plays a vital role in pre-operative assessment of cerebral mass lesions, hence helpful in avoiding intervention in non-neoplastic lesions.

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