

Role of Proton Magnetic Resonance Spectroscopy in Evaluation of Intracranial Space Occupying Lesion

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Abstract

Introduction: Magnetic resonance spectroscopy (MRS) is a potential tool for differential diagnosis between brain abscesses and noninfectious lesion such as a primary brain tumor, lymphoma, brain metastasis, and tuberculoma.

Aims and Objectives: To evaluate the role of MRS in imaging of intracranial space occupying lesion and differentiate between benign and malignant conditions and correlate between imaging findings with histopathological findings.

Materials and Methods: The study was performed on whole body system 1-5 tesla GE Signa HDx magnetic resonance imaging (MRI) at MP MRI scan Centre Medical College, Jabalpur, using a dedicated head coil. Multiplanar, T1 and T2 weighted diffusion, gradient images using spin echo sequences point resolved spectroscopy chemical shift selective.

Result: A total of 70 patients included in our study of the space occupying lesion in the brain, 33 patients had nonneoplastic lesions. Remaining 37 patients had neoplastic lesions. 0-40 years comprising 75% of patients having nonneoplastic pathologies. Only remaining 8 patients (25%) were above the age of 40 years; the majority of patients in our study were males (67%). Only 33% patients were females. Benign pathologies were more common in females 13/23 (56% of females). In males, neoplastic pathologies were more common seen in 27 out of 47 patients (58% of males). Glioma and tuberculoma were most commonly seen in our study in 27 patients comprising 38.5% each, respectively. Mean N-acetylaspartate/creatine (Cr) levels in nonneoplastic and neoplastic category were 1.18 and 1.02, respectively, being higher in the nonneoplastic group. Mean choline/Cr levels were higher in the neoplastic group: 1.9 as compared to 1.07 seen in nonneoplastic group.

Conclusion: MRS is able to distinguish between neoplastic and nonneoplastic intracranial space occupying lesions on the basis of metabolites level. Tuberculoma and pyogenic abscess can be differentiated with the spectroscopic patterns.

Key words: Gliomas, Magnetic resonance spectroscopy, Tumors, Tuberculoma

INTRODUCTION

Medical imaging techniques, beginning with the X-ray in 1895 and followed more recently by ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI), have provided high temporal, spatial, and contrast resolution methods to assess structure.

In 1995, a new era in neuroradiology emerged with the approval of magnetic resonance spectroscopy (MRS) by the United States FDA, as a noninvasive method providing metabolic information about the brain.¹ MRS enables tissue characterization on a biochemical level surpassing that of conventional MRI (c MRI). MRS does not replace c MRI but complements the information provided by it.² MRS may provide additional information as a prognostic indicator while following the progression of the disease and evaluating the response to treatment. MRS can be used to determine the degree of malignancy.¹

The most common nuclei that are used: ¹H (proton), ²³Na (sodium), ³¹P (phosphorus). Proton spectroscopy is easier to perform and provides much higher signal-to-noise ratio than either sodium or phosphorus. Proton MRS can

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be performed within 10-15 min and can be added on to conventional MR imaging protocols.

MRS enables evaluation of metabolic derangements that are specific to certain central nervous system diseases. As a general rule, as malignancy increases, N-acetylaspartate (NAA) and creatine (Cr) decrease, and choline (Cho), lactate (Lac), and lipids increase. NAA decreases as tumor growth displaces or destroys neurons. Very malignant tumors have high metabolic activity and deplete the energy stores, resulting in reduced Cr. Very hypercellular tumors with rapid growth elevate the Cho levels.³

MRS is a potential tool for differential diagnosis between brain abscesses and noninfectious lesions such as primary brain tumor, lymphoma, brain metastasis, and tuberculoma.⁴ Lipids are found in necrotic portions of tumors, and Lac appears when tumors outgrow their blood supply and start utilizing anaerobic glycolysis. Brain abscesses destroy or displace brain tissue, so NAA is not present. Lac, cytosolic acid, alanine, and acetate are characteristic metabolites in bacterial abscesses. Toxoplasmosis and tuberculomas show prominent peaks from Lac and lipids.³ When combined with c MRI and MRS may increase the diagnostic capability of MR, and thus, have a significant impact on the treatment of patients.

MATERIALS AND METHODS

Materials

MRS will be carried out on those patient referred to MP MRI and CT scan center from Neurology OPD/IPD or Medicine Department which are having intracranial space occupying lesions on conventional MRI.

Methods

After taking relevant history and consent patient will be scanned on the GE Signa HDx 1.5T MRS. All patients will be followed up for operative and histopathological findings and for clinical recovery in nonoperative conditions.

Technique

Basic method used to sample a given volume in MRS is point resolved spectroscopy (PRESS) which uses one 90° pulses and two 180° pulses to obtain a spin echo.

Water suppression is accomplished with either a chemical shift selective (CHESS) or inversion recovery (IR) technique. CHESS technique uses a series of selective 90° pulses to reduce the water signal by a factor of approximately 1000.⁶ Water suppression techniques are used with PRESS pulse sequence acquisition. With PRESS, there is a full signal recovery and a good signal-to-noise ratio (requiring fewer signal averages). PRESS allows for sampling of large

volumes of-interest of tissue. PRESS requires a longer TE, with a long TE of 270 ms, only metabolites with a long T2 are seen, producing a spectrum with primarily NAA, Cr, and Cho. One another helpful TE is 144 ms because it inverts Lac at 1.3 ppm.² Short TE allows for identification of other metabolites such as myoinositol (MI), glutamate, glutamine, and glycine.

In our study of single voxel spectroscopy (SV spectroscopy), voxel is placed over the mass lesion to be evaluated but away from the source of susceptibility artifact, i.e., cerebrospinal fluid, hemorrhage, calcification, and lipids. Voxel size of 2 cm × 2 cm × 2 cm is used. Short echo time (TE 35 ms) first followed by SV spectroscopy with intermediate TE (144 ms) is used.

RESULTS

A total of 70 patients included in our study of the space occupying lesion in the brain, 33 patients had nonneoplastic lesions. Remaining 37 patients had neoplastic lesions.

As evident from the Table 1, the majority of patients ($n = 25$) were in the range of 0-40 years comprising 75% of patients having nonneoplastic pathologies. Only remaining 8 patients (25%) were above the age of 40 years. The minimum and maximum age of presentation was 5 and 74 years.

In the neoplastic group, trend toward higher age group was seen. Out of the 37 patients, 24 patients (65%) belong to 41-80 years was had most neoplastic pathologies. Only two patients of less than 20 years had neoplastic pathologies.

The majority of patients in our study were males (67%). Only 33% patients were females as evidence from Table 2.

Benign pathologies were more common in females 13/23 (56% of females). In males, neoplastic pathologies were more common seen in 27 out of 47 patients (58% of males).

Glioma and tuberculoma were most commonly seen in our study in 27 patients comprising 38.5% each, respectively as evident from Table 3.

Tuberculoma was a predominant lesion in the benign category comprising 82% of patients. Abscess⁴ and neurocysticercosis as shown in Table 4.²

Glioma was the predominant pathology in the neoplastic group (73%) followed by metastasis seen in 4 of the patients ss shown in Table 5.

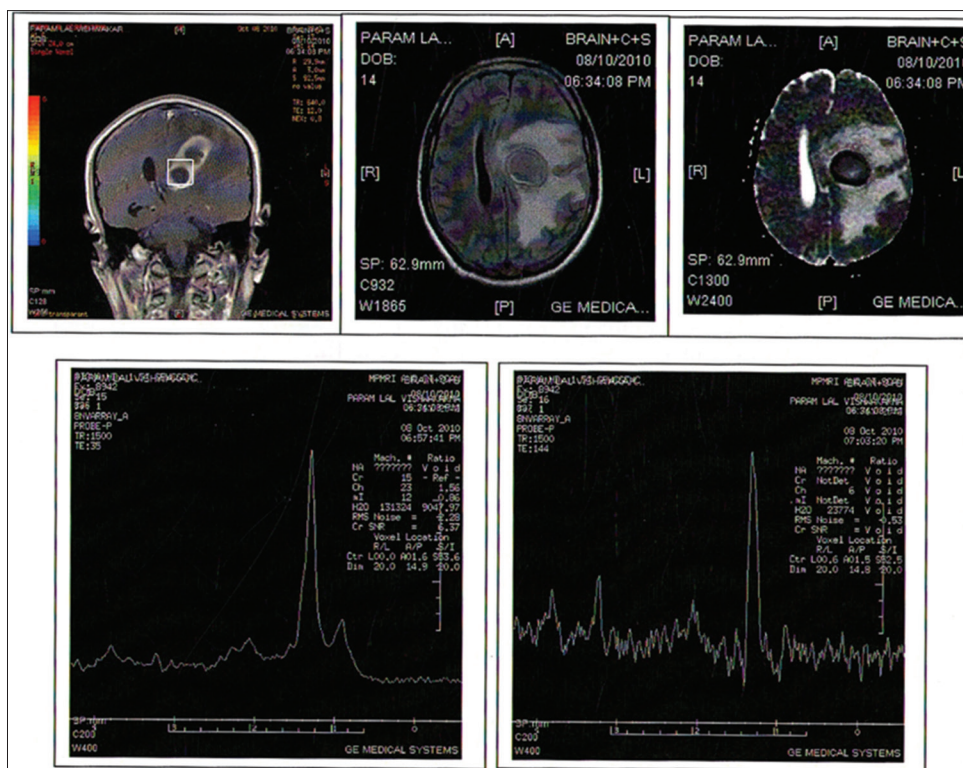


Figure 1: Case 1 – Lobulated cystic peripheral enhancing lesion with surrounding edema and diffusion restriction, spectroscopy showing very high lipid peaks with undetectable N-acetyl aspartate and cytosolic AA. Abscess

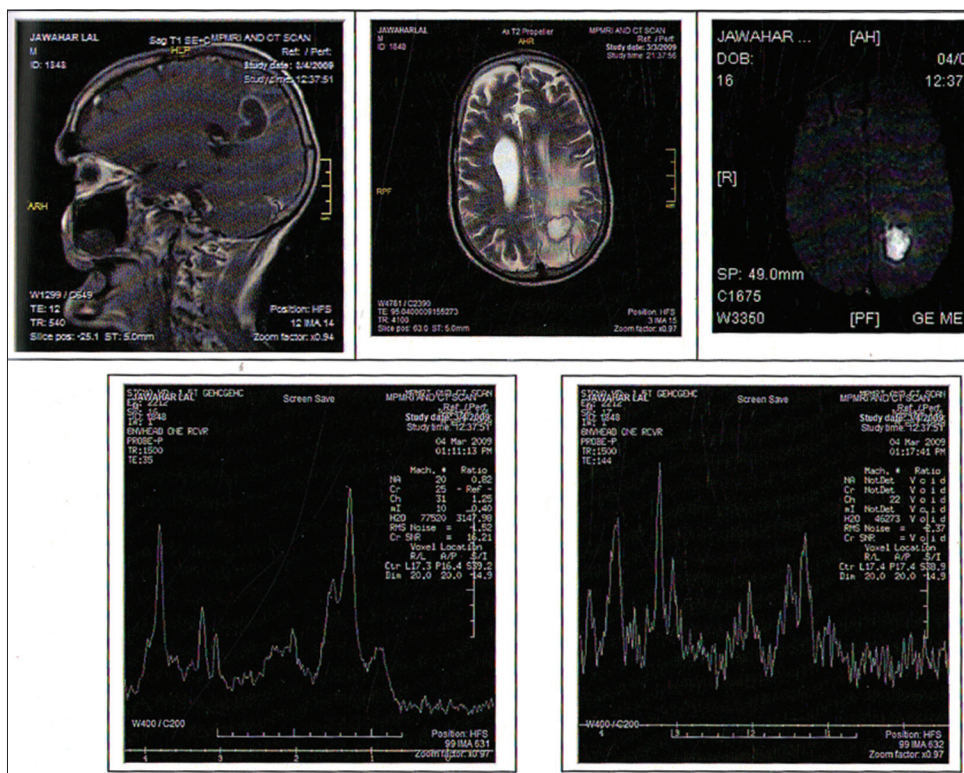


Figure 2: Case 2 – Ring enhancing lesion with diffusion restriction and prominent lipid peak with normal N-acetyl aspartate/ creatine (Cr) and choline/Cr levels s/o tuberculoma

On intravenous gadolinium, ring enhancement pattern of contrast enhancement was seen in 49 patients in

the study. Based on MRI along with spectroscopic evaluation, 25 patients were attributed to the tuberculoma.

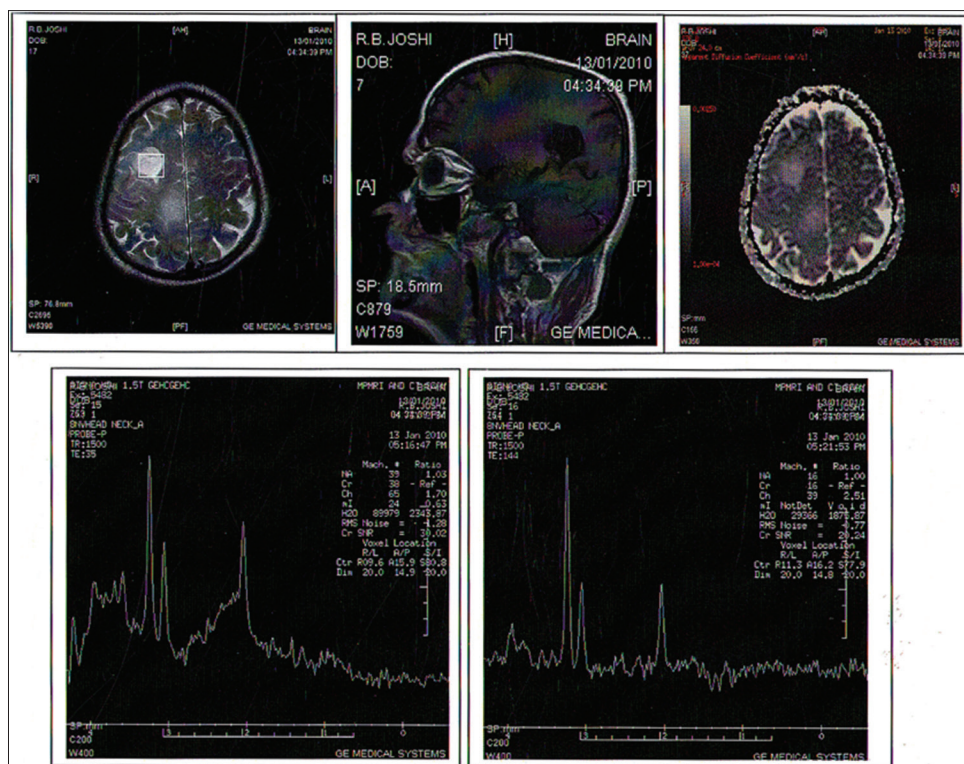


Figure 3: Case – 3 Cortical-subcortical T1 hypointense and T2 hyperintensity without diffusion restriction or contrast enhancement. Spectroscopy showing mild reduced N-acetyl aspartate, mild elevated choline, no lipid peak s/o low grade glioma. Biopsy turned out to be WHO Grade II astrocytoma

Fifteen patients of high-grade glioma comprising 11 of glioblastoma multiforme (GMB) and 4 patients of anaplastic astrocytoma had ring enhancement pattern seen.

Mean NAA/Cr levels in nonneoplastic and neoplastic category were 1.18 and 1.02, respectively, being higher in the nonneoplastic group. Mean Cho/Cr levels were higher in the neoplastic group: 1.9 as compared to 1.07 seen in nonneoplastic group as evident from Table 6.

Statistically significant difference was observed in Cho/Cr and NAA/Cho levels between low- and high-grade glioma groups ($P < 0.05$).

Although the values of NAA/Cr and MI were low in the high-grade glioma patients as compared with low-grade glioma group, the difference was not statistically significant $P > 0.05$ as shown in Table 7 and Table 8. Patient of tuberculoma showed strong lipid resonances at 0.9 and 1.3.

Lac peak was seen in only one of the low-grade glioma patients while none of the high-grade glioma patient had Lac peak in the diagnostic spectra.

Presence of lipid was seen in 3 metastasis patients as shown in Table 9.

Two patients of meningioma had increased Cho peaks, and no lipid or Lac resonance was obtained in any of the patient. Both the cases of epidermoid cyst did not showed any significant alteration in metabolite except mild increased Cho levels and elevated Lac peak (Figures 1-3 and Table 1-9)).

DISCUSSION

NAA is a neuronal marker and decreases in all tumors because of the invasiveness of tumor cells within the normal tissue. NAA accounts for the majority of the resonance at 2.01 ppm. Proton MRS-visible Cho-containing compounds include acetylCho, glycerol phosphor Cho, and phosphor Cho. Cho is increased in all tumors because of increased membrane turnover and cell proliferation. Cr/phosphocreatine, an indicator of energy metabolism, shows variable signal intensity in proton MRS of intracranial tumors.

In our study, it was possible to differentiate neoplastic pathologies from nonneoplastic conditions with as NAA levels were reduced and Cho/Cr levels were higher in neoplastic group as evident in case 3. In one of the patient with low-grade glioma had normal NAA levels. This finding could be due to lesion size being smaller than the voxel size

Table 1: Age-wise distribution of the intracranial space occupying lesions

Age group (in years)	Nonneoplastic	Neoplastic
0-20	11	2
21-40	14	10
41-60	6	13
61-80	2	11
81-100	0	1
Total	33	37

Table 2: Age wise distribution

Gender	Benign	Malignant	Total
Male	20	27	47
Female	13	10	23
Total	33	37	70

Table 3: Etiological distribution of intracranial space occupying lesions

Etiology	Number of cases (%)
Tuberculoma	27 (38.5)
Glioma	27 (38.5)
Abscess	4 (6)
Metastasis	4 (6)
Epidermoid	2 (3)
Meningioma	2 (3)
Neurocysticercosis	2 (3)
Lymphoma	1 (1)
Pineal tumor	1 (1)
Total	70 (100)

and due to partial voluming with normal tissue may falsely elevated NAA signal. Our findings corroborated with the findings by Poptani,⁶ Sanghvi *et al.*⁷

Gliomas have been graded on the basis of NAA/Cho, Cho/Cr, NAA/Cr ratios, and Lip/Lac metabolites in the spectra. NAA/Cho and Cho/Cr ratios have shown consistency in predicting the tumor grade.^{8,9} We observed NAA peak was significantly reduced in almost all the cases of high-grade gliomas. In remaining two cases, diagnostic spectra could not be obtained due to signal contamination due to hemorrhage. The comparison of NAA/Cho and Cho/Cr ratios in these cases of high-grade glioma with that of the low-grade gliomas provided a statistically significant difference between the two groups. These findings corroborated with the findings by Gupta,⁸ Harting.⁹

Server *et al.*, recently in the year 2010, had found out that the statistically significant difference exists between NAA/Cr ratio between high- and low-grade gliomas.¹⁰ However, in our study, though levels of NAA/Cr were low in high-grade tumors, this was found out to be statistically insignificant with low-grade glioma group.

Table 4: Non neoplastic categories

Category	Number of patients (%)
Tuberculoma	27 (82)
Abscess	4 (12)
Neurocysticercosis	2 (6)

Table 5: Neoplastic pathologies

Category	Number of patients (%)
Glioma	27 (73)
Metastasis	4 (11)
Epidermoid	2 (5)
Meningioma	2 (5)
Lymphoma	1 (3)
Pineal neoplasm	1 (3)
Total	37 (100)

Table 6: Spectroscopy findings

Metabolite ratio	Nonneoplastic	Neoplastic
NAA/Cr	1.18	1.02
Cho/Cr	1.07	1.9

NAA: N-acetyl aspartate, Cr: Creatine, Cho: Choline

Table 7: Mean metabolites levels (mean±SD) in the low-grade versus high-grade glioma

Grades of glioma	Metabolite levels			
	NAA/Cr	Cho/Cr	NAA/CH	MI
Low-grade glioma	0.98±0.37	1.26±0.27	0.75±0.18	0.72±0.13
High-grade glioma	0.83±0.19	2.01±0.77	0.48±0.31	0.65±0.13

NAA: N-acetyl aspartate, Cr: Creatine, Cho: Choline, SD: Standard deviation, MI: Myoinositol, CHO: choline

MI is a glial marker located in astrocytes and is a cell volume regulator. In our study, mean MI levels in the high-grade glioma were lower compared to the low-grade glioma patients. Our finding can be corroborated with the findings by Castillo *et al.* In the year 2000, published a paper correlating the levels of MI with the grading of cerebral astrocytomas. They had concluded that higher peak levels of MI were associated with lower tumor grade.¹¹ Our study also yielded same results.

Most tumor cells have low respiration and high glycolysis rates even when oxygen levels are sufficient for respiration. The high glycolytic rate results in increased accumulation of pyruvate, which converts to Lac, because there is a decrease in the tricarboxylic acid cycle activity in brain tumors. Alternatively, Lac also may be produced by anaerobic glycolysis in tumors with hypoxia. Lac levels may be present in the entire spectrum of grades of astrocytomas. Lac may arise not only from hypoxia developing within brain tumor but also seen in region of necrosis or cyst within brain tumor.⁶

Table 8: Lipid lactate peak in benign pathologies

Benign pathologies	Only lipid peak	Only lactate peak	Both lipid+lactate
Tuberculoma (n=27)	23	0	4
Abscess (n=4)	2	0	2
Neurocysticercosis (n=2)	0	2	0

Table 9: Lipid lactate peak in neoplastic category

Tumor category	Only lipid	Only lactate	Both lipid+lactate
High-grade glioma (n=18)	10	0	8
Low-grade glioma (n=8)	0	1	0
Mets (n=4)	3	0	0
Epidermoid (n=2)	0	2	0
Meningioma (n=2)	1	0	0
Gliomatosis cerebri (n=1)	0	0	1
Lymphoma (n=1)	0	1	0
Pineal neoplasm (n=1)	1	0	0

Lac levels were found to be increased in some of the glioma patients. 50% of high-grade glioma patients had Lac peak as against of only single patient of low-grade glioma had lac peak. In highly vascular tumor, Lac may be removed rapidly from the tumor as a result of increased blood flow; therefore, even in high-grade vascular tumors lac levels may not be seen in the Spectra. However, the presence of lac peak alone could not be used to grade the malignancy of glioma.

The presence of elevated lipids can also be used to differentiate the high- and low-grade neoplasms. In our study, elevated lipid levels were seen in all 17 patients of high-grade glioma as against low-grade glioma where no lipid peak was observed. Mobile lipids tend to be present in higher grades of neoplasms with highest levels noted in GMB. The presence of lipids in these cases suggested necrosis and higher grade of malignancy. Our findings corroborated with the findings by Poptani *et al.*⁸ and another study by Grand *et al.*¹² However, elevated lipid is not the sole criteria for high-grade malignancy as lipid elevation often occurs in and necrotic centers of abscesses as evident in case 1 tuberculomas, and thus this has to be correlated with higher levels of Cho and reduced NAA found in malignancy.

Metastasis usually does not pose much of the diagnostic challenge when they are multiple based on the conventional MRI; metastases can be problematic when they are solitary because it may be difficult to distinguish them from primary brain neoplasms. Unfortunately, proton MR spectra of intracranial metastases are often nonspecific and indistinguishable from those of primary brain tumors.

Metastases patients in our study showed low NAA levels and elevated Cho levels. Theoretically, NAA should be

absent in spectra because of lack of neural components. Low levels of NAA were seen presumably secondary to voxel contamination with adjacent brain parenchyma, the presence of N-acetylated metabolites on their cell membranes or the presence of normal brain parenchyma in infiltrating lesions. Three patients with metastasis had mild increased Cho levels with resonance from lipid. This study of MRI with SV spectroscopy could not be reliably differentiated between high-grade glioma and metastasis in 5 patients although high-grade glioma patients (confirmed on histology) had more elevated Cho levels. Our findings corroborated with findings by Server *et al.* in the year 2010. However, trends toward higher values of elevated Cho/Cr were seen in the higher grade glioma patients as against mild elevation in Metastasis group in our study, and more study with the large sample is needed in the future to enable differentiation of high-grade glioma and single necrotic metastasis lesion.

Meningioma patient had marked elevation of Cho levels. Nobile lipids can be seen as also alanine although not present in all cases, detection of alanine is characteristic with meningiomas. However with lipid peak in the spectra, lac resonance can be overlapped. In our study, lipid peaks with highly raised Cho were seen in both the meningioma patients. However, no alanine peak could be attributed in the spectra. Although characteristic c MRI features usually allow confident diagnosis of these tumors, proton MRS may be useful in atypical cases. Our study had two characteristic meningioma patients with typical MRI features on conventional imaging.

As evident in case 2 prominent lipid resonances were noted in intracranial tuberculomas, with particularly important signals at the 1.3 and 0.9 ppm, corresponding to the methylene and terminal methyl groups of fatty acids, respectively. In our study, 25 of the 27 patient with tuberculoma had lipid resonance remaining two cases were showing signs of healing tuberculoma and did not had prominent lipid peak. Lipid peaks were not observed in both the neurocysticercosis patients; instead they had Lac peak in their spectra. However, this has to be evaluated with larger sample value to have a significant impression.

Three patients with bacterial abscess also had lipid/Lac peak. However, those could be differentiated from the tuberculoma patients as former showed the presence of cytosolic AA peak at 0.9 ppm in the spectra. This finding corroborated with findings by Vatsal *et al.*,¹³ found in the year 2001.

Two patients of epidermoid cyst had prominent Lac peak in their spectra. Although we did not had any patient of arachnoid cyst in our study, this finding of the presence of

prominent Lac peak could be used to differentiate between epidermoid cyst and arachnoid cyst,¹⁴ as both epidermoid cyst and arachnoid cyst are having resembling features on conventional MRI.

CONSLUSION

MRS is able to distinguish between neoplastic and nonneoplastic intracranial space occupying lesions on the basis of metabolites level. Proton MRS is a useful and promising diagnostic modality to aid in diagnosing solid brain tumors. Cho/Cr and NAA/Cho ratios and the presence of lipid peak have potential application in pre-operative grading of gliomas. Spectrums from metastasis are in the most cases similar and hence indistinguishable from high-grade gliomas. Tuberculoma and pyogenic abscess can be differentiated with the spectroscopic patterns.

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