Original Article

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Radiology Section

Magnetic Resonance Spectroscopy in Evaluation of Focal Brain Lesions- A Cross-sectional Prospective Study

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ABSTRACT

Introduction: The characterisation of intracranial mass lesions only with the help of conventional magnetic resonance imaging alone may be inconclusive. Magnetic Resonance Spectroscopy (MRS) is a non invasive technique which is superior to Magnetic Resonance Imaging (MRI) in the characterisation of brain lesions. Magnetic resonance spectroscopy is comparatively fast, non-invasive method that gives biochemical analysis of the normal brain parenchyma and of the pathological processes. Magnetic resonance spectroscopy has the advantage of providing characterisation of tissues based on their molecular composition. It gives information about neuronal vitality, cell proliferation, degradation and energy metabolism.

Aim: To describe the spectrum of magnetic resonance spectroscopy in focal brain lesions and to detect the metabolic and biochemical changes in various focal brain lesions. Also, to distinguish neoplastic from non-neoplastic lesions.

Materials and Methods: This prospective study was carried out at Department of Radiodiagnosis, Sri Manakula Vinaynagar Medical College and Hospital, Puducherry, India for a period of 18 months from November 2017 to April 2019. A total of 40 MRI brain with clinically suspected brain lesions were included in the study. Magnetic resonance spectroscopy studies were performed in all patients with focal brain lesions. On the basis of spectral and distribution patterns of the pathologic spectra seen in MR spectroscopy, a qualitative analysis was done. The metabolic area ratios Choline/Creatinine (Cho/Cr)/Cr, NAA/Cho and NAA/Cr were evaluated (NAA- N-acetyl, Cho- choline, Cr- creatine). Data was collected using prescribed proforma and analysed using Statistical Package for the Social Sciences (SPSS) 22 version software.

Results: Out of the 40 patients evaluated 11 cases were high grade gliomas, seven cases were Neurocysticercosis, five low grade glioma, five meningioma, four metastasis, four tubercular abscesses, two tuberculoma and two lymphoma. Increased Cho/Cr ratio was noted in neoplastic lesions when compared to non neoplastic lesions.

Conclusion: The MRS in addition to appropriate conventional MRI sequences provides useful supplementary information and has a potential to validate treatment strategies. Neoplastic lesions show elevated choline and Cho Cr ratio with reduction in N-acetyl aspartate (NAA), whereas non neoplastic lesions show decreased Cho/Cr ratio. Hence, MRS could be a problem solving tool in differentiating neoplastic from non neoplastic lesions.

Keywords: Choline, Creatinine, Glioma, Magnetic resonance imaging, Neurocysticercosis, Seizures

INTRODUCTION

The characterisation of brain lesions only with the help of conventional MRI is quite challenging. It requires histopathological examination of the mass lesion- an invasive technique for definitive diagnosis. Hence, there is a need for some advanced MRI techniques to overcome this difficulty and to provide particularity of the diagnosis. Magnetic Resonance Spectroscopy (MRS) is one such non-invasive technique which is superior to conventional MRI in the identification of intracranial mass lesion [1].

MRS holds the superiority of providing a characterisation of tissues based upon the composition of the molecules. It gives information about neuronal vitality, cell proliferation, degradation, and energy metabolism [2]. The strategies for management of infectious, inflammatory and neoplastic brain lesions definitely differ.

Proton magnetic resonance is the method of choice currently due to the abundance of hydrogen atom. Choline (Cho), Creatine (Cr), N-acetyl aspartate (NAA), Lactate (LAC), lipids, Myo-inositol (MI), Glutamate, glutamine, and amino acids-leucine and alanine are the major metabolites in the brain [3].

Salih M et al., in their study showed that Cho/Cr and Cho/NAA ratios are increased along with choline peaks and unchanged NAA in malignant brain lesions. In addition, Glioma was classified as high and low grade, depending upon Cho/Cr and the presence of lipid/lactate peak. In their study there was total agreement between MRS and histopathological results [2].

Rehman L et al., in their analytical study revealed that out of 50 patients, 27 patients (51%) were diagnosed with neoplastic lesions by MRI. Furthermore, MRS showed 44 (88%) as neoplasms, and histopathology revealed 42 (84%) to have neoplasm. The accuracy of MRS was 94%, with 97.6%, sensitivity, 71.42% specificity, 95.45% PPV and 83.3% NPV. They have concluded in their study that MRS can readily help in differentiating neoplasm from non neoplastic brain tumours, thus an invasive brain biopsy procedure can be avoided [4] and is open to further research.

Differentiating neoplastic from non-neoplastic lesion is not always possible with conventional MRI sequences. Hence additional imaging like MRS could be a non-invasive problem solving tool. This study aimed to describe the various spectrum of MRS in focal brain lesions and to detect the metabolic and biochemical changes in various focal brain lesions.

MATERIALS AND METHODS

The present cross-sectional prospective study was carried out in the Department of Radiodiagnosis, Sri Manakula Vinayagar Medical College and Hospital, Kalitheerthalkuppam, Puducherry, India with clinically suspected 40 brain lesions. The study was carried out for a period of 18 months from November 2017 to April 2019 after ethical approval from the Institutional Ethics Committee. (Code no. 91/2017).

Sample size calculation: The sample size was determined by the average total number of cases referred to the Department of Radiodiagnosis for MRI brain based on previous records and found to have focal brain lesions. The sample size was fixed at 40 participants.

Inclusion criteria: All patients referred for MRI scan with neurological symptoms and who were found to have brain lesions in MRI or those who were incidentally detected with focal brain lesions were included in the study.

Exclusion criteria: Patients with vascular lesions and who were already diagnosed with brain lesions and under treatment were excluded from the study.

Patients who were fulfilling the inclusion criteria were considered for the study. After obtaining an informed consent from patients own language, any queries from the patients was cleared and information was collected by questionnaires.

For most of the cases, diagnosis was confirmed based on the histopathological findings. For cases where histopathology is not possible, taking into account the clinical, imaging features and treatment response, provisional diagnosis were made.

Magnetic Resonance Spectroscopy (MRS) Technique

MRS study was done with 1.5 Tesla PHILIPS whole-body MR systems using standard imaging head coil. Single voxel MRS was used to acquire images. Initially, imaging was performed to localise the lesion and then voxel was placed on the volume of interest. After water suppression, the appoint-resolved spectroscopy (RESS) technique was used for localisation, and the studies were obtained with parameters including Echo Time (TE) and Repetition Time (TR).

The metabolites which were mapped using MRS included choline {(Cho, 3.20 parts per million (ppm)}, creatine (Cr, 3.02 ppm), N-acetylaspartate (NAA, 2.02 ppm), lactate (Lac, 1.33 ppm) and lipids (1.28-1.33 ppm). Neoplastic lesions have elevated choline and reduced NAA peaks in MR spectrum with increase choline/creatine ratio. Reduced Cho, Cr and NAA peaks on MR spectrum are suggestive of non-neoplastic lesions [3].

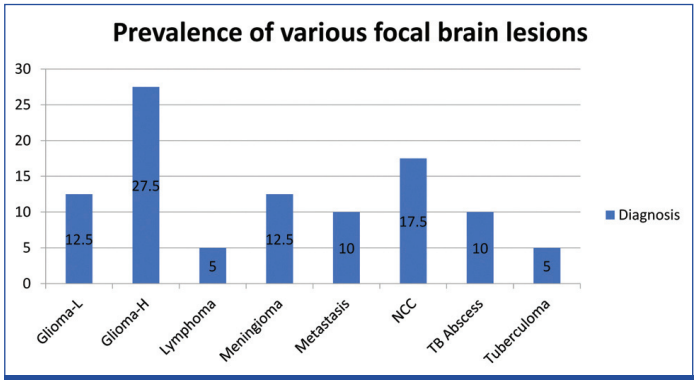
STATISTICAL ANALYSIS

The data was recorded in a proforma and was analysed using Statistical Package for the Social Sciences (SPSS) 22 version software. Categorical data was represented in the form of Frequencies and proportions. Continuous data were represented as mean and standard deviation.

RESULTS

The study comprised of a total of 40 patients with 75% females and 25% males. The mean age of study participants was 47.1±17.17 years. Majority was in the age group of 51-60 years (32.5%), followed by >60 years (20%). The most common presenting complaint was seizures (48.8%), followed by headache (45%) and weakness (20%).

In this study, 12.5% of subjects had low grade glioma, 27.5% had high grade glioma, 5% had lymphoma, 12.5% had meningioma, 10% metastasis, 17.5% had NCC, 10% had tubercular abscess and 5% had tuberculoma [Table/Fig-1]. In the present study, 32.5% had a right sided lesion, 50% had left sided lesion and 17.5% had bilateral lesions. Based upon the location of the lesions, 87.5% of subjects had intra-axial lesions and 12.5% had extra-axial lesions. Tuberculoma showed T1 hypointense, T2 heterogenously hypointense and ring enhancement in post contrast T1. Tubercular abscess appeared heterogenously hypointense on T1, heterogenously hyperintense on T2 and ring enhancement in post contrast T1. T2 hypointense rim was seen in both tuberculoma and tubercular abscess. Neurocysticercosis showed T1 hypointense, T2 hyperintense, and post contrast ring enhancement with scolex seen in majority of cases. Metastasis appeared hypointense on T1, hyperintense on T2 with post contrast heterogenous enhancement. Lymphoma showed T1 hypointense, T2 heterogenously hyperintense, post contrast homogenous/heterogenous enhancement. Meningioma appeared hypointense on T1, heterogenously hyperintense on T2 with post contrast intense homogenous enhancement with dural tail. High grade Glioma showed T1 hypointense, T2 heterogenously hyperintense, post contrast heterogenous enhancement. Low grade glioma appeared iso to hypointense on T1, hyperintense on T2, heterogenous or no enhancement post contrast [Table/Fig-2]. A 55% of the subjects had lesion with diffusion restriction and 45% had no diffusion restriction.



[Table/Fig-1]: Bar diagram showing Prevalence of various focal brain lesions. Y axis is percentage

The composition of the lesion was classified as solid, solid-cystic and ambiguous with 47.5% having solid lesion, 45% having solid-cystic lesions and 7.5 % having an ambiguous lesion.

Out of the 40 patients evaluated, choline peak was noted in 34 cases, lipid peak in 24 cases, lactate peak in 26 cases, myoinositol peak in seven cases, reduced NAA in 40 patients, reduced creatine in 15 cases, and non-specific peak at 3.8 ppm in four cases. In present study, 27 subjects had neoplastic lesions and 13 subjects had non neoplastic lesions. For most of the cases, diagnosis was confirmed by histopathology. The results of the study are summarised in the [Table/Fig-3].

MRI characteristics of focal brain lesions				
Lesion	**T1**	**T2**	**T1 contrast**	**Other specific features**
Tuberculoma	Hypointense	Heterogenously hypointense	Ring enhancement	T2 hypointense rim
Tubercular abscess	Heterogenously hypointense	Heterogenously hyperintense	Ring enhancement	T2 hypointense rim
Neurocysticercosis	Hypointense	Hyperintense	Ring enhancement	Scolex seen in CISS imaging
Metastasis	Hypointense	Hyperintense	Heterogenous enhancement	-
Lymphoma	Hypointense	Heterogenously hyperintense	Homogenous/heterogenous enhancement	-
Meningioma	Hypointense	Heterogenously hyperintense	Intense homogenous enhancement	Dural tail
Glioma- High grade	Hypointense	Heterogenously hyperintense	Heterogenous enhancement	-
Glioma- Low grade	Iso to hypointense	Hyperintense	Heterogenous or no enhancement	-

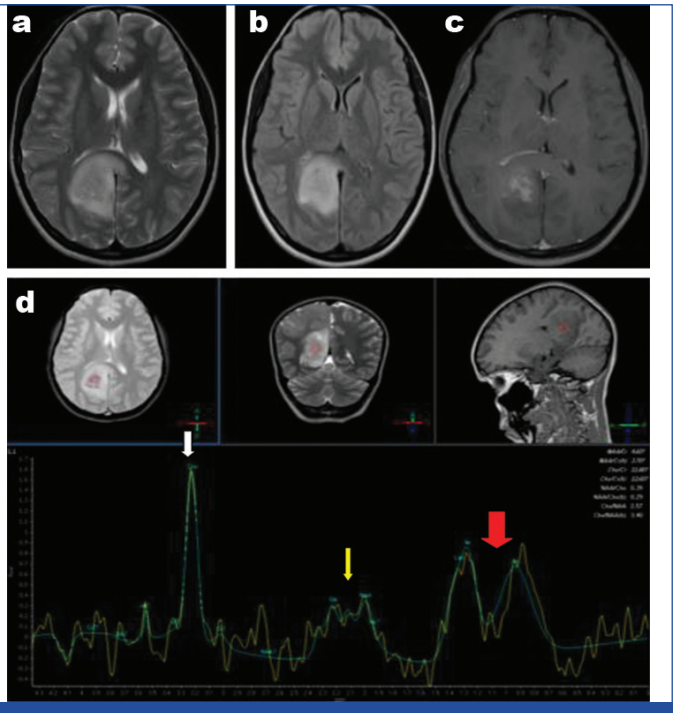
[Table/Fig-2]: MRI characteristics of various focal brain lesions.

Spectral analysis	Cho	Lip	Lact	MI	NSP-3.8 PPM	RNAA	RCR	Ala	Glu
Tuberculoma	1 (2.9%)	2 (8.3%)	2 (7.7%)	0	0	2 (5%)	0	0	0
Tubercular abscess	2 (5.9%)	4 (16.7%)	4 (15.4%)	0	0	4 (10%)	1 (6.7%)	0	0
Neurocysticercosis	5 (14.7%)	5 (20.8%)	5 (19.2%)	0	0	7 (17.5%)	3 (20%)	0	0
Metastasis	4 (11.8%)	2 (8.3%)	3 (11.5%)	0	0	4 (10%)	1 (6.7%)	0	0
Lymphoma	2 (5.9%)	2 (8.3%)	2 (7.7%)	0	0	2 (5%)	1 (6.7%)	0	0
Meningioma	4 (11.8%)	0	0	2 (28.6%)	4 (100%)	5 (12.5%)	2 (13.3%)	1 (100%)	1 (100%)
Glioma high	11 (32.4%)	7 (29.2%)	8 (30.8%)	2 (28.6%)	0	11 (27.5%)	5 (33.3%)	0	0
Glioma low	5 (14.7%)	2 (8.3%)	2 (7.7%)	3 (42.9%)	0	5 (12.5%)	2 (13.3%)	0	0
Total	34	24	26	7	4	40	15	1	1

[Table/Fig-3]: MRS findings of various focal brain lesions.
Cho: Choline; Lip: Lipid; Lact: Lactate; MI: Myoinositol; NSP: Nonspecific protein; RNAA: Reduced; N-acetylaspartate; RCR: Reduced creatinine; Ala: Alanine; Glu: Glutamine; PPM: Parts per million

DISCUSSION

Glioma: In our study, gliomas were reported as low grade and high grade based upon the MR characterisation like heterogeneity of the lesion and significant perilesional infiltration commonly seen in high grade gliomas. Out of 40 patients, high grade gliomas were seen in 11 patients (27.5%) and low grade gliomas were seen in 5 patients (12.5%). The typical MR spectroscopic characterisation of gliomas includes a choline peak with a reduction in NAA and Creatine peak and in some cases, there are associated lipid and lactate peaks. The elevated Cho/Cr ratio is related to an increase in tumour malignancy [Table/Fig-4]. The reduction of NAA indicates the loss of neuronal elements [5]. High grade gliomas in our study showed lipid, lactate peaks when compared with low grade gliomas, which was in concordance with the study done by Horská A et al., [6]. Cho/Cr ratio was significantly increased with decreased NAA/Cho ratio in this study. This is in concordance with the study done by Kumar A et al., [1].

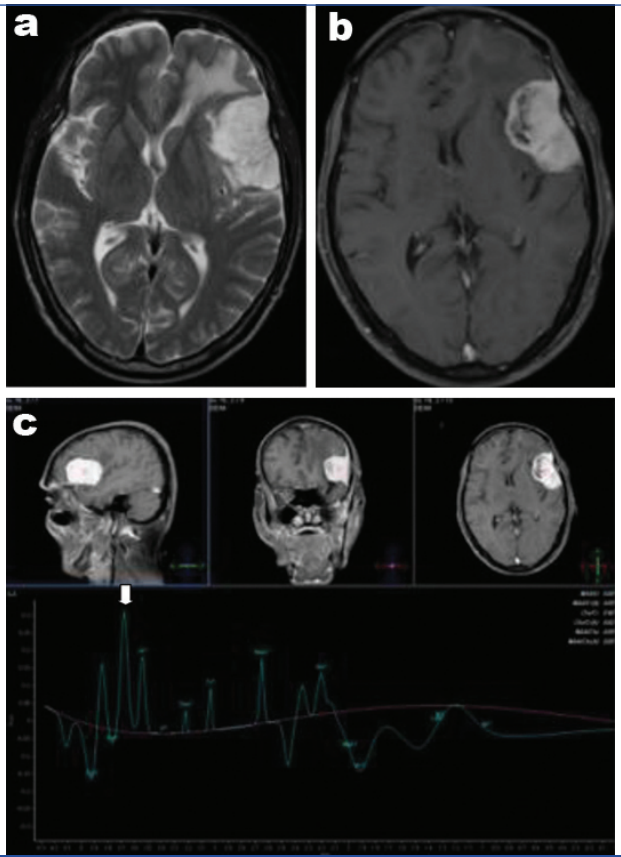


[Table/Fig-4a-d]: Case of High grade Glioma. a) Axial T2 weighted MRI shows moderately defined hyperintense lesion in right posterior parietal region causing mass effect over the ipsilateral lateral ventricle; b) FLAIR images demonstrate hyperintensity of the lesion; c) Post contrast T1 weighted images shows moderate scattered enhancement of the lesion; d) MRS show choline peak (white arrow), reduced NAA(yellow arrow) and lipid, lactate peaks (red arrow).

Three patients (42.9%) with low grade glioma and two patients (28.6%) with high grade glioma showed myoinositol peak in this study.

Neurocysticercosis: Out of 40 patients evaluated, neurocysticercosis was seen in seven patients (17.5%). The intraparenchymal form of neurocysticercosis was observed in all cases. Scolex was recognised in six cases. MRS showed choline peak, reduced NAA. Five cases showed lipid, lactate peaks. The features of parenchymal forms of neurocysticercosis in this study are analogous to the study conducted by Dayananda L et al., [7]. Cho/Cr ratio was comparatively less in neurocysticercosis which is similar to a study done by Kumar A et al., [1].

Meningioma: Meningioma was found in five cases (12.5%). All the cases were extra-axial lesions. Gadolinium-enhanced images show dural tail in four out of five cases. MRS shows elevated choline in four cases (11.8%), Myoinositol peak in two cases (28.6%), and non-specific peak at 3.8 ppm in four cases and reduced NAA in all five cases in this study [Table/Fig-5]. There is no clear explanation for the alanine peak in meningioma. Alanine peak was noted only in one patient in our study.



[Table/Fig-5a-c]: Case of Meningioma. a) Axial T2 weighted MRI shows wedge shaped dural based extra axial lesion which is hyperintense on T2 with adjacent vasogenic edema in left fronto-temporal region; b) Post contrast T1 weighted images show intense homogenous enhancement with dural tail; c) MRS show decreased NAA and MI and non specific peak (white arrow) after 3.8 ppm.

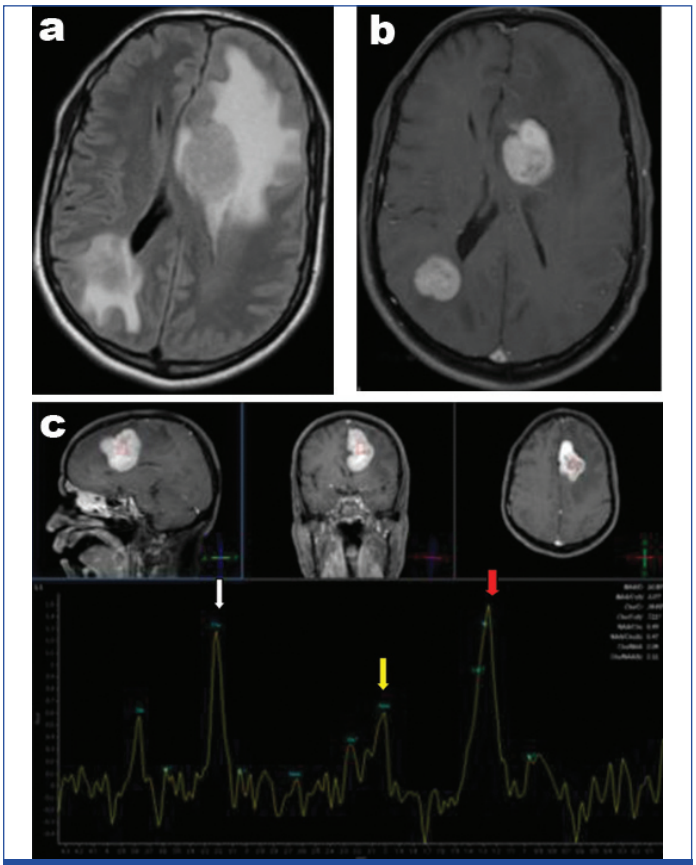
In this study, four of five cases of meningioma showed a distinct peak at 3.8 ppm which is similar to the study done by Kousi E et al., [8].

Lymphoma: Two cases (5%) of lymphoma were evaluated. It was observed that in this study the metabolite ratios obtained were comparable to those in high grade gliomas. However, the presumptive

diagnosis was made based on their characteristic appearances on MRI as a highly cellular enhancing tumour predominantly located in the ependymal surface. Cho/Cr ratio was increased and NAA/Cho ratio was decreased in the total two cases of lymphoma in this study.

Horská A et al., have reported that spectroscopic analysis of lymphomas demonstrated markedly elevated levels of choline and mild to moderately elevated concentrations of lipids and lactate [7].

Metastasis: This study had four patients (10%) with metastasis. The primary malignant lesion was found in three patients in the breast and lung. MRS in this study shows choline peak, lipid, and lactate peak with reduced NAA. Reduced creatine was noted in one case. Cho/Cr ratio was significantly increased in four cases of metastasis with decreased NAA/Cho ratio [Table/Fig-6]. These findings were in concordance with the study done by Fink KR et al., [9].

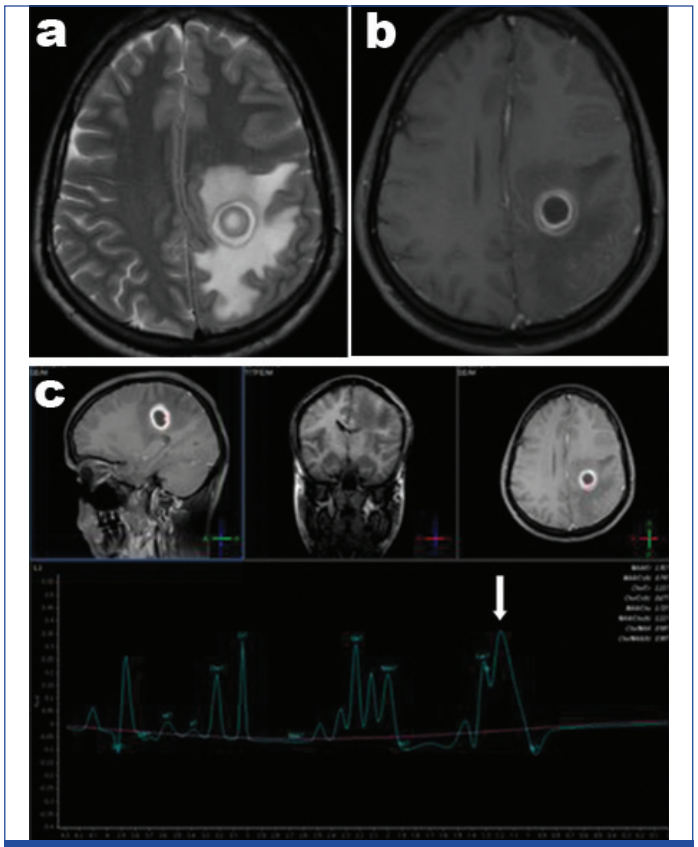


[Table/Fig-6a-c]: Case of Cerebral metastasis. a) Axial FLAIR MRI Image shows two well defined heterogenous lesions in left frontal and right parieto-occipital region; b) Post contrast T1 weighted images shows intense heterogenous enhancement of the lesions; c) MRS show choline peak (white arrow), reduced NAA levels (yellow arrow), lipid, lactate peak (red arrow).

Tuberculoma: Out of 40 patients evaluated, tuberculomas were observed in two cases (5%). On conventional MRI, they were seen as T1/T2 hypointense. Gadolinium-enhanced images show peripheral ring enhancing lesions with adjacent perilesional edema in this study. MRS showed lipid peak and it has an essential role in the detection of tuberculomas from other granulomas.

Tuberculomas occur in four stages: non-caseating granuloma, caseating granuloma, caseating granuloma with central liquefaction, and calcified granuloma. Non-caseating granuloma appears iso to hypointense on T1, hyperintense on T2 and shows homogenous post contrast enhancement. Caseating granuloma appears iso to hypointense on T1 with hyperintense rim, hypointense on T2 and shows homogenous or ring enhancement. Caseating granuloma with central liquefaction shows Isointense to hypointense with hyperintense rim on T1, Hypointense rim with central hyperintensity on T2 and ring enhancement on T1 postcontrast [10].

Tubercular abscess: Out of 40 patients evaluated, tubercular abscesses were found in four cases (10%). The lesions were heterogenous on T1 and T2 with a T2 hypointense rim in all four cases. Post contrast T1 weighted images showed ring enhancement of all the lesions. MRS showed lipid, lactate peak in all four cases in our study suggesting anaerobic glycolysis because of lactate peak [Table/Fig-7]. Choline peak was noted in two cases of the tubercular abscess. The MRS findings of our study were similar to the study conducted by Luthra G et al., [11].



[Table/Fig-7a-c]: Case of Tubercular abscess. a) Axial T2 weighted MRI Image shows a well defined lesion with a hypointense rim in left parietal centrum semiovale with surrounding perilesional edema; b) Post contrast T1 weighted images shows rim enhancement of the lesion; c) MRS show lipid, lactate peak (white arrow). No amino acid peak.

Limitation(s)

A smaller sample size and even a lesser number of samples when taking into consideration the individual lesions and their metabolite characteristics. Histopathological confirmation of the diagnosis could not be obtained for all the lesions. The future recommendations include larger sample size and histopathological correlation for all the cases.

CONCLUSION(S)

MRS in addition to appropriate conventional MRI sequences provides useful supplementary information and has a potential to validate treatment strategies. Neoplastic lesions show elevated choline and Cho/Cr ratio with reduction in NAA, whereas non neoplastic lesions show decreased Cho/Cr ratio. Hence, MRS could be a problem solving tool in differentiating neoplastic from non-neoplastic lesions.

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