Original Research Article

Role of proton MR spectroscopy in evaluation of intracranial space occupying lesions

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Abstract

Background: The term "Intra-cranial space occupying lesion" is defined as any neoplasm, benign or malignant, primary or secondary, as well as any inflammatory or parasitic mass lying within the cranial cavity. It is important to distinguish tumours from nonneoplastic mimics as the appropriate treatment is very different in each pathology. **Aims and Objective:** To evaluate the role of proton MR spectroscopy in evaluation of intracranial space occupying lesions. **Materials and Method:** In the present study total 30 patients who presented with complaints and examination findings suggestive of intracranial space occupying lesion (SOL) and underwent MR brain with proton MR spectroscopy in the study institute between the study duration were selected. After receiving the informed consent and relevant history the scans were performed with BRIVO MR355 1.5 tesla magnetic resonance system, GE Healthcare. **Results:** Majority of the patients were more than 40 years of age. 53.33% of patients were male. Majority of the patients were suffering from Glioblastoma Multiforme and metastasis (26.67% patients each) followed by Tuberculoma and Meningioma (16.67% each). In the present study 3 tuberculomas showed decrease in the NAA / Creatine ratio (60%) and 4 cases showed decrease in NAA / choline ratio (in 80% cases). The choline/Creatine ratio was greater than 1 in all cases tuberculomas (100%). Tuberculomas had a high peak of lipids, more choline, and less N-acetyl aspartate and creatinine (in 80 % of cases). The glioblastomas showed raised choline levels as compared to NAA with high choline / NAA ratio, increased choline / creatine ratio. Out of 8 cases of GBM 6 cases showed lipid and / or lactate peaks suggestive of areas of necrosis and / or anaerobic glycolysis. **Conclusion:** Thus we conclude that proton MR Spectroscopy is an important adjunct to anatomical imaging for evaluation of tumour type and tumour grade. The MR spectroscopy features which favored high grade tumours are high choline levels, highly raised choline / NAA.

Key Words: Proton MR spectroscopy, intracranial space occupying lesions, Tuberculomas, Gliomas.

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Received Date: 12/10/2017 Revised Date: 17/11/2017 Accepted Date: 02/12/2017

DOI: https://doi.org/10.26611/1004127

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 24 December 2017

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.[1] The term "Intra-cranial space occupying lesion" is defined as any neoplasm, benign or malignant, primary or secondary, as well as any inflammatory or parasitic mass lying within the cranial cavity. It also includes haematomas, different types of cysts, and vascular malformations. Among the intracranial space occupying tumours, those of central neurogenic origin i.e. derived from parenchymatous neuroepithelial elements; claim priority in number and complexity. They account for 40-50% of all the intra-cranial space occupying tumours.[2] It is important to distinguish tumours from nonneoplastic mimics as the appropriate treatment is very different in each pathology. The various neuroimaging techniques which help us reach diagnosis are pneumoencephalography, plain X ray skull, cerebral angiography, computed tomography (CT), magnetic resonance imaging (MRI), SPECT and PET scans and the recent functional imaging methods like electroencephalography (EEG), functional magnetic resonance imaging (fMRI), positron emission tomography (PET), magnetoencephalography (MEG). CT and MRI are the methods of choice as these provide the important morphological and structural details. Although magnetic resonance imaging (MRI) is important for the diagnosis of intracranial disease, sometimes the appearances on conventional contrast-enhanced MRI may

How to cite this article: Vikas R Lonikar, Chetan S Ravi, Vivek A Chaudhary. Role of proton MR spectroscopy in evaluation of intracranial space occupying lesions. *MedPulse – International Medical Journal.* December 2017; 4(12): 1043-1047. http://www.medpulse.in

not be specific. This limits the accuracy and capability of MRI for distinguishing tumour from non-neoplastic conditions and benign from malignant disease. Therefore, a non-invasive imaging method that can improve the diagnostic accuracy would be desirable, especially in ambiguous or atypical cases, to avoid delay in starting treatment and unnecessary biopsy. Recent developments in MR spectroscopy (MRS) show great promise in providing additional functional and metabolic information in the study of intracranial tumours and can provide biomarkers of neuronal integrity, cell proliferation or degradation, energy metabolism and necrotic transformation of tissues. Various spectroscopic methods, including single-voxel (SV MRS) and multivoxel MR spectroscopic imaging (MRSI), have been used to study tumour biology, grade gliomas and plan treatment. Our study intends to evaluate the role of proton MR spectroscopy in evaluating various intracranial space occupying lesions.

MATERIALS AND METHOD

The present study was conducted in the department of radiology of Jupiter lifeline hospital and Jupiter scan center, Thane. For the study purpose total 30 patients who presented with complaints and examination findings suggestive of intracranial space occupying lesion (SOL) and underwent MR brain with proton MR spectroscopy in the study institute between the study duration were selected. Following inclusion and exclusion criteria was used to select the study subject.

Inclusion Criteria

Patients who present with the following entities:

Known or suspected cases of brain tumors, Known or suspected cases brain metastasis, Known or suspected cases of CNS infective granulomas/abscess.

Exclusion Criteria

Intracranial SOL like SDH, EDH and AVMs, Patients with infarcts / encephalitis / multiple sclerosis, Patients not consenting for the study, Intracranial aneurysm clips, Intra-orbital metal fragments, Any electrically, magnetically or mechanically activated implants (including cardiac pacemakers, biostimulators, neurostimulators, cochlear implants, and hearing aids), Pregnancy

Written informed consent was obtained from the selected subjects fulfilling inclusion and exclusion criteria.

After receiving the informed consent and relevant history the scans were performed with BRIVO MR355 1.5 tesla magnetic resonance system, GE Healthcare.

Routine MR Brain protocol

- Axial T1 w
- Axial and sagittal T2 w
- Coronal T2 FLAIR
- Axial Gradient echo
- Axial diffusion weighted with apparent diffusion coefficient map
- Post Gadolinium axial, coronal and sagittal T1w sequences taken.

MR Specroscopy protocol-

MRS was performed using 2D multi-voxel PRESS CSI at short echo time (TE 20 ms).

- Volume of interest size modified to best suit the lesion. Some part of normal brain was always included inside the volume of interest to aid in the lesion diagnosis. A smaller volume of interest results in the improved shim and spectrum.
- Volume of interest was taken in such a way that it avoided structures that can contaminate the baseline, such as cerebrospinal fluid and major blood vessels. Where such protocol was not possible in axial planes volume of interest was taken in coronal plane.
- Volume of interest was planned according to imaging slice. Whenever patient exam was repeated only for MR spectroscopy, A T2 localizer was taken in best plane and angle of lesion and volume of interest was planned according to it. Post processing always done with reference to anatomical imaging.
- Spatial saturation bands were used to cover the scalp, skull and blood vessels. six saturation bands were used in 3D on all sides of volume of interest. If saturation bands kept too close to volume of interest some baseline distortion was seen. To overcome it buffer of one voxel width space was kept in between volume of interest and saturation bands.
- Fully excited volume was selected as it helps to attain homogenous excitation of all the metabolites in the selected volume of interest whilst suppressing the interference from outside the volume of interest.
- MR Spectroscopy was always performed at the isocenter of the magnet.
- Always ensured that patient is comfortably positioned as it is important that patient remain still while performing MR spectroscopy

RESULTS

In the present study total 30 patients with intracranial space occupying lesions were enrolled. The patients were referred for MRI either from the neuro med / neuro surgery department of the study institute or referred from the private practitioners.

Table 1: Age and sex distribution of study patients

Group		No. of patients	Percentage
Age group	≤12yrs	2	6.67
	13-30	6	20.00
	31-45	4	13.33
	41-60	8	26.67
	>60	10	33.33
Sex	Male	16	53.33
	Female	14	46.67

It was observed that out of total 30 patients; majority of the patients were more than 40 years of age. 53.33% of patients were male with male: female ratio of 1.14:1.

Table 2: Distribution of patients according to final diagnosis

Diagnosis	No. of patients	Percentage
Tuberculoma	5	16.67
Glioblastoma Multiforme	8	26.67
Anaplastic Astrocytoma	1	3.33
Pilocytic Astrocytoma	1	3.33
Oligodendroglioma	1	3.33
Meningioma	5	16.67
Lymphoma	1	3.33
Metastasis	8	26.67

It was seen that majority of the patients were suffering from Glioblastoma Multiforme and metastasis (26.67% patients each) followed by Tuberculoma and Meningioma (16.67% each).

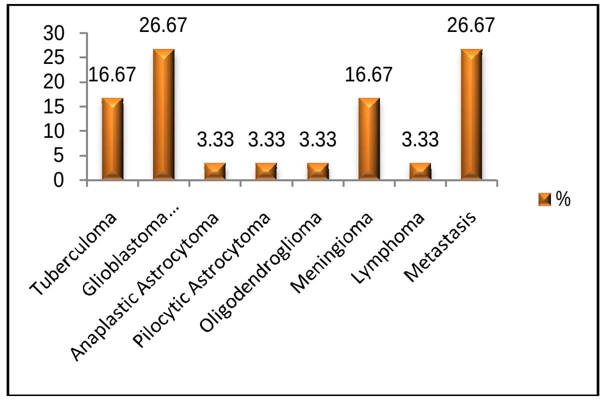

Figure 1: Distribution of patients according to final diagnosis

Table 3: Dirdtibution of Tuberculoma cases

Test	Case 1	Case 2	Case 3	Case 4	Case 5
NAA / creat ratio	1.6	0.852	0.569	0.238	0.60
NAA / Choline ratio	0.469	0.402	1.06	0.973	0.657
Choline / creat. Ratio	3.5	2.1	1.7	2.7	2.2
Lipid and / or lactate peak	Present	Present	Present	Present	Present

Out of total 30 patients 5 cases (16.67%) were diagnosed as tuberculomas. All the patients were under 30 yrs of age. Out of 5 patients 3 were females and 2 males. In the present study 3 tuberculomas showed decrease in the NAA / Creatine ratio (60%) and 4 cases showed decrease in NAA / choline ratio (in 80% cases). The choline/Creatine ratio was greater than 1 in all cases tuberculomas (100%). Tuberculomas had a high peak of lipids, more choline, and less N-acetyl aspartate and creatinine (in 80 % of cases).

Table 4: Distribution of cases of Glioblastoma multiforme (WHO grade 4)

Test	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
choline / NAA ratio	4.9	4.2	4.5	6.9	3.8	4.4	5.1	3.7
choline / creatine ratio	1.6	2.3	4.5	2.7	2.2	3.0	1.9	2.3
Lipid and / or lactate peak	Present	Absent	Present	Absent	Present	Present	Present	Present

In the study out of 30 patients 11 patients were diagnosed as gliomas. Out of 11 patients 8(26.67%) were diagnosed as glioblastoma multiforme (WHO grade 4) while anaplastic astrocytoma (WHO grade3), pilocytic astrocytoma and oligodendroglioma was diagnosed in one (3.33%) cases each. The glioblastomas showed raised choline levels as compared to NAA with high choline / NAA ratio, increased choline / creatine ratio. Out of 8 cases of GBM 6 cases showed lipid and / or lactate peaks suggestive of areas of necrosis and / or anaerobic glycolysis.

Table 2: Distribution of cases of Anaplastic astrocytoma, Low grade glioma and Oligodendroglioma

Type	Test	Level observed
Anaplastic astrocytoma	Choline / NAA ratio	2.0
	Choline / creatine ratio	5.6
	Lipid and / or lactate peak	Present
Low grade glioma	Choline / NAA ratio	2.0
	Choline / creatine ratio	5.6
	Lipid and / or lactate peak	absent
Oligodendroglioma	Choline / NAA ratio	10.5
	Choline / creatine ratio	8.1
	Lipid and / or lactate peak	absent

It was observed that the case of anaplastic astrocytoma (who grade 3) has raised choline / NAA ratio and increased choline / creatine ratio and also showed positive Lipid and / or lactate peak. Low grade glioma showed raised Choline / NAA ratio and Choline / creatine ratio but Lipid and / or lactate peak was absent. Oligodendroglioma also showed raised Choline / NAA ratio and Choline / creatine ratio but Lipid and / or lactate peak was absent.

DISCUSSION

The present study was conducted with the aim to study the role of proton MR spectroscopy in evaluation of intracranial space occupying lesions. For this purpose total 30 patients presenting with complaints and examination findings suggestive of intracranial SOL were selected and underwent MR brain with proton MR spectroscopy. It was seen that majority of the patients were more than 40 years of age. Male (53.33%) were slightly more affected than the females (46.67%). It was seen that majority of the patients were suffering from Glioblastoma Multiforme and metastasis (26.67% patients each) followed by Tuberculoma and Meningioma (16.67% each). Out of total 30 patients 5 cases (16.67%) were diagnosed as tuberculomas. All the patients were under 30 yrs of age. Out of 5 patients 3 were females and 2 males. In the present study 3 tuberculomas showed decrease in the NAA / Creatine ratio (60%) and 4 cases showed decrease in NAA / choline ratio (in 80% cases). The choline/Creatine ratio was greater than 1 in all cases tuberculomas (100%). Tuberculomas had a high peak of lipids, more choline, and less N-acetyl aspartate and creatinine (in 80 % of cases). However, there was significant contamination of the adjacent brain parenchyma in smaller tuberculoma lesions in the MR spectroscopy. Tuberculosis (TB) in any form is a devastating disease, which in its most severe form involves the central nervous system (CNS), with a high mortality and morbidity. Early diagnosis of CNS TB is necessary for appropriate treatment to reduce this morbidity and mortality. However only 30% of patients with brain tuberculoma have a positive chest radiograph.[3] The absence of features of tuberculosis on chest X-rays should therefore does not rule out the possible existence of brain tuberculomas. And this is precisely why it is important to diagnose tuberculomas / CNS tuberculosis on non invasive modalities like CT / MRI and MR spectroscopy. Santy, K., P. and Nan, *et al.*[4] stated that H-MRS allows to non-invasively identifying TB with high specificity and may allow early installment of targeted antimicrobial treatment. Turan Suslu H, *et al.*[5] stated that MR spectroscopy is characterized by a prominent decrease in NAA/creatinine and slight decrease in NAA/choline. The choline/creatinine ratio is greater than 1 intuberculomas. Tuberculomas have a high peak of lipids, more choline, and less N-acetylaspartate and creatine at MR spectroscopy. The findings were comparable with present study. In the study out of 30 patients 11 patients were diagnosed as gliomas. Out of 11 patients 8(26.67%) were diagnosed as glioblastoma multiforme (WHO grade 4) while anaplastic astrocytoma (WHO grade3), pilocytic astrocytoma and oligodendroglioma was diagnosed in one (3.33%) cases each. In the present study all the glioblastomas showed raised choline levels as compared to NAA with high choline / NAA ratio, increased choline / creatinine ratio. Out of 8 cases of GBM 6 cases showed lipid and / or lactate peaks suggestive of areas of necrosis and / or anaerobic glycolysis. One case of anaplastic astrocytoma also showed similar MR spectroscopic features as seen in glioblastomas above and it was not possible to differentiate anaplastic astrocytoma from glioblastoma on spectroscopic findings. However one case of pilocytic astrocytoma showed absence of lipid and /or lactate peak and lower choline levels as compared to NAA with lower choline / NAA ratio and lower choline / creatinine ratio as compared to glioblastomas. Hence absence of lipid and /or lactate peak may help to differentiate between high grade and low grade gliomas. We also had one case of oligodendroglioma which also showed spectroscopic findings similar to glioblastomas and we were not able differentiate it from glioblastoma on spectroscopic findings. Noninvasive preoperative prediction of cerebral glioma grade is important for treatment planning and prediction of prognosis. Although in vivo proton MR spectroscopy (^{1}H- MR spectroscopy) at 1.5T has been attempted to predict the degree of malignancy of the gliomas, some studies have yielded the somewhat disappointing result that there was no reliable indicator for tumour grading.[6-8] Shimizu H *et al.*[9] concluded that Higher grades of brain tumours in their study were associated with higher Cho/reference and lower NAA/reference values. These results suggest that clinical proton MR spectroscopy may help predict malignancy. Yuan-Yu Hsu, *et al*[10] concluded that Proton MRSI can provide in vivo information about the metabolic status of cerebral gliomas, and the (Cho+Cr)/NAA ratio can discriminate different grades better than other metabolite ratios. However, substantial overlap of metabolite ratios among different severities of malignancy makes it impossible to confirm the WHO grade of a specific cerebral glioma by using clinical MRSI. Out of 30 cases included in our study 8(26.67%) cases were diagnosed as metastasis. There were 5 male patients and 3 female (62. 5 % males, 37.5 % females). Most of the patients were more than 60 yrs of age (75%). 3 cases were of metastatic lung cancer, 2 metastatic breast cancer, 1 metastatic non

Hodgkin's lymphoma and remaining cases of 2 metastasis were from unknown primary. On MR spectroscopy all the metastasis showed lipid and/ or lactate peak, All except one showed elevated choline as compared to NAA, decreased NAA levels with high choline NAA ratio and raised choline / creatinine ratio. However we could not differentiate metastasis from high grade gliomas on spectroscopic findings. Out of cases 8 metastasis in 5 cases metastatic lesion showed prominent reduction in the choline levels in the perilesional edema region or the so called peritumoral region (in 62.5 % of cases). Out of 8 cases of glioblastoma multiforme 7 cases showed choline peak in perilesional edema region (87.5%). Out of 8 cases 6 cases had multiple brain metastases. (75% cases). The findings observed by Bruhn *et al*[11], Burtscher *et al*[12] and Law *et al*[13] were comparable with the present study. In the present study out of 30 patients 5 (16.67%) cases were diagnosed as typical meningiomas (who grade 1). Male to female ratio was 2:3 and all the patients were more than 30 yrs of age. All the meningiomas were correctly diagnosed on routine plain and contrast enhanced MR imaging and there was no diagnostic dilemma. On MR spectroscopy all the meningiomas showed high choline levels (100%), 4 out of 5 cases showed absence of NAA (80%), 1 out of 5 lesions showed NAA peak suggestive of contamination by adjacent brain parenchyma. 1 out of 5 lesion showed lactate peak (20% of cases). In our study none of the lesion showed alanine peak which is characteristic of meningioma. The above findings were consistent with the Zhao, Liang *et al*[14]. The Presence of an alanine peak (a doublet at 1.48 ppm), when present, is fairly characteristic and helps todifferentiate a meningioma from a glial tumor.[9,15,16] In vitro studies appear to demonstrate alanine in meningiomasconsistently; however, in clinical practice (in vivo studies), less than 50% of meningiomas will express alanine.[8]

CONCLUSION

Thus we conclude that proton MR Spectroscopy is an important adjunct to anatomical imaging for evaluation of tumour type and tumour grade. The MR spectroscopy features which favored high grade tumours are high choline levels, highly raised choline / NAA.

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Source of Support: None Declared
Conflict of Interest: None Declared