

Role of Magnetic Resonance Spectroscopy in the Evaluation of Ring Enhancing Lesions of the Brain

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ABSTRACT

Introduction: The ring enhancing lesions of the brain are a challenging group of lesions with the variable possibilities of diagnosis under conventional Magnetic Resonance Imaging (MRI). Employing advanced techniques such as Magnetic Resonance Spectroscopy (MRS) could increase the success rates of the diagnosis.

Aim: To assess the role of MRS in evaluating varying ring enhancing lesions of the brain.

Materials and Methods: This prospective observational study involved 50 patients aged between 3-82 years who were detected with ring enhancing lesions of the brain on contrast MR studies. The patients underwent MRS evaluation. Categorical data was represented as frequency (%). The metabolite peaks of choline, lipid, lactate, N-Acetyl Aspartate (NAA), succinate and amino

acids were recorded. The choline/creatine ratio was calculated and associated with the type of lesion the patients exhibited.

Results: Among the 50 patients screened, the most prevalent pathologies were tuberculoma (36%) and neurocysticercosis (22%). While the patients diagnosed with tuberculoma presented with higher peak level of lipids and choline/creatine ratio of >1-2. Increased lactate, succinate, choline peak concomitant with no or insignificant lipid peak, were noted in the cases of neurocysticercosis. Primary brain tumour showed high choline peaks and elevated choline/creatine ratio (>2). Metastasis showed increased choline peak. Cerebral abscess showed increased amino acids and lactate peak.

Conclusion: The diagnosis of varying ring enhancing lesions of the brain was accurately investigated by MRS. This accuracy enables delineating a treatment plan void of any dilemma.

Keywords: Metabolites, Neurocysticercosis, Tuberculoma

INTRODUCTION

Ring enhancing lesions of the brain are considered challenging neuroimaging abnormalities for the radiologists [1,2]. Imaging modalities like the Computed Tomography (CT) and MRI are commonly used to diagnose such lesions [3]. These lesions are typically located at the junction of grey-white matter in the superficial or deeper areas of the brain parenchyma in the sub-cortical area. Lesions may be confined to a single location or may be in multiple locations when detected on MRI that are characterised by a non-enhancing centre surrounded by a contrast enhancing halo. The central region may present a low intensity signal on T1 and a high intensity signal on T2 weighted images [1].

Identifying varying ring enhancing lesions by conventional MRI can be challenging, as the technique cannot distinguish between neoplastic, non-neoplastic lesions and infections [4]. It does not provide any information regarding the tumoral vascularity, metabolism and cellularity [5,6]. Advanced techniques such as Diffusion Weighted Imaging (DWI) and perfusion and proton MRS (1H-MRS) have been employed for the differential diagnosis of lesions, with varying success rates. A combination of the advanced techniques with conventional MRI can increase the specificity to detect lesions [4].

MRS is a non-invasive technique that can provide information regarding tissue chemistry. Its patient-friendly feature can be highlighted as it is devoid of ionising radiations. Information is acquired in the form of a high-quality spectra and not images. Metabolites such as NAA, lactate, phosphocreatine, choline containing compounds and adenosine triphosphates can be measured by MRS. The quantification in MRS is due to the relative spectral peak regions compared to the reference metabolites, which do not vary pointedly with most pathologies. Absolute metabolite concentration can also be measured with a reference to that of unbound water in the tissue, which as an approximation, is assumed not to vary

distinctly with the disease [7]. These features enhance the specificity and sensitivity of MRS in comparison to MRI [8-10].

Though there are numerous studies conducted to differentiate varying types of ring enhancing lesions of the brain, the differentiation between tuberculoma and neurocysticercosis is a dilemma for the radiologist till date, as these two lesions look similar to each other in conventional MRI sequences [11,12]. In a study conducted by Morales H et al., MRS could clearly differentiate tuberculoma over other lesions, based on the metabolite level [13]. In another study conducted by Sharma BB and Sharma S, in which tuberculoma and neurocysticercosis lesions resembled the same in many aspects based on CT and MRI scans but could be differentiated on the basis of location, number of lesions, enhancement pattern and constitutional symptoms, but however, MRS could differentiate between these two lesions based on their metabolite levels [14].

The MRS imaging technique is widely used in many hospitals/imaging centres. Therefore, this study was conducted with an aim to differentiate tuberculoma and neurocysticercosis, along with characterising various other ring enhancing lesions of brain in the state of Pondicherry, India, using MRS. The study focused on differentiating neoplastic, infections, inflammatory and vascular lesions in the brain. The analysis of metabolite peaks and choline/creatine ratio in the ring enhancing lesions was conducted.

MATERIALS AND METHODS

This prospective observational study was conducted at a Tertiary Care Hospital between November 2017-November 2019, after acquiring the approval from the Institutional Ethics Committee (Reg. No. ECR/451/Inst/PO/2013/RR-16) and informed consent from the patients involved in the study was obtained. Considering an effect size of 0.566, power of 0.8 and significance level of 0.05, the sample size was calculated as 50 for this study.

This study included patients, aged between 3-82 years, who experienced seizures and headache, who were incidentally diagnosed with ring enhancing lesions of brain based on CT and contrast MR studies. Patients with a history of claustrophobia, metallic implants, cardiac pacemakers, chronic kidney diseases, diagnosed with schizophrenia and pregnant women were excluded from the study.

MRI scan was performed using the MR Philips Achieva, possessing an ultracompact, superconducting, active shielded superconducting magnet with a magnetic field strength of 1.5 Tesla (T). Conventional spin echo sequences, axial T1, T2 and Fluid Attenuated Inversion Recovery (FLAIR); Coronal T2; Sagittal T1; Post-contrast axial, coronal and sagittal; Diffusion Weighted Imaging (DWI); T2 Gradient Echo Sequences (GRE) spectroscopy was performed at echo time (TE) of 20ms and 144ms. The same instrument was used to perform MRS. With the application of single voxel MRS, the operation was quicker and easier, when compared to that of multi-voxel MRS. The voxel was placed on the lesion such that the maximum area of the lesion, its margin and the normal brain tissue were covered in a single voxel. Spectroscopy was avoided in small lesions close to the bone.

STATISTICAL ANALYSIS

The quantitative data was analysed using R v386 3.6.0 software. The categorical data were represented as frequency (%). The graph was plotted by the MRI machine software, and the peak amplitude of choline, lipid, lactate, reduced NAA and amino acids in the ring enhancing lesions were recorded. The choline/creatine ratio were calculated and associated with the type of lesion the patients exhibited.

RESULTS

Amongst the patients included, the age group of 21-30 years was most prevalent [Table/Fig-1]. Among the clinical manifestations, seizures were the most prevalent presentation (33, 66%) followed by headache (19, 38%), vomiting (12, 24%), fever (11, 22%), weakness (5, 10%) and ataxia (2, 4%).

Age (years)	No. of patients (%)
0-10	6 (12)
11-20	7 (14)
21-30	10 (20)
31-40	6 (12)
41-50	7 (14)
51-60	8 (16)
>60	6 (12)
Gender	
Male	33 (66)
Female	17 (34)

[Table/Fig-1]: Age and gender distribution of patients in the study.

The ring enhancing lesions were positioned on the right side of the brain for 13 (26%) patients, on the left side for 20 (40%), bilateral for 15 (30%) and midline region of the brain for 2 (4%) of them. About 16 (32%) patients presented a single lesion, 22 (44%) patients had 2-4 and 12 (24%) of them presented >4 lesions in this study. The size of the lesion was <2 cm in 30 (60%) patients, 2-4 cm in 14 (28%) and >4 cm in 6 (12%) patients.

Majority of patients presented with tuberculoma (18, 36%), where a single lesion was noted in eight patients and multiple lesions in 10 patients [Table/Fig-2].

The highest peak was observed for choline in 33 (66%) patients, which was prevalent in patients diagnosed with neurocysticercosis [Table/Fig-3]. Choline/creatine ratio >2 with respect to primary brain tumour was observed in patients [Table/Fig-4].

Lesion	No. of male patients	No. of female patients	Total (%)
Tuberculoma	11	7	18 (36)
Neurocysticercosis	8	3	11 (22)
Metastasis	8	2	10 (20)
Primary brain tumour	4	4	8 (16)
Cerebral abscess	0	1	1 (2)
Tumefactive demyelination	1	0	1 (2)
Radiation necrosis	1	0	1 (2)

[Table/Fig-2]: Gender wise incidence of varying ring enhancing lesions of the brain.

MRS diagnosis	Metabolite peak (No. of cases)					
	Choline	Lipid	Lactate	Reduced NAA	Succinate	Amino acid
Tuberculoma	3	18	8	2	0	0
Neurocysticercosis	11	0	9	1	11	0
Metastasis	10	3	3	1	0	0
Primary brain tumour	8	1	1	2	0	0
Cerebral abscess	0	1	1	0	0	1
Tumefactive demyelination	1	1	1	0	0	0
Radiation necrosis	0	1	1	0	0	0
Total	33 (66%)	25 (50%)	24 (48%)	6 (12%)	11 (22%)	1 (2%)

[Table/Fig-3]: Association of metabolite peaks with ring enhancing lesions.

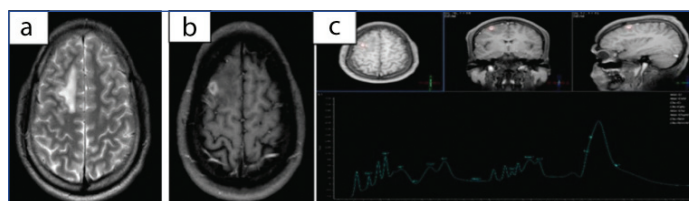
NAA: N-acetyl aspartate

Lesion	Choline/Creatine ratio	No. of patients (%)
Neurocysticercosis	<1	9 (18)
Tuberculoma	>1 to 2	18 (36)
Primary brain tumour	>2	8 (16)

[Table/Fig-4]: Representation of choline/creatine ratio in ring enhancing lesions of the brain.

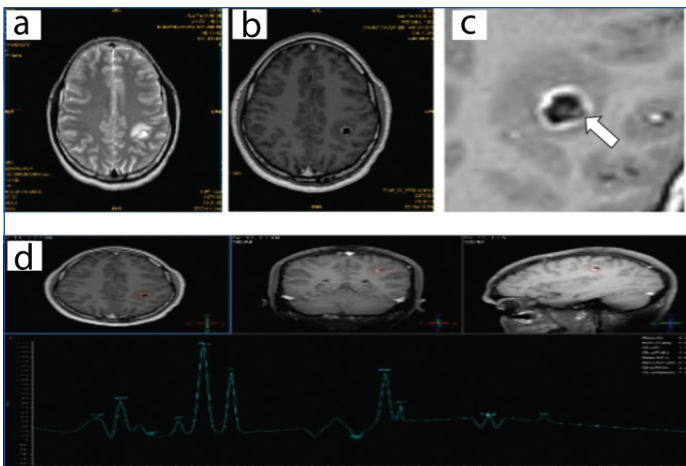
*No data was collected for Metastasis, tumefactive demyelination

Multiple ring enhancing lesions which appeared hyperintense in T2/FLAIR with mild perilesional oedema were seen scattered in brainstem and bilateral cerebellar hemispheres. There was an evidence of diffusion restriction. T1W post-contrast study revealed ring enhancing lesion. On MRS, evidence of lipid peak was noted. The features likely representing multiple tuberculomas were observed [Table/Fig-5].



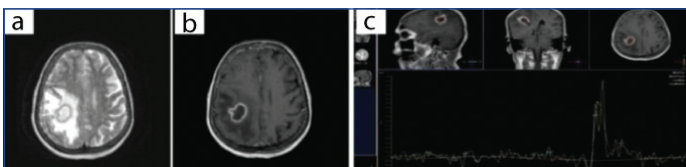
[Table/Fig-5]: Case representation of tuberculoma: a) Axial T2WI showing T2 hyperintense area in the right frontal lobe (superior and medial frontal gyrus) representing oedema; b) Axial T1W postcontrast study revealed ring enhancing lesion; c) MRS taken at ring enhancing lesion of right frontal lobe shows peaking of lipid peak.

Well defined cystic lesion measuring ~12x10 mm which was T2 hyperintense and suppressed in FLAIR (CSF intensity), was noted in the left parietal lobe at grey-white matter junction with perilesional oedema. On post-contrast study-ring enhancement with eccentric scolex was noted within the lesion. MRS showed elevated doublet peak lactate (which got inverted at TE 144 ms) at 1.3 ppm. Lipid peak at 0.9 ppm was insignificant - features suggestive of Colloid vesicular stage of NCC (active stage). Two other small ring enhancing lesions measuring ~5 mm and 7 mm were noted on the right basal frontal lobe and left occipital lobe at grey-white matter junction without perilesional oedema, which showed mild blooming on gradient sequence- suggesting nodular calcified stage of Neurocysticercosis (NCC) [Table/Fig-6].



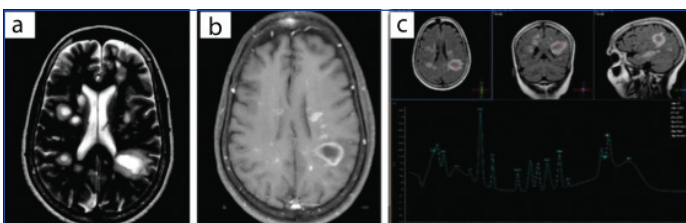
[Table/Fig-6]: Case representation of Neurocysticercosis: a) Axial T2W shows well defined T2 hyperintense cystic lesion with perilesional oedema in left parietal lobe; b) Axial T1W post-contrast sequence shows typical peripheral ring enhancing lesion in the left parietal lobe; c) Zoomed image of B2 left parietal lobe lesion showing eccentric scolex (arrow); d) MRS with 144 ms TE shows inverted doublet lactate peak at 1.3ppm, succinate peak at 2.4ppm, choline peak at 3.2 ppm and mildly reduced NAA at 2 ppm. Lipid peak at 0.9ppm is insignificant.

T2 hyperintense lesion with a hypointense rim noted in the right cerebral hemisphere which showed ring enhancement on post-contrast study with perilesional oedema. MRS showed increased lactate and amino acid. The features were suggestive of cerebral abscess [Table/Fig-7].



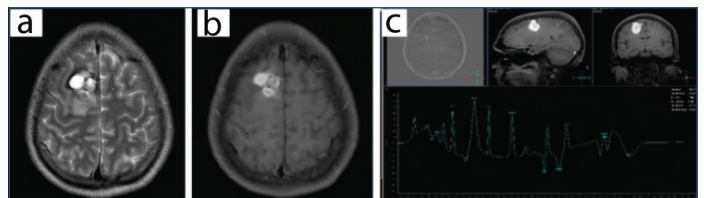
[Table/Fig-7]: Case representation of cerebral abscess with the lesion noted in the right cerebral hemisphere: a) Axial T2W sequence- shows T2 hyperintense lesion with a hypointense rim in the right cerebral hemisphere with surrounding perilesional oedema; b) Axial post-contrast T1W sequence shows peripheral ring enhancement of the lesion; c) MRS showed increased lactate and amino acid peak.

Multiple T2 hyperintense lesions of varying sizes, involving the periventricular and subcortical regions (predominantly in white matter) were observed in the bilateral frontal, parietal, temporal and occipital lobes, which showed incomplete central suppression on FLAIR. Post-contrast Axial T1W study showed multiple ring enhancing lesions. MRS showed elevated choline and lipid lactate peak. The features were likely suggestive of multifocal tumefactive demyelination [Table/Fig-8].



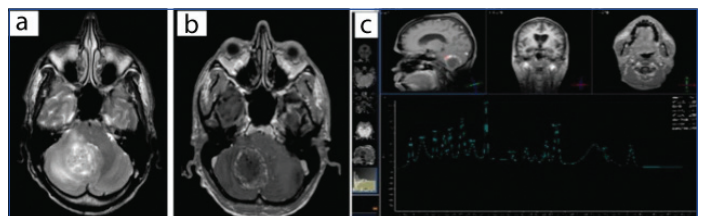
[Table/Fig-8]: Case representation of multifocal tumefactive demyelination: a) Axial T2W sequence shows multiple T2 hyperintense lesions of varying sizes with perilesional oedema seen involving the periventricular and subcortical regions (predominantly in white matter) in bilateral frontal, parietal, temporal and occipital lobes, which showed incomplete central suppression on FLAIR (not shown here); b) Post-contrast Axial T1W study shows multiple ring enhancing lesions; c) MRS showed elevated choline and lipid lactate peak.

A large well defined intra-axial space occupying lesion on the right high frontal lobe and adjacent multiple clusters of lesions was noted with surrounding vasogenic perilesional oedema and haemorrhagic component. Post-contrast axial T1W sequence showed peripheral enhancement of the lesions. MRS showed increased choline and reduced NAA. No other parenchymal lesions were observed. The diagnosis was suggestive of a glioblastoma [Table/Fig-9].



[Table/Fig-9]: Case representation of glioblastoma with the lesion noted in the right high frontal lobe: a) Axial T2W sequences showing a large well defined intra-axial space occupying lesion in the right high frontal lobe and adjacent multiple clusters of lesions was noted with surrounding vasogenic perilesional oedema and haemorrhagic component; b) Post-contrast axial T1W sequence shows peripheral enhancement of the lesions; c) MRS showed increased choline and reduced NAA.

A large well defined solid intra-axial lesion was noted in the right cerebellar lobe with perilesional oedema. Lesion exhibited T1 iso to hypointense signal and T2 iso to hyperintense signal. Mass effect was noted in the form of compression of 4th ventricle and upstream hydrocephalus with periventricular ooze, compression and displacement of brain stem, tonsillar herniation for a distance of 10 mm. On post-contrast study, the lesion showed peripheral ring enhancement. MRS showed increased choline and lactate peak and decreased NAA. The features were suggestive of metastasis [Table/Fig-10].



[Table/Fig-10]: Case representation of metastasis in right cerebellar lobe: a) Axial T2W and shows- large well-defined lesion which exhibits T2 iso to hyperintense signal with surrounding perilesional oedema and mass effect; b) Post-contrast axial T1W study shows sharply demarcated peripherally enhancing lesion with distinct margin. (c) MRS showed increased choline and lactate peak and decreased NAA.

DISCUSSION

Dissimilar aetiologies of the intracranial ring enhancing lesions appear similar on conventional MRI. Differential diagnosis of the neoplastic and non-neoplastic lesions is better diagnosed by MRS because of its higher specificity (93.3%) and sensitivity (87.5%) that produced varying success rates [15,16].

In present study, 50 patients were evaluated by MRS to diagnose ring enhancing lesions of the brain. The mean age of patients in the study was 36.76±21.62 years, where 20% of the patients belonged to the age group of 21-30 years. The study involved large number of male patients (66%). A significant number of patients in this study experienced seizures (66%) followed by headache (38%) and vomiting (24%). Similar findings were reported by Seth S et al., where seizures (80%) was the most common presentation, followed by headache (28%) and vomiting (18%) [4]. An earlier study reported by Elsadway ME and Ibrahim Ali H stated that majority of the patients experienced headache, although these symptoms tend to vary amongst individuals [2]. Tuberculoma (36%) and neurocysticercosis (22%) were the most prevalent lesions in this study. Similar findings have been reported earlier by Bava JS et al., and Mirchandani S et al., [17,18].

Various metabolites (choline, lipid, lactate, reduced NAA, amino acids, creatine, succinate) that are identified by MRS aid in determining the type of ring enhancing lesion of the brain [7]. Tuberculoma and neurocysticercosis feature similarities in clinical and neuroimaging and is an enigma to the radiologist regarding their diagnosis. Differentiation and characterisation of tuberculoma and neurocysticercosis are based on the metabolite peaks that each lesion represents. Tuberculomas are representative of lipid peaks with a choline/creatine ratio of >1 [3,11,12,19]. In case of neurocysticercosis, elevated lactate, succinate and choline levels concomitant with no or insignificant lipid peaks are noted [19,20].

In this study, 18 patients diagnosed with tuberculoma had higher peak levels of lipids, which could be attributed to the lipid fractions in tuberculosis bacillus as reported in the earlier studies [11,21]. An increase in the lipid/lactate peaks and decrease in choline/NAA peaks were noted in the case of tuberculoma diagnosed patients. In the case of neurocysticercosis, increased lactate, succinate and choline with no or insignificant lipid peaks were noted. High choline peaks were noted in the case of primary brain tumour. Lactate peak and amino acids peak was noted in the case of cerebral abscesses. The findings from present study were comparable to that reported by Elsadway ME and Ibrahim Ali H [2]. In the case of metastasis, an increase in choline peak was noted, which was comparable to the findings reported earlier [18,22]. However, the results were contradictory to a study conducted by Elsadway ME and Ibrahim Ali H where a mild elevation of choline/NAA ratio and increase in the lipid and lactate levels were noted [2]. This may be due to the encapsulation of metastatic lesions that do not express higher choline signals [23,24]. With regards to the tumefactive demyelination and radiation necrosis, reduced peaks of only choline, lipid and lactate were noted in a few patients, comparable to an earlier study conducted by Shah R et al., [25].

Overall, higher choline peaks were noted in 66% of the patients as abnormal choline metabolism was identified in multiple cases of cancer followed by lipid peaks (50%) due to bacterial infection [26]. Lactate peaks were also high in 48% patients as it acts as a fuel regarding tumour growth and progression towards metastasis [27]. Decrease in NAA levels as detected by MRS have earlier been understood to designate a compromised neuronal metabolism and in the study, 12% of patients were noted to have reduced NAA [28].

Increase in the levels of choline suggests an increase in choline/creatinine ratio, rather than its absolute concentration. Increased choline levels cognates a higher turnover in the cell membrane along with a higher cellular density that results from tumour cell proliferation. Hence, choline/creatinine ratio is most frequently used to differentiate low and high-grade tumours. A choline/creatinine ratio >2.0 is considered as a strong indicator of high-grade neoplasm [29,30]. In this study, higher choline/creatinine ratio (>2) was noted in 16% patients with primary brain tumour followed by 36% subjects with tuberculoma, with a ratio >1-2, with an increased likelihood of tumour characteristics. Similar findings have been reported in previously conducted studies [31,32].

MRS could be incorporated into standard MRI protocols during the initial diagnostic imaging to further ensure accurate diagnosis. Till date, MRS implementation has been hampered by lack of acquisition protocols, analysis techniques and quality control measures for specific clinical scenarios. Processing and presenting of information, assessing the quality of spectra, and accurately interpreting data is a challenge. There is a paucity of research to implement the diagnostic evidence from MRS however; further research is required to evaluate the efficacy of MRS as a standard diagnostic tool [33].

In this study, MRS was helpful in differentiating neoplastic and infectious brain lesions. This led to the diagnostic delineation of the ring enhancing lesions of the brain, especially in the case of tuberculoma and neurocysticercosis. Thus, this accurate diagnosis paved the way for prudent medical management of the patients.

Limitation(s)

One of the limitations of this study was the smaller sample size. With a larger sample size, correlations of various metabolite peaks to their respective type of ring enhancing lesion can be tested. Gender bias could be excluded in future studies. Histopathological analysis was not possible to further confirm the diagnosis to avoid causing injury during brain biopsy. Also, MRS was avoided in small lesions

closer to the bone, as it is helpful only in the cases of larger lesions and those away from the bony skull.

CONCLUSION(S)

Magnetic Resonance Spectroscopy (MRS) is a useful tool in the diagnosis of the ring enhancing lesions of the brain. It guided in delineating lesions with similar presentations (tuberculoma and neurocysticercosis). However, further research in this regard is required to enable MRS as a diagnostic tool of choice. Until then, MRS sequence can be used as an adjunct, along with other conventional techniques.

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- Plagiarism X-checker: May 11, 2020
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- iThenticate Software: Sep 30, 2020 (9%)

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