

Characteristics of Ring enhancing lesions in brain in correlation with MRI and MR spectroscopy

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Abstract

Background: The aim of this study was to analyze and identify various characteristic changes of multiple ring-enhancing lesions in the brain on conventional MRI and proton MR spectroscopy which leads to an early diagnosis, treatment, response assessment and minimize the complications in such patients. **Materials and method:** It is a type of descriptive study, consisting of 50 patients that were suspected clinically with ring-enhancing lesions were referred to the department of Radio-diagnosis and underwent scanning in 1.5 Tesla MRI over a period of 2 years. **Results:** Out of 50 patients, 19 were diagnosed as neurocysticercosis, 16 as Tuberculomas, 7 as Intracranial Abscess, 4 as metastasis, 3 as primary brain neoplasms, and 1 as Tumefactive Demyelination. Neurocysticercosis was found to be the most common of the pathology diagnosed with Seizures being the most common complaint in patients. **Conclusion:** The use of MRI along with MR spectroscopy is of vital importance and primary research tool in neuro diagnosis. The most common ring enhancing lesions experienced in developing countries like India is NCC and tuberculomas. Accurate diagnosis and characteristics of these lesions can be achieved by MR spectroscopy on a routine MRI scan by analyzing the quantity and ratio of tissue metabolites.

Keywords: MR spectroscopy, brain, ring enhancing lesions, Neurocysticercosis, Tuberculosis

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Introduction

MRI helps in early diagnosis of the diseases which is visually demonstrated as by contrast between grey-white matter junction differentiation, tumour ischemia and infarction, edema, multiple sclerosis plaque, infection, abscess and hemorrhage. MRI has inherent sensitivity and also the capability to visualize all the regions of brain without the need for reformatting the image. MRI helps to correctly diagnose and identify various causes of ring enhancing lesions. Magnetic resonance spectroscopy is a vital tool for identifying and diagnosing infective etiologies like intracranial abscesses and non-infectious lesions like primary intraparenchymal neoplasms, demyelination, lymphoma and cerebral metastasis. The

possible nature and characteristics of these lesions can be achieved by MR spectroscopy (MRS) on a routine MRI scan by analyzing the quantity and ratio of tissue metabolites such as lipid, choline, amino acids, N-acetyl aspartate etc. These lesions located in the sub-cortical area and also at the gray-white matter interface, superficial or deep to the brain parenchyma [1]. Clinical symptoms in these lesions are quite non-specific and hence it is difficult to reach a final diagnosis [2]. Longitudinal studies have demonstrated that proton MR spectroscopy (H-MRS) is useful in monitoring the progression of disease and response to the treatment. MR Spectroscopy also has a vast prognostic implication [1]. Almost all MR localization procedures today are image-guided; in the sense that they use ¹H MR images to guide the placement of ROI for RF excitation. Therefore, spectroscopy protocols typically include an MR study. The various volume localization strategies are classifiable into two broad methodological approaches that are feasible in the clinical setting. One involves detection of signals from a single, well-defined region of tissue called

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single-voxel localization, while the other involves the simultaneous acquisition of signal data from several different regions. Both approaches use magnetic field gradient, as in imaging, to obtain spatial information, but are also able to provide the acquired molecule-level information selectively. A normal MR spectrum (Fig 1) is read from viewers right to left with metabolite peaks at various locations on X-axis, starting from lipids at 0.9 and 1.3 ppm, lactate at 1.3 ppm, (as a doublet), N-acetyl aspartate peak (NAA) at 2.0 ppm, choline peak (Cho) at 3.2 ppm, creatine peak (Cr) at 3.0 ppm, and Myo-inositol peak (mI) at 3.6 ppm. A line joining mI, Cr, Cho and NAA forms 45-degree angle to x axis when they are present in normal proportions which is called as Hunters angle. The variation from short echo time to long echo time (TE), change in the location of the voxel from peripheral cortex to the midbrain and changing repetition time (TR) all leads to change in the Hunters angle[3]. This helps in analysing the chemical properties of a tissue based on the intensity and distribution of energy measured after a certain frequency or wavelength is allowed to interact with the tissue sample. It provides in vivo chemical information that is represented by the spectrum by peaks which is obtained that corresponds to the various metabolites. Below (Table 1) are the various brain metabolite peaks noted that corresponds to different pathological processes [4]. The aim of this study was to analyze and identify various characteristic changes of these ring enhancing lesions in brain on conventional MRI and proton MR spectroscopy which leads to an early diagnosis, treatment, response assessment and minimize the complications in such patients [1].

Material and methods

It was a descriptive study conducted on 50 patients over a period of 2 years from August 2018 to September 2020.

Results

Normal Single Voxel MR Spectrum- Normal MR Spectroscopy obtained at TE of 30 msec. [3]

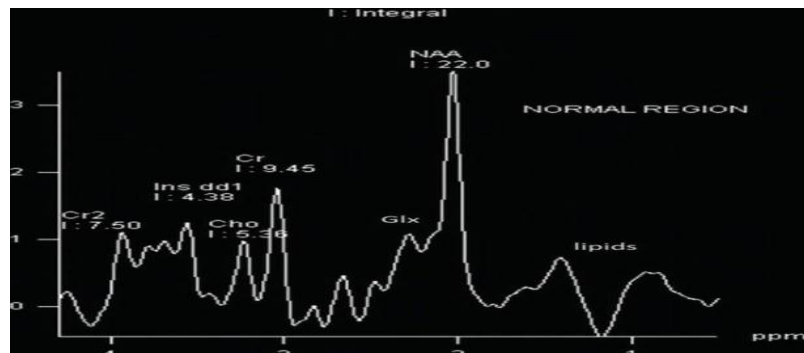


Fig 1: Normal Single Voxel MR Spectrum

All the patients were referred to the Department of Radiology those with strong suspicion of intracranial space occupying lesions. On gadolinium contrast injection, all ring enhancing lesions of the brain detected on MR imaging were retrospectively studied of all age groups irrespective of sex were included in the study. Patients having history of claustrophobia, history of metallic foreign body or implants in situ, cardiac pacemakers, contrast allergy, and those with poor kidney function were excluded from the study. Furthermore, supportive investigations were requested such as Complete blood count, CSF examination, tuberculin test/Chest X-ray, ELIZA test, Radiograph of the extremity to look for intramuscular cysticercosis, Visual evoked potential (VEP) and biopsy to help correlate the findings with imaging and clinical examination. These results were used as references to reach the final diagnosis. The MRI scan was performed using:

EQUIPMENT AND TECHNIQUE USED: All the patients were scanned under MR SIEMENS AVANTO 1.5 T strength. It contains an active shielded, ultra-compact, superconducting magnet equipped by Matrix head coil of 12-element capable of ultra-fast parallel acquisition. mSENSE coils were used for acquisition of images. All the patients underwent axial T1W, T2W, FLAIR sequences, coronal T2 and Sagittal T1 sequences. DWI, GRE and Special sequences such as CISS 3D, VEBOLD and perfusion imaging were used as and when required. Contrast enhanced images were requested for better delineation of these lesions. Single voxel spectroscopy was performed at TE of 144 msec. The voxel is placed on the lesion so that it covers the maximum area of the lesion as well as the enhancing walls. We used PRESS and T1 post contrast sequence which are applied with orthogonal gradient. Spectroscopy was avoided in small lesions close to the bone and ventricles.

Table 1: The brain metabolites that correspond to various pathological processes. [7]

Chemical Compound	Chemical (PPM)	Comments
N-Acetyl Aspartate (NAA)	2.0	Neuronal Marker.
Creatine/Phosphocreatine	3.0,3.9	Supplier Of Phosphate To Convert Adp. Energy Metabolism.
Choline (Cho)	3.2	Cell Membrane Marker.
Myo-Inositol(MI)	3.6	Glial Cell Marker, Osmolyte Hormone Receptor Mechanisms
Glutamate (Glu) Glutamine (Gln) (Glu+Gln=Glx)	2.1-2.5	An Excitatory Neuro Transmitter And Regulator
Lipids (Lip)	0.9-1.4	Cell Break Down/ Brain Destruction Indicator.
Lactate(Lac)	1.3	Degradation Of Pyruvate In The Anaerobic Glycolysis Pathway

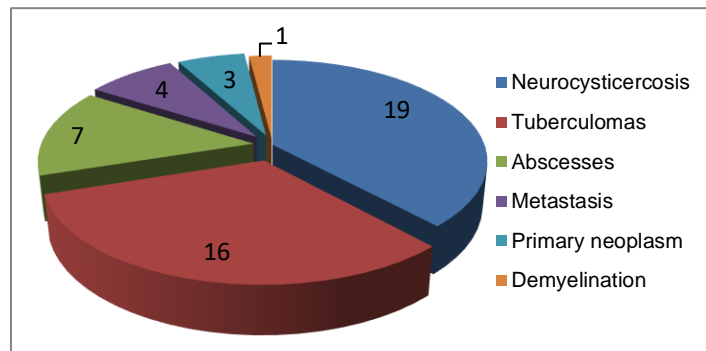


Fig 2: Incidence of various pathologies presenting as Ring enhancing lesion

Table 2: MRI characteristics of various ring enhancing pathologies and their supportive findings that help to reach a conclusive diagnosis.

Radiological diagnosis	No. of patients	Most common Complaint	T1WI	T2WI	DWI (Restriction)	MR Spectroscopy peak	Supportive findings to confirm the diagnosis
Neurocysticercosis	19	Seizures	Hypointense	Hyperintense	No	Choline, Lactate, succinate	Extremity Radiographs and/or ELISA positive for cysticercosis
Tuberculoma	16	Seizures, neurologic deficit	Hypointense	Hyperintense	No	Lipid, Lactate	Past history of TB and/or Seizure stoppage in 4 weeks after starting Anti-tubercular therapy
Abscess	7	Fever, headache	Hypointense	Hyperintense rim	Yes	Amino acids- e.g.: leucine, valine etc.	High TLC count with improvement on Antibiotics
Metastasis	4	Seizures	Hypo to Isointense	Hyperintense	Yes	Choline, lactate	Primary neoplasm: In lungs- 3 patients In breast-1 patient
Primary neoplasm	3	Headache	Hypointense	Heterogeneously hyperintense	Yes	High Choline/Creatinine ratio, reduced NAA	Biopsy proven High grade glioma in all patients.
Tumefactive demyelination	1	Seizures	Hypointense	Iso to hypointense rim	No	Variable, Choline, NA/Creat. higher	Low CBV on perfusion imaging

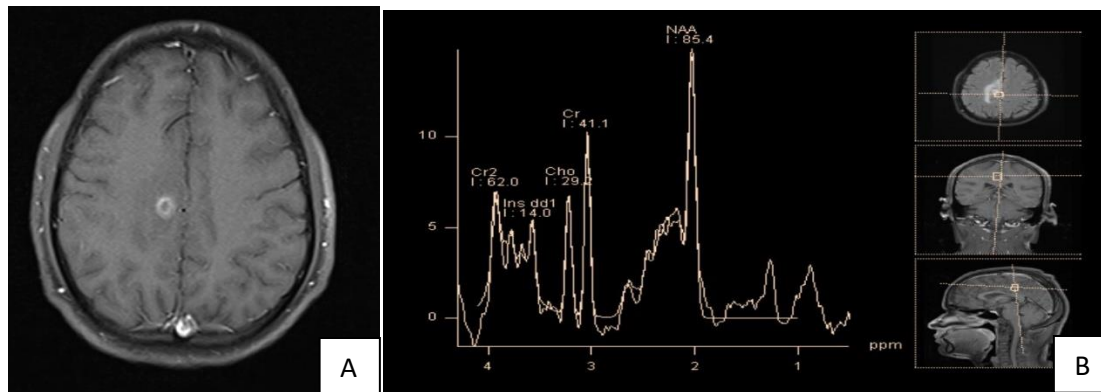


Fig 3: Neurocysticercosis- A well-defined thick-walled ring enhancing lesions (A) in the gray-white junction of left parietal lobe with perilesional edema. On MR Spectroscopy (B), low level of metabolites with poor signal to noise ratio with choline peak at 3.2 ppm and mild succinate peak at 2.4 ppm. Features suggestive of neurocysticercosis (colloidal vesicular stage)

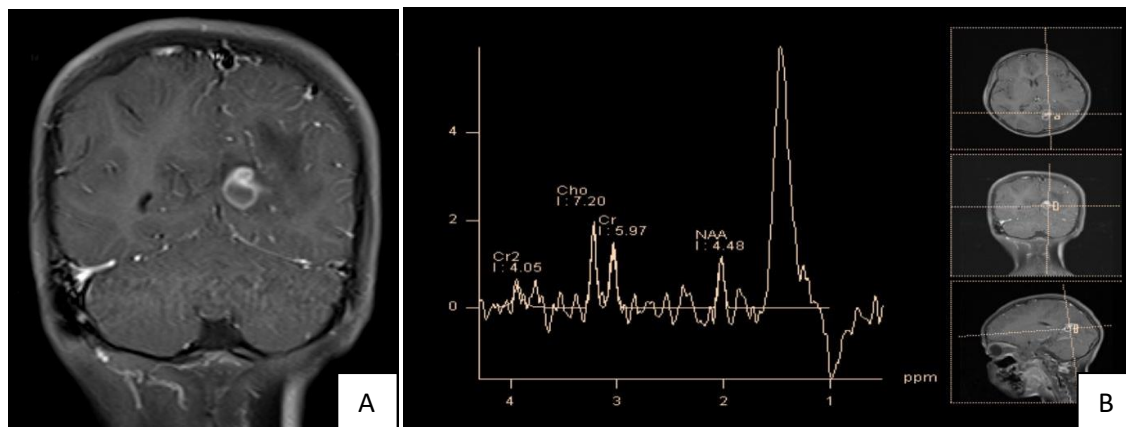


Fig 4: Tuberculoma- Multiple conglomerated well-defined ring enhancing lesions (A) is seen in left occipital lobe. . On MR Spectroscopy (B), low NAA levels with high lipid peak at 1.3 ppm is seen. Features are suggestive of tuberculoma.

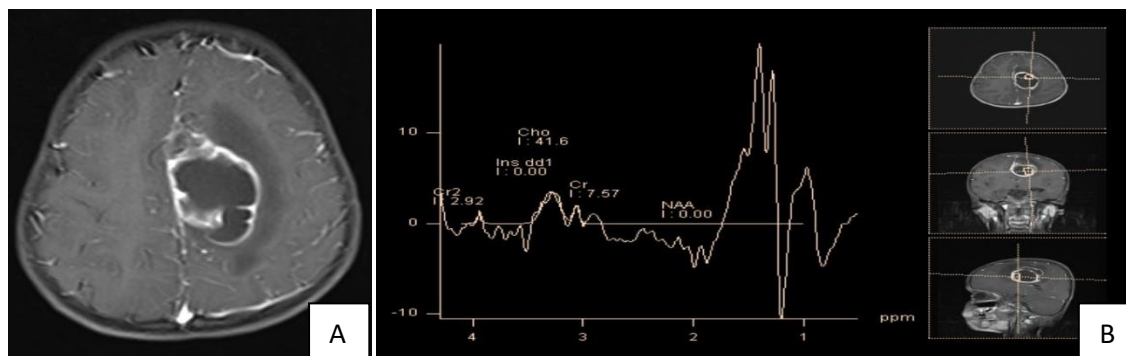


Fig 5: Abscess- A well-defined lobulated thick enhancing walled lesion (A) with perilesional edema and effacement of adjacent sulcal spaces with midline shift is seen adjacent to the falx in the left fronto-parietal region. On MR Spectroscopy (B), low NAA levels with marked elevation of lipid/lactate peak at 1.33 ppm, also high (valine, isoleucine and leucine) peak at 0.9 ppm and an alanine peak at 1.48 ppm are seen. Features are suggestive of abscess.

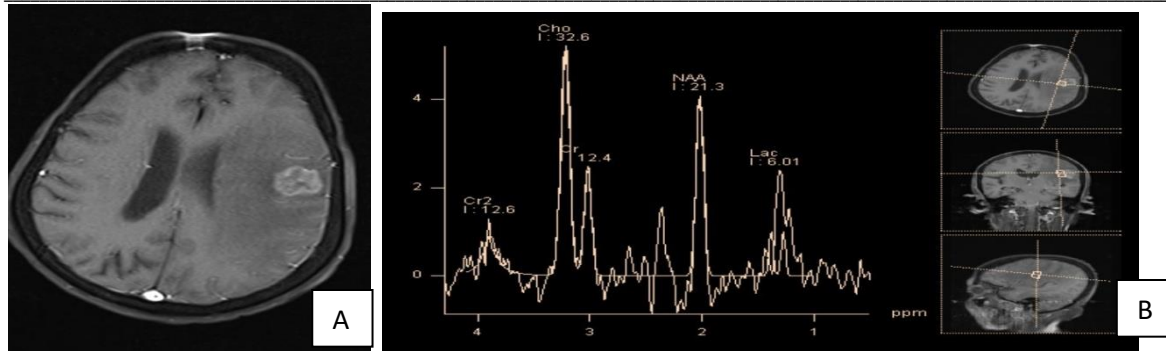


Fig 6: Metastasis- A well-defined thick walled lesion showing peripheral enhancement (A) and surrounding perilesional edema in left frontal subcortical white matter was identified in a patient with past history of carcinoma lung. On MR Spectroscopy (B), marked elevation of choline peak at 3.2 ppm, mild lipid/lactate peak is also noted at 1.33 ppm is seen. Features are suggestive of metastasis.

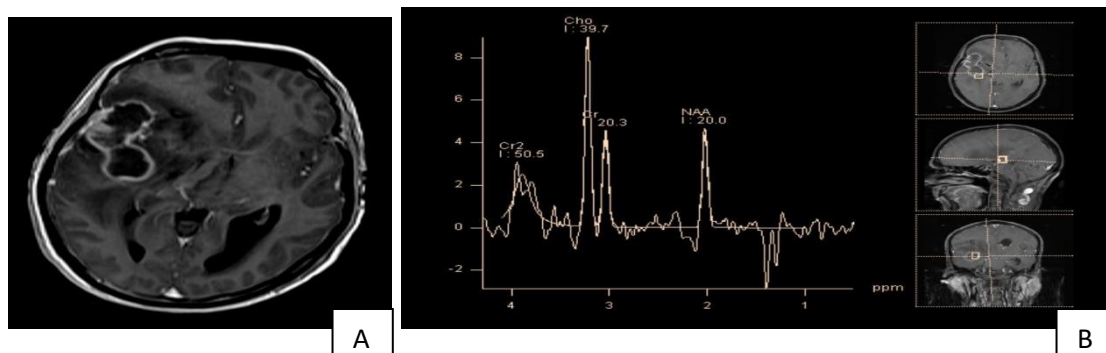


Fig 7: Primary Brain Neoplasm- A well-defined lobulated lesion with marked perilesional edema and post-contrast enhancement (A) is seen in the subcortical white matter of right frontal- temporal lobe. On MR Spectroscopy (B), marked elevation of choline peak at 3.2 ppm, mild lipid/lactate doublet is also noted at 1.33 ppm is seen with reversed Choline:Creatinine ratio- 1.64. Features are suggestive of high grade glioma.

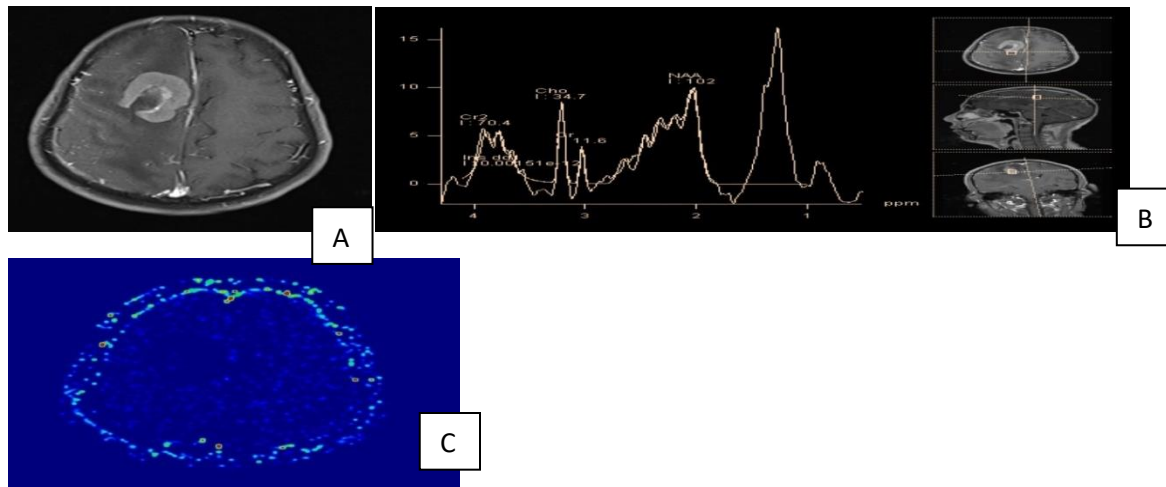


Fig 8: Tumefactive demyelination- A well-defined thick walled lesion is seen in right frontal lobe in superior and middle frontal gyrus and subcortical white matter - temporal lobe. On post contrast study (A), it shows thick peripheral enhancement with incomplete ring open towards cortex. On MR Spectroscopy (B), marked elevation of lipid peak at 1.33 ppm, with markedly reduced NAA and mild glutamate peak at 2.2 ppm is seen. On Perfusion imaging (C), low CBV is noted. Features are suggestive of Tumefactive demyelination.

AGE DISTRIBUTION: 50 patients having ring enhancing lesions were analysed by cross-sectional method using conventional MRI and MR Spectroscopy between the ages of 5 to 69 years. Majority of the patients were in the age group of 20 to 29 years comprising of 18 patients (36%), followed by 12 patients (24%) in the age group of 10 to 19 years.

PATHOLOGIES: (Fig 2) shows most common pathology among them was neurocysticercosis (NCC) that was seen in 19 patients (38%), followed by tuberculomas in 16 patients (32%), abscesses in 7 patients (14%), metastasis in 4 patients (8%), primary neoplasm in 3 patients (6%) and Tumefactive demyelination in 1 patient (2%)

SEX DISTRIBUTION: In our study, 32 patients (64%) were males and 18 patients (36%) were females.

CLINICAL FEATURES: All the patients were symptomatic with a varied and multiple groups of symptoms, most commonly seizures (82%), neurological deficit (34%), headache (64%), vomiting (52%), weakness (48%) and fever (46%).

SIDE OF LESION: Out of 50 patients, 18 patients (36%) had lesion on the right side of brain whereas 16 patients (32%) had lesion on the left side and 16 patients (32%) had lesion bilaterally.

NUMBER OF LESIONS: Also, there were 18 patients (36%) with only single lesion, 24 patients (48%) having 2 to 4 lesions and 8 patients (16%) having more than 4 lesions.

SIZE OF LESION: In our study, 33 patients (66%) had less than 2 cm size of lesions, 13 patients (26%) had 2 to 4 cm size of lesions and 4 patients (8%) had more than 4 cm size of lesions.

DIFFUSION RESTRICTION: Out of 50 patients, 26 patients (52%) showed diffusion restriction whereas 24 patients (48%) did not show any diffusion restriction on DWI.

MR SPECTROSCOPY FINDINGS: Out of the 50 patients evaluated, Choline peak was observed in 32 patients (64%), Lipid in 28 patients (56%), Lactate in 26 patients (52%), reduced NAA peak in 16 patients (32%) and amino acids in 7 patients (14%). (Table 2) shows MRI characteristics of various ring enhancing pathologies and their supportive findings that help to reach a conclusive diagnosis.

Discussion

Neurocysticercosis- Out of fifty patients evaluated neurocysticercosis was seen in 19 (males=12; females=7) cases. 8 patients were diagnosed with single lesion whereas multiple lesions were identified in 11 patients. Intraparenchymal forms of NCC were observed in all the cases with spinal cysticercosis and subarachnoid cysticercosis seen in one case each. CISS 3D sequences were used to identify scolex in 7 cases. MRS shows Choline peak resonating at 3.2 ppm, while peak of succinate was observed at 2.4 ppm and reduced peak of NAA (Fig 3). Gradient echo imaging played a significant role in detecting calcified lesions which were observed in 7 cases (36.8 %). All the lesions were low or isointense signal on T1 weighted images

and hyperintensity was observed in T2 weighted images. Out of these 11 lesions showed inversion on FLAIR that suggested the contents are similar to that of CSF. Strong ring enhancement with adjacent perilesional edematous component was seen in 12 cases suggestive of active lesions. Not even a single case of intraventricular neurocysticercosis was identified in our study, probably due to small sample size. Martinez et al reported intraventricular neurocysticercosis in 22% of cases [5]. MRI is a better modality compared to CT for detection of parenchymal neurocysticercosis according to our study as compared to the study done by Suss Raetal et al [6]. Our study showed similar features of parenchymal forms of NCC as it was found in the study done by Amaral LL et al [7].

Tuberculoma- Tuberculomas were diagnosed in 16 (32%) cases out of the total 50 cases that were studied. Out of these 16 cases (10:6- male: female), single lesion was noted in 8 of them and multiple in 8 cases. Most of the multiple tuberculomas were conglomerating type of lesions and appeared low signal on T1W and T2W images whereas few of them had high signal T2W images. There was no or partial restriction seen in 14 cases. All lesions showed a nodular or irregular ring like enhancement. Lipid peak was noted on MR spectroscopy (Fig 4) in all 16 cases and it plays a crucial role in identifying tuberculomas from other infective granulomas. Ratio of Choline to Creatinine was below 1.1 in all NCC and above 1.2 in all tuberculoma that was similar to the study performed by Kumar et al and Jayasunder et al [8, 9].

Abscess- Out of the 50 patients, abscesses were found in 7 cases- 14% (males=5; females=2). Single abscess was found in 4 cases (57.1%) whereas the other 3 cases had multiple abscesses. One patient presented with history of congenital heart disease -tetralogy of fallot. All the cases showed sizes >2 cm and two cases were >4 cm. All abscesses showed hypointensity on T1W images with a hyperintense ring around it noted in 6 cases. It was having hyperintensity on T2W images with hypointense rim surrounding the lesion. These lesions showed absolute diffusion restriction with corresponding low ADC values within it and high lactate levels in all 7 patients suggesting anaerobic glycolysis with amino acids like valine, leucine and isoleucine peaks seen in 3 cases (Fig 5). Abscesses has been described by Halmes et al MR. Our findings were correlated with the central necrosis, peripheral edematous changes and the characteristic peripheral enhancing capsule of the abscess [10]. Our findings were similar to the study conducted by Leuthardt EC et al [11] and Shukla-Dave A et al [12]

Metastasis

Since lymphatic drainage is absent in the brain, hence the metastatic spread of tumour cells to the brain is via hematogenous route. Most common brain metastasis occurs primarily from breast cancer, lung cancer and malignant melanoma. Although MRI cannot unequivocally differentiate between metastases and other neoplasms, use of MRS helps in reaching the diagnosis. Out of the 50 patients, 4 cases were metastasis (males=2; females=2). All four patients showed more than one lesion. All the cases demonstrated high

Choline to creatinine ratio and Choline to NAA ratio (Fig 6). All 4 patients showed hyperintensity on T2W images; however 2 patients showed FLAIR suppression which suggested it to be a cystic metastasis. Primary neoplasm was detected in all four patients with two patients having breast carcinoma, one lung and prostate. On post-contrast study, irregular, thick ring type of enhancement was noted in all four patients. Our findings were similar to the study conducted by Vieth RG et al [13].

Primary Brain Neoplasm—Out of the 50 patients, 3 cases were of primary neoplasm (2 male; 1 female). All three lesions were single in number. The lesions were ill-defined with peripheral ring enhancement with central necrotic area appearing hypointense on T1, heterogeneously hyperintense on T2 and FLAIR and showing mild diffusion restriction with corresponding low values on ADC and areas of blooming on GRE which are suggestive of hemorrhages. It showed marked peri-lesional edema with effacement and mass effect on adjacent sulcal spaces. On post contrast study (G), it shows peripheral ring like enhancement. On MR spectroscopy, high choline peak with reduced NAA and increase choline-creatine ratio and low Myo-inositol: creatinine ratio (<0.4) was noted in all patients (Fig 7). The sensitivity and specificity of proton MR spectroscopy ranges from 72 to 86% and 60 to 67% respectively in the studies conducted by Lu et al [14], Louis et al [15], and Stadlbauer et al [16].

Tumefactive demyelination—It is important to distinguish demyelination from neoplasm as it can lead to severe repercussions on misdiagnosing, since treatment for both is completely different. Out of the 50 patients, 1 case was of Tumefactive demyelination and it was a male patient. A thick open or irregular ring type of lesion opening towards the cortex noted. On diffusion imaging it did not show diffusion restriction, however foci of blooming was noted in the peripheral thick margin of lesion. On MR spectroscopy, marked elevation of lipid-lactate doublet at 1.33 ppm, choline peak and mild glutamate peak at 2.2 ppm was noted with markedly reduced NAA (Fig 8). Perfusion imaging helps differentiate tumefactive demyelinating lesions can be differentiated from the main differential considerations like high-grade gliomas and lymphomas with the help of perfusion imaging techniques. Tumefactive demyelinating lesions show a substantial low amount of mean cerebral blood volume compared to high-grade gliomas and lymphomas. In our study, perfusion imaging was performed for this patient that showed findings similar to study conducted by Cha S, Pierce S, and Knopp EA et-al [17]. Use of MRI along with MR spectroscopy is a very useful, important and primary research tool in neurodiagnosis. Most common ring enhancing lesions experienced in developing countries like India is NCC and tuberculomas. T2W hyperintensity with no diffusion restriction and presence of scolex helps in differentiating NCC from tuberculomas. Abscess shows T2W hypointense rim with central diffusion restriction, with amino acid peaks. High grade gliomas may be lobulated with central necrotic component with thick irregular ring enhancing lesions with very high Cho/Creat ratios and low NAA whereas,

metastases are well-defined T2W hyperintense lesions with high choline peaks. Tumefactive demyelination most commonly shows incomplete ring enhancement with open part predominantly towards the cortex and low cerebral blood volume on perfusion imaging. Hence, conventional MR imaging along with MR spectroscopy can be useful to reach a correct the diagnosis and also in differentiation of peri-lesional edema from neoplastic invasion.

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Conflict of Interest: Nil

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