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ORIGINAL RESEARCH

Role of MRI with MR spectroscopy in the evaluation of ring enhancing lesions in brain

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ABSTRACT INTRODUCTION

Aims and objectives: To study the role of MR spectroscopy in the evaluation of various ring enhancing lesions in the brain with single and multi-voxel proton MR spectroscopy.Ring enhancing lesions represent an important public health challenge and is a major cause of morbidity and mortality throughout the world.

Materials and methods: 100 cases referred to the Department of Radiodiagnosis and Imaging, Government Medical College, Amritsar with clinically suspected brain lesions were evaluated and statistically analyzed.

Results: Hundred patients with ring enhancing lesions were evaluated using MRI and MR spectroscopy. Various parameters of ring enhancing lesions were evaluated and the spectrum of findings on MRI and MRS were assessed. The patients were followed up for clinical improvement based on the line of treatment. Few cases requiring histopathological correlation were followed up based on biopsy reports and post operative histopathological reports.

Conclusions: Conventional MRI is a great tool in making a sufficient differential diagnosis of the ring enhancing lesions of the brain, but MR spectroscopy further helps in knowing the chemical nature of lesions and accurate diagnosis of brain tumours. This facilitates the clinician to plan the best line of treatment thus reducing the suffering and morbidity of the patients.

Keywords: Magnetic resonance spectroscopy, ring enhancing lesions, metabolite peaks, neoplastic follow up

INTRODUCTION

The basic principle that enables MR spectroscopy (MRS) is that the distribution of electrons around an atom cause nuclei in different molecules to experience a slightly different magnetic field.[1]This results in slightly different resonance frequencies, which in turn return a slightly different signal. Proton MRS plots hydrogen atom (proton) metabolite signal intensity versus an observation frequency. The signal intensity of hydrogen atom (proton) metabolite

metabolites is plotted against an observation frequency in proton MRS. In the MR environment, protons from the main components of the molecule (mostly carbon atoms) can form "peaks" or "resonances," with signal intensity proportional to the relative quantity of protons.

The metabolite peaks' "position" on the x-axis represents the molecule's immediate chemicalandmagneticsurroundings.Thechemicalshiftforaspecificpeakpositionis computed by dividing the frequency difference between two peaks (one of which serves as a reference) by the MR's operating frequency.[2]

Multiple ring-enhancing lesions (RELs) are one of the most commonly encountered neuroimaging abnormalities. Commonly available imaging techniques such as computed tomography and magnetic resonance imaging (MRI) can be used to detect these lesions. A wide range of etiologies can lead to cerebral ring-enhancing lesions.[3] On conventional imaging, these lesions appear as hypodense or isodense mass lesions on non-contrast compute tomography studies. After contrast administration, ring-like enhancements are seen.[4]Ring-enhancing lesions are often variable in size and have variable amounts of vasogenic oedema around them. The ring-enhancing lesions are commonly found at the junction of grey and white matter, but they could also be found in the subcortical area or deep within the brain parenchyma or may be superficial.[5]

MATERIALS AND METHODS

STUDY SITE

Government Medical College, Amritsar.

STUDY POPULATION

100 patients referred to the Department of Radiodiagnosis and Imaging, Government Medical College, Amritsar with clinically suspected brain lesions or with symptoms of intracranial mass were studied.

INCLUSION CRITERIA

- Patients with recurrent seizures, visual impairment, focal neurological deficit,raised intracranial pressure (severe headache, vomiting and papilledema),loss of sensorium and posturing of limbs suggestive of intracranial lesions.
- All cerebral ring enhancing lesions detected on contrast MR studies.
- All patients incidentally diagnosed to have ring enhancing lesions by CT.
- All age groups included irrespective of age or sex.

EXCLUSION CRITERIA

- Patient having history of claustrophobia.
- Patient having history of metallic implants insertion, cardiac pacemakers and metallic foreign body in situ.
- Study design:Observational study
- Sample size:100
- Duration of study:2years
- Ethical clearance was obtained from the Research and Dissertation Committee/ Ethical Committee of the institution for this study.

IMAGING TECHNIQUE

MR Imaging was performed using 1.5 Tesla Siemen Magnetom Aera machine having NUMARIS/4-MR 52149 and SYNGO MR SPECTROSCOPY software system with a standard head coil. Conventional MRI study was done with fast spin echo (FSE) sequences. MRS was acquired after conventional MRI. At 1.5T, single or multi voxel MRS protocol depending on the size and signal intensity of lesions. The voxel was placedonthelesionsuchthatitwasawayfromtheboneandcoveredmaximum area of the lesion.

STATISTICAL METHODS

The MR spectroscopic values were noted and tabulated. Data was subjected to quantitative statistical analysis in terms of sensitivity, specificity, true predictive value, false predictive value and accuracy. Association between different parameters was done using Chi square test and p value <0.05 was considered statistically significant. Kappa values were also calculated to measure the degree of agreement between two parameters.

RESULTS

Table 1 Radiological diagnosis

Radiological diagnosis	No. of cases	%age
Brain Tumour	7	7.0
Fungal abscess	3	3.0
Metastases	7	7.0
Demyelinating disorder	1	1.0
Neurocysticercosis	18	18.0
Pyogenic abscess	4	4.0
Tuberculoma	60	60.0
Total	100	100.0

Out of 100 cases, 60 cases were tuberculomas, 18 cases were neurocysticercosis, 7 cases were brain tumour, 7 cases were metastases, 4 cases were pyogenic abscesses, 3 cases were fungal abscesses and 1 case was demyelinating disorder.

Graph 1: Bar graph showing case distribution based on radiological diagnosis11-20 years age group was mostly affected (29 % cases).

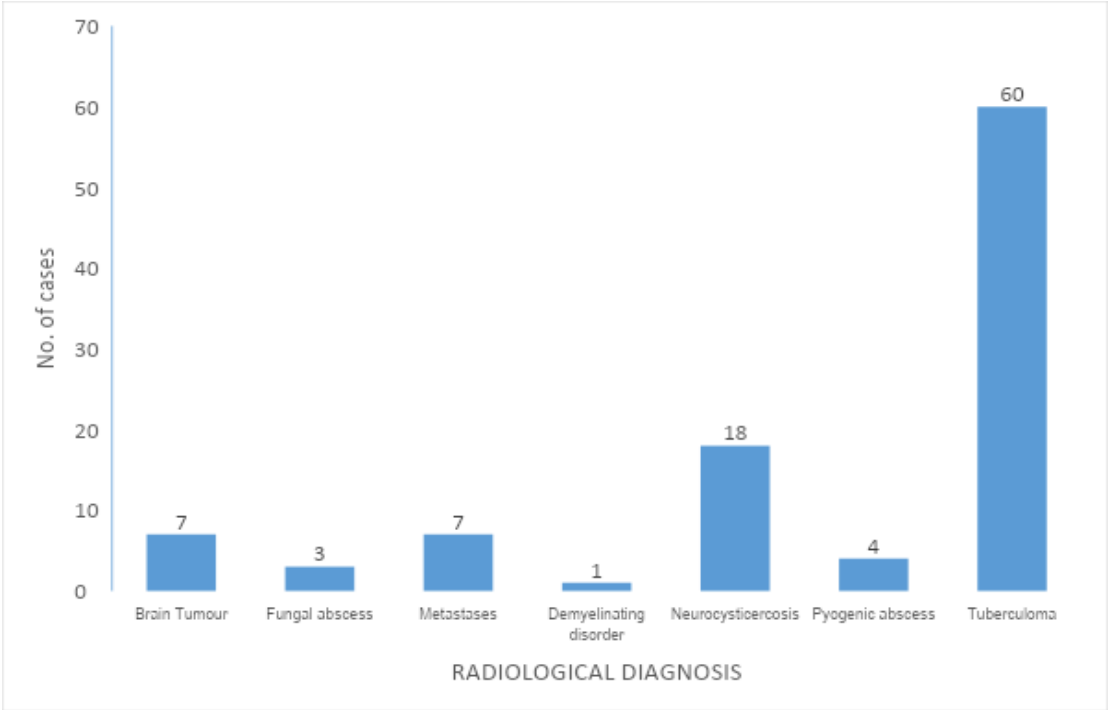

Table 2: Metabolite distribution of various lesions

Radiological diagnosis	I Cho	r NAA	Lip	Lac	AA
Brain Tumour	100.00	100.00	100.00	57.14	0.00
Fungal abscess	0.00	66.67	66.67	66.67	100.00
Metastases	100.00	100.00	71.42	85.71	0.00
Demyelinating disorder	100.00	100.00	100.00	100.00	0.00
Neurocysticercosis	77.77	94.44	0.00	33.33	0.00
Pyogenic abscess	0.00	75.00	75.00	75.00	100.00
Tuberculoma	93.33	81.66	100.00	81.66	0.00

Out of various lesions studied, 100% of brain tumours, 100 % of metastases and demyelinating disorder showed increased choline. 100% of brain tumours, metastases and demyelinating disorders showed reduced NAA. 100% of demyelinating disorders, 100 % of brain tumour and 100% of tuberculomas showed lipid peak. 100% of demyelinating disorders showed lactate peak. 100% of pyogenic and fungal abscesses showed amino acid peak.

Graph 2: Bar graph showing case distribution based on metabolite distribution of various lesions.

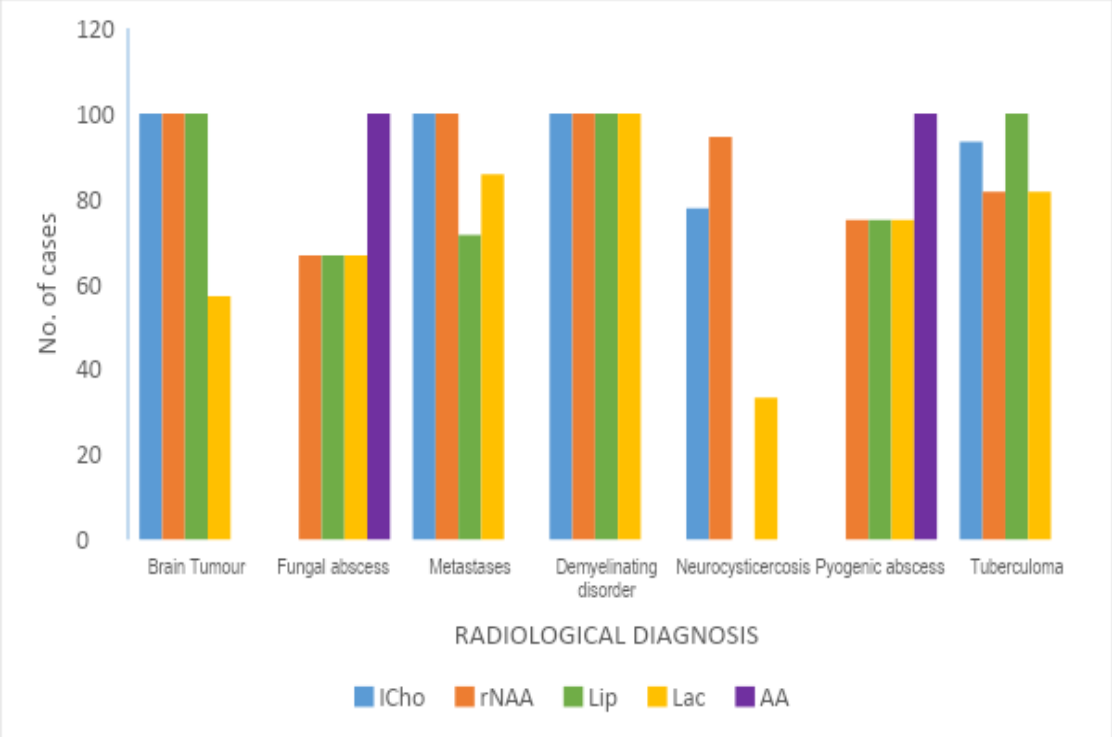

Table 3: TB MRS V/S TB follow up

TB MRS	TB Follow Up				Total	
	Non TB Follow up		TB Follow up			
	No.	%age	0	%age	No.	%age
Non TB MRS	36	37.50	60	62.50	96	96.00
TB MRS	4	100.00	0	0.00	4	4.00
Total	40	40.00	60	60.00	100	100.00

κ : 0.915; p=0.001

Sensitivity	100.00	Specificity	90.00
Positive predictive value	93.75	Negative predictive value	100.00
Accuracy	96.00		

While sensitivity, specificity, PPV and NPV of MR spectroscopy in detecting tuberculomas was increased to 100%,90%,93.75% and 100% respectively with accuracy upto 96%. There was strong agreement between MR spectroscopy and TB follow up. The kappa and p values were 0.915 and <0.001 respectively, which are significant and hence MRS was efficient in detecting tuberculomas in our study.

Table 4: NCC MRS V/S NCC follow up

NCC MRS	NCC Follow up				Total	
	Non NCC Follow up		NCC Follow up			
	No.	%age	No.	%age	No.	%age
Non NCC MRS	82	95.35	4	4.65	86	86.00
NCC MRS	0	0.00	14	100.00	14	14.00

Total	82	82.00	18	18.00	100	100.00

κ : 0.852; p=0.001

Sensitivity	77.78	Specificity	100.00
Positive predictive value	100.00	Negative predictive value	95.35
Accuracy	96.00		

While sensitivity, specificity, PPV and NPV of MR spectroscopy in detecting NCC increased to 77.78%, 100%, 100%, 95.35% respectively with accuracy upto 96%.The kappa and p values were 0.852 and <0.001,which were both highly significant and hence MR spectroscopy was efficient in diagnosis of NCC in our study.

Table 5: DMD MRS V/S DMD follow up

DMD MRS	DMD FOLLOW UP				Total	
	Non DMD Follow up		DMD Follow up		No.	%age
	No.	%age	No.	%age		
Non DMD MRS	99	100.00	0	0.00	99	99.00
DMD MRS	0	0.00	1	100.00	1	1.00
Total	99	99.00	1	1.00	100	100.00

κ : 0.823; p=0.001

Sensitivity	100.00	Specificity	100.00
Positive predictive value	100.00	Negative predictive value	100.00
Accuracy	100.00		

The sensitivity, specificity, PPV and NPV of MRS in detecting demyelinating disorder was 100%, 100%, 100% and 100% respectively with accuracy upto 100%. The MRS revealed kappa and p values1.0and<0.001 respectively, both of which are highly significant, hence conventional MRI was efficient in detecting demyelinating disorders in our study.

TABLE 6: METS MRS V/S METS follow up

METS MRS	METS Follow Up				Total	
	Non METS Follow up		METS Follow up			
	No.	%age	No.	%age	No.	%age
Non METS MRS	93	100.00	0	0.00	93	93.00
METS MRS	0	0.00	7	100.00	7	7.00
Total	93	93.00	7	7.00	100	100.00

κ : 1.000 p=0.001

Sensitivity	100.00	Specificity	100.00
Positive predictive value	100.00	Negative predictive value	100.00
Accuracy	100.00		

The sensitivity, specificity, PPV and NPV of MR spectroscopy in detecting metastases increased to 100%, 100%, 100%, 100% respectively with accuracy upto 100%. The kappa and p values were 1.0 and <0.001 respectively, both of which are highly significant. Hence, MRS was efficient in detecting metastases in our study.

Table 7: Brain tumour MRS V/S brain tumour follow up

Brain Tumour MRS	Brain Tumour Follow up				Total	
	n Brain Tumour Follow Up		Brain Tumour Follow up			
	No.	%age	No.	%age	No.	%age
Non Brain tumour MRS	93	100.00	0	0.00	93	93.00
Brain tumour MRS	0	0.00	7	100.00	7	7.00
Total	93	93.00	7	7.00	100	100.00

κ : 1.000; p=0.001

Sensitivity	100.00	Specificity	100.00
Positive predictive value	100.00	Negative predictive value	100.00
Accuracy	100.00		

While sensitivity, specificity, PPV and NPV of MR spectroscopy in detecting brain tumour increased to 100%, 100%, 100%, 100% respectively with accuracy upto 100%. The kappa and p values were 1.0 and <0.001 respectively, both of which are highly significant. Hence, MRS was efficient in detecting brain tumours in our study.

Table 8: Fungal abscess MRS V/S fungal abscess follow up

Fungal Abscess MRS	Fungal Abscess Follow up				Total	
	Fungal Abscess Follow up		ngal Abscess Follow up			
	No.	%age	No.	%age	No.	%age
Non Fungal abscess MRS	97	100.00	0	0.00	97	97.00
Fungal abscess MRS	0	0.00	3	100.00	3	3.00
Total	97	97.00	3	3.00	100	100.00

κ : 1.000; p=0.001

Sensitivity	100.00	Specificity	100.00
Positive predictive value	100.00	Negative predictive value	100.00
Accuracy	100.00		

While sensitivity, specificity, PPV and NPV of MR spectroscopy in detecting fungal abscess increased to 100%, 100%, 100%, 100% respectively with accuracy upto 100%. The kappa and p values were 1.0 and <0.001 respectively, both of which were highly significant indicating MRS was efficient in detecting fungal abscesses in our study.

Table 9: Pyogenic Abscess MRS V/S pyogenic abscess follow up

Pyogenic Abscess MRS	Pyogenic Abscess Follow Up				Total	
	ogenic Abscess Follow up		genic Abscess Follow up			
	No.	%age	No.	%age	No.	%age
Non Pyogenic abscess MRS	96	100.00	0	0.00	96	96.00
Pyogenic abscess MRS	0	0.00	4	100.00	4	4.00
Total	96	96.00	4	4.00	100	100.00

κ : 0.658; p=0.001

Sensitivity	100.00	Specificity	100.00
Positive predictive value	100.00	Negative predictive value	100.00
Accuracy	100.00		

While sensitivity, specificity, PPV and NPV of MR spectroscopy in detecting pyogenic abscess increased to 100%,100%,100%,100% respectively with accuracy upto 100%.The kappa and p values were 1.0 and <0.001 respectively, both of which were highly significant indicating MRS was efficient in detecting pyogenic abscesses in our study.

DISCUSSION

TUBERCULOMA

Out of 100 cases evaluated, tuberculomas were seen in 60 cases. Among the 60 cases, 50% cases were females and 50% cases were males. On T1 weighted images, 70% of the cases presented as hypointense lesions whereas 30% presented as isointense lesions. On T2 weighted images, 81.66% presented as hypointense lesions, 11.66% presented as hyperintense lesions and 6.66% presented as heterogenous lesions. Most of the lesions (88.33%) showed no diffusion restriction while few (11.66%) presented with diffusion restriction on DWI/ADC maps according to study by Maheshwarappa RP et al.[6]

Most of these lesions were conglomerate lesions with irregular ring like enhancement. All the lesions showed peripheral ring-like enhancement on post contrast scans. MRS showed increased levels of choline in 93.33% cases, reduced NAA in 81.66% cases, lipid peak in100% cases and lactate peak in 81.66% cases. Therefore, our study shows that lipid peak is sensitive in diagnosing tuberculomas on MR spectroscopy in accordance with studies conducted by Seth R et al in 2010.[7]

Our study regarding the tubercular lesions also demonstrates that there is increase in choline levels, decrease in N acetyl aspartate level and lipid peak in the lesions as concluded by study conducted by Shetty G et al in 2014.[8] Elevated Choline/ Creatine ratio was seen in 56/60 cases of tuberculomas and only 5/18 cases of neurocysticercosis which indicates that elevated Ch/Cr ratio >1 has high sensitivity for detecting tuberculoma but low specificity in differentiating from neurocysticercosis as per study conducted by Verma SR et al in 2017.[9]

NEUROCYSTICERCOSIS

Out of 100 cases, 18 cases were neurocysticercosis out of which 66.67% of cases were females and 33.33% of cases were males. On T1 weighted images, 66.67% of these lesions were hypointense, 22.22% of these lesions were iso in tense and11.11% of these lesions were hyperintense.

Lesions that were hyperintense on T1 weighted images were hypointense on T2 weighted images. These were calcified lesions of neurocysticercosis. On DWI/ADC maps, these lesions show 77.77% of neurocysticercosis lesions show no diffusion restriction while 22.22% of them showed restricted diffusion.

On MR spectroscopy, the lesions show reduced NAA in 94.44% cases and increased choline in 77.77% cases.Lactate peak is seen in 33.33% of cases.This interpretation is in accordance with study conducted by Archana R et al in 2018.[10] Choline/Creatine ratio is less than 1 in most of the lesions which is 77.77% of the lesions in accordance with the study conducted by Pretell EJ et al in 2005.[11]

PYOGENIC ABSCESS

Out of 100 cases, 4 cases were pyogenic abscesses. 2 (50%) each of these cases were seen in males and females. All these lesions were hypointense on T1 weighted images, hyperintense on T2 weighted images and showed diffusion restriction.

On MR spectroscopy, all these lesions(100%) showed amino acids peak at 0.9 ppm. 75% of

cases showed reduction in NAA levels (3 cases),75% of cases showed lipid peak(3 cases) and 75% cases showed lactate peak(3 cases).Pyogenic abscesses showed restriction of diffusion on DWI/ADC maps in accordance with the studies conducted by Mishra AM et al in 2004.[12] Pyogenic abscesses show lipid and lactate levels at 1.3ppm and amino acid levels at 0.9ppm corresponding to the study conducted by Gupta RK et al in 2001.[13] Presence of amino acids on in vivo 1H-MR spectroscopy is a sensitive marker of pyogenic abscess and is in accordance with the study conducted by D Pal et al in2010.[14]

FUNGAL ABSCESS

Out of 100 cases, 3cases were diagnosed to be fungal abscesses. The patients presented with invasive sinusitis with intracranial manifestations presenting as intracranial abscesses as described by Orlowski HL et al in his study in 2017.[15] The wall of the abscesses were irregular compared to the pyogenic abscesses on post contrast scans, which mostly had smooth walls as demonstrated by Luthra G et al in their study in 2007.[16]

All cases presented as hypointense lesions on T1 weighted images, hyperintense lesions on T2 weighted images and showed restriction on DWI/ADC maps.

On MR spectroscopy, all the lesions (100%) showed amino acids peak at 0.9ppm. Reduced NAA, lipid and lactate peaks were seen in 75% cases each(2 out of 3 cases). Fungal abscesses show lipid, lactate and amino acids peaks as studied by Luthra G et al in2007.[16]

BRAIN TUMOURS

Out of 100 cases, 7 cases were diagnosed to be malignancies i.e., Glioblastoma multiforme. Most of these lesions appear hypointense on T1 weighted images (71.42%) and 28.57% cases appear hyperintense on T1 weighted images due to haemorrhagic component within them. All the lesions are hyper intense on T2 weighted images. Diffusion restriction is not seen in 71.42% of lesions and is seen in 28.57%of lesions on DWI/ADC maps. On post contrast scans, there is irregular peripheral enhancement.

On MR spectroscopy, all the lesions show choline peak, reduced NAA levels and lipid peaks(100%)while lactate peak is seen in 57.14% of cases as in a study by Ramadan S et al in2011.[17]

Involvement of the adjacent cortex with FLAIR signal intensity abnormality without enhancement was seen in all cases of glioblastoma multiforme and was not seen in metastases in accordance with study performed by Tang YM et al in 2006.[18]

METASTASES

7 cases out of 100 cases were diagnosed to be metastases. All the lesions were hypointense on T1 weighted image. They were heterogenous to hyperintense on T2 weighted images. All the lesions showed diffusion restriction on DWI/ADC maps with thick, irregular type of ring enhancement noted after contrast administration.

MR spectroscopy shows choline peak with reduction in NAA in all the cases (100%), lipid peak in 83.34% cases and lactate peak in 83.34%cases as in a study conducted by Chernov MF et al in 2006.[19]

DEMYELINATING DISORDER

1 case of multiple sclerosis was identified in our study in a female aged 35years who presented with ataxia. She had T1 hypointense lesions, T2/FLAIR hyperintense lesions in the periventricular white matter giving typical “Dawson’s fingers” appearance. The lesions

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showed no restriction on diffusion and showed peripheral enhancement on post contrast scans as in studies conducted by Capello E et al in 2001.[20]

MR spectroscopy revealed reduced levels of NAA, increased levels of choline along with lipid and lactate peaks in accordance with the study conducted by Cianfoni A et al in 2007.[21]

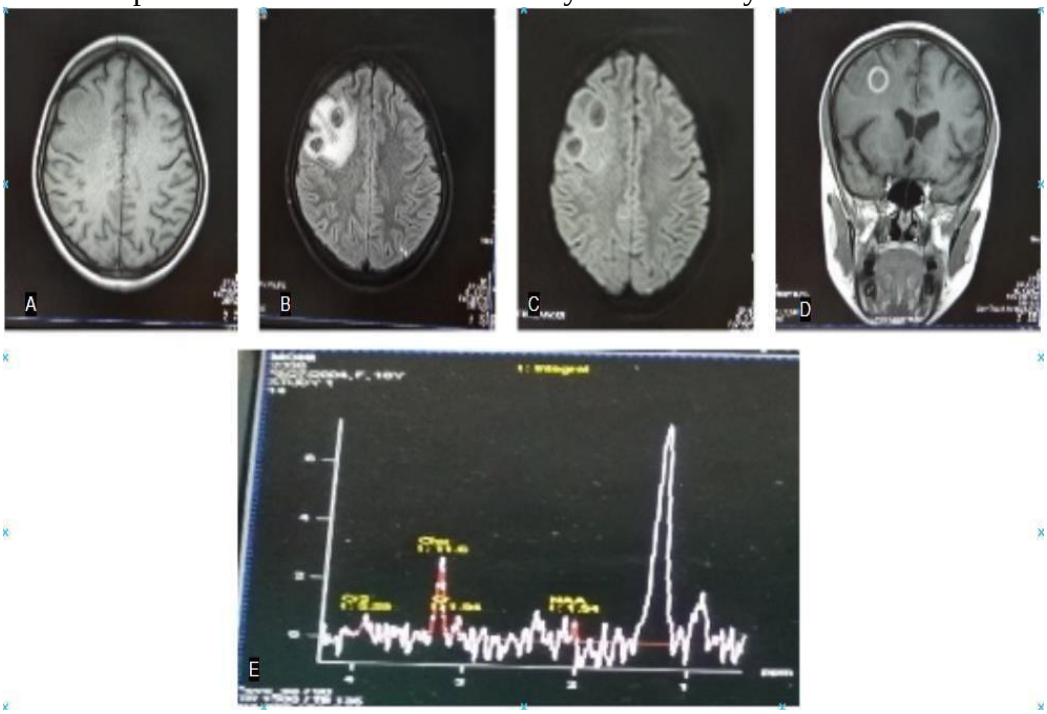

Figure 1: Tuberculoma

A, Axial T1 weighted image showing hypointense lesions in the right frontal region.**B,** Axial FLAIR image showing two well-defined hypointense round to oval lesions with peripheral oedema. **C,** DWI map shows no diffusion restriction.**D,** Coronal T1 weighted post contrast scan showing ring-like enhancement of the lesion. **E,** MR spectroscopy at short TE (30ms) shows lipid/ lactate peak at 1.3ppm with choline/creatine ratio of more than 1.

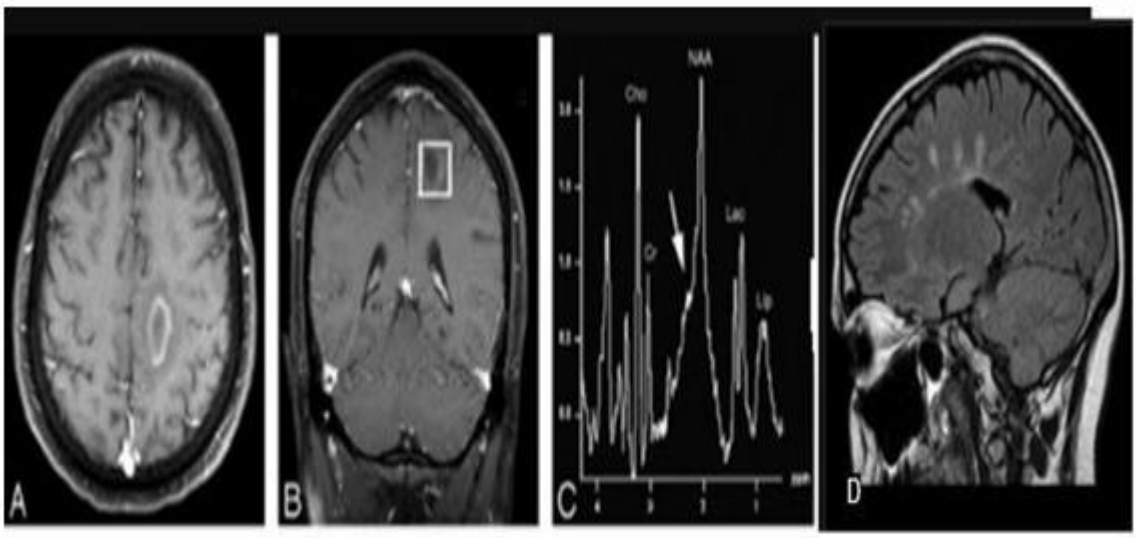

Figure 2: Demyelinating disorder(multiple sclerosis)

A, Axial T1 weighted post contrast image showing a ring-enhancing lesion in the left frontal

lobe with surrounding vasogenic oedema.B, Voxel localization for MR spectroscopy of the lesion.C, On MR spectroscopy, the lesion shows marked elevation of choline, lactate and lipid metabolites. D, FLAIR image showing the classical ”Dawson’s fingers” appearance.

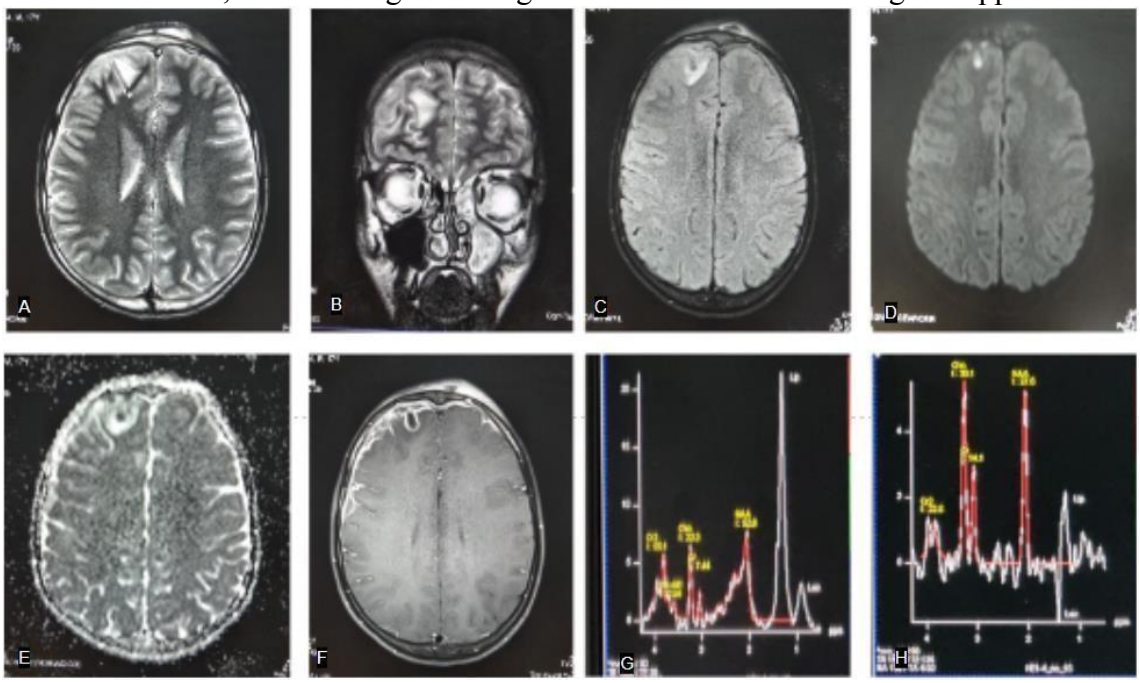

Figure 3: Fungal Abscess

A, Axial T2 weighted image showing a round to oval hyper intense lesion in the right frontal region.B, Coronal T2 weighted image showing a round to oval hyperintense lesion in the right frontal region.C, Axial FLAIR image showing a hypointense with perilesional edema.D and E, DWI and ADC maps respectively, showing diffusion restriction.F, Axial T1 weighted post contrast image showing a ring-like enhancement of a lesion in a patient of invasive fungal sinusitis. G and H, MR spectroscopy at short TE (30ms) and long TE (135ms) respectively, shows lipid and lactate peak at shortTE (30ms) within version of lactate peak at higher TE(135ms).

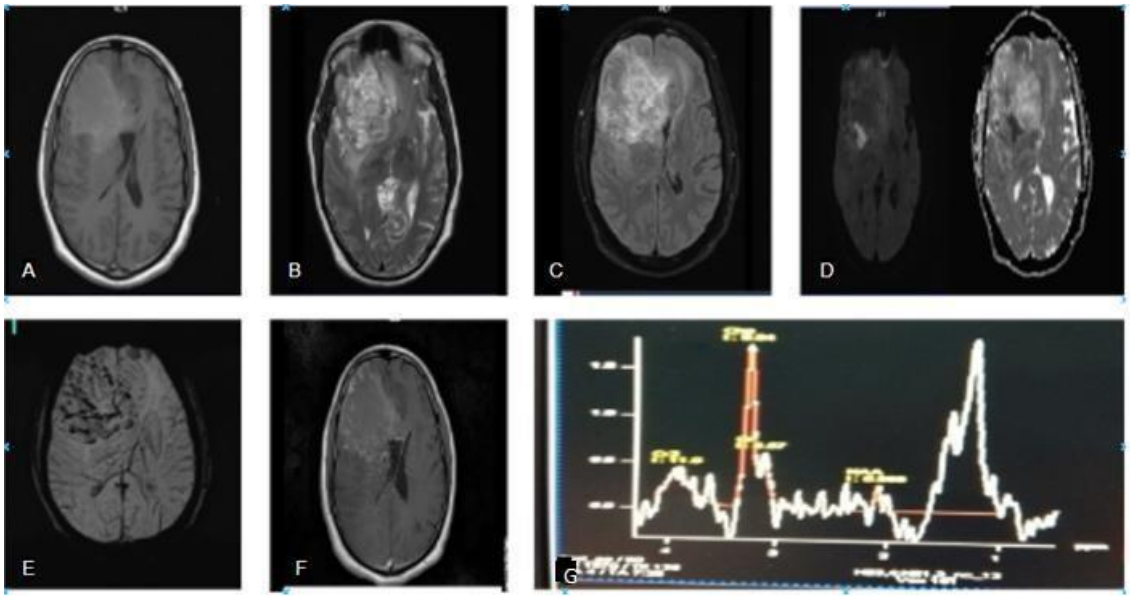

Figure 4: Brain tumour (glioblastoma multiforme)

A, Axial T1 weighted image showing a well-defined, irregular, hyperintense lesion in the right frontal region.Band C, Axial T2 weighted andFLAIR images respectively, showing the well-defined, irregular, heterogenously hyperintense lesion with mild perilesional oedema.D, DWI/ADC maps showing a small area of diffusion restriction in the lesion. E, SWI shows multiple linear blooming foci suggestive of hemorrhagic component.F, Axial T1 weighted post contrast image showing peripheral enhancement.G, MR spectroscopy shows an increased Choline/creatine ratio: 2.08 (>1. 5) with a choline peak.

SUMMARY AND CONCLUSION

Hundred patients with ring enhancing lesions were evaluated using MRI and MR spectroscopy. Various parameters of ring enhancing lesions were evaluated and the spectrum of findings on MRI and MRS were assessed. The patients were followed up for clinical improvement based on the line of treatment. Few cases requiring histopathological correlation were followed up based on biopsy reports and post operative histopathological reports. The following conclusions were drawn.

Conventional imaging (T1, T2, FLAIR, DWI, ADC and post contrast sequences in our study) plays a very important role in characterization of ring enhancing lesions.

Hypointensity on T2 weighted images with lipid peak at 1.3 ppm on MRS favours diagnosis of tuberculoma.Hyperintensity on T2 weighted images with reduced NAA levels and absence of lipid peak at 1.3ppm favours diagnosis of neurocysticercosis. Eccentric hyperintense scolex on T1 weighted images can sometimes be seen. Abscesses (both pyogenic and fungal) appear as hyperintense lesions surrounded by perilesional hypointense signal suggestive of oedema on T2 weighted images with complete diffusion restriction on DWI/ADC maps. MR spectroscopy shows lipid, lactate and amino acids peaks.Brain tumours and metastases show T2 hyperintense signal. Glial tumours (Glioblastoma multiforme in our study) show no restriction of diffusion on DWI/ADC maps while metastases show restricted diffusion. Both the lesions show choline peak and reduced NAA levels. Lipid and lactate peaks may also be seen.

Lipid and lactate peak is more often observed in infective and inflammatory conditions.

Choline/Creatine ratio is moderately elevated in few non-neoplastic lesions while ratios >1.5 is more common in malignant and metastatic lesions.

CONCLUSION

Conventional MRI is a great tool in making a sufficient differential diagnosis of the ring enhancing lesions of the brain, but MR spectroscopy further helps in knowing the chemical nature of lesions and accurate diagnosis of brain tumours. This facilitates the clinician to plan the best line of treatment thus reducing the suffering and morbidity of the patients.

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