IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 7 Ser.3 (July. 2023), PP 44-51
www.iosrjournals.org

Deciphering The Signature Of Magnetic Resonance Spectroscopy In Ring-Enhancing Brain Lesions – A Metabolic Alchemy.

Praveen Kumar Tamminana[1], Lavanya Kilaparthi[2]
(1 - Senior Resident, Department of Radiology, Maharajah's Institute of Medical Sciences, Vizianagaram, Andhra Pradesh, India)
(2 - Post Graduate, Department of Radiology, Maharajah's Institute of Medical Sciences, Vizianagaram, Andhra Pradesh, India)

Abstract:
Background: *Conventional Magnetic Resonance Imaging (MRI) Often Presents Challenges In Diagnosing The Diverse Range Of Ring Enhancing Lesions Found In The Brain. The Use Of Advanced Techniques Such As Magnetic Resonance Spectroscopy (MRS) Can Improve The Success Rates Of Diagnosis. This Prospective Observational Study Was Aimed To Evaluate The Role Of MRS In Assessing Different Types Of Ring Enhancing Brain Lesions.*
Materials And Methods:*The Study Included 100 Patients Aged Between 5-80 Years Who Were Identified With Ring Enhancing Brain Lesions On Contrast MROr CTStudies. MRS Evaluations Were Performed On These Patients. Categorical Data Was Presented 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 Analyzed In Relation To The Type Of Lesion Observed In The Patients.*
Results:*Among The 100 Patients Examined, The Most Common Pathologies Were Tuberculoma (36%) And Neurocysticercosis (22%). Tuberculoma Patients Exhibited Higher Levels Of Lipid Peak And Choline/Creatine Ratio Ranging From >1 To 2. Neurocysticercosis Cases Showed Increased Lactate, Succinate, And Choline Peaks, With No Or Minimal Lipid Peak. Primary Brain Tumors Presented High Choline Peaks And Elevated Choline/Creatine Ratios (>2). Metastasis Was Characterized By Increased Choline Peak. Cerebral Abscess Showed Elevated Levels Of Amino Acids And Lactate Peak.*
Conclusion:*MRS Proved To Be An Accurate Diagnostic Tool In Determining The Different Types Of Ring Enhancing Brain Lesions. This Accuracy Can Aid In Developing Appropriate Treatment Plans Without Any Uncertainty.*
Key Word: *Neurocysticercosis, Tuberculoma, MRS, Choline, Creatine, NAA.*

Date of Submission: 26-06-2023 Date of Acceptance: 06-07-2023

I. INTRODUCTION

Brain imaging has a wide range of imaging findings that pose a great diagnostic challenge to radiologists, ring enhancing lesions being common entities that make a radiologist go for a broad spectrum of differentials which are very difficult to narrow down to a specific diagnosis[1,2,3]. These lesions are typically located at the grey-white matter junction of the brain parenchyma in the sub-cortical area. Lesions can be single or multiple in various locations. On MRI, they are characterized by a non-enhancing center surrounded by a contrast enhancing halo. The central region may be of low intensity signal on T1 and a high intensity signal on T2 weighted images [1].

Differentiating between different types of ring-enhancing lesions using conventional MRI can pose challenges, as this technique is unable to discern between neoplastic, non-neoplastic, and infectious lesions [4]. Moreover, conventional MRI lacks the ability to provide insights into tumoral vascularity, metabolism, and cellularity [5,6]. To address these limitations, advanced imaging techniques such as Diffusion Weighted Imaging (DWI), perfusion imaging, and proton Magnetic Resonance Spectroscopy (1H-MRS) have been employed for the purpose of differential diagnosis, albeit with varying success rates. By combining these advanced techniques with conventional MRI, the specificity in lesion detection can be enhanced.[4]

Magnetic Resonance Spectroscopy (MRS) is a non-invasive technique that provides valuable information about tissue chemistry. It offers the advantage of being patient-friendly, as it does not involve ionizing radiation. Instead of producing images, MRS captures high-quality spectra. It enables the measurement of various metabolites such as NAA, lactate, phosphocreatine, choline-containing compounds, and adenosine

triphosphates. MRS quantification relies on comparing relative spectral peak regions to reference metabolites, which generally show minimal variation with most pathologies. Additionally, absolute metabolite concentrations can be measured by referencing them to the concentration of unbound water in the tissue, assuming that this concentration remains relatively constant across different diseases [7]. These features enhance the specificity and sensitivity of MRS compared to MRI [8-10].

Differentiating between tuberculoma and neurocysticercosis, two similar-looking ring enhancing lesions of the brain, remains a challenge for radiologists using conventional MRI sequences [11,12]. However, a study conducted by Morales H et al. demonstrated that MRS could effectively differentiate tuberculoma from other lesions based on metabolite levels [13]. Similarly, Sharma BB and Sharma S conducted a study where CT and MRI scans showed similarities between tuberculoma and neurocysticercosis lesions, but MRS successfully differentiated between the two based on metabolite levels, in addition to considering factors such as location, number of lesions, enhancement pattern, and constitutional symptoms [14].

Given the widespread use of MRS imaging in hospitals and imaging centers, this study aimed to differentiate tuberculoma and neurocysticercosis, as well as characterize other ring enhancing lesions of the brain in Pondicherry, India, using MRS. The study focused on distinguishing neoplastic, infectious, inflammatory, and vascular lesions in the brain. Analysis of metabolite peaks and the choline/creatine ratio in the ring enhancing lesions was conducted.

II. MATERIAL AND METHODS

Study Design: Prospective observational study

Study Location: The study has been conducted at a tertiary care teaching hospital, in the department of Radiology, Maharajah's Institute of Medical Sciences, Vizianagaram, Andhra Pradesh, India.

Study Duration: January 2020 to April 2023.

Sample size: 100 patients.

Inclusion Criteria:
Age between 5 - 80 years.
Diagnosed with ring enhancing lesions of brain based on contrast CT or contrast MRI studies.

Exclusion Criteria:
Patients with a history of claustrophobia.
Patients with metallic implants, cardiac pacemakers.
Patients with chronic kidney disease.
Pregnant women.

Methodology:

The patients aged between 5 to 80 years, who came to the department of radio diagnosis for CT or MRI brain study and were detected of having ring enhancing lesions on contrast study were taken. They and their attendants were well informed about the study and informed consent was obtained. Detailed questionnaire containing demographic data and any significant past and family history was given to them and the particulars were recorded. The patients who underwent MRI scan proceeded to have MR spectroscopy. The patients who underwent contrast CT scan were sent to MR Imaging with MRS.

MRI scan was performed using the MR Philips Ingenia 1.5 Tesla unit. Conventional spin echo sequences, axial T1, T2 and Fluid Attenuated Inversion Recovery (FLAIR): Coronal T2; Sagittal T1; Post-contrast T1 axial, coronal and sagittal; Post contrast 3D FLAIR; Diffusion Weighted Imaging (DWI); Susceptibility Weighted Imaging (SWI). Epilepsy protocol containing additional T2 oblique coronal and T1 3D Inversion Recovery sequences was included in patients presenting with seizures.

MR spectroscopy was performed with same unit, at echo time (TE) of 20ms and 144ms. Single voxel MRS was used, placing the voxel on the lesion in such a manner that the maximum area of the lesion, its margin and the normal brain tissue were covered. Spectroscopy was not performed in small lesions closer to the bone.

Statistical analysis: Statistical analysis was done using SPSS version 21. Categorical data was represented as frequency in percentage. Chi square test was used to analyse nonparametric data wherever necessary and p value <0.05 is taken as significant.

III. RESULTS

Age and Sex distribution: The age group of 21-30 years was the most represented among the included patients, while distribution of other age groups is almost even as shown in Table/Figure 1 with almost two thirds of patients being males in the study subjects, as shown in Table/Figure 2.

Table 1: Age distribution of patients

Age (years)	No. of patients (%)
0-10	12 (12%
11-20	14 (14%)
21-30	20 (20%)
31-40	12(12%)
41-50	14(14%)
51-60	16 (16%)
>60	12 (12%)

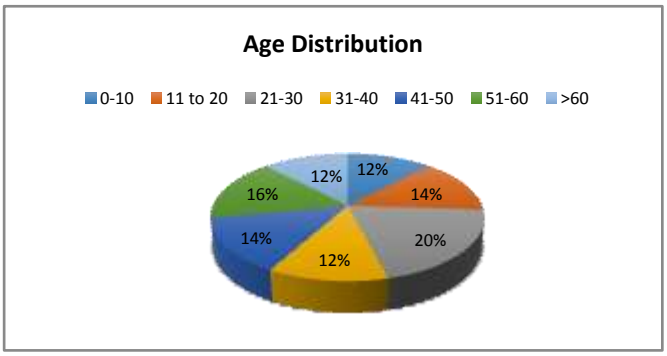
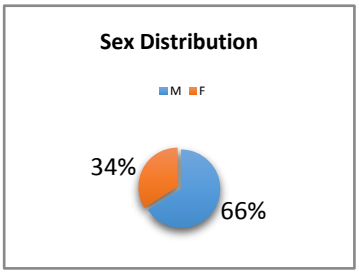


Table 2: Sex distribution.

Gender	
Male	66 (66%)
Female	34 (34%)



The most common clinical manifestation observed in the study was seizures, with 66 patients (66%) experiencing this symptom. Headache was the second most prevalent presentation, reported by 38 patients (38%), followed by vomiting in 24 patients (24%). Fever was observed in 22 patients (22%), while weakness was reported by 10 patients (10%) and ataxia by 4 patients (4%).

Among the included patients, the distribution of ring enhancing lesions was as follows: 26 patients (26%) had lesions on the right side of the brain, 40 patients (40%) had lesions on the left side, 30 patients (30%) had bilateral lesions, and 4 patients (4%) had lesions in the midline region. Regarding the number of lesions, 32 patients (32%) had a single lesion, 44 patients (44%) had 2-4 lesions, and 24 patients (24%) had more than 4 lesions in this study. In terms of lesion size, 60 patients (60%) had lesions smaller than 2 cm, 28 patients (28%) had lesions sized between 2-4 cm, and 12 patients (12%) had lesions larger than 4 cm.

Table 3: Number of lesions identified

No. of lesions	No. of patients
Single	32
2 to 4	44
> 4	24

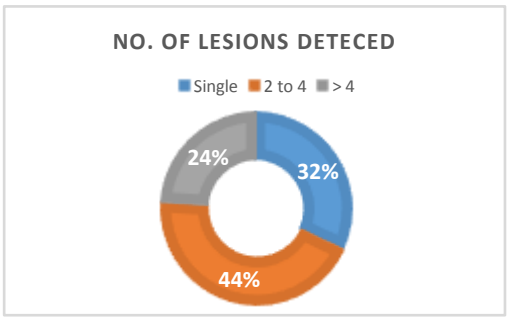


Table 4 : Size of the lesions

Lesion Size	No. of patients
<2 cm	60
2 – 4 cm	28
>4 cm	12

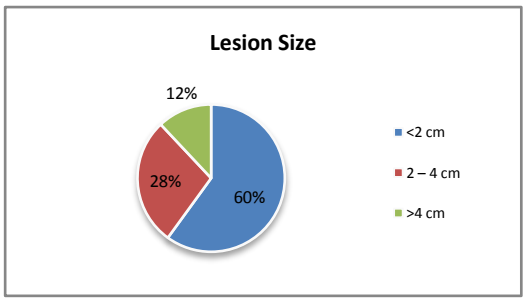


Table 5: Lesions diagnosed.

Lesion	Male patients	Female patients	Total
Tuberculoma	22	14	36
Neurocysticercosis	16	6	22
Metastasis	16	4	20
Primary brain tumor	8	8	16
Cerebral abscess	0	2	2
Tumefactive demyelination	2	0	2
Radiation necrosis	2	0	2

The majority of patients were diagnosed with tuberculoma (36%), with 16 patients having a single lesion and 20 patients presenting with multiple lesions. This was followed by neurocysticercosis (NCC) (22). The next dominant form of diagnoses were of neoplastic etiology, including primary (16) as well as secondaries (20). Cerebral abscess, demyelination, radiation necrosis constituted the rest of the diagnoses.

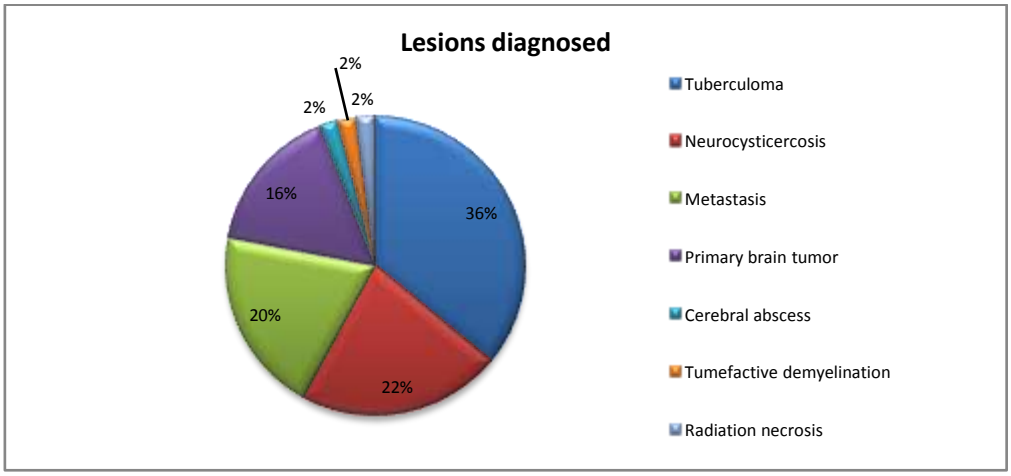
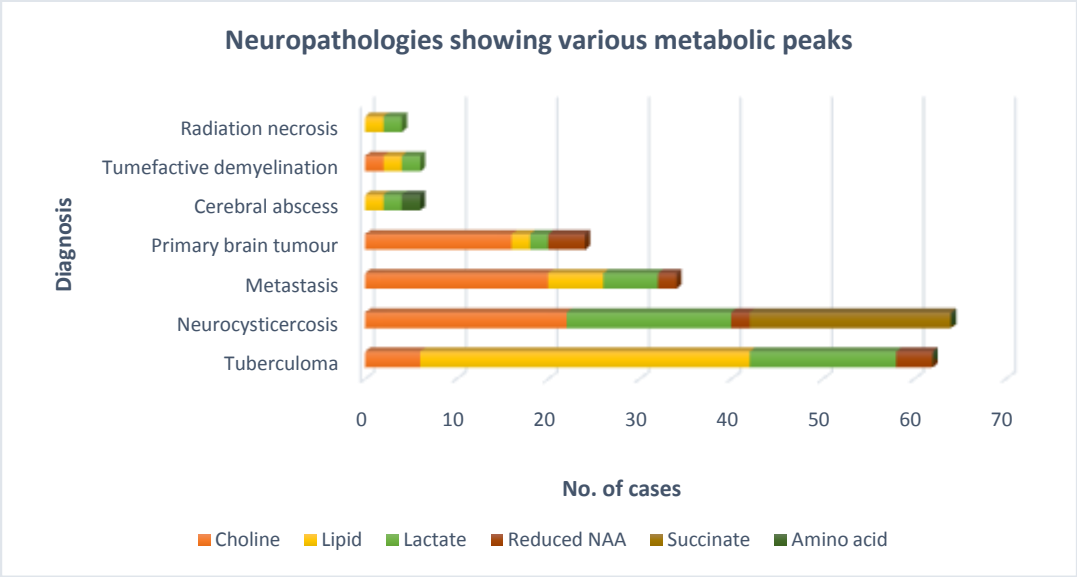


Table 6: Metabolite peaks seen in various neuropatholoogies

MRS diagnosis	Metabolite peak (No. of cases)					
	Choline	Lipid	Lactate	Reduced NAA	Succinate	Amino acid
Tuberculoma	6	36	16	4	0	0
Neurocysticercosis	22	0	18	2	22	0
Metastasis	20	6	6	2	0	0
Primary brain tumor	16	2	2	4	0	0
Cerebral abscess	0	2	2	0	0	2
Tumefactive demyelination	2	2	2	0	0	0
Radiation necrosis	0	2	2	0	0	0
Total	**66**	**50**	**48**	**12**	**22**	**2**



Out of 36 cases of tuberculoma, all the cases showed lipid peak while 16 of them also showed lactate peak.
All 22 cases of neurocysticercosiscases showed choline and succinate peak, while 9 of them also showed lactate peak.

All the neoplastic lesions, including both primary and secondary showed choline peak. However, lipid lactate peak was seen in 6 of metastatic lesions, but only shown by 2 of primary brain tumors.

All cerebral abscess cases showed lipid lactate peak as well as an aminoacid peak, but didn't show any other metabolite peaks.

Tumefactive demyelination showed lipid, lactate peak as well as choline peak.

Radiation necrosis showed only lipid lactate peak and didn't show any other peak.

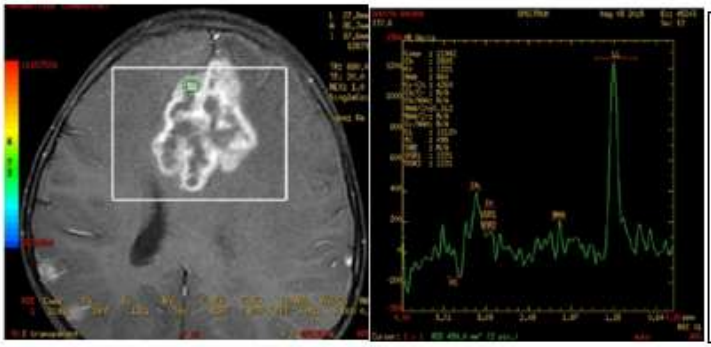
The highest peak observed in the spectra was for choline, which was prevalent in 66 patients (66%). It was statistically significant ($X^2 = 3.921$; $p<0.05$).

Table 7: Choline/creatine ratio of various lesions

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

Choline/creatine ratio is elevated in all the 16 cases of primary brain tumor cases, while it was 1 to 2 in all the tuberculoma cases.
18 out of 22 NCC cases showed low choline creatine ratio (<1)

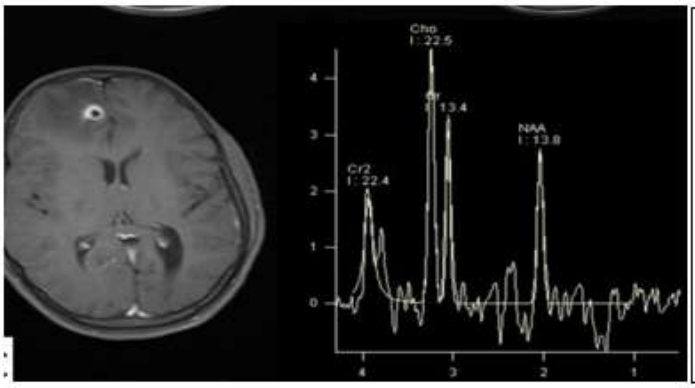
Representative Case Images



MRI brain showing realtively large, ring enhancing lesion in left frontal parafalcine region.

MR spectroscopy showing lipid lactate peak.

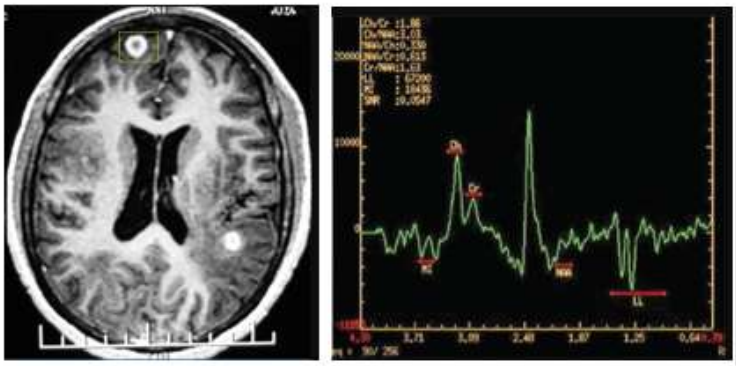
Case diagnosed as Tuberculoma



MRI brain showing small ring enhancing lesion in right frontal lobe, in parafalcine region.

MR spectroscopy showing choline peak.

Case diagnosed as Neurocysticercosis



MRI brain showing small ring enhancing lesion in anterior part of left frontal lobe.

MR spectroscopy showing succinate peak

Case was diagnosed to be Neurocysticercosis

IV. DISCUSSION

The conventional MRI imaging does not distinguish between the different causes of intracranial ring enhancing lesions, making it difficult to differentiate between neoplastic and non-neoplastic lesions. However, Magnetic Resonance Spectroscopy (MRS) provides a more accurate diagnosis due to its higher sensitivity (87.5%) and specificity (93.3%), although success rates may vary [15,16].

In this particular study, 100 patients with ring enhancing brain lesions were evaluated using MRS. The mean age of the patients was 36.76±21.62 years, with 20% falling in the 21-30 age group. A significant majority of the participants were male (66%). Among the patients, seizures were the most common presentation (66%), followed by headache (38%) and vomiting (24%). These findings were similar to a study conducted by Seth S et al., which also reported seizures as the most common symptom (80%), followed by headache (28%) and vomiting (18%) [4]. Another earlier study by Elsadway ME and Ibrahim Ali H found that the majority of patients experienced headache, although the specific symptoms varied among individuals [2].

The most prevalent lesions in this study were tuberculomas (36%) and neurocysticercosis (22%). These findings align with previous studies conducted by Bava JS et al. and Mirchandani S et al. [17,18].

MRS plays a crucial role in identifying various metabolites (such as choline, lipid, lactate, reduced NAA, amino acids, creatine, and succinate) that assist in determining the specific type of ring enhancing brain lesion [7]. Tuberculoma and neurocysticercosis share clinical and neuroimaging similarities, posing a diagnostic

challenge for radiologists. To differentiate and characterize these lesions, the key lies in the distinct metabolite peaks they exhibit. Tuberculomas typically display lipid peaks and a choline/creatine ratio greater than 1 [3,11,12,19]. Conversely, neurocysticercosis is characterized by elevated levels of lactate, succinate, and choline, while lipid peaks are either absent or insignificant [19,20]. This differentiation based on metabolite patterns aids in resolving the diagnostic enigma associated with distinguishing between tuberculoma and neurocysticercosis.

In this study, 18 patients diagnosed with tuberculoma exhibited higher levels of lipid peaks, which can be attributed to the presence of lipid fractions in tuberculosis bacillus, as reported in previous studies [11,21]. These tuberculoma patients showed increased lipid/lactate peaks and decreased choline/NAA peaks. On the other hand, patients with neurocysticercosis displayed elevated lactate, succinate, and choline levels, with little to no lipid peaks. Primary brain tumors were associated with high choline peaks, while cerebral abscesses showed lactate and amino acid peaks. These findings align with a study conducted by Elsadway ME and Ibrahim Ali H [2]. In the case of metastasis, an increase in choline peak was observed, consistent with earlier findings [18,22]. However, these results contradict the study by Elsadway ME and Ibrahim Ali H, where a mild elevation in choline/NAA ratio and increased lipid and lactate levels were noted. This discrepancy may be attributed to the encapsulation of metastatic lesions, which do not exhibit higher choline signals [23,24]. Tumefactive demyelination and radiation necrosis were associated with reduced peaks of choline, lipid, and lactate in a few patients, similar to findings reported by Shah R et al. [25].

Overall, abnormal choline metabolism was identified in 66% of the patients, mainly seen in cases of cancer, followed by lipid peaks (50%) associated with bacterial infections [26]. Lactate peaks were elevated in 48% of patients, as lactate acts as a fuel for tumor growth and metastasis progression +. Decreased NAA levels detected by MRS have been previously linked to compromised neuronal metabolism, and in this study, 12% of patients showed reduced NAA levels [28].

An increase in the choline/creatine ratio, rather than the absolute concentration of choline, indicates higher cellular turnover and density associated with tumor cell proliferation. Therefore, the choline/creatine ratio is commonly used to differentiate between low-grade and high-grade tumors. A ratio greater than 2.0 is considered a strong indicator of a high-grade neoplasm [29,30]. In this study, a higher choline/creatine ratio (>2) was observed in 16% of patients with primary brain tumors and 36% of subjects with tuberculoma, indicating a higher likelihood of tumor characteristics. These findings align with previous studies [31,32].

Incorporating MRS into standard MRI protocols during initial diagnostic imaging could enhance the accuracy of diagnosis. However, the implementation of MRS has been hindered by the lack of standardized acquisition protocols, analysis techniques, and quality control measures for specific clinical scenarios. Challenges include processing and presenting information, assessing spectrum quality, and accurately interpreting data. Currently, there is limited research available to support the implementation of MRS as a standard diagnostic tool, highlighting the need for further investigation [33].

In this study, MRS was proved to be valuable in differentiating between neoplastic and infectious brain lesions, particularly in cases of tuberculoma and neurocysticercosis. This accurate diagnosis facilitated appropriate medical management for the patients, allowing for more informed decision-making.

Limitation(s)

This study had certain limitations, including a relatively small sample size. Conducting future studies with larger sample sizes would allow for testing correlations between metabolite peaks and specific types of ring enhancing lesions. Gender bias could be addressed by including a more balanced distribution of male and female participants in future studies. Additionally, histopathological analysis could not be performed to confirm the diagnoses, as brain biopsy was not feasible due to the risk of injury. Furthermore, MRS was not utilized for small lesions.

V. CONCLUSION

Magnetic Resonance Spectroscopy (MRS) has shown promise as a valuable tool for diagnosing ring enhancing brain lesions. It has provided guidance in distinguishing between lesions with similar presentations, such as tuberculoma and neurocysticercosis. However, additional research is needed to establish MRS as a primary diagnostic tool in this context. In the meantime, MRS sequences can be used as a supplementary tool alongside other conventional techniques. Further studies will contribute to the understanding and utilization of MRS in the accurate diagnosis of these lesions.

References

[1]. Smirniotopoulos JG, Murphy FM, Rushing EJ, Rees JH, Schroeder JW. Patterns Of Contrast Enhancement In The Brain And Meninges. Radiographics. 2007;27(2):525-51.
[2]. Elsadway ME, Ibrahim Ali H. Verification Of Brain Ring Enhancing Lesions By Advanced MR Techniques. Alexandria J Med. 2018;54(2):167-71.
[3]. Garg RK, Sinha MK. Multiple Ring-Enhancing Lesions Of The Brain. J Postgrad Med. 2010;56(4):307-16.

[4]. Seth S, Mahesh P, Raju A. Role Of MRI And MR Spectroscopy In The Evaluation Of Ring Enhancing Lesions In Brain. Glob J Res Anal. 2017;6(6):127-29.
[5]. Burger PC. Malignant Astrocytic Neoplasms: Classification, Pathologic Anatomy, And Response To Treatment. Semin Oncol. 1986;13(1):16-26.
[6]. Choudary GP, Lakshmi AY, Bodagala VL, Chandra VV, Thota N, Chowhan AK. Perfusion-Weighted Imaging In Differentiating Ring-Enhancing Lesions In Brain. J Dr NTR Univ Health Sci. 2019;8(3):162-69.
[7]. Condon B. Magnetic Resonance Imaging And Spectroscopy: How Useful Is It For Prediction And Prognosis? EPMA J. 2011;2(4):403-10.
[8]. Mishra AM, Gupta RK, Jaggi RS, Reddy JS, Jha DK, Husain N, Et Al. Role Of Diffusion-Weighted Imaging And In Vivo Proton Magnetic Resonance Spectroscopy In The Differential Diagnosis Of Ring-Enhancing Intracranial Cystic Mass Lesions. J Comput Assist Tomogr. 2004;28(4):540-47.
[9]. Alam MS, Sajjad Z, Hafeez S, Akhter W. Magnetic Resonance Spectroscopy In Focal Brain Lesions. J Pak Med Assoc. 2011;61(6):540-43.
[10]. Hellstrom J, Romanos ZR, Libard S, Wikstrom J, Ortiz-Nieto F, Alafuzoff I, Et Al. The Value Of Magnetic Resonance Spectroscopy As A Supplement To MRI Of The Brain In A Clinical Setting. Plos ONE. 2018;13(11):E0207336.
[11]. Shetty G, Avabratha KS, Rai BS. Ring-Enhancing Lesions In The Brain: A Diagnostic Dilemma. Iran J Child Neurol. 2014;8(3):61-64.
[12]. Verma SR, Choudhary N, Sardana V. Magnetic Resonance Spectroscopy In Differentiation Of Intracranial Tuberculoma And Neurocysticercosis. Int J Sci Res. 2017;6(3):397-99.
[13]. Morales H, Alfaro D, Martinot C, Fayed N, Gaskill-Shipley M. MR Spectroscopy Of Intracranial Tuberculomas: A Singlet Peak At 3.8 Ppm As Potential Marker To Differentiate Them From Malignant Tumors. Neuroradiol J. 2015;28(3):294-302.
[14]. Sharma BB, Sharma S. Neurocysticercosis (NCC) Vs Central Nervous System (CNS) Tuberculoma In Children-Dilemma Over Clinico-Radiological Diagnosis? Open Journal Of Pediatrics. 2016;6(3):245-51.
[15]. Rudresh K, Krishna MV, Karthik, Jomy S. Clinical And Aetiological Profile Of Ring-Enhancing Lesions On CT Brain. JIACM. 2008;9(2):100-02.
[16]. Jesrani A, Ajmal R, Asad M, Zehra SN. Diagnostic Accuracy Of Magnetic Resonance Spectroscopy In Differentiating Neoplastic From Non-Neoplastic Enhancing Brain Lesions Taking Histopathology As Gold Standard, Experience At Liaquat National Hospital, Karachi, Pakistan. Acta Sci Cancer Biol. 2019;3(10):03-08.
[17]. Bava JS, Sankhe A, Patil S. Role Of MR Spectroscopy In Evaluation Of Various Ring Enhancing Lesions In Brain. Int J Sci Res. 2016;5(7):1512-14.
[18]. Mirchandani S, Dave J, Dave AN. Role Of MRI &MR Spectroscopy (Metabolic Mapping) In Characterisation Of Ring Enhancing Lesions In Brain. J Dent Med Sci. 2019;18(5):55-60.
[19]. Venkat B, Aggarwal N, Makhaik S, Sood R. A Comprehensive Review Of Imaging Findings In Human Cysticercosis. Jpn J Radiol. 2016;34(4):241-57.
[20]. Pretell EJ, Martinot C, Garcia HH, Alvarado M, Bustos JA, Martinot C. Differential Diagnosis Between Cerebral Tuberculosis And Neurocysticercosis By Magnetic Resonance Spectroscopy. J Comput Assist Tomogr. 2005;29(1):112-14.
[21]. Gupta RK, Khader MH, Mishra AM, Jha D, Husain M, Prasad KN, Et Al. High Fractional Anisotropy In Brain Abscesses Versus Other Cystic Intracranial Lesions. Am J Neuroradiol. 2005;26(5):1107-14.
[22]. Kaddah RO, Khalil ME. Malignant Focal Brain Lesions. Value Of MRS Tumour Biomarkers In Preoperative Prediction Of Grades Of Malignancy. Egypt J Radiol Nucl Med. 2014;45(4):1201-08.
[23]. Fan G, Sun B, Wu Z, Guo Q, Guo Y. In Vivo Single-Voxel Proton MR Spectroscopy In The Differentiation Of High-Grade Gliomas And Solitary Metastases. Clin Radiol. 2004;59(1):77-85.
[24]. Chiang IC, Kuo YT, Lu CY, Yeung KW, Lin WC, Sheu FO, Et Al. Distinction Between High-Grade Gliomas And Solitary Metastases Using Peritumoral 3-T Magnetic Resonance Spectroscopy, Diffusion, And Perfusion Imagings. Neuroradiology. 2004;46(8):619-27.
[25]. Shah R, Vattoth S, Jacob R, Manzil FFP, O'Malley JP, Borghei P, Et Al. Radiation Necrosis In The Brain: Imaging Features And Differentiation From Tumor Recurrence. Radiographics. 2012;32(5):1343-59.
[26]. Glunde K, Penet MF, Jiang L, Jacobs MA, Bhujwalla ZM. Choline Metabolism-Based Molecular Diagnosis Of Cancer: An Update. Expert Rev Mol Diagn. 2015;15(6):735-47.
[27]. Goodwin ML, Pennington Z, Westbroek EM, Cottrill E, Ahmed AK, Sciubba DM. Lactate And Cancer: A "Lactatic" Perspective On Spinal Tumor Metabolism (Part 1). Ann Transl Med. 2019;7(10):220.
[28]. Moffett JR, Ross B, Arun P, Madhavarao CN, Namboodiri MAA. N-Acetylaspartate In The CNS: From Neurodiagnostics To Neurobiology. Prog Neurobiol. 2007;81(2):89-131.
[29]. Mcknight TR, Von Dembussche MH, Vigneron DB, Lu Y, Berger MS, Mcdermott MW, Et Al. Histopathological Validation Of A Three-Dimensional Magnetic Resonance Spectroscopy Index As A Predictor Of Tumor Presence. J Neurosurg. 2002;97(4):794-802.
[30]. Brandao LA, Castillo M. Adult Brain Tumors: Clinical Applications Of Magnetic Resonance Spectroscopy. Neuroimaging Clin N Am. 2013:23(3):527-55.
[31]. Maheshwarappa RP, Agrawal C, Bansal J. Tuberculoma Versus Neurocysticercosis: Can Magnetic Resonance Spectroscopy And Diffusion Weighted Imaging Solve The Diagnostic Conundrum? J Clin Diagn Res. 2019;13(6):TC01-06.
[32]. Hafez H, Elmoneim BA, Fawzy T, Omar SF. The Role Of Proton Magnetic Resonance Spectroscopy In Grading Of Brain Gliomas. Menoufia Medical Journal. 2016;29(1):136-40.
[33]. Manias K, Gill SK, Zarinabad N, Davies P, English M, Ford D, Et Al. Evaluation Of The Added Value Of 1H-Magnetic Resonance Spectroscopy For The Diagnosis Of Pediatric Brain Lesions In Clinical Practice. Neurooncol Pract. 2018;5(1):18-27.