Section: Radiology

Original Research Article

A NEW ERA OF BRAIN TUMOR MANAGEMENT: MRS AS A NON-INVASIVE DIAGNOSTIC TOOL

Received : 16/09/2023
Received in revised form : 21/10/2023
Accepted : 02/11/2023

Keywords:
Brain Tumor, MRS.

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DOI: 10.47009/jamp.2023.5.6.16

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (6); 70-76

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Abstract

Background: The primary goal is to improve the diagnosis and treatment of brain tumors by using MRI to identify key characteristics. This includes identifying the conventional MRI characteristic findings of brain tumors, evaluating the accuracy of MRI spectroscopy in grading brain tumors, determining the degree of infiltration of the tumor into surrounding tissues, and identifying biochemical markers of brain tumors using MR spectroscopy. Achieving these objectives is critical to developing more effective treatments for brain tumors and improving patient outcomes. By accurately identifying the characteristics of brain tumors using MRI, one can better diagnose and monitor the progression of the disease, leading to more targeted and effective treatments. **Materials and Methods:** This study aimed to evaluate brain tumors using 3T MRS in a prospective cross-sectional study conducted at the Department of Radiology in Narayana Medical College Hospital from January 2021 to August 2022. The study population consisted of thirty patients who underwent MRI brain with clinically suspected metastasis or brain tumors. MRS imaging was performed using a 3T MRI machine with automatic dynamic high-order shimming and chemical-shift selective water suppression, and the relative signal strengths of metabolites were evaluated. The data was analysed using SPSS, and cases were followed clinically and radiologically as indicated. **Result:** The current study involved 35 instances. Tumor grades were categorized according to WHO criteria and included 5.7% of grade I, 17.1% of grade II, 48.6% of grade III, and 28.6% of grade IV tumors. The analysis of metabolite ratios indicated that NAA/Cr levels were similar in HGG and isolated metastatic lesions in the intratumoral and contralateral regions. However, individuals with a single metastatic lesion in the pertumoral region had considerably higher NAA/Cr levels. MRS correctly identified 26 cases of HGG and 6 cases with other pathologies (LGG and metastatic lesions) but misidentified 3 cases without HGG as having HGG. The study reported the diagnostic accuracy of MRS as 85.7% with a sensitivity of 92.9%, specificity of 57.1%, positive predictive value of 89.7%, and negative predictive value of 66.7%. **Conclusion:** The study found that MRS had a diagnostic accuracy of 85.7%, with a sensitivity of 92.9% and specificity of 5.17%. Patients with a single metastatic lesion had higher levels of NAA/Cr, while those with HGG had higher levels of Cho/Cr and Cho/NAA compared to solitary lesions. Patients with HGG also had higher levels of rCBV in the peritumoral region. The combination of MRS and brain SPECT provided accurate pre-surgical diagnosis and resolved a significant diagnostic puzzle. A multi-modality approach to brain tumor diagnosis could benefit both patients and doctors involved in the treatment plan.

INTRODUCTION

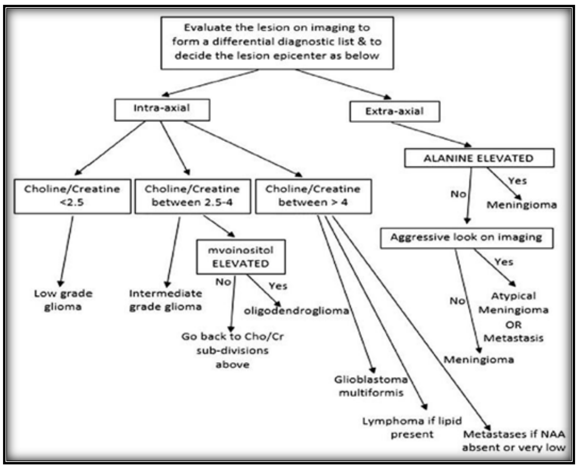
Intracranial tumors pose a serious medical issue with 10 to 17 people per 100,000 diagnosed with primary and secondary CNS neoplasms annually. Supratentorial and infratentorial brain tumors are two types of brain tumors that are challenging to distinguish between low and high-grade gliomas as well as neoplastic from non-carcinomatous brain masses using conventional MRI. MRI techniques such as MR spectroscopy have been developed to increase the accuracy of cancer diagnosis.[1]

Clinicians can assess variables such as neuronal survival, neurotoxins, and membrane turnover within the area of interest and, consequently, the likely underlying pathophysiology, by comparing the relative number of metabolites. 1H-MRS is an attractive, non-invasive addition to MRI that allows for the examination of certain metabolites in the brain to indicate the nature of these diseases, grading of tumors, follow-up, and evaluating the response of these tumors to treatment.[2]

DWI enables us to learn more about the brain by observing the minute movements of water molecules. DWI has been utilized to identify the cellularity of brain tumors and to distinguish between high and low cellular brain tumors. Echo time (TE) in MRS is another significant factor that has a significant impact on the spectrum. It is feasible to find more metabolites at short TE.[3]

PWI is an MR method that examines the tumors' hemodynamics. Although findings on the differentiating of LGG from anaplastic astrocytomas and anaplastic astrocytomas from glioblastomas are contradicting, it is much higher in HGG than in LGG. In recent years, some authors have improved the capacity to distinguish solid tumors from other intra-tumoral or peri-tumoral tissues and among tumor kinds and/or grades by using a variable combination of 1H-MRSI, DWI, and PWI in addition to conventional MRI.[4]

NAA, Cr, and tCho, which are present in normal brain tissue's proton spectra at 2.0, 3.0, and 3.2 ppm, respectively, are the primary metabolites. When short echo durations are used, lipid signals at 1.3 (methylene) and 0.9 ppm (methyl) in brain malignancies can be seen. Metabolic alterations in primary brain tumors that happen after radiation therapy have been studied in the past. Despite conflicting data from various groups, tCho decrease seems to be a reliable indicator of therapy response.[5]



MRS has been shown to be helpful in determining prognosis and treatment response, as well as in the assessment of tumor grade, tumor type differentiation, radiation damage from recurrent gliomas and tumor type differentiation. Studies using 1H-MRS have produced encouraging outcomes for separating glioblastomas from metastasis. These two lesions are treated differently, which may have an impact on the clinical result.

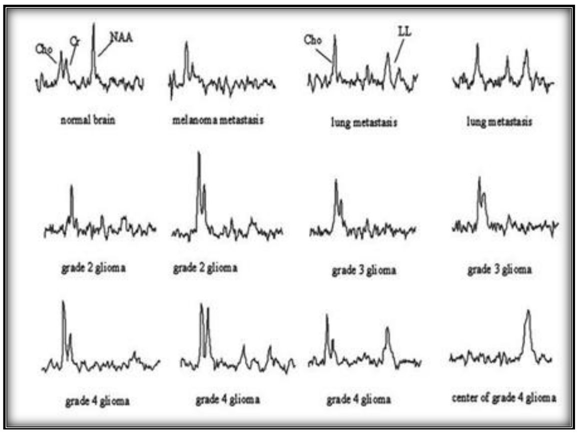


Figure – MRS spectra from normal brain tissue , brain metastasis, necrosis, and gliomas of different grades.

With these backgrounds, this study was conducted for the evaluation of brain tumors using 3T MRS. Despite the advancements in MRI, it is frequently difficult to accurately characterize brain lesions. However, with the use of MRS, clinicians can identify biochemical patterns associated with brain lesions to provide more accurate diagnoses and treatment responses. Using MRS alongside other MRI techniques such as DWI and PWI, the ability to differentiate between solid tumors and other intra-tumoral or peri-tumoral tissues and among tumor kinds and/or grades is improving.

MATERIALS AND METHODS

Study Design: This study was conducted as a prospective cross sectional study for evaluation of brain tumors using 3T MRS.

Study Area: Department of Radiology in Narayana Medical College Hospital

Study population: Cases undergoing MRI brain with clinically suspected metastasis or brain Tumors

Study period: August 2022 to March 2023

Inclusion criteria:

- Cases with suspected brain tumors
- Both male and females

Exclusion criteria:

- Subjects who are detected to have intracranial bleed/ hypoxic-ischemic injury/ ischemia/ infarction
- Subjects who failed to give consent.
- Subjects who are claustrophobic.
- Subjects having a history of metallic implant insertion, cardiac pacemakers, and metallic foreign body insitu.

Sample size: A total of thirty patients presented with suspicious of brain tumors on MRI were included in this study.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Ethical committee approval: Ethical committee approval was obtained for this study from the Institutional Human Ethics Committee.

Data Collection: After receiving written informed consent, the principal investigator evaluated all of the cases for the demographics and clinical presentation using a pre-structured proforma. In every case, MRS came after MRI.

MRS and MRI techniques: The experiments were conducted using a 3 Tesla magnetic resonance imaging (MRI) machine, which had the capability to produce amplitude gradients of 80 mT/m and 200 mT/m/ms, and an eight-channel receiver head coil. The MRI protocol involved various imaging techniques such as T2-weighted TSE, T1-WIR, FLAIR, DWI, and T1-WSE, which were performed after administering a contrast medium. In addition, multivoxel 2D 1HMRS was carried out on a VOI (volume of interest) location using the PRESS pulse sequence on three reference images. To ensure the quality of spectroscopic data, the VOI was chosen from within the tumor, peritumoral edema, and adjacent normal-appearing white matter as a control. Special care was taken to minimize interference from subcutaneous fat and lipids of the skull, and saturation slabs were used in certain areas to further reduce the risk of artifacts. Lastly, automatic dynamic high-order shimming and chemical-shift selective water suppression were employed to enhance the accuracy of the imaging.

MRS data evaluation: Automated checks were conducted on the signal strengths of NAA, creatine-phosphocreatine complex, and Cho-containing molecules in the spectra. The Cho/Cr, Cho/NAA, and NAA/Cr ratios were calculated for post-processing analysis, which included operations like frequency shift, baseline correction, phase correction, and peak fitting/analysis, using the software provided by the manufacturer. The spectral analysis window was limited to a range of 0.50 to 4.30 ppm, and a single representative voxel from the tumor core and surrounding tissue was used to quantify the metabolites. In order to minimize the impact of the partial volume effect, cystic or necrotic regions and adjacent normal tissues were avoided as much as possible when determining the greatest Cho/Cr and Cho/NAA ratios and the lowest NAA/Cr ratios using spectral maps at the two aforementioned places. Every spectrum was also examined for the presence of lipids and lactate. The MRS study was performed by a radiologist and an MR physicist who have experience in quantitative spectroscopic imaging, and only data from high-quality spectra were used in the study. Each report was entered using the same proforma.

Data analysis: The information was initially inputted into Excel and then processed using SPSS software version 16. The descriptive statistics, including mean, standard deviation, and proportions, were generated for the quantitative variables. The Mann Whitney U test and chi square test were also performed accurately. A p-value of less than 0.05 was used as the threshold for determining statistical significance.

Image Reconstruction: The medical imaging data was reformatted into axial, coronal, and sagittal views using volume rendering techniques. Maximum and average intensity projection images were created to aid in the evaluation of the vascular system. The cases were then monitored over time using clinical and radiological methods as needed.

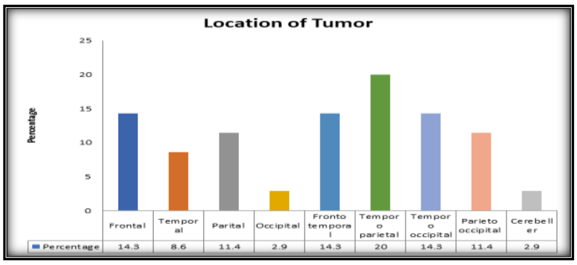
RESULTS

Thirty five instances were included in the current investigation. Most of the cases (57.1%) belongs to age group 41–60 category, while 25.7% of cases belongs to age group 21–40, 14.3% of cases belongs to age group more than 60, and 2.9% of cases belongs to age group less than or equal to 20 years.

In this study, there were 68.6% male participants and 31.4% female participants.

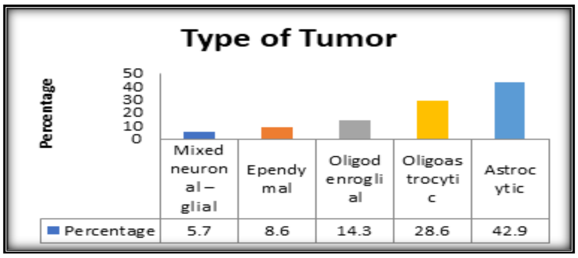
According to an analysis of the study participants' presenting complaints, headaches were reported in 91.4% of cases, seizures in 40%, loss of consciousness in 31.4%, and altered sensorium in 14.3% of cases.

In the present study, meningeal signs were present in 25.7% of cases and the rest 74.3% of cases did not show any meningeal signs.

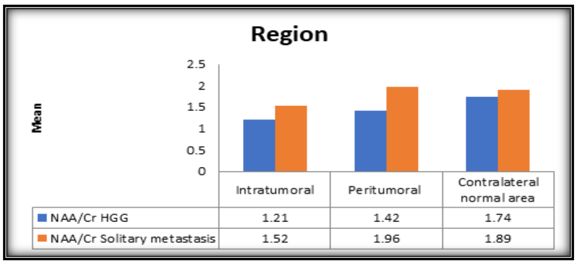


Graph 1: Proportion of cases based on tumor location

On assessing the types of tumors, mixed neuronal glial tumors were noted in 5.7% of cases, ependymal tumors in 8.6% of cases, oligodenroglial tumors in 14.3% of cases, oligoastrocytic tumors in 28.6% of cases and astrocytic tumors in 42.9% of cases.

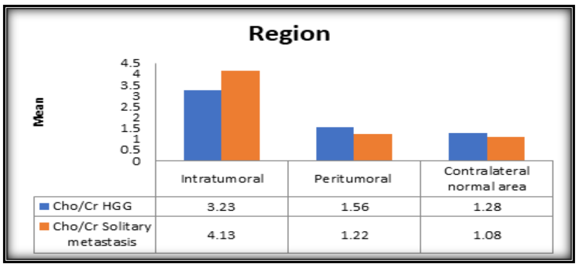


Graph 2: Proportion of cases based on tumor type



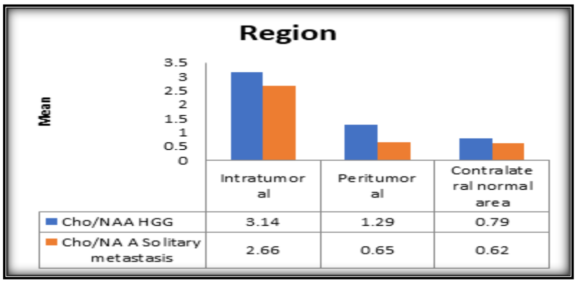
Graph 3: Comparison of NAA/Cr between HGG and solitary metastasis in different regions

When the metabolite ratios were examined in the intratumoral and contralateral areas, Cho/Cr levels were discovered to be comparable in cases with HGG and cases with a single metastatic lesion. However, cases with HGG were found to have noticeably elevated levels of Cho/Cr in the peritumoral area.

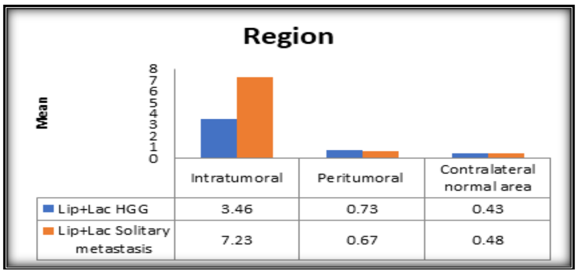


Graph 4: Comparison of Cho/Cr between HGG and solitary metastasis in different regions

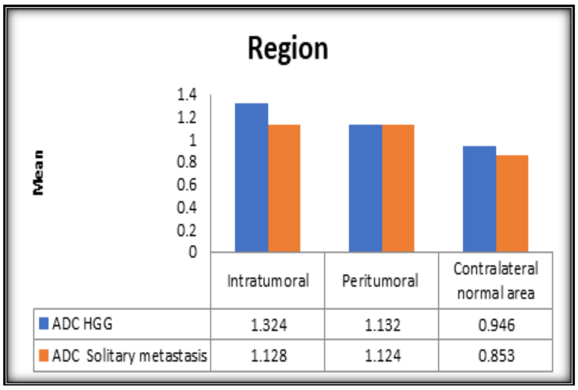
When the metabolite ratios were examined in the intratumoral and contralateral areas, Cho/NAA levels were discovered to be comparable in cases with HGG and cases with a single metastatic lesion. However, cases with HGG were discovered to have noticeably elevated levels of Cho/NAA in the peritumoral area.



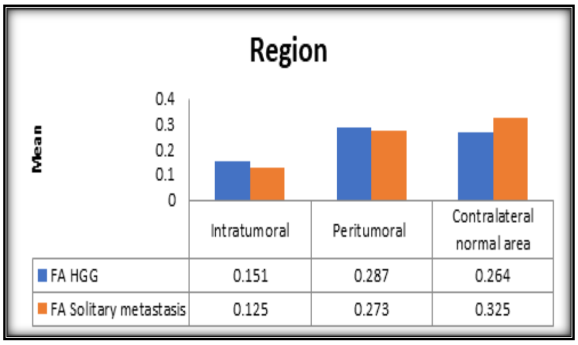
Graph 5: Comparison of Cho/NAA between HGG and solitary metastasis in different regions



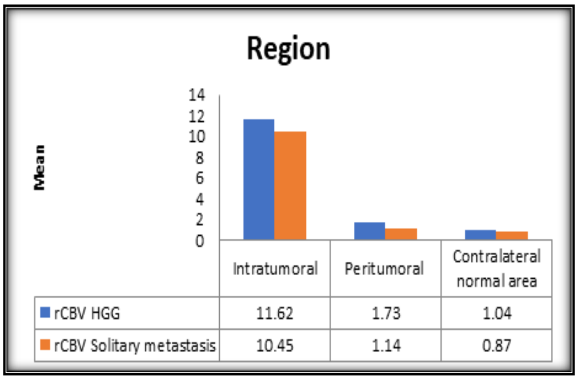
Graph 6: Comparison of Lip+Lac between HGG and solitary metastasis in different regions



Graph 7: Comparison of ADC between HGG and solitary metastasis in different regions



Graph 8: Comparison of FA between HGG and solitary metastasis in different regions



Graph 9: Comparison of rCBV between HGG and solitary metastasis in different regions

Diagnostic efficacy of MRS was reported as 85.7% in this study with Sn of 92.9%, Sp of 57.1%, PPV of 89.7% and NPV of 66.7%, in this study.

Table 1: Findings of MRI- T1 and T2 WI

MRI findings- T1-WI	Frequency	Percentage
Low signal	20	57.1
Iso signal	10	28.6
High signal	5	14.3
Total	35	100.0
MRI findings- T2-WI	**Frequency**	**Percentage**
Low signal	19	54.3
High signal	16	45.7

Table 2: Enhancement pattern noted in MRI

Enhancement pattern	Frequency	Percentage
Spotty	9	25.7
Heterogenous	21	60.0
Homogenous	1	2.9
None	4	11.4
Total	35	100.0

Table 3: Proportion of cases with Edema in MRI

Edema	Frequency	Percentage
None	3	8.6
1+	15	42.9
2+	12	34.3
3+	5	14.3
Total	35	100.0

Table 4: Findings of MRI - DWI

DWI	Frequency	Percentage
Low signal	9	25.7
Iso signal	6	17.1
High signal	20	57.1
Total	35	100.0

Table 5: Pattern of Contrast enhancement in MRI

Contrast enhancement	Frequency	Percentage
Minimal	2	5.7
Moderate	9	25.7
Intense	24	68.6
Total	35	100.0

Table 6: Proportion of cases based on tumor location

Location of Tumor	Frequency	Percentage
Frontal	5	14.3
Temporal	3	8.6
Parital	4	11.4
Occipital	1	2.9
Fronto temporal	5	14.3
Temporo parietal	7	20.0
Temporo occipital	5	14.3
Parieto occipital	4	11.4
Cerebeller	1	2.9
Total	35	100.0

Table 7: Proportion of cases based on WHO- tumor grade

Tumor grade –WHO	Frequency	Percentage
Grade I	2	5.7
Grade II	6	17.1
Grade III	17	48.6
Grade IV	10	28.6
Total	35	100.0

Table 8: Proportion of cases based on pathological condition

Pathological condition	Frequency	Percentage
Low grade gliomas	4	11.4
High grade gliomas	29	82.9
Metastatic lesions	2	5.7
Total	35	100.0

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 9: MR spectroscopy findings versus Actual diagnosis

MR spectroscopy	Diagnosis		Total
	HGG	Others	
HGG	26	3	29
Others	2	4	6
Total	28	7	35

DISCUSSION

The investigation included 35 cases with most (57.1%) in the 41-60 age group, 25.7% in the 21-40 age group, 14.3% over 60, and 2.9% under 20. The study had 68.6% male and 31.4% female participants. Headaches were the most common complaint (91.4%), followed by seizures (40%), loss of consciousness (31.4%), and altered sensorium (14.3%). Meningeal signs were present in 25.7% of cases. MRI showed low, iso, and high signals in 57.1%, 28.6%, and 14.3% of cases, respectively, on T1 weighted imaging and 54.3% and 45.7% on T2 weighted imaging. Contrast enhancement was minimal in 5.7%, moderate in 25.7%, and intense in 68.6% of cases. Tumor location involved the frontal lobe (14.3%), temporal lobe (8.6%), parietal lobe (11.4%), and occipital lobe (2.9%). In 14.3% of cases, frontotemporal involvement was found, and in 20%, temporal parietal, in 14.3%, temporal occipital, in 11.4%, parietooccipital involvement was identified. Cerebellar involvement was found in 2.9% of cases.[6-10]

CASE 1

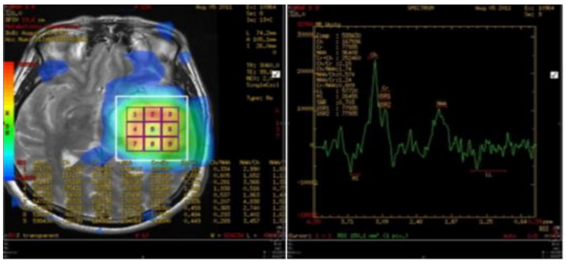


Figure 1: A – Axial T2 image showing a lesion in the left anterior temporal lobe. B- MRS image showing choline peak and NAA reduction. The HPE of the tumor turned out to be Low Grade Glioma.

CASE 2

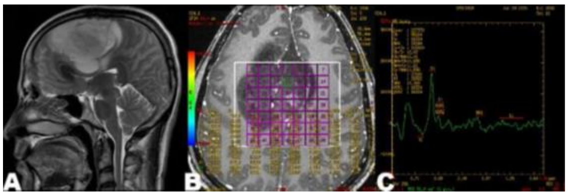


Figure 2: A – SagT2 image showing a lesion in the mild line frontal lobe causing compression on the corpus callosum. B – Contrast image showing subtle contrast enhancement. C- MRS image showing choline peak and NAA reduction. The HPE of the tumor turned out to be Anaplastic astrocytoma

CASE 3

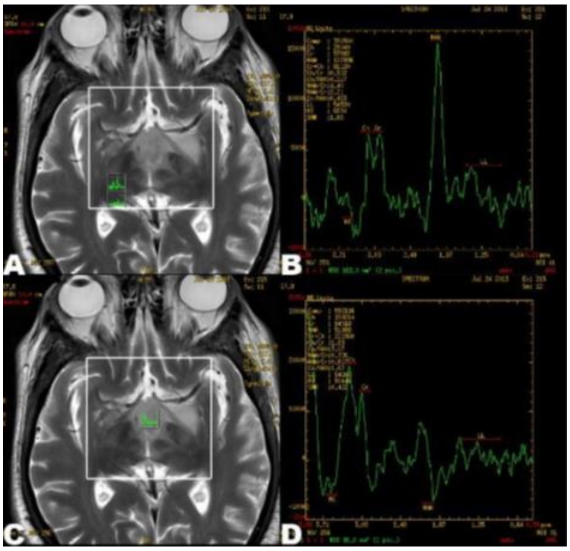


Figure 3. A,B – Axial T2 image and MRS image showing normal NAA peak at the level of right half of mid brain. C, D – Axial T2 image and MRS image showing a T2 iso to hyper intense lesion in the interpeduncular cistern which on MRS showing elevated Choline and Creatinine peaks which on histopathology turned out to be high grade glioma.

CASE 4

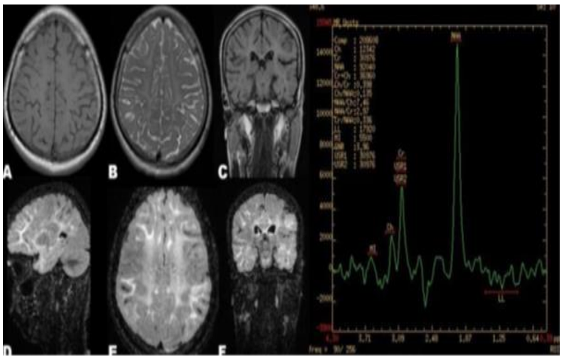


Figure 6: A,B,C,D,E,F– Axial T1,T2,Cornal T1, Sag, Axial, and Coronal FLAIR images showing diffuse increase in signal intensity in the bilateral cerebral white matter on T2 and FLAIR images including subcortical U fibers also. Adjacent MRS image showing NAA peak in the above-mentioned white matter which is suggestive of Canavan's Disease.

The study included 35 cases with gliomas. Most cases (57.1%) were in the 41-60 age group and 68.6% were male. Headaches were reported in 91.4% of cases, while meningeal signs were present in 25.7% of cases. MRI showed low, iso, and high signals in 57.1%, 28.6%, and 14.3% of cases, respectively. Astrocytic tumors were found in 42.9% of cases, while 28.6% of cases were grade IV. NAA/Cr levels were comparable in cases of HGG and isolated metastatic lesions. Cho/Cr levels were elevated in the pertumoral area of HGG cases. Cho/NAA levels were elevated in the pertumoral area of HGG cases as well. Lip+Lac levels were comparable in both cases of HGG and cases of solitary metastatic lesions

The study was conducted to compare the Magnetic Resonance Spectroscopy (MRS) findings between cases of High-Grade Glioma (HGG) and cases of isolated metastatic lesion. ADC levels were found to be equal in both cases without any significant difference. FA was also found to be at comparable levels in both cases. rCBV was reported to be in similar values in both cases, but instances with HGG were discovered to have noticeably higher levels of rCBV in the pertumoral region. MRS identified 26 cases with HGG correctly, along with 6 cases with other pathology, but three cases without HGG were incorrectly identified. Diagnostic efficacy of MRS was reported as 85.7% in this study. The study findings were comparable with other studies that showed MRS variations in connection to the density of glioma cells. Inositol, alanine, glycine, and PEA concentrations grew in accordance with the degree of malignancy in glioblastoma. Taurine was found in medulloblastoma. Total creatine concentrations declined with malignancy, and NAA was not able to be found in non-neuroectodermal brain tumors. Ishimaru et al. performed a study to evaluate how well MRS distinguishes HGG from metastases, and found that each tumor displayed a robust Cho peak at a lengthy TE. All metastatic and glioblastomas displayed obvious lipid or a lipid/lactate mixture at short TE, while anaplastic gliomas did not.

CONCLUSION

The current study found that MRS had an 85.7% diagnostic accuracy, with a sensitivity of 92.9%, specificity of 5.17%, positive predictive value of 89.7%, and negative predictive value of 66.7%. By analysing metabolite ratios, it was discovered that cases with a single metastatic lesion in the area around the tumor had higher levels of NAA/Cr compared to cases with HGG. However, patients with HGG had significantly higher levels of Cho/Cr and Cho/NAA than those with solitary lesions in the same area. Similar to patients with single lesions, those with HGG had higher levels of rCBV in the area around the tumor.

The study concluded that 1H-MRS accurately diagnosed the tumor before surgery, which resolved a significant diagnostic issue. The use of additional information from the brain SPECT further confirmed this. The study suggests that both patients and doctors would benefit from a multi-modal approach to brain tumor diagnosis

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