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Research Article

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

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Abstract

Objective: To determine the diagnostic accuracy of Magnetic Resonance spectroscopy in differentiating neoplastic from non - neoplastic enhancing brain lesions taking histopathology as gold standard.

Design: Cross sectional study.

Patients and Methods: A total of 51 patients with enhancing lesions detected on MRI brain contrast studies were included in this study. MRS was performed. On MRS, lesion was categorized and final diagnosis was made on histopathology results. All the information was recorded into predesigned proforma.

Results: The average age of the patients was 40.37 ± 11.56 years. Sensitivity, specificity, PPV, NPV and accuracy of MRS was 87.5%, 93.3%, 95.5%, 89.7% and 92.1% respectively.

Conclusion: Magnetic resonance spectroscopy can readily help in differentiating neoplasm from non-neoplastic ring enhancing brain tumors, thus an invasive brain biopsy procedure can be avoided in many cases where diagnosis is straight forward and with this we can reduce the morbidity and mortality which can be associated with invasive procedure as well as reducing the manpower, time to start treatment and cost.

Keywords: Magnetic Resonance Spectroscopy; Neoplastic; Non - Neoplastic Ring; Brain Lesions

Introduction

Magnetic resonance spectroscopy is a noninvasive diagnostic tool of MRI which assesses and compares the chemical information and metabolites of abnormal tissue of brain with the normal one [1]. The first clinical use of MRS was established in 1980s [2]. Since then, patients with brain cancer have become the primary focus of MRS applications.

Ring - enhancing lesions are one of the most commonly encountered neuro imaging abnormalities. Typically, the ring-enhancing lesions are located at the junction of the gray and white matter, but they could be located in the sub - cortical area, deep in the brain parenchyma or may even be superficial [3,4]. A wide range of etiologies may present as cerebral ring - enhancing lesions which includes primary brain tumor (high grade lesions), metastasis, non-tumorous conditions like abscess, tuberculomas, multiple sclerosis, resolving hematoma (10 - 21 days) or post radiation necrosis [5,6].

Distinguishing neoplastic from non - neoplastic ring enhancing lesions is extremely important because a misdiagnosis can lead to

unwarranted neurosurgery and exposure to toxic chemotherapy or potentially harmful brain irradiation. Despite the excellent soft tissue contrast provided by MRI, literature has shown that conventional MRI has only 61.4% [7] sensitivity in differentiating ring enhancing neoplastic lesions from non - neoplastic lesions.

Newer imaging methods such as magnetic resonance spectroscopy (MRS) is shown to light the blind spots of conventional MRI with significant increase in diagnostic accuracy when used as an adjunct. MRS is a noninvasive diagnostic technique which can determine the concentration of specific metabolites in a pre-selected volume of tissue [8,9]. These metabolites have been used to assess the pathophysiology of different neurological abnormalities. In recent years, MRS is finding a role in practice, as a promising diagnostic technique in detecting various neurological and neurosurgical disorders with sensitivity and specificity of 97.6% [1] and 71.42% [10] respectively.

The high morbidity and mortality associated with ring enhancing brain lesions necessitates their early and accurate diagnosis. This can be done by combined use of conventional magnetic resonance imaging and noninvasive technique of magnetic resonance spectroscopy.

Therefore the rationale of this study has been designed with the intention to determine the diagnostic accuracy of magnetic resonance spectroscopy which is cost effective, noninvasive and does not involve ionizing radiations in detecting neoplastic from non - neoplastic ring enhancing brain lesions and to standardize its use to determine the best management. For example brain abscess can be stereo tactically aspirated, followed by intravenous antibiotics hence avoiding craniotomy.

Material and Method

This cross - sectional study was conducted from October 2018 to March 2019 in Radiology department of Liaquat National Hospital, Karachi, Pakistan after approval from ethical committee. Total 51 patients with enhancing brain lesions detected on MRI brain contrast studies were selected with patient's age ranging from 18 to 65 years. The mean age was 40.37 ± 11.56 years of both genders. Cases were referred from Outpatient Department of Neurology Clinics who were suspected of having space occupying lesions in brain. Full history, clinical examination and laboratory investigations (Complete Blood Count, ESR and Urea Creatinine levels) were carried out.

The patients having claustrophobia, metallic implants, cardiac pacemaker and having metallic foreign body in situ were excluded from the study. Informed consent was taken from the research and ethical committee of the institution. Sample size was calculated considering both the sensitivity and specificity of magnetic resonance spectroscopy to differentiate neoplastic from non neoplastic enhancing brain lesions. Nonprobability consecutive sampling technique was applied to collect the samples which were being referred with provisional diagnosis as cases of some space occupying lesion in brain on clinical basis according to presenting signs and symptoms. Patient's history regarding duration of symptoms and demographic details like patient's age and gender was noted. Patients were subjected to Toshiba 1.5 Tesla MR Scanner using head coil. Axial T1, T2, Sagittal T2, coronal Fluid Attenuated Inversion Recovery (FLAIR) and post - contrast axial, coronal and sagittal images were acquired. MRS was performed through single voxel technique and the studies were obtained with TE and TR of 135 and 1500 respectively. Metabolites were plotted on the X axis on the MR Spectrum in parts per million (ppm). The height of peak on the Y axis indicated their relative concentrations. Major metabolites were NAA which appears at 2.01ppm, Cho at 3.22ppm, Cr at 3.02, lipid at 0.8 to 1.3ppm and lactate at 1.32 to 1.33ppm.

On MRS, lesions was categorized as neoplastic if there was increased Cho and decreased NAA levels, and increased Cho/Cr ratio greater than1.5and decreased NAA/ Cho ratio less than1.2and non - neoplastic if there was decreased Cho, Cr and NAA levels [2]. Final diagnosis was made on histopathology results.

Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS 21.0) as to obtain sensitivity and specificity of magnetic resonance spectroscopy in the differentiation of neoplastic from non neoplastic brain lesions taken histopathology as gold standard. Frequency and percentage was calculated for qualitative variables, i.e, presenting complains, detailed history of presenting complains; magnetic resonance spectroscopy findings and histopathological findings.

Mean ± SD was computed for quantitative variable, i.e. Age of the pateint. Taken histopathological findings as gold standard, all statistical parameters, (sensitivity, specificity, positive predictive value, negative predictive value) were calculated to obtain diagnostic accuracy of shear wave elastography.

Patients Data was entered and analyzed by using Statistical Package for Social Sciences (SPSS 21.0). Mean + SD was calculated for age, gender, duration of symptoms and size of the lesion. Frequency and percentage was computed for qualitative variables like neoplastic and non - neoplastic ring enhancing brain lesions using MRS and histopathology. With histopathology findings as gold standard; the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of magnetic resonance spectroscopy findings was calculated using 2 x 2 tables. Stratification was done on age, gender, duration of symptoms and size of the lesion.

Results

A total of 51 patients with enhancing lesions detected on MRI brain contrast studies were included in this study. Age distribution of the patients is shown in figure 1. The average age of the patients was 40.37 ± 11.56 years similarly average duration of symptoms and lesion size is also presented in table 1. There were 60.78% (31/51) male and 39.22% (20/51) female. Out of 51 patients MRS diagnose neoplastic lesions in 21 patients and histopathology also proves these lesions as neoplastic in all these 21 patients. Out of 51 patients there was case which MRS diagnosed as neoplastic but histopathology proved it as non neoplastic lesion and it is considered as false positive on MRS. In 26 patients out of 51 MRS diagnosed the cases as non neoplastic which were also proven non neoplastic on histopathology while there were 3 cases which were falsely diagnosed as non neoplastic on MRS as these were proven neoplastic on histopathology.

Diagnostic accuracy of magnetic resonance spectroscopy in differentiating neoplastic from non - neoplastic enhancing brain lesions is presented in table 2. Sensitivity, specificity, PPV, NPV and accuracy of MRS was 87.5%, 93.3%, 95.5%, 89.7% and 92.1% respectively. (Figure 2 a and b) shows lesion in left frontal lobe of brain with perilesional edema, its MRS shows reduced peak of N - acetylasparate (NAA) and significantly raised peak of Choline and high choline to creatine ratio, findings on MRS are suggestive of neoplastic lesion, later proven by histopathology as neoplastic lesion.

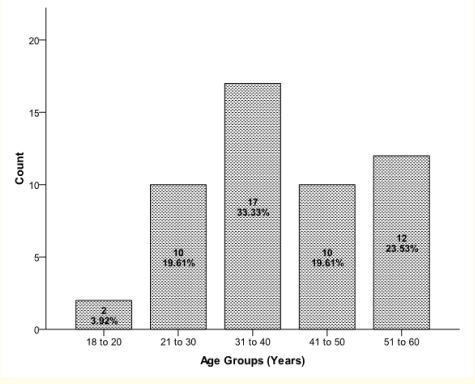

Figure 1: Age distribution of patients (n=51).

Statistics		Age (Years)	Duration of Symptoms (Days)	Size (cm)
Mean		40.37	13.71	5.56
Std. Deviation		11.56	3.51	1.25
95% Confidence Interval for Mean	Lower Bound	37.12	12.72	5.21
	Upper Bound	43.62	14.70	5.92
Median		39.00	14.00	5.00
Inter quartile Range		18	5	1.00

Table 1: Descriptive statistics of characteristics of Patients (n=51).

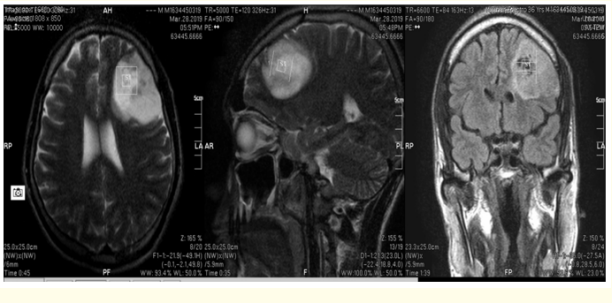

Figure 2(a): Lesion in left frontal lobe with perilesional edema.

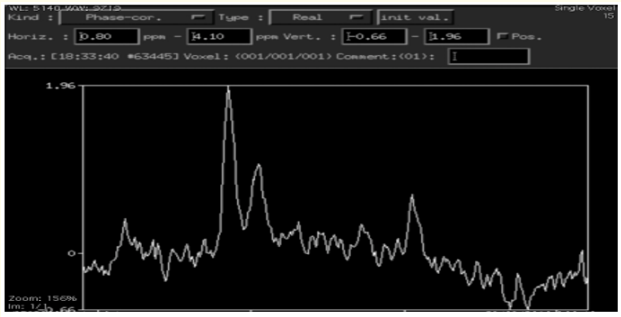

Figure 2(b): MRS of lesion in left frontal lobe shows elevated choline peak and reduced NAA peak.

Magnetic Resonance spectroscopy Findings	Histopathology		Total
	Positive	Negative	
Neoplastic	21 (TP)	1 (FP)	22(43.1%)
Non neoplastic	3 (FN)	26 (TN)	29(56.9%)
Total	**24(47.1%)**	**27(52.9%)**	**51**
Sensitivity		87.5%	
Specificity		93.3%	
PPV		95.5%	
NPV		89.7%	
Accuracy		92.1%	

Table 2: Diagnostic accuracy of MRS in differentiating neoplastic from non-neoplastic enhancing brain lesions taking histopathology as gold standard.

Discussion

Magnetic resonance spectroscopy is alluring in providing chemical information about diseased metabolites and comparing them with the normal brain tissue [11]. Clinically, it was first used in the 1980s [12]. Since then, MRS has become more diagnostic in evaluating the patients of brain cancer [11-13]. Brain tumors exhibited markedly different spectra from normal brain tissue, which was realized earlier in the development of human brain proton MRS [14].

It was found that nearly all brain tumors have often elevated Choline (Cho) levels and decreased N - acetyl aspartate (NAA) signals, hence leading to increased Cho/NAA ratios. In this study, patients with heterogeneous brain lesions evaluated for suspected neoplasm, analysis proved a high rate of success of 94% accuracy in correctly classifying lesions as neoplastic and non - neoplastic lesions on the basis of the ratios of NAA/Cho and NAA/Cr. Elevated levels of Cho were detected in tumors compared with non - neoplastic lesions. Elevated signal intensity in Cho results from increased attenuation of proliferating tumoral cells with Cho - containing compounds including membrane precursors and products of degradation. Tumoral levels of NAA were presumably originating from residual brain tissue within an infiltrating tumor. The study showed that MRS absolute lipid and macromolecular signals could be helpful in differentiating GBM from metastasis. LM13 class was found to be a discriminated parameter with an accuracy of 85%. Another metabolite MM12 - fucose peak may also have a role in understanding molecular biology of brain metastasis and should be further investigated to address specific metabolic phenotypes [15], which were lower than in non - neoplastic lesions. Moreover, the relation of existence of malignancy and the intensity of the Cho signal is not easy to interpret; for instance, in glioblastoma, which is an inhomogeneous texture, the relation between the Cho signal and brain cancer is not so straightforward [16].

In present study the average age of the patients was 40.37 ± 11.56 years. There were 60.78% (31/51) male and 39.22% (20/51) female. In Rehman., *et al*. study [1] 40% females and 60% males with mean age of 37 ± 13.24 years. In Surur., *et al*. study [17] women (57.9%) and 24 men (42.1%), aged between 12 and 81 years (35 years average).

Our results show sensitivity (87.5%), specificity (93.3%) and accuracy (92.1%) in differentiating neoplastic from non-neoplastic lesions using Magnetic resonance Spectroscopy and these are comparable to the previous studies reporting sensitivities of 97.6%), specificity (71.42%) and accuracy (94%) [1]. And in other study sensitivity 87%, specificity of 85% and diagnostic accuracy of 88.2%3 for spectroscopy [18,19]. In this study, PPV and NPV were 95.45% and 83.3%; while one study has found 93% PPV and 70% NPV [2].

Other useful application of MR spectroscopy is in detecting the organisms responsible for abscess, because the presence of anaerobic bacteria tends to cause elevated acetate and succinate peaks, whereas absence of acetate and succinate signals are more likely

with obligate aerobes or facultative anaerobes [18]. MRS can also differentiate high - grade gliomas from metastases, especially with peritumoral measurements, supporting the hypothesis that MRS can detect infiltration of tumor cells in the peritumoral edema. The important point which should be considered is that the spectroscopic changes observed in MS plaques resemble metabolic changes due to brain tumors (high Cho, low NAA, increased Lac) [19].

MRS has also proved in classifying many types of brain tumors [20]. Gliomas of each grade have some specific MRS features and these can be further used for improvement of the diagnostic value of conventional magnetic resonance imaging in non-invasive assessment of glioma grade [21].

Conclusion

Magnetic resonance spectroscopy can readily help in differentiating neoplasm from non - neoplastic ring enhancing brain tumors, thus an invasive brain biopsy procedure can be avoided in many cases where diagnosis is straight forward and with this we can reduce the morbidity and mortality which can be associated with invasive procedure as well as reducing the manpower, time to start treatment and cost.

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