COMPARISON OF HISTOPATHOLOGIC FEATURES WITH PRE OPERATIVE MAGNETIC RESONANCE IMAGING AND MAGNETIC RESONANCE SPECTROSCOPY DIAGNOSIS OF PRIMARY BRAIN TUMORS

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ABSTRACT

Background and Objective: Brain tumours account for major portion of neurosurgical disease burden. The outcome of the patient depends on preoperative neurologic deficits and imaging features in magnetic resonance imaging which is very helpful for evaluation of brain tumours. Magnetic resonance spectroscopy is even more beneficial in making a plan for extent of resection. The present study was designned to compare the histopathological diagnosis using pre-operative Magnetic resonance imaging (MRI) and Magnetic resonance spectroscopy (MRS) diagnosis for primary brain tumors and to find if one technique is better than the other.

Methods: This study was conducted at Neurosurgery department Jinnah Hospital Lahore in collaboration with the Pathology department, Allama Iqbal medical college and Radiology department Jinnah Hospital Lahore from January 2014 to December 2016. Fifty patients provisionally diagnosed as low and high grade primary brain tumor on MRI and MRS were included in the study before surgical biopsy or resection. Tissue for histopathology was obtained via biopsy or resection and all enrolled tumors were graded according to WHO criteria. Histopathological diagnosis was compared with the pre-operative diagnosis after application of Chi square test. The sensitivity, specificity, positive predictive value and negative predictive value of MRI and MRS were also calculated in radiological diagnosis characterization.

Results: The age of patients ranged from 4 to 62 years. Out of the total, 30 (60%) patients were male and 20 (40%) were female. Among all, 35 (70%) patients were having supratentorial brain tumors and 15 (30%) as infratentorial brain tumors. MRI and MRS revealed 20 (57.2%) patients of supratentorial group had Glioma features and among them 13 (65%) had high grade while 7 (35%) were low grade. Among infratentorial group, 9 (60%) patients had medulloblastoma features with 7 (77.8%) patients having high grade and 2 (22.2%) patients have low grade. These MRI and MRS features were compared with histopathological diagnosis and no significant difference was found (p-value > 0.05). Sensitivity, specificity, positive predictive value and negative predictive value of MRI and MRS in detecting tumor necrosis were 95 %, 74%, 77% and 90% respectively.

Conclusion: Pre-operative MRI and MRS are effective in accurate characterization of primary brain tumors which was confirmed by histopathology.

Key Words: Magnetic resonance imaging (MRI), Primary brain tumor, Magnetic resonance spectroscopy (MRS).

INTRODUCTION

In the modern era of neurosurgery, brain tumors account for the major portion of neurosurgical diseases. They can be divided into intra and extra-axial tumors depending on the location with respect to neuronal tissue.[1] In the United States it accounts for 9.5/100,000 cases.[2] Common clinical presentations of brain tumors are headache, vomiting, seizures, behavioral changes, vertigo, neurological deficits etc.[3] Gliomas are the most common brain tumors followed by meningiomas. The outcome of patient with brain tumors depends on the pre-operative neurological deficit and imaging features on Magnetic Resonance Imaging (MRI). Pre-operative imaging used for evaluation of brain tumors can help the neurosurgeon's plan for attaining the safest resection which is essential for the possible functionally active life after surgery.[4] The imaging techniques are getting better day by day just like the evolving technique of neurosurgery. MRI is the modality of choice for accurate pre-operative diagnosis

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due to its multiplanar capabilities and better contrast resolution as compared to CT scan. The addition of Magnetic Resonance Spectroscopy (MRS) in pre-operative imaging is even more beneficial in making a plan for accurate extent of resection. Moreover, its utilization for evaluation of brain tumors has increased because it provides much more information about tumor activity and nature of tumor tissue compared to standard MRI alone. MRS findings are based on the metabolites of tumor tissue and various peaks on MRS help the operating surgeon. Creatine, choline, N-acetylaspartate (NAA)etc. are the common metabolites studied on MRS. Gliomas/Astrocytomas have variety of histological characteristics i.e. variable cellular and nuclear pleomorphism, vascular proliferation, necrosis and mitotic activity.[5] The pattern of MRS peaks can help to determine neoplastic nature of tumor e.g. Increased Cho/Cr ratio, decreased NAA and presence of lactate.[6] Astrocytomas are classified into low grade, anaplastic and GBM (Glioblastoma Multiforme).[7] Grading of astrocytoma is essential for the decision of surgery, post-operative adjuvant treatment and functional outcome.[8] Accurate pre-operative diagnosis is of immense importance in planning the limits of maximal safe resection.[9] A patient diagnosed as a case of primary brain tumor has concerns regarding complete resection for which the pre-operative diagnosis is very important.[10] This study was designed to determine the sensitivity and specificity of MRI and MRS in diagnosis of characteristics of brain tumors and comparing it with the final histopathological diagnosis.

MATERIALS AND METHODS

This study was conducted at Neurosurgery department Jinnah Hospital Lahore, Pathology department AIMC and Radiology department Jinnah Hospital Lahore from January 2014 to December 2016. Fifty patients who were diagnosed as cases of primary brain tumors were included in the study. MRI and MRS were obtained and provisional diagnosis was made on the basis of radiological features. Patients were divided according to age, sex, location and characteristics of the tumor i.e. high grade or low grade. On the basis of MRI and MRS features, treatment modality was planned and patients underwent surgical resection ranging from simple biopsy to gross total resection and results were compared with histopathological diagnosis. Specimens were sent and processed primarily in Pathology department Jinnah hospital Lahore. Few specimens were sent to other private laboratories. Their reports were followed. The tumors were classified according to 2007 WHO classification of CNS tumors. Grading of the tumors was done according to WHO grading scheme (Fig. 1). Grade I applies to lesions with low proliferative potential. Neoplasms designated grade II are generally infiltrative in nature and exhibit low-level proliferative activity. The designation WHO grade III is generally reserved for lesions with histological evidence of malignancy, including nuclear atypia and brisk mitotic activity. The designation WHO grade IV is assigned to cytologically malignant, mitotically active, necrosis-prone neoplasms which may show widespread infiltration of surrounding tissue and a propensity for craniospinal dissemination. Grade 1 and Grade 2 tumors are classified as low grade. Grade 3 and Grade 4 tumors are classified as high grade. Histopathological diagnosis was compared with the pre op diagnosis after application of Chi square test. The sensitivity, specificity, positive predictive value and negative predictive value of MRI and MRS were also calculated in radiological diagnosis characterization.

RESULTS

A total of fifty patients were enrolled in the study who were diagnosed having primary brain tumors and their MRI and MRS characteristics were noted on Performa. The age of patients ranged from 4 to 62 years with mean of 33. 30. 30 (60%) patients were male and 20 (40%) were female. Among all patients, 35 (70%) patients were diagnosed as cases of supratentorial brain tumors and 15 (30%) as infratentorial brain tumors. Regarding supratentorial tumors 19 (54.3%) were male and 16 (45.7%) were female. While among infratentorial tumors 11 (73.3%) were male and 4 (26.7%) were female. MRI and MRS revealed 31 (62%) patients having high grade and 19 (38%) patients having low grade features (Table 1). Further stratification showed that 20 (57.2%) patients of supratentorial group had Glioma features out of which 13 (65%) had high grade while 7 (35%) had low grade characteristics. About 9 (25.7%) patients from supratentorial group had characteristics of meningioma and out of which 4 (44.5%) had low grade and 5 (55.5%) had high grade features. While 6 (17.1%) patients from supratentorial group were diagnosed as oligodendroglioma with low grade and anaplastic features in 4 (66.7%) and 2 (33.3%) respectively. On the other hand 15 (30%) patients from infratentorial group were found to have three characteristic type of tumors including medulloblastoma, ependymoma and astrocytoma. About 9 (60%) patients had medulloblastoma features with 7 (77.8%) patients having high grade and 2 (22.2%) patients having low grade features. Around 3 (20%) patients from infratentorial group had ependymoma with high grade characteristics in 2 (66.7%) patients and low grade in 1 (33.3%). Whereas 3 (20%) patients from infratentorial group had features of astrocytoma with high grade features in 2 (66.7%) patients and low grad in 1 (33.3%). These MRI and MRS features were compared with histopathological diagnosis and no significant difference was found (p-value > 0.05) (Table 2). Sensitivity, specificity, positive predictive value and negative predictive value of MRI and MRS in detecting tumor necrosis were 95%, 74%, 77% and 90% respectively. Preopera-

tive diagnosis on basis of MRI and MRS was confirmed in 47 patients.

MRS showed that patients with high grades of malignancy had high peaks of choline, decreased peaks of NAA while choline creatine ratio was more than 1.5. Regarding gliomas the choline peak was observed at 3.2 ppm and it was found that for high grade gliomas, average choline peak was 0.7 and 0.60 for low grade. NAA peak was observed at 2.9 ppm and for high grade gliomas it was 0.15 and 0.2 for low grade.

In case of meningiomas choline was 0.5 in high grade and 0.4 for low grade while NAA was depressed to 0.2 for both grades. High grade oligodendrogliomas showed that choline peak was 0.65 while in low grade it was 0.5 and NAA was 0.30 for low grade and 0.15 for high grade. In case of infratentorial group, medulloblastomas showed choline peak of 0.8 for high grade and 0.4 for low grade and decreased peak of NAA with an average of 0.1 in low and 0.005 in high grade. Ependymomas showed almost same peak of choline as in medulloblastomas of 0.7 in high grade and 0.4 in low grade. In astrocytomas, low grade had choline peak of 0.5 and high grade had 0.7 while NAA was 0.5 in low grade and 0.05 in high grades. Choline creatine ratio was > 1.5 in all the brain tumors.

Table 1: *Location, type and grading of primary brain tumors.*

Tumor Location	*Tumor Type*	*Grade*		*Total*
		High Grade	*Low Grade*	
Supratentorial group (n = 35)	Glioma	13 (65%)	7 (35%)	20 (57.2%)
	Meningioma	5 (55.5%)	4 (44.5%)	9 (25.7%)
	Oligodendroglioma	2 (33.3%)	4 (66.7%)	6 (17.1%)
Infratentorial group (n = 15)	Medulloblastoma	7 (77.8%)	2 (22.2%)	9 (60.0%)
	Ependymoma	2 (66.7%)	1 (33.3%)	3 (20.0%)
	Astrocytoma	2 (66.7%)	1 (33.3%)	3 (20.0%)

Table 2: *Choline and NAA peaks.*

MRS Supratentorial	Glioma		Choline	NAA
		High Grade	0.7	0.15
		Low Grade	0.6	0.2
	Meningioma		Choline	NAA
		High Grade	0.5	0.2
		Low Grade	0.4	0.2
	Oligodendroglioma		Choline	NAA
		High Grade	0.65	0.15
		Low Grade	0.5	0.30
MRS Infratentorial	Medulloblastoma		Choline	NAA
		High Grade	0.8	0.005
		Low Grade	0.4	0.1
	Ependymoma		Choline	NAA
		High Grade	0.7	0.05
		Low Grade	0.4	0.1
	Astrocytoma		Choline	NAA
		High Grade	0.7	0.05
		Low Grade	0.5	0.5

Choline/creatine peak > 1.5 in both supratentorial and infratentorial group.

DISCUSSION

Gross total resection of primary brain tumors is always the prime concern for neurosurgeons in order to provide the best functional outcome of the patient. Incomplete excision of tumors leads to increased morbidity and mortality. In the modern era of MRI and MRS, the pre-operative diagnostic accuracy has increased and it is helpful for the surgeon in planning operative intervention. The addition of MRS has revolutionized the pre-operative accuracy as it can tell us the nature of contents of the tumor. The recent standard for grading tumors has been histopathological diagnosis which carries with it significant risks of morbidity along with possibility of sampling error and confusing results that may be misinterpreted. MRS can also show the tumor extension and increased choline peak beyond the boundaries apparent on conventional MRI. MRS analysis of the voxel on tumor margin can clarify the grade. If margin is low grade we do not rem-

ove the margin. Various peaks in MRS indicate the nature of tumors.[11] High choline peak is indication of high grade tumor and informs the surgeon that it should be completely resected. Similarly depressed NAA and high choline creatine ratio points towards high grade tumor. MRS enhances the ability of the surgeon

Astrocytic Tumours	**I**	**II**	**III**	**IV**
Subependymal giant cell astrocytoma	*			
Pilocytic astrocytoma	*			
Pilomyxoid astrocytoma		*		
Diffuse astrocytoma		*		
Pleomorphic xanthoastrocytoma		*		
Anaplastic astrocytoma			*	
Glioblasteoma				*
Giant cell glioblastoma				*
Gliosarcoma				*
Oligodendroglial tumours				
Oligodendroglioma		*		
Anaplastic oligodendroglioma			*	
Oligoastrocytic tumours				
Iligoastrocytoma		*		
Anaplastic oligoastrocytoma			*	
Choroid plexus tumours				
Choroid plexus papilloma	*			
Atypical choroid plexus papilloma		*		
Choriid plexus carcinoma			*	
Other neuroepithelial tumours				
Angiocentric glioma	*			
Chordoid glioma of the third ventricle		*		
Neuronal and mixedx neuronal-glial tumours				
Gangliocytoma	*			
Ganglioglioma	*			
Anaplastic ganglioglioma			*	
Desmoplastic infantile astrocytoma and ganglioglioma	*			
Dysembryoplastic neuroepithlial tumour	*			

	I	**II**	**III**	**IV**
Central neurocytoma		*		
Extraventricular neurocytoma		*		
Cerebellar liponeurocytoma		*		
Paraganglioma of the spinal cord	*			
Papillary glioneuronal tumour	*			
Rosette-forming glioneuronal tumour of the fourth ventricle	*			
Pineal tumours				
Pineocytoma	*			
Pineal parenchymal tumour of intermediate differentiation		*	*	
Pineoblastoma				*
Papillary tumour of the pineal region		*	*	
Embryonal tumours				
Medulloblastoma				*
CNS primitive neuroectodermal tumour (PNET)				*
Atypical teratoid/rhaboid tumour				*
Tumours of the cranial and paraspinal nerves				
Meningioma	*			
Atypical meningioma		*		
Anaplastic/malignant meningioma			*	
Haemangiopericytoma		*		
Anaplastic haemangiopericytoma			*	
Haemangioblastoma	*			
Tumours of the sellar region				
Craniopharyngioma	*			
Granular cell tumour of the neurohypophysis	*			
Pituicytoma	*			
Spindle cell oncocytoma of the adenohypophysis	*			

Fig. 1: *WHO Grading of Tumours of the Central Nervous System. Reprinted from Ref. 13.*

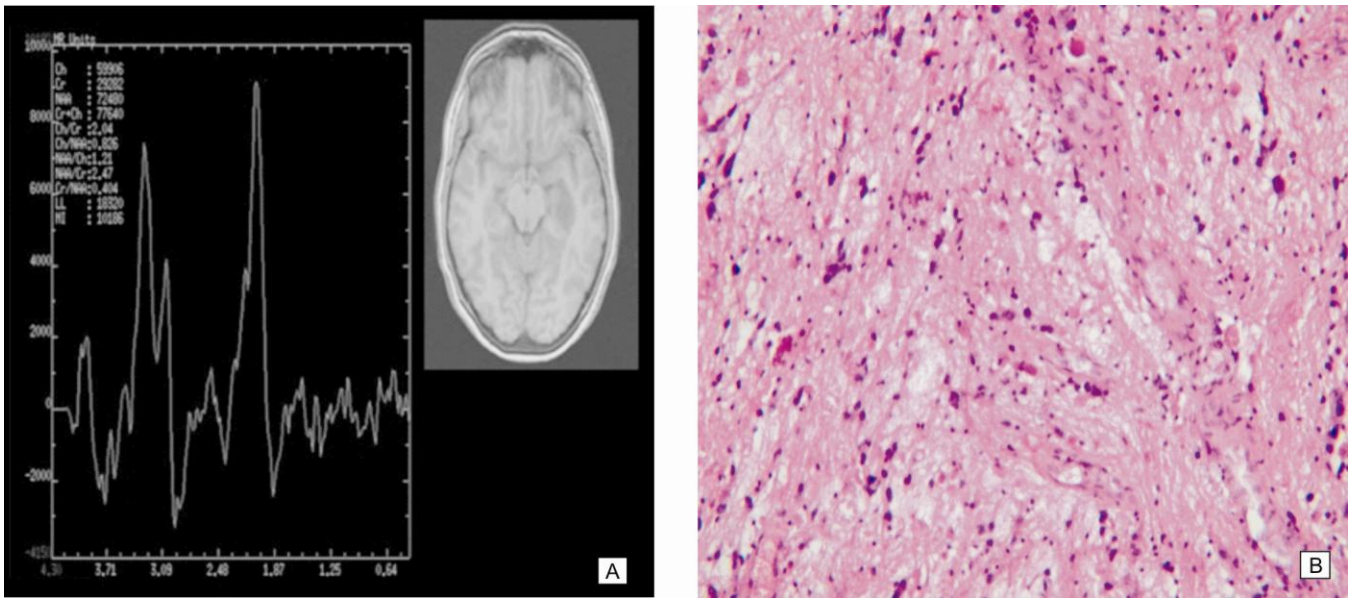

Fig. 2: *A: Left temporal low grade glioma showing mildly elevated choline, decreased NAA and creatine and increased choline/creatine ratio. B: Photomicrograph showing Pilocytic Astrocytoma WHO G I (H/E; 200X).*

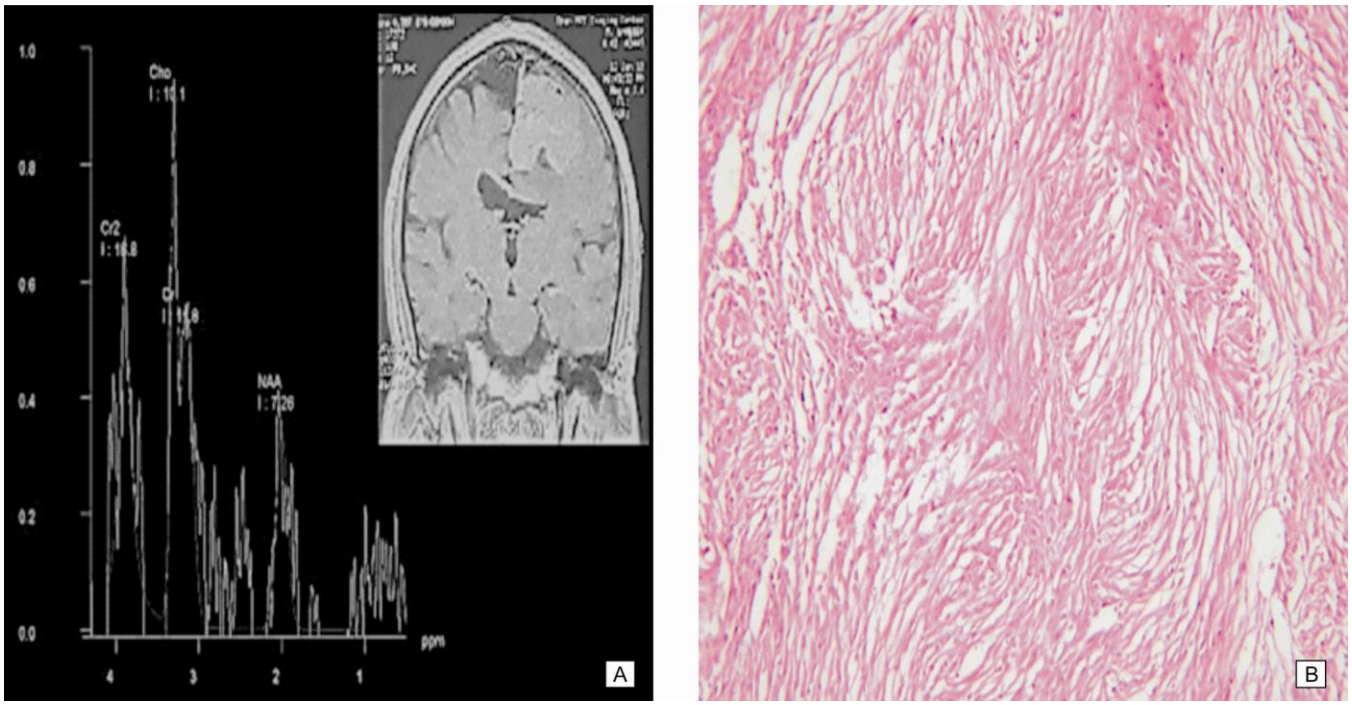

Fig 3: A: Left parafalcine Meningioma showing choline peak at 3.2 ppm and increased alanine.
B: Photomicrograph showing Meningiotheliomatous meningioma WHO G I (H/E; 200X).

to noninvasively characterize the features of the tumor which leads to appropriate planning for surgical management.

In this study, the pre-operative MRI and MRS radiological diagnosis was compared with post-operative histopathological diagnosis and it is found that combination of MRI and MRS will guide the surgeon about the nature and grading of tumor. It is useful for the primary diagnosis and planning of treatment whether to take a simple biopsy or complete excision would be proceeded. It is also helpful in making a demarcation of normal brain tissue from tumor tissue.[12]

It is ***concluded*** that MRS features augment the diagnostic ability of conventional MRI in noninvasive

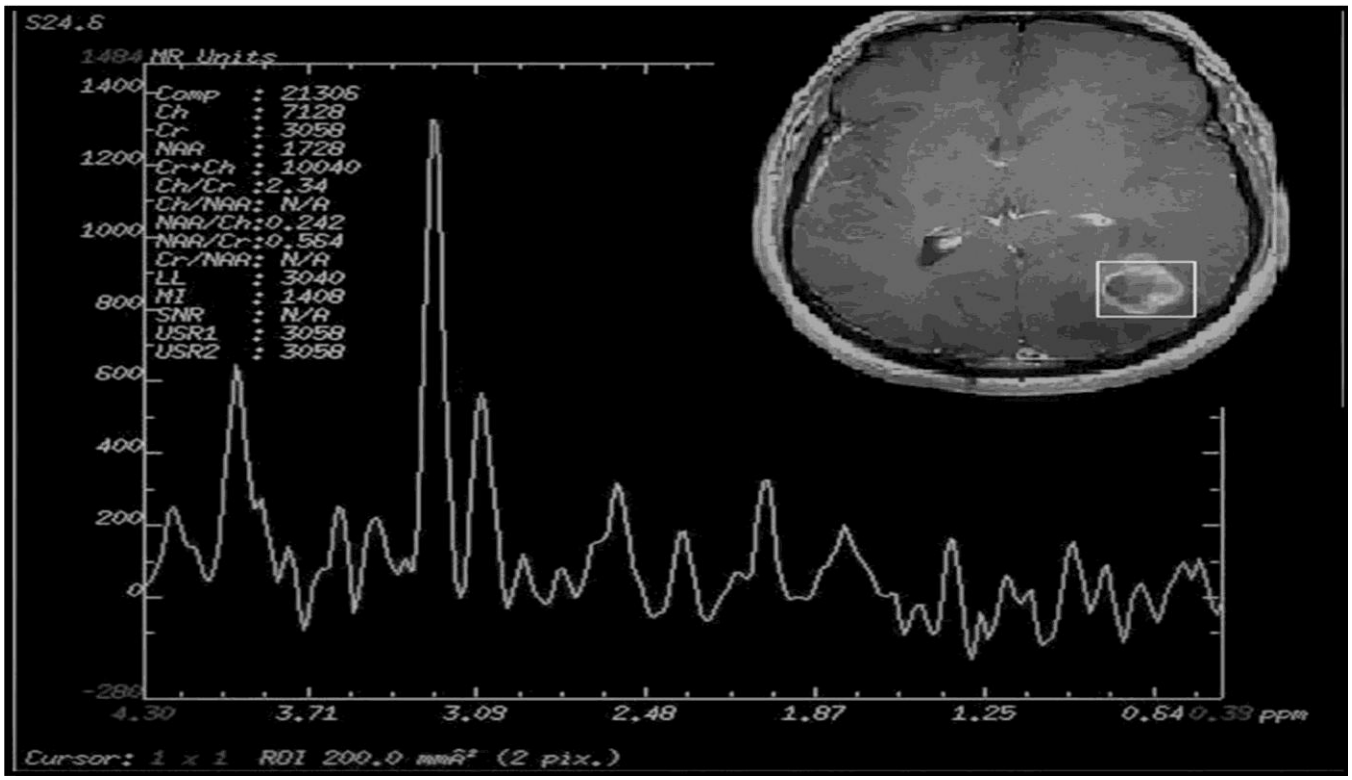

Fig 4: *Left Parietal Glioblastoma showing choline peak, decreased NAA peak, Increasedcholine and choline/creatine ratio and decreased NAA.*

characterization of nature, boundaries and grading of brain tumors. This, also, contributes in appropriate preoperative surgical planning. In the present study, histopathological results show excellent congruence with the preoperative MRS based radiological diagnosis.

Authors' Contribution

UAK: Conception of research, collection of data from neurosurgery department and contribution in data analysis. HAA: Contribution in data analysis and interpretation, Writing and formatting of discussion, introduction and results. MS: Follow up of patients with the radiology department in order to evaluate MRI and MRS, contribution in data analysis. AA: Overall supervision for the histopathology diagnosis and paper writing.

ACKNOWLEDGEMENT

The authors are obliged to Departments of Neurosurgery, JHL and Pathology Department, AIMC, Lahore for helping and facilitating this research project.

Funding

Nil.

Conflict of Interest

None.

Permission of IRB

Yes.

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