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Research Article

Magnetic Resonance Spectroscopy : Metabolites and Their Clinical Applications

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ABSTRACT:

The basic principles and procedures of proton magnetic resonance spectroscopy (MRS), with emphasis on clinical and work in humans, are illustrated in this study. MR spectroscopy (MRS) is a modality that is available on most state-of-the-art clinical MR scanners. For the brain in particular, MRS has been a powerful research tool and has also been proven to provide additional clinically relevant information for several disease families such as brain tumors,metabolic disorders, and systemic diseases.
(MRS) could be used for dozens of metabolites . In this study we will focus especially on proton (hydrogen) MRS. In this article, we will try to explain basically how MRS could be used in daily practice of radiologists. With collection of all this data and information in already clinically diagnosed and treated patients , this article can be used as a common guide for radiologists and a useful tool while reporting MRS.

Keywords : MRS, Metabolites , NAA , Choline, Hydrogen.

INTRODUCTION

Magnetic resonance spectroscopy (MRS) provides information about the metabolite profile of the tissue under investigation and has long been under the domain of biochemists and researchers. The technique has evolved into a clinical tool and with its use it is possible to obtain information on a routine clinical scanner in a reasonably short time.
MR spectroscopy provides a measure of brain chemistry. The most common nuclei that are used are 1H (proton), 23Na (sodium), 31P (phosphorus). Proton spectroscopy is easier to perform and provides much higher signal-to-noise than either sodium or phosphorus. MRS can be performed within 10-15 minutes and can be added on to conventional MR imaging protocols. It can be used to serially monitor biochemical changes in tumors, stroke, epilepsy, metabolic disorders, infections, and

neurodegenerative diseases. They require interpretation and should always be correlated with the MR images before making a final diagnosis.

MATERIALS & METHODS :

MRI was performed on a 1.5 tesla MR imaging unit (Avanto Siemens). MRI protocols conducted are as sagittal , axial and coronal spin echo T2W , T1W1 , coronal T2, axial FLAIR and SWI / gradient sequences.

A group of around three hundred patients during period of January 2017 to June 2018 was studied. All positive cases are selected for MRS having ring enhancing or other non specific enhancing lesions including abnormal cortex enhancement , lesions crossing mid line and suspected patients of mesial temporal sclerosis or other involving abnormality and volume loss in hippocampus.

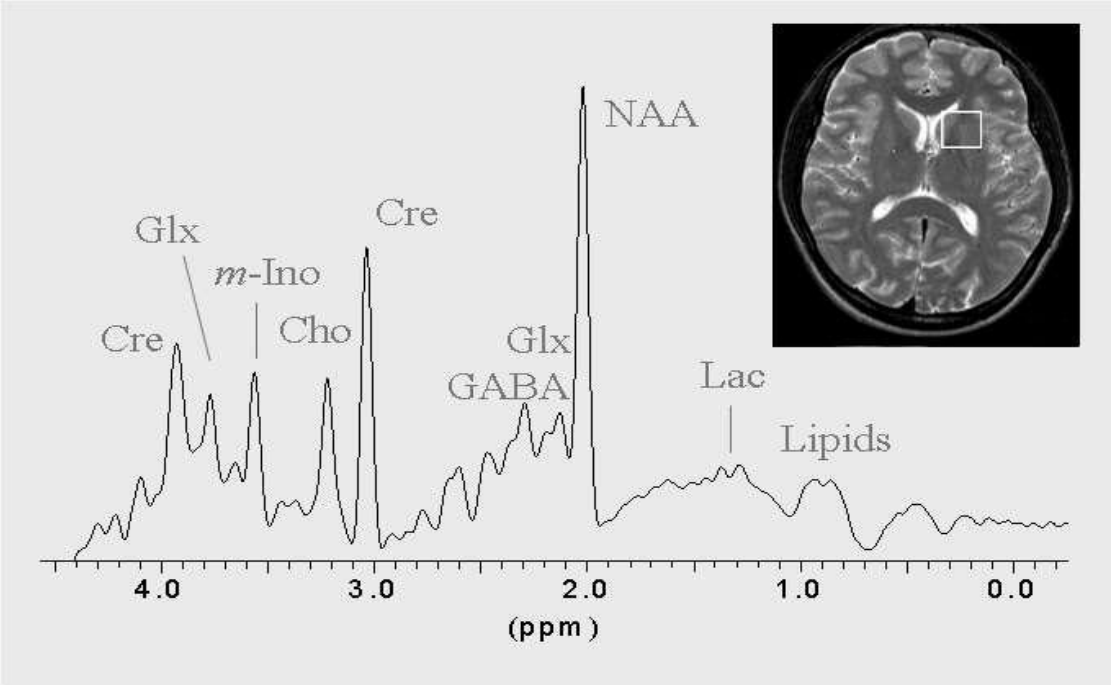
Single voxel and multi voxel MR spectroscopy is done depending upon the abnormality and area of brain parenchyma was involved. Multi voxel technique is used in the lesions more than 2 cms in size.

RESULTS :

MR spectroscopy is conducted on the same machine as conventional MRI. Spectroscopy is a series of tests that are added to the MRI scan of brain or spine to measure the chemical metabolism of a suspected lesion. There are several different metabolites, or products of metabolism, that can be measured to differentiate between tumor Types and infective etiology

The brain metabolites that are commonly seen on the MR spectrum are

Metabolite	Properties
Lipids	Products of brain destruction
Lactate	Product of anaerobic glycolysis
NAA	Neuronal marker
Glutamine/GABA	Neurotransmitters
Creatine	Energy metabolism
Choline	Cell membrane marker
myo-inositol	Glial cell marker, osmolyte hormone receptor mechanisms



Each metabolite appears at a specific ppm, and each one reflects specific cellular and biochemical processes. NAA is a neuronal marker and decreases with any disease that adversely affects neuronal integrity. Creatine provides a measure of energy stores. Choline is a measure of increased cellular turnover and is elevated in tumors and inflammatory processes.

The common way to analyze clinical spectra is to look at metabolite ratios, namely NAA/Cr, NAA/Cho, and Cho/Cr.

Metabolite Ratios

	Normal	Abnormal
NAA/Cr	2.0	< 1.6
NAA/Cho	1.6	< 1.2
Cho/Cr	1.2	> 1.5

For MR imaging, the total signal from all the protons in each voxel is used to make the image. If all the signal were used for MRS, the fat and water peaks would be huge and scaling would make the other metabolite peaks invisible. Fat and water are eliminated.

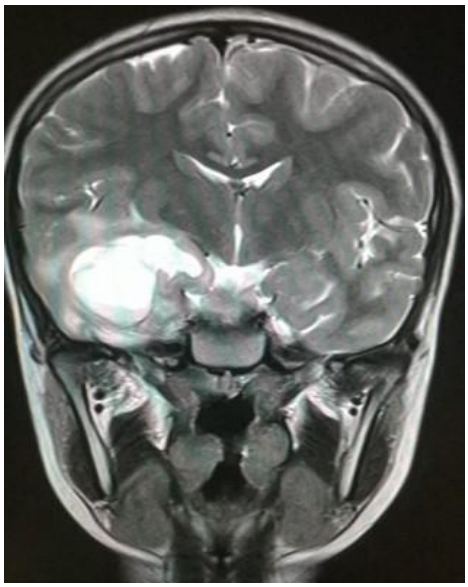
Fat is avoided by placing the voxel for MRS within the brain, away from the fat in bone marrow and scalp.

MRS IN BACTERIAL INFECTIONS :

Pyogenic Abscess : Brain abscesses are characteristically defined as a focal suppurative process within the brain parenchyma. The abscesses result from cerebritis (1–9 days) to well-developed abscess (days 14 onwards).

The fully developed mature abscess with central liquefactive necrosis appears as hypointense on T1-weighted and hyperintense on T2-weighted images.

It is not always possible to differentiate pyogenic abscesses from other cystic intracranial mass lesions solely from conventional MR imaging features. In vivo MRS may help in suggesting the definitive diagnosis of pyogenic abscess among the various lesions with comparable imaging features. The spectral pattern permits the differentiation of pyogenic abscess from tumors by demonstrating the presence of amino acid peak (0.9 ppm), The abscess with true aerobes (Nocardia asteroides and Pseudomonas aeruginosa) shows peaks of cytosolic amino acids, lactate, alanine, and glycine (3.56 ppm), along with mobile lipid peaks at various chemical shifts (0.9, 1.3 ppm).



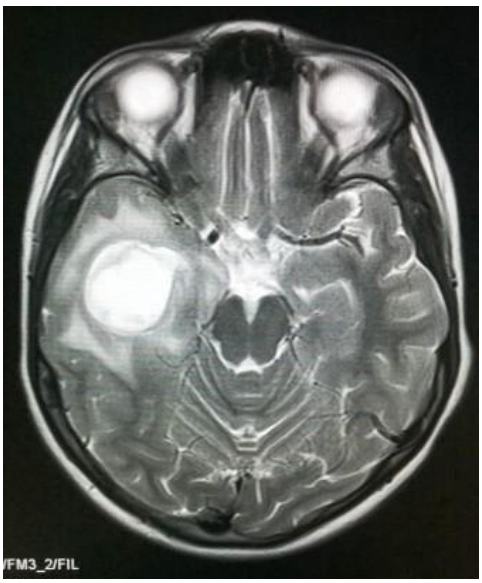


Fig.1a T2 coronal image showing hyper intense lesion on right.
Fig.1b axial T2 image with well defined lesion and edema in right temporal lobe.

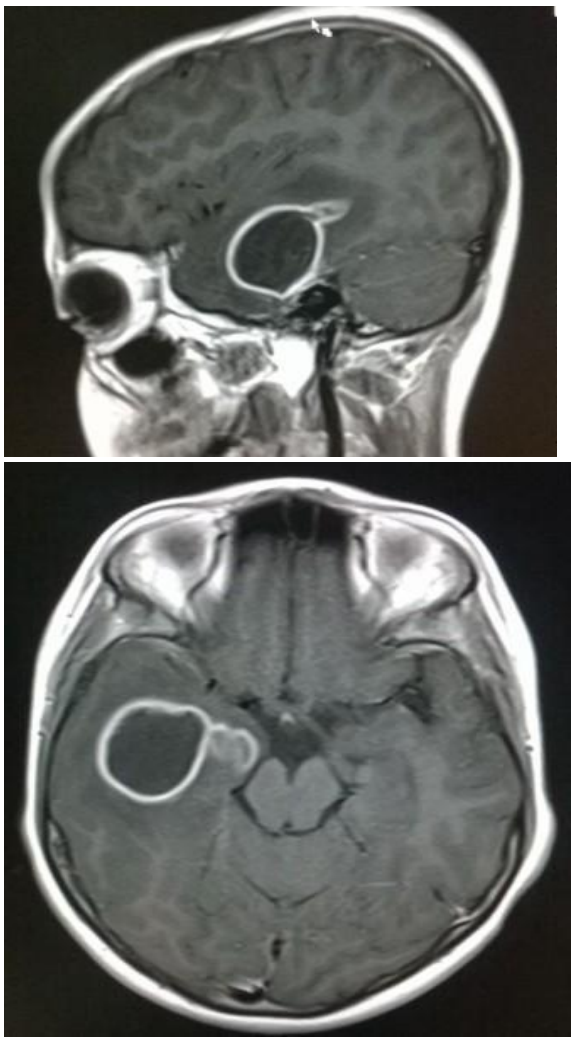


Fig. 2a sagittal T1 , post contrast image with marginal enhancement.
Fig. 2b post contrast ring enhancing lesion in right temporal lobe with extension to limbic system .(Amygdala), A case of cerebral abscess.

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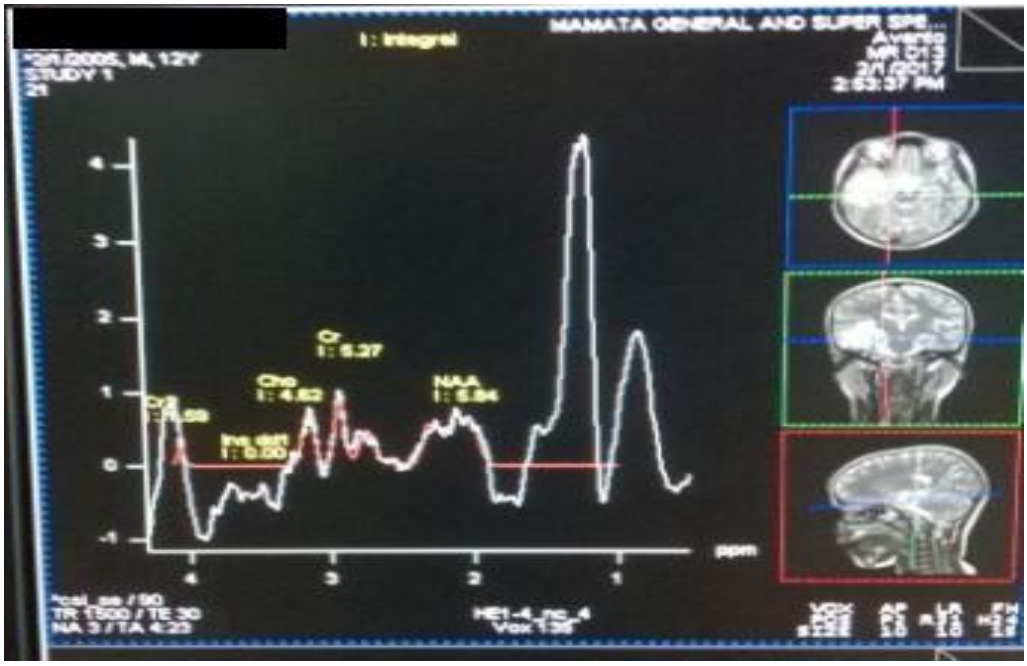

Fig. 3 MRS reveal significant lactate peak at 1.3 and lipid peak below 1 ppm.significant NAA peak reduction is also noted due to destruction of neuronal cells.No significant choline peak is noted .

MRS IN TUBERCULAR INFECTIONS :

Tuberculosis (TB) of the CNS is always secondary to TB elsewhere in the body and is caused by Mycobacterium tuberculosis. The incidence of CNS TB has increased following the emergence of acquired immunodeficiency syndrome (AIDS). TB causes a granulomatous inflammatory reaction, which may involve the meninges, causing TB meningitis, and/or brain parenchyma, causing tuberculoma or tuberculous abscess. Tuberculoma is a space-occupying mass of granulomatous tissue. The definitive diagnosis is necessary, as most tuberculomas respond to medical management. On MR imaging, tuberculoma's appearance varies depending on its stage of maturation (i.e, whether noncaseating, caseating with solid or liquid center).

The noncaseating tuberculoma usually appears as hyperintense on T2-weighted and slightly hypointense on T1-weighted images. Metastases, lymphoma, and other infective granulomas also have similar imaging features. On T1-weighted magnetization transfer (MT) imaging, the cellular component of the lesion appears brighter and is considered relatively specific for the disease.

One of the characteristic features of mycobacterium is the presence of a lipid-rich cell wall that contributes to the lipid peaks in tuberculomas. On spectroscopy caseating tuberculomas show peaks attributed to cyclopropane rings (0.5 and 0.1 ppm) and phenolic glycolipids (7.1–7.4 ppm). These peaks have also been reported from the lipid extracts of

pure strain of M tuberculosis. Phenolic glycolipids represent the biochemical fingerprint of M tuberculosis in a granuloma.

Restriction on DWI with low ADC values has also been observed in tubercular abscess and is considered to be the result of the presence of intact inflammatory cells in the pus.

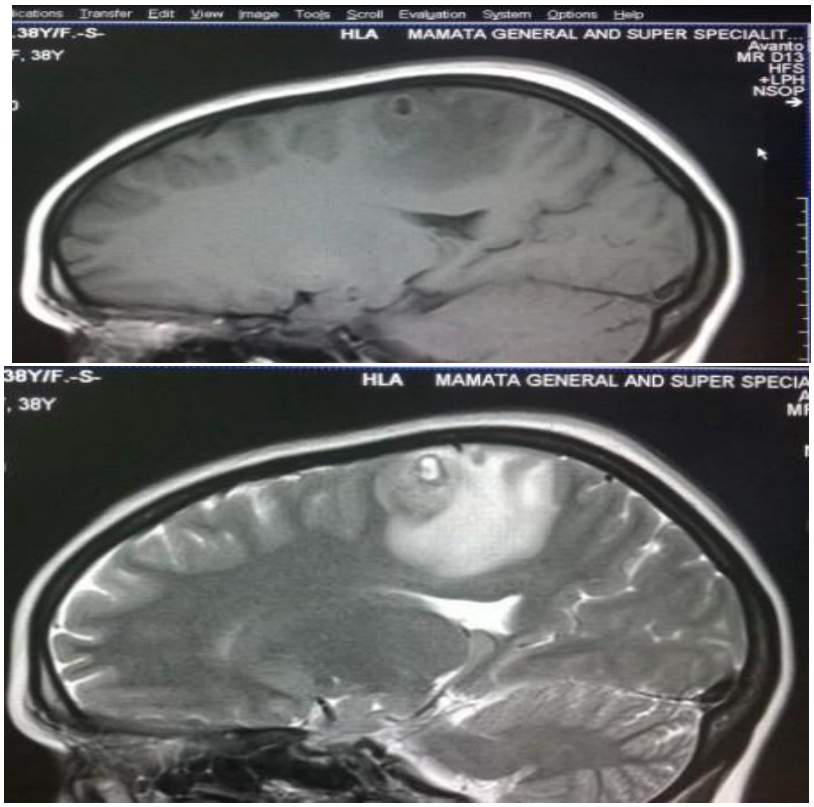

Fig.4a T1 image showing ring lesion in high parietal lobe with peri lesional vaso genic white matter edema.

Fig.4b T2W2image showing ring lesion with central necrotic area and perilesional edema.

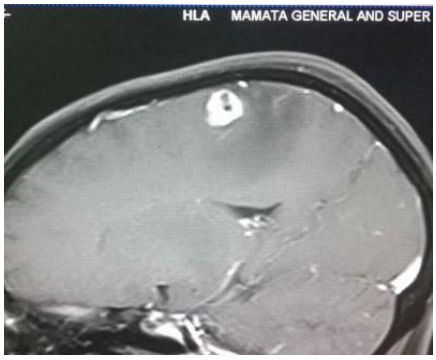

Fig. 5a

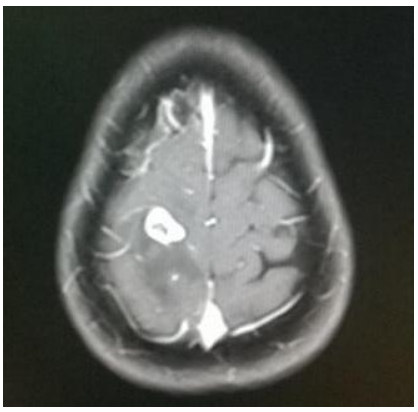

Fig. 5b

Fig. 5a post contrast image showing thick ring enhancing lesion.

Fig. 5b post contrast ring enhancing lesion in right high parietal region with typical white matter location.

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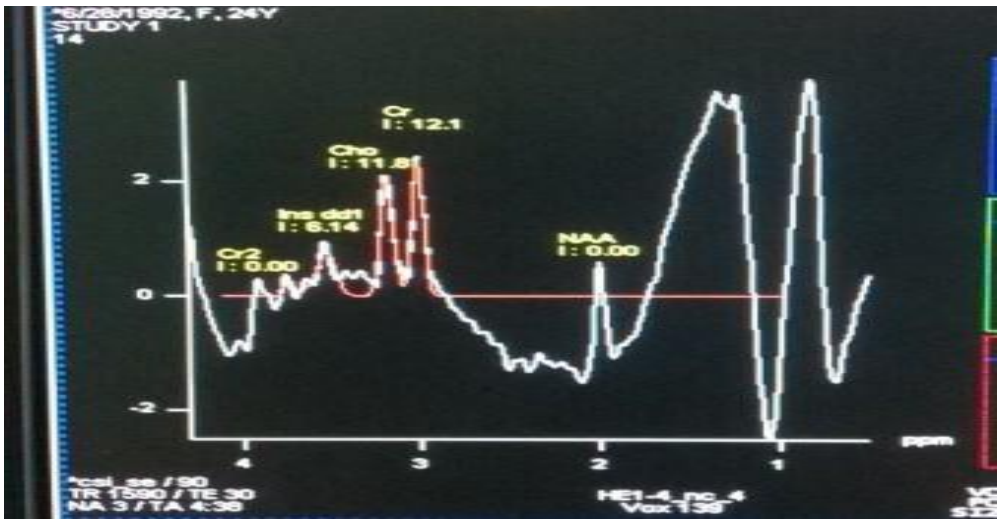
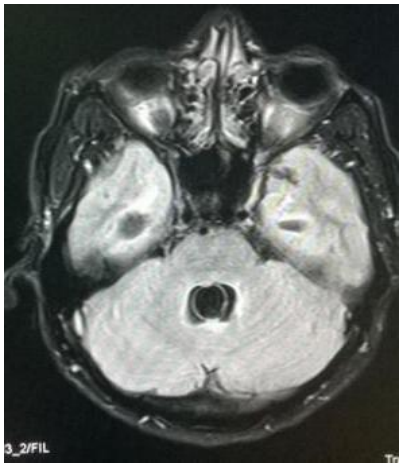
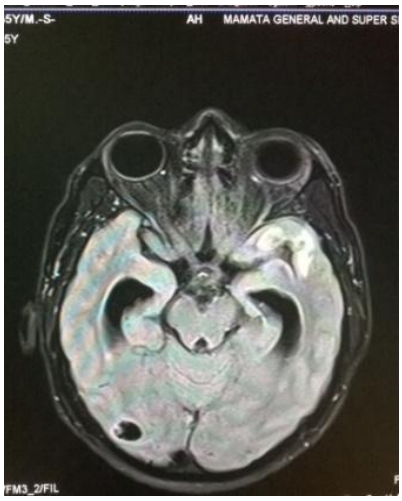


Fig.6 showing multi voxel MRS with reduced NAA peak and dominant lipids, lactate and amino acid peaks. Note normal choline peak, In a case of tuberculoma.





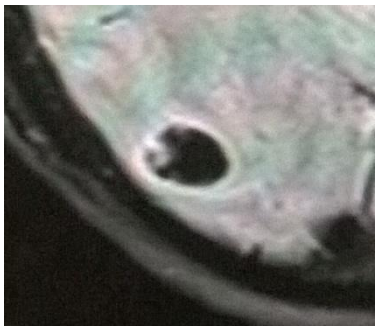


Fig. 7a image showing intra ventricular cyst in 4th ventricle.

Fig. 7b FLAIR image showing hypo intense cyst in right occipital region with scolex inside.few focal areas of cerebral edema noted in left temporal region. Note dilated temporal horns.

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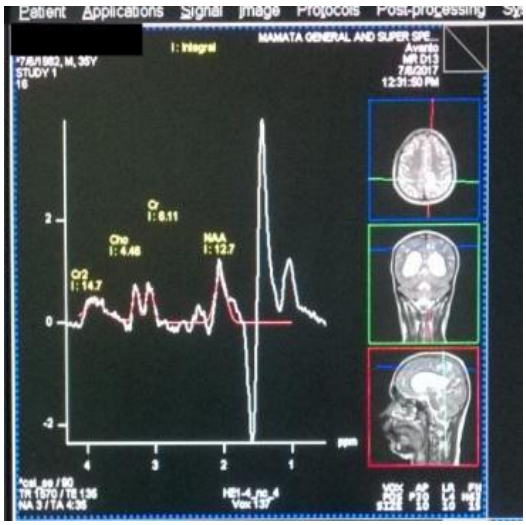


Fig.8 MRS showing lipid ,lactate and small alanine peak with reduced NAA peak and flat choline and creatine peaks.

MRS IN PARASITIC INFECTIONS :

Neurocysticercosis :- Cysticercus cysts may remain viable for many years. Locations of cysts vary; they may be intracranial (parenchymal, ventricular, subarachnoid [cisternal]) or spinal. During the course of development, cysticercus cysts in the brain go through a cystic or vesicular stage, the viable stage; colloidal or granular stage, and the chronic calcified stage.

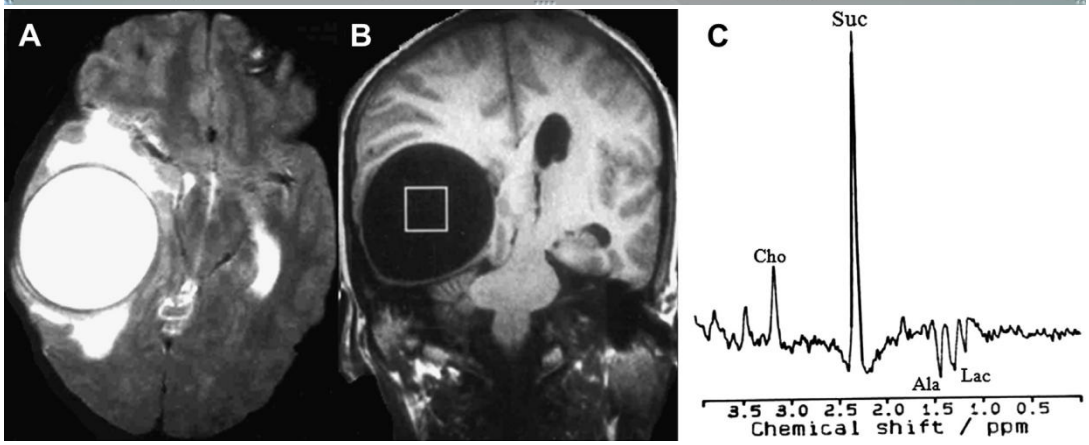
In vivo spectroscopy in neurocysticercosis shows peaks ofcytosolic amino acids (valine, leucine, and isoleucine), Lac, alanine, succinate, NAA, Cr, and Cho. The peaks of NAA, Cr, and Cho are assumed to be due to contamination from normal brain parenchyma within the voxel. Lac, alanine, succinate, and Cho peaks on ex vivo MRS of fluid aspirated from cerebral cysticercus cysts have been demonstrated.

On starting to examination, single or multi voxel protocol must be selected considering the purpose of the study. In research of brain tumour which has got a heterogeneous or infiltrative pattern we should use multi-voxel protocol [4]. But in small lesions, posterior fossa tumors, or if there is a non removable metallic implant near the FOI, we should use single voxel protocol. Different components of metabolites could be useful for defining the different peak values of the same product. For example: NAA 2.02 and 2.6 ppm, Cr at 3.02 and 3.9 ppm, Glx between 2.05 - 2.4 and 3.65 - 3.8 ppm, glucose at 3.43 and 3.48 ppm, myo-inositol between 3.56 and 4.06. But, generally, only the established dominant ones to be considered for diagnosis. Main metabolites: Cho (choline, 3.2 ppm), Cr (creatine, 3.0 ppm), NAA (n-acetile aspartic acid, 2.02 ppm), Mi (myo-inositole, 3.56 ppm) Lip (Lipid, 0.8 - 1.5 ppm), Lac (lactate, 1.3 ppm) .

In infantile periods, mI is the dominant peak at first months and Cho is also high at these times. But then mI's and Cho's peak values decreases as NAA, Cr increases. After the end of age 2, MRS patterns of metabolites becomes similar with adult level.

Table 1. Example of normal metabolite ratios for children and adults.

Normal	Neonatal	Infantile	Child	Adult
NAA/Cho	0.67 ± 0.17	1.56 ± 0.67	3.43 ± 1.04	2.37 ± 0.40
Cho/Cr	1.27 ± 0.40	0.84 ± 0.21	0.49 ± 0.16	1.05 ± 0.2



Hydatid cyst located on the right temporal region. MRS shows peaks of Lac at 1.33 ppm; alanine (ala) at 1.48 ppm, succinate (Suc) at 2.4 ppm, and choline (Cho) at 3.2 ppm.

Brain Tumors :-

MRS can be used to determine the degree of malignancy. As malignancy increases, NAA and creatine decrease, and choline, lactate, and lipids increase.

NAA decreases as tumor growth displaces or destroys neurons.Very malignant tumors have high metabolic activity and deplete the energy stores, resulting in reduced creatine. Very hypercellular tumors with rapid growth elevate the choline levels.Lipids are found in necrotic portions of tumors Lactate appears when tumors outgrow their blood supply and start utilizing anaerobic glycolysis. In our study we studied most of the common brain tumors by their morphology location and spectroscopy.

Proton MR Spectroscopy (^{1}H MR spectroscopy) is a noninvasive technique that is acquiring an important role in the diagnosis of brain tumors before surgery.

Epidermoid cyst :

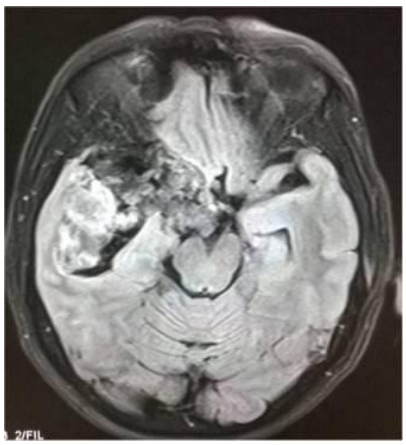
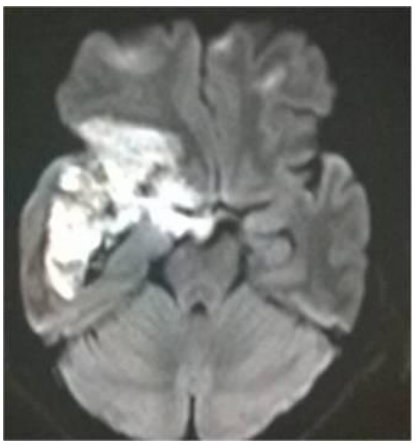
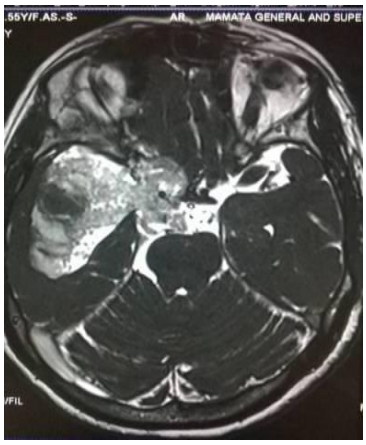




Fig. 9 FLAIR image showing mixed intensity lesion in right peri sylvian region with its extension to the right para sellar,pre pontine and basal cistern.

Fig. 10 diffusion image showing restricted diffusion in the lesion with extension to the basal cisterns, an Epidermoid cyst.

Fig. 11 3D CISS image showing more details of cisternal extension and encircling nature of the tumor to adjacent vessels and cranial nerves.

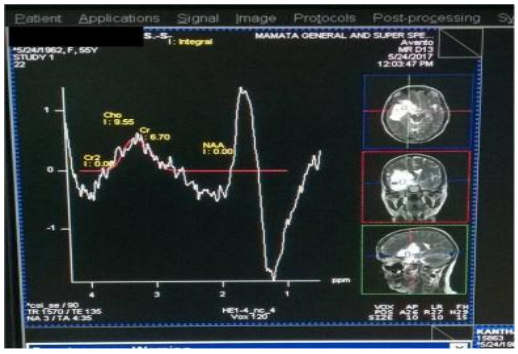


Fig. 12 epidermoid.

Malignant transformation of intracranial epidermoid cysts is very rare. If MRS show increased choline peak , than lipids and lactate one should suspect malignant transformation.

Meningioma was the only tumor group in which long TE performed better than short TE. Proton MR Spectroscopy

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Elevated levels of alanine has been detected previously in grade -1 meningioma patients. However, there has been no study to date that compares various metabolite levels between grade-1 and grade-2 (atypical) meningiomas. MRS show choline peaks in atypical meningiomas with decrease in NAA levels and change in NAA/CHO ratio. Involvement of adjacent dura, bone hyperostosis and some times angiomatous / sarcomatous changes are also observed in atypical meningiomas. Recurrence is more likely in patients with increased choline peak on spectroscopy.

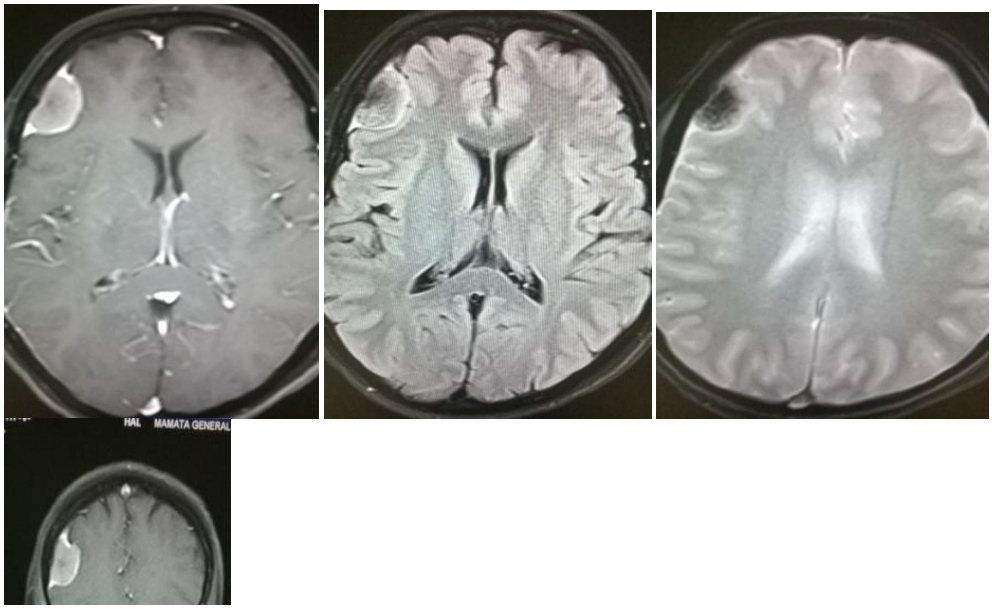

Fig. 13 Meningioma : calcified, extra axial lesion with post contrast typical dural tail sign.

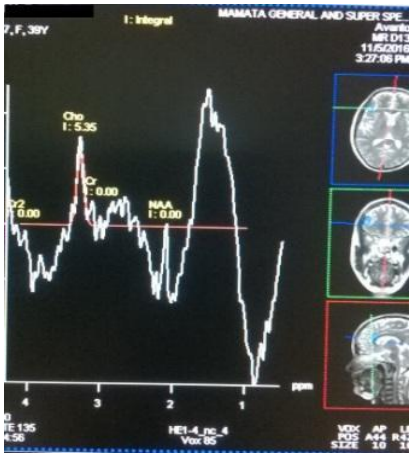

Fig. 14 Alanine peak in meningioma with mild choline peak prominence.

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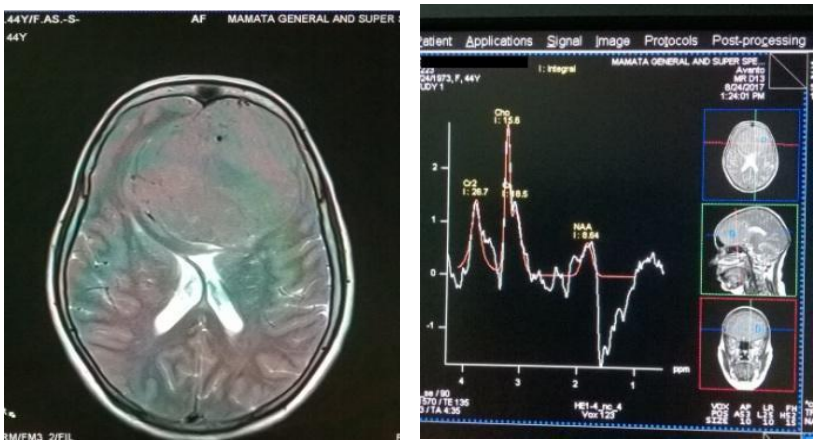

Fig. 15 a ,b Atypical meningioma frontal region with choline ,alanine and creatinine peak on spectroscopy.

MRS can be used to determine the degree of malignancy. As malignancy increases, NAA and creatine decrease, and choline, lactate, and lipids increase. NAA decreases as tumor growth displaces or destroys neurons. Very malignant tumors have high metabolic activity and deplete the energy stores, resulting in reduced creatine .Very hypercellular tumors with rapid growth elevate the choline levels. Lipids are found in necrotic portions of tumors Lactate appears when tumors outgrow their blood supply and start utilizing anaerobic glycolysis.

Key feature of gliomas is elevated choline beyond the margin of enhancement due to infiltration of tumor into the adjacent brain tissue.

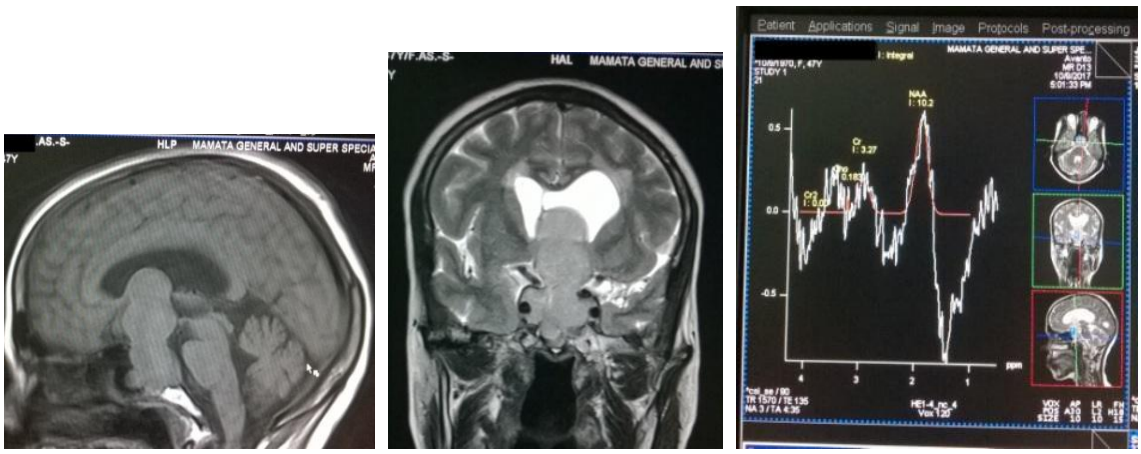

Fig. 16 Reveal pituitary macro adenoma with supra and para sellar extension with mass effect on 3rd ventricle. Non specific metabolite peaks on MRS with out choline raise.

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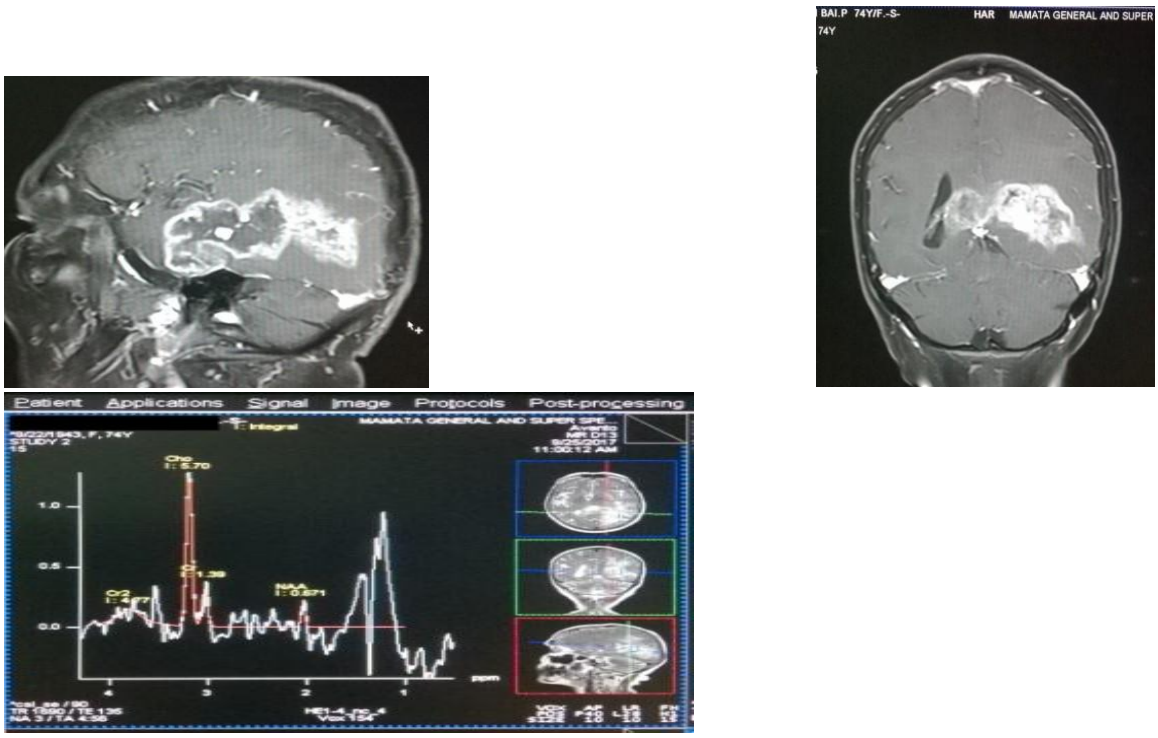

Fig. 17 post contrast MR images showing butterfly glioblastoma, crossing mid line through corpus callosum. MRS show significant choline peak parallel to its malignant nature.

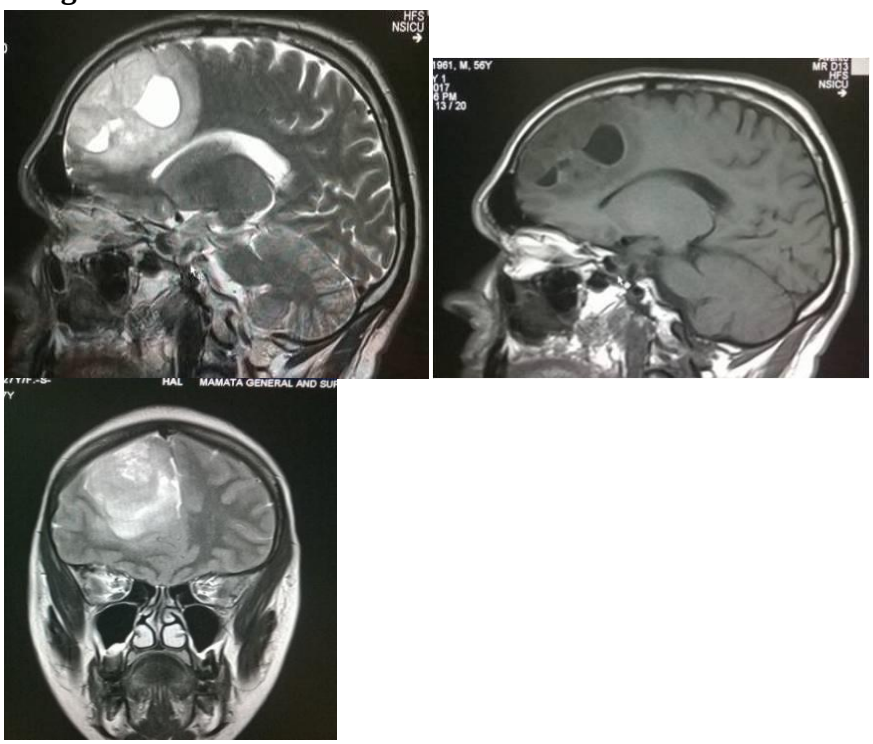

Fig . 18 Dysplastic/Anaplastic oligodendroglioma, right frontal lobe.

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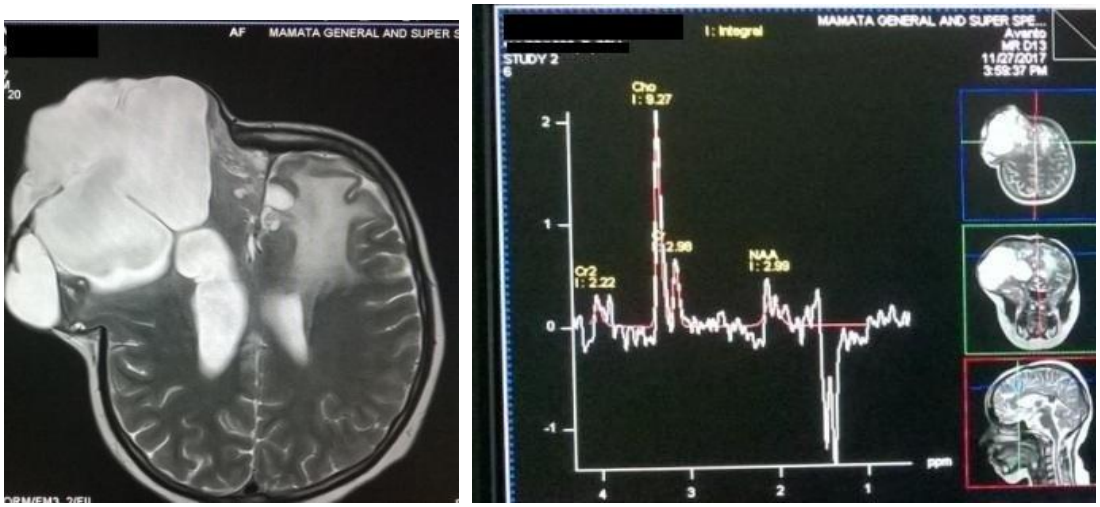


Fig. 19, post operative follow up of the same patient showing recurrence, dominantly cystic, anaplastic with high degree of malignancy denoted by significant choline peak and flat NAA . Lesion also show multiple dural enhancing areas and along lepto meninges.

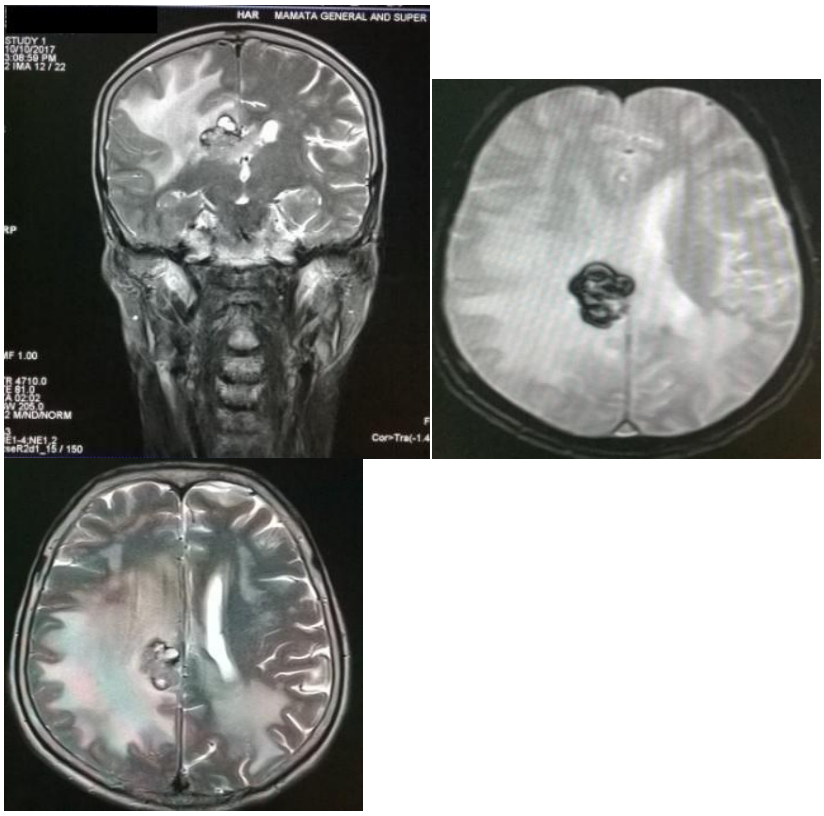
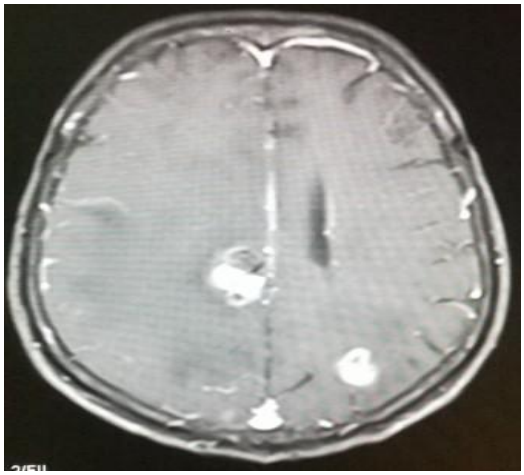


Fig. 20 Multiple metastatic lesions at grey and white matter junction with significant white matter peri lesional edema. Gradient image showing significant bloomimg in the lesion suggesting hemorrhagic nature of the secondaries.



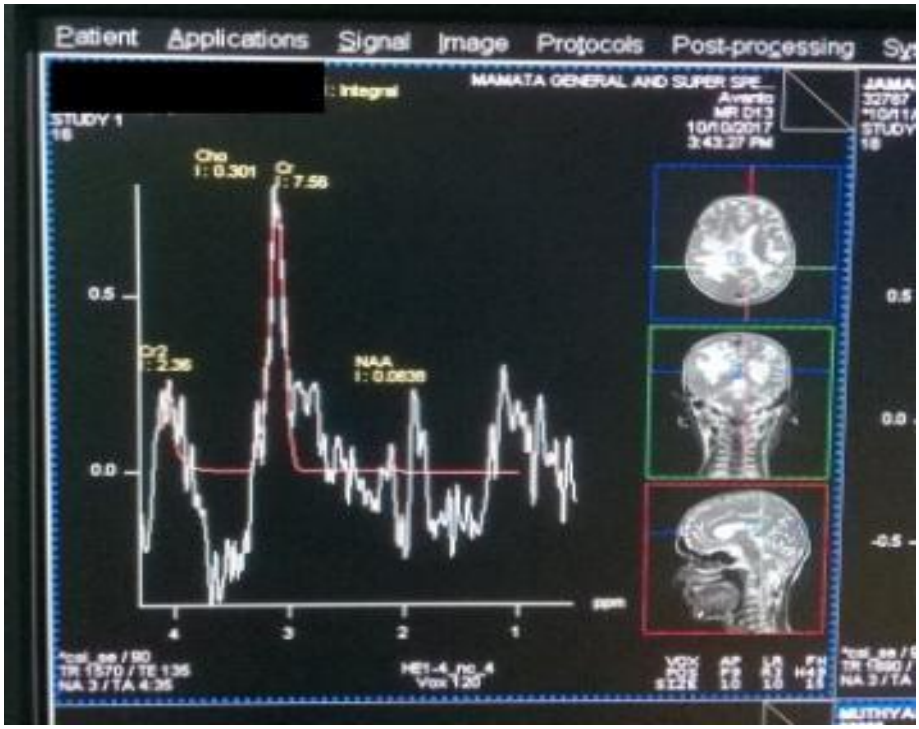


Fig. 21 post contrast enhancement in multiple metastatic lesions with significant choline peak showing aggressive nature of the disease.

DISCUSSION:

The current evidence on the accuracy of ^{1}H-MR spectroscopy in the characterization of brain tumors is promising. Conventional MR imaging provides highly detailed anatomic information and has become a mainstay in the diagnosis of suspicious brain lesions.

Proton MR spectroscopy (^{1}H-MR spectroscopy) provides additional information on the metabolic composition within an area of tissue. By comparing the relative concentration of these metabolites, clinicians can judge factors such as neuronal viability, neurotoxins,

and membrane turnover within the volume of interest and, thereby, the likely underlying pathology and post operative consequences.

The first aim of this study is to provide an updated systematic review ,the value of ^{1}H-MR spectroscopy for characterizing brain tumors. The second aim is to develop methodologic guidelines for measuring the efficacy of ^{1}H-MR spectroscopy to help focus future research in this area and plan a good treatment protocol and post operative follow ups for the patients.

A number of large diagnostic performance on current patients have demonstrated that ^{1}H-MR spectroscopy can accurately distinguish between high- and low-grade astrocytomas / benign and malignant brain tumors. This work now needs to be extended to demonstrate: (1) diagnostic thresholds selected a prior, rather than post operative histopathological diagnosis and can achieve similar diagnostic accuracy. The incremental diagnostic yield of ^{1}H-MR spectroscopy compared with anatomic MR imaging, and that any improvement in tumor grading by ^{1}H-MR spectroscopy leads to a reduction in biopsy rates or changes in therapy. Evidence in other clinical subgroups, such as the use of ^{1}H-MR spectroscopy to distinguish neoplastic and non-neoplastic lesions or to differentiate recurrent tumors from radiation necrosis, is limited by the small number of studies.

CONCLUSION:

In conclusion, MR spectroscopy is used worldwide as an adjunct to MR imaging in several common neurologic diseases, including brain neoplasms, inherited metabolic disorders, demyelinating disorders, and infective focal lesions. Single voxel MRS is useful in small lesions and multi-voxel MRS is useful in large lesions

The spectrum of disorders for which MR spectroscopy will be clinically used is likely to expand more and include neurodegenerative diseases and epilepsy. The standardization of MR spectroscopy data acquisition and analysis techniques for clinical use is encouraged, along with the publication of normative data obtained with these techniques.

Where possible, these should include assessment of the impact on clinical outcome and economic benefit. Clinical imaging centers specializing in combined use of MR imaging and spectroscopy are already established . MR spectroscopy is a definite diagnostic tool to differentiate between benign and neoplastic lesions, to map a pathway for better patient management , to judge a severity and aggressiveness of the lesion.

In future we hope to develop MR spectroscopy involving crucial malignancies all over the human body which can be a better milestone in the management and the treatment of the patients.

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