The Most Commonly Seen Metabolites in Intracranial Space Occupying Lesions - A Prospective Study

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ABSTRACT

Background: Intracranial space occupying lesions are defined as lesions occurring within the cranial vault, which can be intra-axial or extra-axial. Magnetic Resonance Spectroscopy can be performed in 10-15 minutes and combined with conventional imaging protocols. Thus, MRS offers the possibility of not just visualization of the lesion but also biochemical characterization simultaneously. The present study was aimed at establishing the most commonly seen metabolites in the intracranial space occupying lesions. Methods: The present observational study was conducted in the Department of Radiodiagnosis, Ananta Institute of Medical sciences and Research Centre, Udaipur, Rajasthan, on a 1.5 Tesla Siemens MAGNETIC RESONANCE IMAGING equipment and 3.0 TESLA MAGNETIC RESONANCE IMAGING equipment. As reference standards, values of Cho/Cr > 1.5, NAA/Cr < 1.6, Cho/NAA > 0.8, Lactate > 1.34, Lipids >1.4, Glutamate > 2.5, Glutamine > 2.38, Alanine >1.48 were taken as abnormal. Based on these the lesions were characterised as benign/ malignant and grades of malignancy was determined. The data was arranged in a tabulated version and analysed using SPSS software. Results: Mean Cho/ Cr ratio was high in gliomas, metastasis and meningiomas, while it was normal in DNETs and infections. Highest Mean Cho/Cr value was seen in metastasis (3.48). Abscesses showed presence of lactate, acetone and amino acids peaks, while acetone and amino acids were not seen in Tuberculosis or NCC. Lipid peaks were seen in 100% of the cases of Tuberculosis. Conclusions: From the above study, we can conclude that presence of alanine in 100% of meningiomas makes it a useful marker for these tumors. Tuberculomas showed intense signals from lipids, and hence could be separated from Neurocysticercal cysts.

Key words: Intracranial, Neurocysticercal, Tuberculosis,

INTRODUCTION

Intracranial space occupying lesions are defined as lesions occurring within the cranial vault, which can be intra-axial or extra-axial and they expand in volume leading to displacement of normal intracranial contents and increasing the intracranial pressure. MR spectroscopy is a non-invasive method of obtaining metabolic information about tissues. Conventional MR imaging measures signals emitted by hydrogen (proton) nuclei from small pixels that have been selected by spatial variations in frequency and phase. This spatial mapping enables the signal to be formed into images. Magnetic Resonance Spectroscopy (MRS) can extract information about the chemicals that reside on the frequency scale between water and fat in both a qualitative and quantitative manner. MRS uses the same principles as Magnetic Resonance Imaging (MRI) but rather than generating an image, a plot representing chemical composition of a region is generated.[1-3] Magnetic Resonance Spectroscopy can be performed in 10 - 15 minutes and combined with conventional imaging protocols. Thus, MRS offers the possibility of not just visualization of the lesion but also biochemical characterization simultaneously. MR spectroscopy enables characterization of metabolic changes that are associated with growth of tumor, degree of malignancy, tumor grading, response and sequelae to treatment. Brain tumors generally have different imaging
features by which low-grade growths can be differentiated from malignant types. Magnetic Resonance Spectroscopy does not replace conventional MRI but compliments the information provided by it. It may provide information as a prognostic indicator, help follow progress of the disease and evaluate response to treatment. The present study was aimed at establishing the most commonly seen metabolites in the intracranial space occupying lesions.

METHODS

The present observational study was conducted in the Department of Radiodiagnosis, Ananta Institute of medical science and research Centre, Udaipur, Rajasthan, on a 1.5 tesla Siemens equipment MAGNETIC RESONANCE IMAGING equipment. Purposive sampling was done during the study and all the subjects with intracranial lesions were included in the study. The ethical committee clearance was obtained by the institutional ethical committee and all the subjects were informed about the study and a written consent was obtained from all in their vernacular language. Initially, each patient was subjected to routine spin echo (SE) sequences. Volume of interest from the lesion was selected on SE T2 weighted images or in heterogenous lesions; areas of solid enhancement were selected. For necrotic and cystic lesions spectrum from within the lesion were analyzed separately. Single voxel (SVS) (voxel 2 cm) and multivoxel spectroscopy (Chemical shift imaging, CSI) (voxel 1-8 cm) were performed in these lesions. Corresponding contralateral areas were also analyzed for the metabolite ratios as control. SVS studies were performed with Point Resolved Spectroscopy (PRESS) sequence (TR/TE/Ac (repetition time/time to echo/acquisitions) (1500/135 and 30/128)). CSI was performed using (1690/135 and 30/4) parameters. The SVS-SE-135 spectra were used for metabolite ratio calculations. As reference standards, values of Cho/Cr > 1.5, NAA/Cr < 1.6, Cho/NAA > 0.8, Lactate >1.34, Lipids >1.4, Glutamate >2.5, Glutamine >2.38, Alanine >1.48 were taken as abnormal. Based on these the lesions were characterized as benign/ malignant and grades of malignancy was determined. The data was arranged in a tabulated version and analyzed using SPSS software.

RESULTS

The present study enrolled 65 subjects, out of which 39 were males and 26 were females. Majority of the subjects were aged between 20-39 years of age. Table 1 and Graph 1 show the average metabolite ratios in various lesions. Mean Cho/ Cr ratio was high in gliomas, metastasis and meningiomas, while it was normal in DNETs and infections. Highest Mean Cho/Cr value was seen in metastasis (3.48). Mean Cho/NAA ratio was high in all the lesions, with highest values seen in the meningiomas (7.86) and gliomas (5.15). Mean NAA/Cr ratio was below normal in all the lesions, lowest values seen in the meningiomas (0.53) and Gliomas (0.67). Table 2 and Graph 2 show the other metabolites detected by spectroscopy in malignant tumours. Lactate peak was seen in above 60% of all high grade gliomas and in metastasis, and only in 33% of the meningiomas. Lipid peak was found in the high grade gliomas, particularly in grade IV gliomas (100%). Alanine was seen in all the meningiomas, but not in any other malignancy. All the cases of grade 4 gliomas had lactate. Grade 3 gliomas had both lactate and lipids in equal proportions.

Table 3 shows the ratio of metabolites in infectious lesions. Abscesses showed presence of lactate, acetone and aminoacids peaks, while acetone and aminoacids were not seen in Tuberculosis or NCC. Lipid peaks were seen in 100% of the cases of Tuberculosis, while being absent in Neurocysticercosis.

DISCUSSION

Single voxel Proton MRS, using STEAM or PRESS, has been performed to study brain lesions in clinical settings (Demaerel et al, Kugel et al, Sutton et al, Ott et al).
The utility of these sequences in the differentiation of lesions have been assessed by various workers in the past. Proton MRS is useful only when the voxel of interest is taken from well within the lesion. For very small lesions, the possibility of partial averaging from surrounding tissues and hence obtaining a misleading spectrum is a limiting factor (Kugel et al.[9] Ott et al[11]). The presence of prominent areas of hemorrhage, calcification or sometimes necrosis, or the peripheral location of the lesion close to calvarium or CSF, also result in poor spectrum which does not serve any diagnostic purpose. In the present study, of the 65 patients with intracranial space occupying lesions, diagnostic spectrum was obtained in 60, i.e., 92% of cases. The study was done from the most homogenous part of the lesion in case of predominantly solid lesions. For cystic lesions and suspected abscesses, the cystic or necrotic parts were analyzed separately. In most of the studies in the past on intracranial lesions a short echo time sequence (30 or 20 ms) has been used along with a long echo time (270ms) sequence (Poptani et al[12]), or two long echo time sequences have been used employing PRESS or STEAM for localization (Kugel et al 9, Sutton et al [10], Ott et al[11]). Kugel et al[9] have used SE 135 and 270 ms sequences for better signal to noise ratio and a smooth spectrum devoid of contributions from short T2 metabolites, such as inositols and lipids. Kim et al[13] compared the diagnostic accuracy of short (35 ms) and intermediate (144ms) TE in the grading of gliomas and concluded that a combination of the two is preferable. In the present study a combination of STEAM 30 ms and 135 ms sequences have been used. The 135 ms sequence was used to obtain the metabolite ratios. The results of the present study reveal that the spectral pattern of tumors is markedly different from the normal brain and from other non-neoplastic lesions. In general, the results are consistent with the earlier studies on brain tumors. Most of the tumors revealed an elevated Choline (Cho) peak along with a decrease in N-Acetyl Aspartate (NAA) resonance. However, these resonances were normal or absent in the non-neoplastic lesions. (Bruhn et al[14], Arnold et al[15], Fulham et al[16], Kugel et al[9], Sutton et al[10], Ott et al[11]) All malignant tumors, gliomas, metastasis and meningiomas, were characterized by increased Cho, decreased NAA and Creatine (Cr) along with the presence of lactate (Lac), lactate and lipid (Lip), or lipid resonances in all the cases. Increased Cho has been observed in most brain tumors, attributed to the increased membrane turnover and cell proliferation. Presence of Cho was an essential feature of all gliomas, even when cystic; though the choline levels in cystic neoplasms were lower than in the solid lesions. The latter appears to be due to the degraded pool of Cho in the cystic fluid with no active membrane turnover. (Bruhn et al[14]) The increased Cho may either indicate increased cell proliferation (increased PC) or necrotic process (increased GPC). It is probable that the concentration of free Cho does not change in tumors as reported by Usenius et al.[17] This may also explain the presence of increased choline in some infectious lesions. (Cabello and Coher[18]) The correlation between the tumor grade and prognosis is well established (Adamson et al).[19] Histological classification from biopsy specimens is the reliable and standard method for this purpose. However, biopsies are associated with considerable morbidity especially the risk of irreversible neurological deficit. Proton MRS with its potential to differentiate lesions, promises to provide a preoperative diagnosis, thus obviating the need for surgical biopsy (Son et al,[20] Tzikka et al[21]). Lactate in tumor cells is believed to be formed by conversion from pyruvate, which accumulates as a result of the increased glycolytic activity in the tumor cells, due to the decrease in the tricarboxylic acid cycle activity (Peeling and Sutherland).[22] Hence, the presence of lactate does not appear to correlate significantly with grade of malignancy. Similar results were obtained by Kugel et al[9] in their study of brain tumors.

CONCLUSION
From the above study, we can conclude that presence of alanine in 100% of meningiomas makes it a useful marker for these tumors. Dysembryoplastic neuroepithelial tumors show normal spectrum, a characteristic that enables its differentiation from more malignant lesions. Presence of lactate, acetate and amino acids in brain abscesses was a differentiating feature from the spectral pattern of glioblastomas and metastasis which showed varying levels of choline, lactate and lipids. Tuberculomas showed intense signals from lipids, and hence could be separated from Neurocysticercal cysts. Absence of prominent Cho/NAA ratio differentiated them from metastasis.

REFERENCES


