Role of magnetic resonance spectroscopy & diffusion weighted imaging in differentiation of supratentorial brain tumors

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KEYWORDS
Magnetic resonance imaging; Brain tumor; MRS; DWI

Abstract  Purpose: To evaluate the role of magnetic resonance spectroscopy & diffusion weighted imaging (DWI) in differentiating between primary and secondary brain tumors.
Patients & methods: This prospective study was performed for 40 patients. Diffusion weighted image (DWI) and apparent diffusion co-efficient (ADC) maps were acquired by using b-values of 0 and 1000 mm²/s. Standard mean ADC values were calculated automatically and expressed in 10⁻³ mm²/s in both intra-lesional and peri-lesional regions. Multi voxel MR spectroscopy was performed using a spin-echo mode sequence. The metabolites were identified including the following: N-acetylaspartate (NAA) at 2.0 ppm, creatine (Cr) at 3.0 ppm, choline (Cho) at 3.2 ppm, lipid at the range of 0.7–1.3 ppm, lactate at 1.33 ppm and myoinositol at 3.56 ppm. The ratios that were calculated include the following: Cho/NAA and Cho/Cr in both intralesional and perilesional regions.
Results: Intralesional ADC values showed no difference between the metastases (0.6: 1 x 10⁻³ mm²/s with mean 0.86) and high grade primary tumors (0.6: 1.1 x 10⁻³ mm²/s with mean 0.73). Perilesional ADC value Findings in the study revealed that primary tumors have low ADC values (0.9: 1.1 x 10⁻³ mm²/s with mean 0.95) in their perilesional voxels denoting perilesional infiltration, while higher ADC values in metastasis (1.3–1.6 x 10⁻³ mm²/s mean 1.41) due to the absence of perilesional infiltration increase in CHO/Cr ratios (>1) in primary high grade tumors (indicating perilesional infiltration) while there was no increase in CHO/Cr ratio in cases of metastases. Low grade primary tumors showed low lactate and lipid, with increasing malignancy, and tumors showed increasing levels of lactate and lipid peaks (indicating necrosis) with remarkable difference in lipid peaks between low and high grade tumors. There was no significant difference between primary & metastatic brain tumors as regards lactate peak.

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Conclusion: Intra-lesional ADC values are not useful in the differentiation between primary and metastatic tumors. Perilesional ADC values can differentiate between primary & metastatic brain tumors. Intralesional MRS values (CHO/Cr ratio) were able to grade the tumor and differentiate between high and low grade tumors, while Perilesional MRS values (CHO/Cr ratio) could be able to differentiate primary tumors from metastasis.

1. Introduction

Intracranial tumors are a significant health problem. The annual incidence of primary and secondary central nervous system neoplasms ranges from 10 to 17 per 100,000 persons (1). Brain tumors are subdivided into supra-tentorial & infra-tentorial brain tumors (2). Differentiation of low grade from high grade glioma, neoplastic from non-neoplastic brain masses by using conventional MRI is frequently difficult, and many cases require biopsy or follow-up imaging. Gadolinium enhancement is useful in evaluation of brain tumors. Recent MR imaging techniques, such as MR spectroscopy, can further improve the diagnostic accuracy of MR imaging in the diagnosis of such tumors (2,3). Magnetic resonance spectroscopy is a technique that allows the study of some metabolites in the brain or neoplasms that point to the nature of these lesions, grading of brain tumors, and follow-up and to evaluate the response of these lesions to treatment (4). Magnetic resonance spectroscopy is an analytical method used to identify molecules and to determine their biophysical characteristics (5). Thus, this technique is a multi-parametrical molecular imaging method that can complete MRI study enabling the detection of biochemical patterns of different features and aspects of brain tumor (6). Diffusion-weighted imaging (DWI) helps us to obtain additional information about the brain from the microscopic movement of water molecules. DWI has been used to detect the nature of brain tumors according to their cellularity and to differentiate between high cellular and low cellular brain tumors (7,8).

2. Patients and methods

The study protocol was approved by the local Ethics Committee, and informed consent was obtained from all patients. This prospective study included 40 patients, and their age ranged from 30 to 65 years old with suspicious of intra-axial supratentorial brain tumors by CT.

2.1. Image protocol

All examinations were performed using a 1.5 T MR Unit (SIGNA Horizon, General Electric Medical System, Milwaukee, WI) using head coil.

2.2. Magnetic resonance spectroscopy (MRS)

Multi voxel MR spectroscopy was performed using a spin-echo mode sequence (SE) with long TE (144 mm/s) and short TE (35 mm/s). Water suppression was achieved with chemical shift selection (CHESS) technique. The voxels were placed on the lesions and perilesional areas away from CSF and scalp fat to avoid contamination and voxel was placed in normal region. The metabolites were identified including the following: N-acetyl aspartate (NAA) at 2.0 ppm, creatine (Cr) at 3.0 ppm, choline (Cho) at 3.2 ppm, lipid at the range of 0.7–1.3 ppm, lactate at 1.33 ppm and myoinositol at 3.56 ppm. The ratios were calculated including the following: Cho/NAA and Cho/Cr in both intralesional and perilesional regions.

2.3. Diffusion weighted imaging with apparent diffusion coefficient calculation

DW images were obtained by using an axial echo-planar SE sequence, average, 5 mm section thickness. DW images and ADC maps were acquired by using b values of 0 and 1000 s/mm². Post processing of ADC maps was performed. Standard mean ADC values were calculated automatically and expressed in 10⁻³ mm²/s.

2.4. Statistical analysis

Statistical analysis was undertaken to prove the efficacy of MRS & diffusion in the evaluation of supratentorial brain tumors. Statistical analysis was performed using the SPSS software package version 16.0 (statistical package for social science TM) and P < 0.05 was considered to be statistically significant. The sensitivity and specificity for each protocol were compared in order to evaluate the reliability of each of them and when they are combined.

3. Results

In this prospective study, forty patients were included in this study with supra-tentorial brain tumors. Their age ranged from 30 to 65 years old.

3.1. MRS evaluation

MRS evaluation of the studied 40 patients revealed that 36 cases of the 40 patients (90%) had primary tumors and 4 patients (10%) had metastatic tumors as shown in Table 1 & Fig. 1.

3.1.1. Calculated CHO/Cr ratios from intralesional areas

Calculated CHO/Cr ratios from the intra-lesional areas showed significant increase from low grade to high grade tumors with no significant difference between high grade primary and metastases as shown in Table 2 & Fig. 2.
3.1.2. Calculated CHO/Cr ratios from perilesional areas

Calculated CHO/Cr ratios from the perilesional areas showed increase in CHO/Cr ratios (>1) in primary high grade tumors (indicating perilesional infiltration) while there was no increase in CHO/Cr ratio (≤1) in cases of metastases (indicating no perilesional infiltration) as shown in Table 3 & Fig. 3.

3.1.3. Lipid & lactate levels

Low grade primary tumors showed low lactate and lipid, with increasing malignancy, tumors showed increasing levels of lactate and lipid peaks (indicating necrosis) with remarkable difference in lipid peaks between low and high grade tumors. There was no significant difference between primary to metastatic brain tumors as regards lactate peak.

3.2. Diffusion image evaluation

(a) Intralesional evaluation: As shown in Table 4 & Fig. 4, the calculated ADC value could not distinguish between primary and metastatic brain tumors but calculated ADC values were effective in grading of malignant tumors. High grade malignant tumors had significantly lower ADC values than those of low grade malignant. Intralesional ADC values calculated from Low grade primary tumor areas were (1.2–1.6 × 10⁻³ mm²/s).

(b) Perilesional evaluation: As shown in Table 5 & Fig. 5.

The final histopathological results of 40 patients revealed 35 case primary tumors (85%) which were divided into 4
categories “13 cases of low grade glioma (30%), 3 cases of anaplastic astrocytoma (10%), 17 cases of glioblastoma multiformis (40%), 2 case of lymphoma (5%)”, and 5 cases of metastases (15%) as shown in Table 6 & Fig. 6.

Comparison between MRI & histopathological results were obtained postoperatively by frozen section, as shown in Table 7 & Fig. 7.

4. Discussion

Conventional magnetic resonance imaging is still the basic imaging requirement for initial evaluation of brain tumors. It gives basic information about anatomical features of these tumors such as edema, mass effect, pattern of enhancement (9). MRS limits the use of invasive diagnostic approaches such as brain biopsy, as histopathology is the gold standard for diagnosis of brain tumors (10). In contrast to the structural information provided by MRI, MRS provides a qualitative analysis of a number of metabolites within the brain. These metabolites reflect aspects of neuronal integrity, cell membrane proliferation or degradation, energy metabolism and necrotic transformation of brain or tumor tissue (11). Our MRS results showed that all of them showed variable degrees of increased CHO peak and CHO/NAA ratios using long TE (144 m sec) with significant increase from low grade and high grade tumor without any significant difference between primary and metastatic brain tumors. This agreed with result of Martinez-Bisal and Celda (12) and Shokry (9) that increase in CHO/NAA ratio in lesion could only differentiate low grade primary tumors from high grade primary tumors. A decreased Cr peak was also detected in all cases with significant increase from low grade to high grade tumor but without significant difference between primary and metastatic brain tumors and this also agreed with result of Delorme and Weber (13). While in the short (TE 35 m s), the lactate levels showed significant difference between low grade and high grade tumors also with-

out any significant difference between primary and metastatic brain tumors. This agreed with result of Van der Graaf (14) who stated that the presence of the lactate peaks was usually consistent with aggressive tumors, reflecting increased anaerobic metabolism and cellular necrosis and this pathology don’t differ a lot from primary to metastatic brain tumors. However, short (TE 35 m s), showed the higher lipid peaks in metastatic brain tumors and showed significant difference levels from primary lesions. This agreed with Shokry (9), Opstad et al. (15) & Van der Graaf (14) who gave a possible explanation for the elevated lipids in metastatic lesions as the cancer cells of different origin, contain mobile spectroscopically detectable lipids in their cell membrane. In this study there was another important result; intralesional voxels in primary tumors have also showed different levels of CHO/Cr ratios which showed increase in CHO/Cr ratios with the increase in the grade of the tumor. So CHO/Cr ratios have shown consistency in predicting the tumor grade, and the comparison of CHO/Cr ratios in high grade tumors with that of low grade tumors proved a significant difference between two groups. Chen et al. (16) and Faria et al. (17) added that the increase in CHO/Cr ratios in high grade tumors than those found in low grade tumors was significantly correlated with the expression of proliferating cells. This result showed increase in perilesional CHO/Cr ratio in high grade primary tumors with significant level differences from metastatic brain tumors which did not show increase in perilesional CHO/Cr ratio. This agreed with Opstad et al. (15) & Faria et al. (17) result and they added that primary high grade tumors have been reported to have peritumoral infiltrating neoplastic cells. So perilesional edema showed spectroscopic malignant changes in the form of higher CHO/Cr ratio in primary tumors than metastatic, and this matched agreement with Shokry (9).

![Fig. 4](image1.png)

**Fig. 4** The estimated intralesional ADC values in the studied cases.

![Fig. 5](image2.png)

**Fig. 5** The estimated perilesional ADC values in the studied cases.

<table>
<thead>
<tr>
<th>Type of tumor</th>
<th>Range</th>
<th>Mean ± SD</th>
<th>t value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low grade</td>
<td>0.9–1.2 × 10⁻³ mm²/s</td>
<td>1.10</td>
<td>0.10</td>
<td>3.63</td>
</tr>
<tr>
<td>High grade</td>
<td>0.9–1.1 × 10⁻³ mm²/s</td>
<td>0.95</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td>*Metastases</td>
<td>1.3–1.6 × 10⁻³ mm²/s</td>
<td>1.41</td>
<td>0.09</td>
<td></td>
</tr>
</tbody>
</table>

**Table 5** The estimated perilesional ADC values in the studied cases.

<table>
<thead>
<tr>
<th>Type of tumor</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary tumors</td>
<td>35</td>
<td>85</td>
</tr>
<tr>
<td>Low grade glioma (I-II)</td>
<td>13</td>
<td>30</td>
</tr>
<tr>
<td>Anaplastic astrocytoma (III)</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Glioblastoma multiformis</td>
<td>17</td>
<td>40</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>*Metastases</td>
<td>5</td>
<td>15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>χ²</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.025</td>
<td>0.042</td>
</tr>
</tbody>
</table>

**Table 6** The final histopathological results of the studied cases.
This result showed no significant difference in intraslesional ADC values between primary and metastatic brain tumors and so failed to differentiate primary tumors from metastatic brain tumors by intraslesional ADC values only. This result matched with Pavlisa et al. (18) & Ja Lee et al. (19) & Ohba et al. (20) which referred this result due to the increase in the cellularity of all these lesions to the level that DWI could not differentiate, but this results mismatched with Chiang et al. (3) that found that ADC values in the tumoral regions of metastasis were significantly higher than primary tumors, but his study was done using 3 T MR unit. Another valuable result was that intraslesional ADC values were higher in low grade primary than high grade tumors with significant different ADC values (1.2–1.6 × 10⁻³ mm²/s) for low grade tumors and (0.6–1 × 10⁻³ mm²/s) for high grade tumors. So in our study it could be able to differentiate low grade tumors from high grade tumors using ADC values, and this agreed with the result of Ohba et al. (20) who added that ADC values can be used to grade primary tumors. Also we found that perilesional ADC values were higher in metastatic brain tumors.
than primary high grade tumors with significant ADC value changes between both. Perilesional ADC values calculated around tumor areas were higher in metastasis (vasogenic edema) denoting no perilesional infiltration (1.3–1.6 × 10⁻³ mm²/s) than high grade primary tumors (0.9–1.1 × 10⁻³ mm²/s) denoting peri lesion infiltration. So in the current study it could be able to differentiate primary from metastatic brain tumors which means high sensitivity of ADC values to differentiate between primary and metastatic brain tumors. This matched with the result of Faria et al. (17) who referred this result to perilesional infiltration of primary high grade tumors which increase cellularity in perilesional area while metastatic cases show no perilesional infiltration raising ADC values in perilesional edema. In our study, ADC values calculated from primary tumoral area had the lowest values in high-grade malignant tumors. We could not find any difference among the ADCs of the tumor types in the same grade.

5. Conclusion

From the current study it can be concluded that the combination of MR spectroscopy and DWI with ADC values calculation could improve the diagnostic efficacy of MR imaging in the diagnosis and grading of malignant brain tumors. Intralesional ADC values are not useful in the differentiation between primary and metastatic tumors with no valuable changes. Perilesional ADC values can differentiate between primary & metastatic brain tumors.

MRS may enable differentiation between lesions showing similar aspects on conventional MRI. Choline is considered the most specific marker of intracranial neoplasm. Increase in Choline levels and Choline/NAA ratios are very suggestive of the malignant nature of the neoplasm, its grading and its follow-up to evaluate the response of the treatment.

Conflict of interest

The authors declare that they have no conflict of interest.

References