Role of diffusion weighted imaging and proton magnetic resonance spectroscopy in ring enhancing brain lesions

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Abstract  Aim of the work: To assess and compare the usefulness and efficacy of both diffusion weighted imaging (DWI) and proton magnetic resonance spectroscopy (1HMRS) in brain lesions with ring enhancement in post contrast T1WI and to determine which method is more effective.

Subjects and methods: Thirty patients with ring-enhanced brain lesions were classified into 2 groups, abscess group (11 patients) and tumor group (19 patients), were examined using diffusion-weighted imaging (DWI) and H-proton magnetic resonance spectroscopy (1HMRS).

Results: Restricted diffusion and low ADC value were seen in 9 (81%) patients of brain abscesses, however, free diffusion and high ADC value were found in 18 (94%) patients with necrotic brain tumor. The abscess group showed aminoacids, acetate and lactate in 9 patients and extra peak of succinate was found in 1 patient; however in the tumor group lactate alone was found in 12 patients, lactate and choline were seen in 5 patients, none of the patients showed amino acids, succinate or acetate.

Conclusion: Both DWI and 1HMRS are useful and efficient imaging techniques in ring enhancing brain lesions and differentiate between pyogenic brain abscesses and necrotic tumors, but DWI is accurate, has less imaging time than 1HMRS, also is available in many imaging centers.

1. Introduction

Intracranial cystic mass lesions represent a significant neurosurgical dilemma. Depending upon non-specific clinical findings and tumor appearances on imaging modalities including CT scan and conventional MRI, differentiation of various intracranial cystic lesions may be challenging (1).

It is shown that conventional MRI has only 61.4% sensitivity in differentiating brain cystic neoplasms from abscesses as...
their main differential diagnosis (1). Recent imaging modalities such as diffusion weighted imaging (DWI) and proton magnetic resonance spectroscopy (MRS) were shown to light the blind spots of conventional MRI with a significant increase in diagnostic accuracy when used as an adjunct (1,2).

The medical management strategies for abscess and neoplasms are different, correct diagnosis must be obtained before the treatment of cystic brain lesions (2), knowledge of the exact nature of the lesion helps neurosurgeon to determine the best management. For example, cerebral abscess can be stereotactically aspirated, followed by intravenous antibiotic therapy, hence avoiding craniotomy (3).

An early and correct diagnosis of aerobic abscesses by in vivo MR spectroscopy as a non-invasive method will reduce the morbidity and mortality rates that occur when diagnosis is delayed (4).

Diffusion-weighted imaging provides a way to assess the diffusion properties of the water molecules in tissue and has been used in clinical applications such as ischemia, tumors, epilepsy and white matter disorders (5).

Diffusion weighted MRI can be used to identify brain abscess and can help to differentiate it from a cystic brain tumor (6).

Combined use of MRS and DWI may improve results compared with the use of a single technique to differentiate brain abscess from cystic tumor. MRS and DWI are complement to conventional MRI for better characterization of intracranial cystic brain lesions (7).

The aim of this study: to assess and compare the usefulness and efficacy of both diffusion weighted imaging (DWI) and proton magnetic resonance spectroscopy (1H MRS) in differentiation between brain lesions with ring enhancement in post contrast T1WI and to determine which method is more effective.

2. Patients and methods

2.1. Study participants

This retrospective study was performed between August 2013 and January 2014, thirty patients (23 males, 7 females) with pyogenic brain abscesses, cystic and necrotic brain tumors were included in the present study, age range between 22 and 70 years, mean 43 years, all patients referred from the neurosurgery department of our institution, these patients had ring-enhanced brain lesions on post contrast T1 images, all were examined with both DWI and proton MRS, we excluded patients with brain lesions that showed hemorrhage in T1WI, lesions less than 1 cm in diameter that were too small to be evaluated by MRS, post-radiation states, large area of calcifications detected by CT.

Patients were classified into two groups according to the final diagnosis, the abscess group included 11 cases, while the tumor group included 19 patients, glioblastoma multiforme (11%) was the most frequent tumor in the tumor group, and the distribution of the patients in the tumor group is shown in Table 1.

In the abscess group (11 patients), the final diagnosis was made by pathology or aspiration biopsy or on the base of clinical symptoms, improvement in the follow up imaging after antibiotic therapy and laboratory data, however in the tumor group (19 patients) primary tumors were finally diagnosed by histopathology obtained by surgery, however metastasis was diagnosed on the base of clinical and radiological findings and had pathologically proven primary tumors, in 5 patients with metastasis; the primary tumor was from cancer breast in 3 patients and cancer lung in 2 patients.

The protocol of the study was approved by the local ethics committee of our institution and informed consent was obtained from all patients.

2.2. Imaging procedures

All patients showing evidence of ring enhancing brain lesion in post contrast T1WI of conventional MRI were examined by both DWI and 1H MRS using 1.5 Tesla MR unit (Signa Horizon SR 120, General Electric Medical Systems, Milwaukee, WI, USA) with a standard quadrature head coil.

The conventional MRI included T1W (TR/TE = 500/15 ms), T2WI (TR/TE = 4000/126 ms) and FLAIR (TR/TE = 8000/142 ms, inversion time = 2200 ms) sequences, contrast enhanced MRI was done for all patients after intravenous injection of gadolinium-diethylene triaminopenta-acetic acid, with dose 0.1 mmol/kg body weight.

2.3. Diffusion weighted imaging (DWI)

Diffusion weighted imaging was performed for all patients and acquired in the axial plane using single shot echo-planar spine echo sequence using the following parameters, TR = 3000–4500, TE = 80–100, field of view = 32–40 cm, matrix size = 192 × 256, slice thickness = 5 mm, number of excitations = 3, diffusion gradient encoding in 3 orthogonal directions at b = 1000 s/mm². The time of scanning was 40 s. The signal intensity of the cystic or necrotic portion of the lesion was defined by visual assessment as low or high compared with normal brain parenchyma.

2.4. Post-processing of ADC map

It was done using the standard software supplied on the machine console to obtain the ADC value and map, the ADC values were measured in the regions of interest in the center of the lesion (cavity of the abscess and necrotic portion of the tumor) and in comparable normal contralateral regions in the white and gray matter of the brain. The ADC values of the gray and white matter were 0.85 ± 0.13 × 10⁻³ and 0.8 ± 0.13 × 10⁻³ mm²/s, respectively (2).

Brain abscess was defined as ring enhancing lesion with restricted diffusion (hyper intense) and had low ADC value than that of normal-appearing brain, while necrotic tumor

### Table 1 Distribution of patients in the tumor group in relation to their final diagnosis.

<table>
<thead>
<tr>
<th>Final diagnosis</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glioblastoma multiforme</td>
<td>11 (57.89%)</td>
</tr>
<tr>
<td>Metastasis</td>
<td>5 (26.32%)</td>
</tr>
<tr>
<td>Astrocytoma</td>
<td>2 (10.53%)</td>
</tr>
<tr>
<td>Ependymoma</td>
<td>1 (5.26%)</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
</tr>
</tbody>
</table>
was defined as ring enhancing lesion with free diffusion (hyperintense) and had high ADC value than that of normal-appearing brain.

2.5. MR spectroscopy

The selection of voxel position in the estimated center of the lesion was determined visually by examining the MR images in three orthogonal planes (sagittal, coronal, and axial) to define the volume of interest, a voxel 1.5 × 1.5 × 1.5 cm to 2 × 2 × 2 cm was used depending upon the lesion size, single voxel MRS was applied by using a point-resolved spectroscopy sequence (PRESS), these spectroscopic sequences were taken in the center of the lesion, short TE (TR/TE = 1500/35 ms), intermediate TE (TR/TE = 1500/144 ms), and an additional long TE of 270 ms were obtained to confirm the phase inversion associated with J-coupled metabolites of lactate and amino acids but not of lipids, which is helpful to discriminate lactate or amino acids from lipid signals (2). The acquisition time for each sequence was 7 min 54 s.

The spectral data post-processing were carried out through the workstation spectroscopic package using semi-automated software (Functool, version 2.33, GE Medical Systems, Milwaukee, WI, USA).

The presence or absence of resonance peaks was recorded for each patient as the following: choline (Cl) at 3.2 ppm, creatine (Cr) at 3.04 ppm, NAA at 2.02 ppm, lactate at 1.3 ppm, amino acids (AAs) at 0.9 ppm and lipids at 0.8–1.3 ppm, acetate (1.9 ppm) and succinate (2.4 ppm) assignments of these various resonance were based on previously published 1HMRS studies of necrotic brain tumors and brain abscesses (2).

Based on MR spectroscopic findings, diagnosis of abscess depends on the presence of amino acids with or without lactate, acetate and succinate, while the diagnosis of tumor cysts depends on the absence of amino acids and the presence of lactate or lactate and choline.

2.6. Statistical analysis

Data were entered into a computer using computer programs Microsoft Excel version 12 (Microsoft Corporation USA) and SPSS version 19 (Statistical Package for the Social Science, IBM corporation USA). Data were statistically described in terms of range, mean and standard deviation (±SD), frequencies (number of cases) and relative frequencies (%). Comparison between different groups was done using student’s t-test for independent samples in comparing 2 groups of quantitative data when normally distributed and Mann–Whitney U test for independent samples when not normally distributed, P value < 0.05 was considered statistically significant.

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of both DWI and 1HMRS in relation to the final diagnosis for differentiation between pyogenic brain abscesses and cystic and necrotic brain tumors were calculated using 2 × 2 contingency table (Table 2).

3. Results

This study included 30 patients with evidence of ring enhancement in post contrast T1WI and they were classified into two groups based on the their final diagnosis; the abscess group included 11 patients (9 male, 2 female), age range 22–70 years, mean age 46 years, and the tumor group included 19 patients (14 male, 5 female), age range 31–67 years, mean age 39 years.

Nine cases with pyogenic brain abscesses were hyperintense on diffusion-weighted images and had low ADC values when compared those in normal-appearing brain.

The ADC value ranged from 0.71 to 0.83 ± 0.31 × 10⁻³ mm²/s (mean ± SD); two cases of brain abscess showed low signal intensity in DWI with high ADC values and it was found that these changes in the signal intensity were due to a 3-week course of IV antibiotic treatment and their mean ADC ranged from 1 (10⁻³ mm²/s) to 1.2 (10⁻³ mm²/s).

We found that, the necrotic areas of 18 tumors had low signal intensity on DWI with high ADC values, ADC values of necrotic tumors ranged from 2.73 to 3.5 ± 0.34 × 10⁻³ mm²/s, 1 patient showed high signal intensity on DWI and low ADC values, mimicking that of abscess; It was low grade astrocytoma. The reason for restricted diffusion was possibly due to necrosis of the central portion of the tumor containing viscous fluid which was found at surgery.

Analysis of the value of ADC using unpaired t test (two tailed Student’s t test) indicates a significant difference between necrotic brain tumor and abscess (P < 0.01) (Table 3).

Interpretation of 1HMRS findings in the abscess group showed that: the main findings were the resonances of amino acids (valine, leucine, and isoleucine), acetate, alanine, and lactate identified in 9 patients with or without other prominent predominant resonance peaks as N-acetylaspartate, choline (Cl), and creatine/phosphocreatine and these visible resonances of Cho, Cr, and NAA which may be seen in the abscess may be due to partial volume effects caused by a combination of the resonances from the central cavity and surrounding contrast-enhancing tissue. A resonance peak for succinate was also detected in 1 patient, AAs could not be detected in 2 patients which was probably due to the fact that, these patients underwent treatment with antibiotics for 3 weeks, an extra peak of lipids was found in 3 patients.

In the tumor group, lactate alone was found in 12 patients, lactate and choline were seen in 5 patients, neither lactate nor

### Table 2 2 × 2 contingency table

<table>
<thead>
<tr>
<th></th>
<th>Tumor</th>
<th>Abscess</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor</td>
<td>a</td>
<td>b</td>
<td>a + b</td>
</tr>
<tr>
<td>Abscess</td>
<td>c</td>
<td>d</td>
<td>c + d</td>
</tr>
<tr>
<td>Total</td>
<td>a + c</td>
<td>b + d</td>
<td>a + b + c + d</td>
</tr>
</tbody>
</table>

Sensitivity: a/a + c, specificity: d/b + d, positive predictive value: a/a + b, negative predictive value: d/c + d.

### Table 3 Range, mean ± SD of ADC values (value × 10⁻³ mm²/s) of both abscess and tumor groups.

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abscess (n = 11)</td>
<td>0.71–0.83</td>
<td>0.84 ± 0.63</td>
<td>0.01</td>
</tr>
<tr>
<td>Necrotic or cystic tumor (n = 19)</td>
<td>2.73–3.5</td>
<td>2.23 ± 0.73</td>
<td></td>
</tr>
</tbody>
</table>

SD = standard deviation.

* P value, significant.
choline in 2 patients, lipid and lactate seen in 2 metastatic brain patients, none of the patients showed amino acids, succinate or acetate. NAA and creatine were reduced or absent in all patients.

With DWI, 9 cases of abscess were correctly diagnosed and 2 cases of abscess were misdiagnosed as tumor, 18 cases of the tumor group were correctly diagnosed and 1 case of the tumor group was misdiagnosed as an abscess.

With MRS two abscesses were misdiagnosed as tumor, these findings may due to the absence of amino acids because these patients were undergoing treatment with antibiotics and all 19 patients in the tumor group were correctly diagnosed.

We found that: sensitivity, specificity, PPV, and NPV of DWI in ring enhancing brain lesions and in differentiation of brain abscess from necrotic brain tumor were: 94.7%, 81.8%, 90% and 90%, respectively, whereas they were 100%, 82%, 90% and 100% with MRS accurately in the diagnosis in 11 patients (36.7%) with brain abscess and 19 patients (63.3%) with necrotic brain tumor Table 4.3.4.

Table 4 Comparison between DWI and 1H-MRS in differentiating between brain abscess and necrotic tumors.

<table>
<thead>
<tr>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DWI 94.73</td>
<td>81.82</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>1H-MRS 100</td>
<td>82</td>
<td>90</td>
<td>100</td>
</tr>
</tbody>
</table>

DWI = diffusion-weight imaging, 1H-MRS = proton magnetic resonance spectroscopy.

3.1. Cases

Figs. 1–4 demonstrate a sample of selected cases of our study, each figure outline one case.

4. Discussion

It is difficult to differentiate necrotic glioblastomas, cystic metastases, and abscesses with conventional MR imaging. All can appear as expansile rim-enhancing masses with prominent perifocal edema (8).

Spectroscopic, diffusion and perfusion-weighted MRI are advanced MR techniques that are used to add important physiological and metabolic information to that obtained with conventional MRI, the measurements of these advanced techniques can be used to demonstrate differences between cerebral abscesses and necrotic tumors (9).

We present a retrospective analysis of ADC and 1H-MRS spectroscopy data in 30 patients with ring enhancing lesion (11 patients with pyogenic brain abscess and 19 cases with necrotic brain tumors), we compared findings of proton MR spectroscopy (1H-MRS) with those of diffusion-weighted imaging to determine which technique was more effective for this differential diagnosis.

In our study, 9 cases (9/11) with pyogenic abscesses were hyperintense on diffusion-weighted images with low ADC values when compared with those in normal-appearing brain.

Fig. 1 (A–E): A male patient aged 61 years shows ring enhancing lesion in the right deep parietal region giving the radiological appearance of brain abscess but by clinical follow up and with antibiotics, no improvement could be detected and in biopsy, low grade astrocytoma was diagnosed. (A) and (B) Axial pre and post contrast T1WI show well defined ring enhancing brain lesion in the right deep parietal region. (C) Diffusion weighted Images show: The central portion of the lesion displays high signal intensity. (D) ADC shows: The central cavity of the lesion displays low signal (black arrow) (E) 1H-MRS shows: The central portion shows resonance peaks of, lactate (Lact) and lipid (Lip) but no peaks of amino acids which is the signature of abscess.
The ADC value ranged from 0.71 to 0.83 ± 0.31 \times 10^{-3} \text{ mm}^2/\text{s} (mean ± SD); two patients with brain abscess showed low signal intensity in DWI with high ADC values and it was found that these changes in the signal intensity were due to a 3-week course of IV antibiotic treatment and their mean ADC ranged from 1 (10^{-3} \text{ mm}^2/\text{s}) to 1.2 (10^{-3} \text{ mm}^2/\text{s}). However necrotic areas of 18 (18/19) tumors had low signal intensity on DWI with high ADC values ranging from 2.73 to 3.5 ± 0.34 \times 10^{-3} \text{ mm}^2/\text{s}. We found one patient with high signal intensity on DWI and low ADC values, mimicking that of abscess; It was low grade astrocytoma. The reason for restricted diffusion was possibly due to necrosis of the central portion of the tumor containing viscous fluid which was found at surgery.

Analysis of the value of ADC using unpaired t test (two tailed Student’s t test) indicates a significant difference between necrotic brain tumor and abscess (P < 0.01).

So, depending on the results of the present study, most of patients with brain abscesses showed restricted diffusion and low ADC values in contrast to patients with cystic and necrotic tumors which showed free diffusion and high ADC values, these results agreed with many previously published studies as Reiche et al. (10), who reported that all abscess cavities are hyperintense (restricted diffusion) in DWI and low ADC values, 8 of 10 patients with necrotic glioblastoma and all 6 metastatic cysts revealed hypointensity (free diffusion) on DWI and high ADC value.

Also, Leuthardt et al. (11) in their study revealed that: all abscess lesions were markedly hyperintense with diminished ADC value.

Reddy et al. (12) in their study found that: 93 out of 97 patients with brain abscess were hyperintense on DWI with significantly low ADC value (0.87 ± 0.05 \times 10^{-3} \text{ mm}^2/\text{s}), compared with 48 non-abscess lesion (2.89 ± 0.05 \times 10^{-3} \text{ mm}^2/\text{s}).

The causes of restricted diffusion in pyogenic abscesses are microscopic organization of the tissues, high viscosity of pus resulting from high protein, different types of viable or dead cells and necrotic tissue and bacteria, all of these impede microscopic motion of water particles (13).

However, in necrotic or cystic brain tumors which consist of tissue debris and fewer inflammatory cells, cyst fluid is almost clearer and more serious than pus, so, there are less diffusion barriers in tumor cysts than in the abscess cavities (10).

Lai et al. (1) described that 1 out of 21 patients with pyogenic brain abscess showed hypointensity in DWI and high ADC, this patient received antibiotic therapy for about 21 days, this agrees with the results of the present study.

In a study by Chang et al. (14), they reported 1 case of ring-enhanced fibrillary low grade astrocytoma with high signal on DWI and low ADC value, similar to that of abscess, surgery revealed the presence of viscous creamy material within the tumor.

Park et al. (15) reported 2 cases of necrotic brain metastasis with markedly high signal intensity on DWI, after surgery it was found that the cyst had a thick and creamy necrotic content similar to pus, these metastasis were from colonic adenocarcinoma.

In the present study, DWI correctly diagnosed 9/11 patients with brain abscess, the sensitivity, specificity, PPV, and NPV of DWI in group of brain abscess were: 94.7%, 81.8%, 90%, 90% and these results matched with Hassan et al. (7) who reported that DWI correctly classified patients into abscess or tumor in 46 patients (92%) out of total 50 patients with 96.88% sensitivity, 83.33% specificity, 91.18% PPV, and 93.75% NPV.

Findings from several studies have suggested that in vivo proton magnetic resonance spectroscopy (1HMRS), a non-invasive examination, might contribute to the establishment.
of the differential diagnosis between brain tumors and abscesses (16).

In our study, 8 patients in the abscess group and 12 patients in the tumor group showed findings of increased lactate, the lactate signal was of variable peak height. An extra peak of lipids was found in 3 patients in the abscess group and in 2 patients from the tumor group; lactate and lipid signals were observed however it was stated that lactate and lipids are non-specific metabolites produced by anaerobic glycolysis and necrotic brain tissue in brain abscesses. Both lactate and lipid peaks can also be observed in necrotic tumors (16).

Pyogenic brain abscesses contain large amounts of neutrophils and proteins, which are released in the necrotic cavity. The breakdown of the neutrophils results in the release of a large amount of proteolytic enzymes that hydrolyze the proteins into amino acids at 0.9 ppm, as seen on in vivo PMRS in pyogenic brain abscesses (17).

In the study by Garg et al. (16) who studied etiologic categorization of brain abscess with in vivo proton MR spectroscopy, they revealed the presence of amino acids in 89 of 91 abscesses along with lipid and lactate, acetate and succinate. Acetate and succinate are the end products of heterolactic and homolactic fermentation and were seen only in pyogenic abscesses, though occurrence in a single case of cerebral mucormycosis has been shown (17).

These findings agree with our results as amino acids were detected in 9 out of 11 patients with pyogenic brain abscess. Our findings also agree with the study by Mishra et al. (18), who reported that amino acids and lactate with or without other metabolites were observed in 25 out of 29 patients with brain abscess and also agree with Pal et al. (19) who found that amino acids were present in 80% of 194 patients with pyogenic abscesses with a sensitivity of 72% in vivo 1HMRS spectroscopy, also in their study they could not find amino acids in some of the patients having sterile cultures. The absence of amino acids in sterile abscesses was probably due to the fact that these patients were undergoing treatment with antibiotics (20).
Hassan et al. (7) reported in their study that patients with brain abscess were characterized by demonstration of amino-acids with or without other resonances of lactate, acetate and succinate on MRS, one of patients with spectra not consisting with abscess was on antibiotic therapy before MRS study.

Interpretation of the results of HMRS in the tumor group in this study showed that: lactate alone was found in 12 patients, lactate and choline were seen in 5 patients, neither lactate nor choline in 2 patients, lipid and lactate seen in 2 metastatic brain patients, none of the patients showed aminoacids, succinate or acetate. NAA and creatine were reduced or absent in all patients, and these results matched with those reported by Mishra et al. (18) who found that only lactate was seen in 14 out of 23 patients whereas both lactate and choline were visible in 6 out of 23 patients with cystic brain tumors, and also matched with results of Lai et al. (1) who found lactate was present only in 14 out of 23 patients with tumor cysts whereas both lactate and choline were visible in 9 patients with tumor cysts.

In our study MRS had 100% sensitivity, 82% specificity, 90% PPV and 100% NPV in the diagnosis of 19 patients (63.3%) with necrotic brain tumor, Lai et al. (1) reported that MRS had 85.7 sensitivity, 100% specificity, 100% PPV, 88.5% NPV, Hassan et al. (7) reported that MRS had 93.75% sensitivity, 77.78% specificity, 88.24% PPV, and 87.5% NPV.

According to the results of the present study, diagnosis of pyogenic brain abscess can be made if the ring-enhancing lesion had restricted diffusion with low ADC and the diagnosis of necrotic or cystic brain tumor had free diffusion with high ADC value, the specific spectrum of abscess cavity showed characteristic peak of aminoacids with or without other resonances of lactate, succinate and acetate and this spectrum looks different from spectra of cystic or necrotic brain tumors.

This study has some limitations, first, it is a retrospective study with small number of patients, second, lack of good history taking as 2 patients of brain abscess received antibiotic treatment before examination also MRS has its own limitation, so further studies with large sample of patients are recommended and patients on antibiotic treatment should be excluded.

In conclusion: Both DWI and 1HMRS are useful and efficent imaging techniques in ring enhancing brain lesions and differentiate between pyogenic brain abscesses and necrotic tumors, but DWI is accurate, had less imaging time than 1HMRS, also DWI is available in many imaging centers.

Conflict of interest

We have no conflict of interest to declare.

References


