The diagnostic value of diffusion weighted imaging in patients with meningioma

Sherif A. Khedr a, Mohamed A Hassaan a,b,*, Amal Refaat a,c

a Radiology department, Cairo University, Egypt
b Radiodiagnosis Cairo, Cairo University, Egypt
c Cancer Institute, Cairo University, Egypt

Received 17 December 2011; accepted 10 January 2012
Available online 14 February 2012

Abstract  Purpose: This study aims to determine the use of diffusion-weighted (DW) magnetic resonance imaging (MRI) in differentiating typical and atypical meningiomas.

Patients and methods: In total, 31 patients aged 37–77 years with meningiomas were included in this study. Using routine MRI sequences, the meningiomas were diagnosed and DW images were performed using factor of b-0 and b-1000. Apparent diffusion coefficient (ADC) values were measured in the lesion, in the normal area of brain parenchyma. Student t-test was used for statistical analysis. P < 0.05 was considered significant.

Results: Showed that the mean ADC of atypical/malignant meningiomas (0.42–0.69 × 10^−3 mm^2/s; P < .0001) was significantly lower compared with benign meningiomas (0.72–1.5 × 10^−3 mm^2/s). Mean NADC ratio in the atypical/malignant group (0.61) was also significantly lower than the benign group (1.21; P < .0001), without overlap between groups. The difference between the ADC values of the subtypes of typical meningiomas was insignificant.

In conclusion: Typical meningiomas have higher ADC values than atypical cases. DW MRI may be of help in differentiating typical and atypical meningiomas.

1. Introduction

Meningiomas are readily diagnosed by MR imaging, and most are asymptomatic [1]. Meningiomas comprise approximately 14–20% of all intracranial tumors [1,2]. Atypical meningiomas account for 7.2% of all meningiomas, whereas malignant meningiomas are rare and constitute approximately 2.4% [1]. Malignant and atypical meningiomas are more prone to recurrence and aggressive growth, which increases patient morbidity and mortality [3–4]. It would be useful to distinguish among benign, malignant, and atypical meningiomas before resection,
because this would aid in surgical and treatment planning. This distinction between benign and malignant or atypical meningioma is neither easily nor reliably accomplished to date when assessing the imaging features of meningiomas on routine MR images [5,6].

Diffusion-weighted MR imaging has been used to investigate primary brain neoplasms. Correlations between apparent diffusion coefficient (ADC) values, tumor cellularity, and tumor grade have been made [7–8], and the use of diffusion-weighted imaging to monitor treatment response has been evaluated [8]. Whether diffusion-weighted imaging has a similar potential role in the diagnosis or prognosis of non-primary brain neoplasms or extraxial neoplasms is unclear [8].

The purpose of this study was to examine the signal characteristics of meningiomas retrospectively on diffusion-weighted images and to correlate the ADC value from the ADC maps with the histopathological findings. We hypothesized that the ADC value may be helpful in distinguishing benign from malignant and atypical meningiomas, and we hypothesized that the ADC value may be able to predict the histopathological results of meningiomas.

2. Methods

Between June 2008 and May 2010, 31 patients (13 women and 18 men; average age, 55 years) with brain meningiomas were retrospectively included in this study. All of the patients had non-focal neurologic examinations at the time of presentation. Indications for MR imaging included headache (1), migraine [2], transient ischemic attack [3] change in mental status [4], and fall down [5].

2.1. Imaging techniques

2.1.1. (A) Conventional magnetic resonance imaging (MRI)

All MRI studies were done using Magnetom symphony, syngo, 1.5 T machine. The patients were informed about the duration of the examination, the position of the patient and the importance of being motionless.

MRI study was done with the patients in the supine position using the standard head coil. The examination was done before contrast administration, a scout sagittal T1-weighted view was obtained to verify the precise position of the patient and to act as a localizer for subsequent slices, then multiple pulse sequences were used to obtain axial images followed by coronal and/or sagittal images based on the location of the pathology encountered. In midline lesions sagittal planes were used while in laterally located lesions coronal images were more helpful.

The contrast media used were either Omniscan or Magnivist (Gadolinium (Diethelene Triamine Penta acidic acid) (‘‘Gd-DTPA’’), it was administrated intravenously in a dose of 0.1 mmol/kg body weight. T1-WIs was obtained immediately after the end of contrast injection.

All cases were examined using the following protocol:

- Sagittal T1-WI as a localizer:
  - TE = 10–12 m/s.
  - TR = 400–600 m/s.

- Axial and coronal spin-echo sequences, short TR/TE (T1-weighted images):
  - TE = 10–12 m/s.
  - TR = 400–600 m/s.
  - Axial fast spin-echo, long TR/TE (T2-weighted images):
    - TE = 70–90 m/s.
    - TR = 2800–3500 m/s.
  - Post-contrast axial, sagittal and coronal spin-echo sequences, short TR/TE (T1-weighted images):
    - TE = 10–12 m/s.
    - TR = 400–600 m/s.
  - FOV = 24–18 cm in axial images and 30–22 cm in coronal images.
  - Matrix (frequency × phase) 192 × 160.
  - Slice thickness = 6 mm with 2 mm interval (In all sequences).

2.1.2. (B) Diffusion-weighted MR imaging (DWI)

The imaging sequence for DWI was a multi-section single shot spin-echo EPI sequence (TR/TE/NEX: 4200/140 ms/I) with diffusion sensitivities of b values = 0, 500 and 1000 s/mm². The diffusion gradients were applied sequentially in three orthogonal directions (X, Y and Z directions). Sections of 5 mm thickness, interslice gap of 1 mm, FOV 240 mm and a matrix of 128 × 256 were used for all images. The total acquisition time was 80 s.

Three types were obtained; orthogonal images, trace images and ADC maps. The ADC maps were calculated automatically by MRI software and included in the sequence.

2.2. Imaging analysis

Experienced neuroradiologists reviewed the MR and diffusion-weighted images without any knowledge of the histopathological findings or the ADC value. The signal intensity of the meningiomas was assessed on the short- and long-TR images and the diffusion-weighted sequences. Signal intensity was judged as hypo intense, isointense, slightly hyper intense, or hyper intense to cortex, and enhancement patterns were marked as either homogeneous or heterogeneous. Typical meningiomas had homogeneous signal intensity similar to that of gray matter, intense homogeneous enhancement (no cystic/necrotic/hemorrhagic foci), smooth and distinct margins, and no evidence of brain invasion.

2.3. Statistical analysis

ADC values and normalized ADC ratio (ADCmeningioma/ADCnormal appearing white matter) of the neoplastic tissue (avoiding calcifications and cystic or necrotic areas) were measured and compared with histological findings. Student t-test was used for statistical analysis. P < 0.05 was considered significant.

2.4. Results

The 31 patients included in our study were classified into 24 patients had typical meningioma and the 7 patients had atypical and malignant meningiomas according to WHO classification. DWI and ADC values of the examined meningioma were correlated with histopathological data (Table 1). Histopathological grading of meningiomas was based on WHO classification: Grade-I (typical meningioma), Grade-II (atypical meningioma) and Grade-III (malignant meningioma)
Histopathological examination revealed typical meningiomas \((n = 24)\), and atypical/malignant meningiomas \((n = 7)\).

All cases of typical meningiomas \((n = 24)\) appeared hypo intense, isointense or slightly hyper intense on DWIs obtained at b0 and b1000. The ADC values ranged from 0.72 to \(1.5 \times 10^{-3}\) mm\(^2\)/s (Table 2).

In 7 (22.5\%) of 31 cases, the meningiomas were malignant \((n = 2)\) or atypical \((n = 5)\) appeared hyper intense on DWIs obtained at b0 and b1000. The ADC values were lower than normal brain ranged from 0.42 to 0.69 \(\times 10^{-3}\) mm\(^2\)/s (Table 2). Mean NADC ratio in the atypical/malignant group (0.61) was also significantly lower than the benign group (1.21; \(P < .0001\)), without overlap between groups.

Histopathological examination revealed that two of these cases were classified as malignant or World Health Organization (WHO) grade III (Figs. 1 and 2). Brain invasion, multifocal areas of necrosis, hypercellularity, and cytological pleomorphism with numerous abnormal mitoses were seen. These lesions had no atypical features on routine MR images; they had smooth, well-circumscribed borders and intense, homogeneous enhancement.

Five of these meningiomas were classified as atypical (WHO grade II) based on histopathological examination (Fig. 3). These meningiomas contained multiple foci of tumor necrosis and the presence of a high mitotic rate as determined by the MIB-1 index. MIB-1 is a nuclear antigen expressed by

<table>
<thead>
<tr>
<th>Site of meningioma</th>
<th>Number of cases</th>
<th>WHO classification</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Grade-I Grade-II Grade-III</td>
</tr>
<tr>
<td>Right parietal</td>
<td>6</td>
<td>4 1 1</td>
</tr>
<tr>
<td>Left parietal</td>
<td>4</td>
<td>2 1 1</td>
</tr>
<tr>
<td>Right parieto-occipital</td>
<td>3</td>
<td>3 – –</td>
</tr>
<tr>
<td>Left parieto-occipital</td>
<td>2</td>
<td>2 – –</td>
</tr>
<tr>
<td>Right temporal</td>
<td>2</td>
<td>1 1 –</td>
</tr>
<tr>
<td>Left temporal</td>
<td>2</td>
<td>1 1 –</td>
</tr>
<tr>
<td>Right frontal</td>
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<td>2 – –</td>
</tr>
<tr>
<td>Right sphenoidal</td>
<td>2</td>
<td>2 – –</td>
</tr>
<tr>
<td>Left sphenoidal</td>
<td>3</td>
<td>2 1 –</td>
</tr>
<tr>
<td>Anterior falx</td>
<td>1</td>
<td>1 –</td>
</tr>
<tr>
<td>Posterior falx</td>
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<td>3 – –</td>
</tr>
<tr>
<td>Right CPA</td>
<td>1</td>
<td>1 –</td>
</tr>
<tr>
<td>Total number</td>
<td>31</td>
<td>24 5 2</td>
</tr>
</tbody>
</table>

Table 2 The DWI findings in the examined cases lesions \((n = 31)\).

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>No. of patients</th>
<th>SI on DWIs (b1000)</th>
<th>Range of ADC ((10^{-3}) mm(^2)/s)</th>
<th>Mean ADC ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical meningioma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Isointense</td>
<td>0.72–1.5</td>
<td>1.21</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>Slightly hyperintense</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Hypointense</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atypical and malignant meningioma</td>
<td>7</td>
<td>Hyperintense</td>
<td>0.42–0.69</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Figure 1 Right parietal malignant meningioma. Isointense in T1WI (a), hyperintense in T2 WI (b), hyperintense in FLAIR (c), uniform contrast enhancement in axial T1WI (d), markedly hyperintense in DWI (e), and isointense in ADC (f). ADC value \(0.58 \times 10^{-3}\) mm\(^2\)/s.
all cycling cells, which is a measure of cell proliferation. Most tumors with an MIB-1 proliferation index greater than 10% that show malignant histopathological findings, and levels between 2% and 5% are usually atypical. The MR imaging characteristics of these tumors were typical of benign meningiomas, and atypical histopathological findings were not anticipated on the basis of the MR imaging findings.

Twenty-four (77.5%) of 31 meningiomas were benign as revealed by histopathological examination (WHO grade I). These meningiomas had the ADC values that ranged from 0.72 to \(1.4 \times 10^{-3}\) mm\(^2\)/s. These meningiomas were usually iso-intense on the short-TR images and predominantly hyper intense on the long-TR images (Fig. 4). One of these benign meningiomas, which appeared densely calcified, had low ADC \((0.72 \times 10^{-3}\) mm\(^2\)/s\) (Fig. 5).

**Figure 2** Bifrontal recurrent malignant meningioma. Isointense in T1WIs with hemorrhagic element (a), heterogenous iso and hyperintense in T2 WIs (b), homogenous contrast enhancement in sagittal (c), coronal T1 WIs (d), heterogenous hyperintense in DWI (e), and hypointense in ADC (f). ADC value 0.56.

**Figure 3** Left tentorial atypical meningioma. Hypointense in T1 WIs (a), heterogenous hpo and hyperintense in T2 WIs (b), hyperintense in FLAIR (c), homogenous contrast enhancement in coronal T1 (d), heterogenous hyperintense in DWI (e), and hypointense in ADC (f). ADC value 0.63.
Two of these benign meningiomas had distinct histopathological features. Both of these meningiomas had high ADC value (average \(1.4 \times 10^{-5} \text{ mm}^2/\text{s}\) and \(1.5 \times 10^{-5} \text{ mm}^2/\text{s}\)), (Fig. 6). These meningiomas tend to be hypo intense on diffusion-weighted images and hyper intense on ADC maps. Histopathological analysis revealed that these meningiomas represented a benign subtype of meningioma with unique features. One of these meningiomas had undergone micro cystic change, a feature of the histological subtype called the micro cystic meningioma (Fig. 6). Another meningioma was classified as a secretory meningioma, which is another distinct subtype characterized by marked edema in the surrounding brain parenchyma (Fig. 7).

Mean NADC ratio in the atypical/malignant group (0.61) was also significantly lower than the benign group (1.21; \(P < .0001\)), without overlap between groups the difference between the ADC values of the subtypes of typical meningiomas was insignificant.

Figure 4  Left tentorial typical meningioma. isointense in T1 WIs (a), isointense in T2 WIs (b), homogenous contrast enhancement in axial T1WI (c), isointense in DWI (d), and in ADC (e). ADC value 1.1.

Figure 5  Left CPA calcified meningioma. Axial CT (a) isointense in T1 WIs (b), hypointense in T2 WIs (c), non uniform contrast enhancement in axial T1WI (d), markedly hypointense in DWI (e), and ADC (f). ADC value 0.72.
3. Discussion

Diffusion-weighted MR imaging has been evaluated as a diagnostic tool in cases of primary brain neoplasms. Tumor cellularity and tumor grade have been correlated with ADC values from ADC maps [9,10]. Primary brain neoplasms with higher cellularity or higher grades typically have lower ADC values when compared with normal brain tissue [10]. Furthermore, the ADC value correlates with specific histopathological features of high-grade glioma. Cystic or necrotic portions of these tumors are associated with the highest ADC values [10]. The ability of diffusion-weighted imaging to distinguish between peri tumoral edema and undemanding tumor reliably remains controversial [11].

Because meningiomas are commonly occurring benign tumors that constitute approximately 20% of all intracranial tumors [1,2] and are easily diagnosed using routine MR imaging, we chose to examine the signal characteristics of meningiomas.

Figure 6  Left frontal microcystic meningioma. Hypointense in T1 WIs (a), isointense in T2 WIs (b), FLAIR (c), uniform contrast enhancement in axial T1WI (d), hypointense in DWI (e), and iso to hyperintense in ADC (f). ADC value 1.4.

Figure 7  Left frontal secretory meningioma. Hypointense in T1 WIs (a), isointense in T2 WIs (b), heterogenous hyperintense in FLAIRWI (c), contrast enhancement in axial T1WI (d), hypointense in DWI (e), and hyperintense in ADC (f). ADC value 1.5.
on diffusion-weighted images retrospectively and to correlate the ADC values from ADC maps with histopathological findings. Furthermore, malignant and atypical meningiomas, although relatively uncommon and accounting for approximately 7.2% and 2.4% of all meningiomas, respectively [1,2], are associated with less favorable clinical outcomes because they are more prone to recurrence and aggressive growth [4–7]. To date, investigators have been unsuccessful when attempting to predict the histological or physical characteristics of meningiomas preoperatively, and there is no reliable way to distinguish benign from atypical or malignant meningiomas on routine MR images [5,8]. Having the ability to distinguish benign from atypical or malignant meningiomas accurately would provide useful diagnostic information to aid in surgical and treatment planning and prognostication.

In this series, most of the meningiomas (n = 24) had benign results of their histopathological examinations. According to the WHO classification of meningiomas, those meningiomas with low risk of recurrence and aggressive growth are classified as WHO grade I [4]. The grade I classification includes the most common types of meningioma (fibrous or fibroblastic, transitional or mixed, and meningothelial) and the following benign subtypes: psammomatous, angiomatous, micro cystic, secretory, lymphoplasmacytoid-rich, and metaplastic [4].

The appearance of these 24 meningiomas on the diffusion-weighted images was variable. They showed hypo intense, iso-intense and slightly hyper intense texture on the diffusion-weighted sequences and on the ADC maps. Furthermore, it is difficult to draw firm conclusions regarding any relationship between the appearances of these lesions on routine MR images and on diffusion-weighted images. In all cases, the meningiomas were isointense on the short-TR images, most appeared isointense to hyper intense on the long-TR images, and all enhanced homogeneously, as expected.

All except one of these benign meningiomas in our series had elevated ADC value compared with normal brain. Of note is that one meningioma showed the lowest ADC value (0.72 × 10^{-3} mm²/s). This meningioma exhibited benign but distinct histopathological results. This particular meningioma was a psammomatous meningioma, which was densely calcified, as readily seen on MR images and CT scans. These meningiomas with abundant psammoma bodies form irregular calcified and occasionally ossified masses [4]. The decreased ADC value may relate to the paramagnetic properties of calcium. It is reasonable to postulate that a densely calcified mass would create a cellular environment in which the presence of this mineral would change the normal translational movement of water molecules across membranes [13].

In this study, it seems that the calculation of the ADC value from the isotropic diffusion map (ADC map) may reliably predict some histopathological findings. We had two benign meningiomas with the high ADC values which had distinct histopathological features. One was a micro cystic meningioma, which is rich in intracellular fluid [12]. Another meningioma was a secretory meningioma, which produces marked edema out of proportion to tumor size, which may be related to the prominent pericytic proliferations often seen in this tumor type [13]. These results were in agreement with previous studies [13] that reported that some benign meningiomas with distinct histopathological features have high ADC value as micro cystic meningioma, secretory meningioma, angiomatous meningioma, intratumor hemorrhage and cystic degeneration in meningioma. The increased ADC value of these meningiomata may be explained by the presence of increased amounts of fluid within these lesions. The presence of the increased fluid may allow for free movement of water molecules or less restriction to water diffusion, much in the same way that CSF diffuses freely without restriction and appears hypo intense on the diffusion-weighted MR sequences [12,13].

In this series, there were seven meningiomas that were malignant or atypical. Five were classified as atypical (WHO grade II), and two were classified as malignant (WHO grade III). According to WHO criteria, atypical meningiomas must have increased mitotic activity or three or more of the following: small cells with high nucleus to cytoplasmic ratio, prominent nucleoli, uninterrupted patternless or sheet like growth, and foci of “spontaneous” or “geographic necrosis” [4]. Increased mitotic activity has been defined as four or more mitoses per 10 high-power fields [4]. To be classified as a malignant meningioma, the meningioma must exhibit features of frank malignancy. Such features include malignant cytology (e.g., having an appearance similar to sarcoma, carcinoma, or melanoma) and a high mitotic index, which is defined as 20 or more mitoses per high-powered field [5].

All of the malignant or atypical meningiomas in this series had markedly increased signal on diffusion-weighted images, hypo intense signal on the ADC maps, and low ADC value indicative of marked restriction to water diffusion. All of these meningiomas had imaging characteristics suggestive of benign disease, which included homogeneous signal intensity similar to that of gray matter, intense homogeneous enhancement (no cystic/necrotic/hemorrhagic foci), smooth and distinct margins, and no evidence of brain invasion. Atypical or malignant histopathological results were not anticipated on the basis of routine MR imaging [14,15].

It seems that the histopathological findings of these atypical and malignant meningiomas correlated well with their appearance on diffusion-weighted images and the ADC value. These meningiomas showed hypercellularity, multifocal areas of necrosis, brain invasion, numerous abnormal mitoses, or cytological pleomorphism. There are several possible explanations for this observed correlation. One factor is that malignant and atypical meningiomas have less extracellular water and space, which reduces the ADC value. [16,17]. Furthermore, these meningiomas have higher nuclear-to-cytoplasmatic ratios and more prominent nucleoli, and this increased amount of intracellular, complex protein molecules likely restricts the free translation of intracellular water [18–20].

The ADC values of atypical/malignant meningioma were lower than normal brain ranged from 0.42 to 0.69 × 10^{-3} mm²/s. Mean NADC ratio in the atypical/malignant group (0.61) was also significantly lower than the benign group (1.21; P < .0001), without overlap between the groups. These results were in agreement with other studies [21].

Limitation of this study is the limited number of the patients and this study not including the different histopathological subtypes of meningioma.

4. Conclusion

Albeit a small sample size, atypical and malignant meningiomas tend to be markedly hyper intense on diffusion-weighted
MR images and exhibit marked decreases in the ADC values when compared with normal brain parenchyma. Although benign meningiomas have a variable appearance on diffusion-weighted images, they tend to have high ADC values compared with normal brain, with the exception of densely calcified or psammomatous meningiomas, which may have a low ADC value. Benign meningiomas with the highest ADC value seem to have increased water content because of either a specific histological subtype of meningioma or distinct histopathological features. Furthermore, the average ADC values of malignant and atypical meningiomas were significantly lower compared with benign meningiomas ($P < .00029$).

It seems that the use of ADC value may reliably predict the histopathological features of meningiomas before resection. Because atypical and malignant meningiomas are more prone to recurrence and aggressive growth, diffusion-weighted MR imaging with calculation of the ADC value should be performed when meningiomas are detected because this may provide useful diagnostic information for presurgical planning, treatment, and prognostication.

References


