Role of MRI Diffusion in Assessment of Mediastinal Lymphadenopathy

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Abstract

Background: Diffusion MR imaging is a non-invasive functional imaging technique that can be incorporated into routine morphological MR examination to provide functional assessments of mediastinal lymphadenopathy. It can be used in differentiating benign from malignant lymph nodes as well as differentiating lymphoma from sarcoidosis.

Patients and Methods: This study included 23 patients; 15 males and 8 females in the period from June 2013 to July 2014. The mean age was 46.1 ± 16.1 (range: 22-76 years). Cases were referred from the Chest and Oncology Departments to Radiology Department in Kasr El Aini Hospital for MRI assessment. The complaints varied between dyspnea, chest pain, cough, hemoptysis, fatigue and loss of weight. A superconducting 1.5 T MRI machine with a four-channel body phased-array coil was used for the examination. Biopsy and histopathological assessment was done after that.

Results: MRI examination with diffusion weighted imaging was able to detect metastatic mediastinal lymph nodes that showed restricted diffusion with mean ADC value measuring (1.067 ± 0.33) x 10^-3 mm^2/s. MRI diffusion weighted imaging can differentiate lymphoma from sarcoidosis in the setting of mediastinal/hilar lymphadenopathy. The mean ADC for lymphoma was (1.22 ± 0.23) x 10^-3 mm^2/s and for sarcoidosis was (1.9 ± 0.28) x 10^-3 mm^2/s. The ADC value in the lymphoma group was lower than in the sarcoidosis group, and the difference was statistically significant (p-value < 0.001).

Conclusion: MRI with diffusion weighted images can detect malignant mediastinal lymph nodes, detect metastatic lymph nodes and differentiate lymphoma from sarcoidosis.

Key Words: Magnetic resonance imaging – Diffusion – Bronchogenic Carcinoma – Lymphoma – Sarcoidosis

Introduction

MRI of the mediastinum using fast acquisition sequences with a high temporal resolution has become applicable with the recent advances in gradient technology and multichannel coils. Thoracic applications of diffusion weighted imaging (DWI) techniques are still growing, and preliminary studies have reported promising results [1].

DWI depends on the acquisition of a magnetic resonance signal related to random thermal motion (Brownian motion) or the “diffusion” of water protons in tissue [2].

In solid malignant lesions, the extravascular extracellular space is relatively diminished compared with the intracellular space due to an increased number of tightly packed cells, cellular pleomorphism, large cell volume and neoangiogenic vessels. This increased microstructural density will restrict random water molecule movement [3].

The evaluation of the data provided by DWI can be either qualitative or quantitative. Malignant lesions, in general, show restricted diffusion in the form of bright signal on diffusion-weighted images acquired using a high b value and dark signal on the ADC map (lower ADC values) as compared with benign lesions [4].

Lymphadenopathy is the most common cause of multiple mediastinal masses. Lymphoma and sarcoidosis form a great part of the differential diagnosis of mediastinal-hilar lymphadenopathy [5].

Primary mediastinal lymphoma usually occurs in the anterior mediastinum. Malignant lymphoma accounts for nearly 20% of all mediastinum neoplasms in adults and 50% in children [6].

Sarcoidosis is a chronic inflammatory disease of unknown etiology. The disease most commonly affects right paratracheal and hilar lymph nodes (90% of cases) [7].

Distinction is critical because lymphoma is managed with chemotherapy and radiotherapy,
while sarcoidosis is generally managed by clinical follow-up or with different therapeutic options such as immunosuppressive therapy [5].

Diffusion-weighted imaging can be used beside other modalities in differentiating lymphoma from sarcoidosis in the setting of mediastinal and hilar lymphadenopathy. The ADC value in the lymphoma patients is lower than in the sarcoidosis [5].

Quantitative analysis of DWI also enables differentiation of lymph nodes with and without metastasis [8].

Diffusion weighted MR imaging can be used for the diagnosis of metastatic lymph nodes with a high degree of accuracy (95%). The mean ADC value in metastatic lymph nodes is less than that in nodes without metastases and is similar to that in primary lesions [9].

MRI is emerging as a valuable mediastinal imaging modality besides digital radiography and computed tomography. It offers a unique combination of morphological and functional information in a single examination without any radiation harm to the patient. New users should make themselves familiar with the particular advantages, uses and limitations of DWI and its diagnostic scope to appreciate its potential benefits [1].

Patients and Methods

This study included 23 patients; 15 males and 8 females in the period from June 2013 to July 2014. The mean age was 46.1 ± 16.1 (range: 22-76 years).

Cases were referred from the Chest and Oncology Departments to Radiology Department in Kasr El-Aini Hospital for MRI assessment.

The complaints varied between dyspnea, chest pain, cough, hemoptysis, fatigue and loss of weight.

Inclusion criteria included: Patients with mediastinal lymphadenopathy.

Exclusion criteria included: Patients with pacemaker, cochlear implants, cerebral aneurysm clips, ocular metallic foreign body, bullets or gunshots near great vessels or vital organs.

All cases were subjected to the following:
- Proper clinical evaluation for all patients with relevant laboratory investigations including: CBC, random blood sugar, liver functions and kidney functions.
- Computed tomography of the chest.
- Magnetic resonance imaging using a 1.5-T superconducting imager using a four-channel body phased-array coil.

° MRI protocol: Respiratory gating has been used. The MR scanning sequences were T1WI, T2WI, T2 STIR & DWI, quantitative DWI analysis (ADC measurement).

° T1WI was obtained with the spin echo sequence with the following parameters: Repetition time/echo time: 10ms/5 ms; number of excitations: 2; direction of frequency encoding: R/L; section thickness: 8mm; gap: 0.5mm; field of view: 36-40cm; matrix: 288x224.

° T2WI was obtained with the following parameters: Repetition time/echo time, 664ms/80ms; number of excitations, 3; direction of frequency encoding: R/L; section thickness, 8mm; gap, 1.5mm; field of view, 36–40cm; matrix, 288x224.

° T2 STIR was obtained with the following parameters: Repetition time/echo time, 1.6ms/20ms; number of excitations, 3; direction of frequency encoding: R/L; section thickness, 10mm; gap, 1mm; field of view, 36–40cm; matrix, 288x224.

° DWI is typically acquired in a transverse plane, using at least two b values; low (0-50s/mm²) and intermediate-to-high b values (500-1000s/mm²). The typical slice thickness is 4-9mm with an interslice gap of 0-1.5mm, and the number of excitations ranges from 1 to 10.

° Quantitative DWI analysis (ADC measurement).

- Biopsy and histopathological assessment was done after that.

MR Imaging analysis:

MR images were analyzed for the following:
- Mediastinal lymph nodes were first evaluated on conventional images for location, size and the presence of cystic-necrotic parts.
- Presence of pleural effusion.
- Presence of hepatic or splenic focal lesions.

Quantitative analysis:

ADCs were calculated from the ADC maps which were constructed from b=0 and b=1000 sec/mm² values. A ROI was drawn centrally, and the size of ROI was kept as large as possible on the ADC map avoiding the macroscopic necrosis and major blood vessel in the light of the conventional images. The average of three measurements was recorded as the final result.
In the assessment of mediastinal/hilar lymph nodes; only lymph nodes appropriate to criteria were measured for ADC value. The exclusion criteria were as follows; (a) lesions containing large amounts (more than 50% of total size) of necrosis or calcification; (b) lesion size less than 15 mm in short axis diameter in view of the limited planar resolution of DWI.

Statistical analysis:

ADC was statistically described in terms of mean ± standard deviation (±SD), median and range. Comparison of ADC between lymphoma and sarcoidosis was done using Student t-test for independent samples. Accuracy of ADC in differentiating lymphoma from sarcoidosis was represented using the terms sensitivity, and specificity. Receiver operator characteristic (ROC) analysis was used to determine the optimum cut off value. 

$p$-values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 15 for Microsoft Windows (2006).

Results

This study included 23 patients; 15 males and 8 females (mean age 46.1 ± 16.1) which were diagnosed as summarized in the following table (Table 1).

MRI Findings in patients with metastatic lymphadenopathy from bronchogenic carcinoma:

This group included 10 patients diagnosed as bronchogenic carcinoma associated with metastatic mediastinal lymphadenopathy. Nine males and one female patient with mean age 59.4 ± 11.4 years (range: 36-76 years).

Quantitative analysis has also been used to assess mediastinal/hilar lymph nodes. Only lymph nodes appropriate to criteria were measured (number of total lymph nodes measured = 14 lymph nodes).

Lymph nodes were localized and defined as follows; 5 right paratracheal, 3 prevascular, 2 subcarinal, 2 hilar, 1 aorto-pulmonary and 1 cardiophrenic lymph node.

Among the 14 nodes measured: 12 showed restricted diffusion with mean ADC value (1.067 ±0.33) x 10⁻³ mm²/s (range 0.6-1.5), whereas 2 lymph nodes showed facilitated diffusion and were hyperintense on the calculated ADC map (Fig. 1).

Table 1: Patients’ diagnosis.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic lymphadenopathy from bronchogenic carcinoma</td>
<td>10</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>7</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>6</td>
</tr>
</tbody>
</table>

Fig. (1): (a) Axial MR T2WI, (b) Axial DWI, (c) Axial inverted grey-scale high b-value PET- like diffusion weighted MRI image (d) ADC map, showing right upper lobar soft tissue mass lesion diagnosed as bronchogenic carcinoma and right paratracheal lymph node. They both showed restricted diffusion evident by high signal on DWI and low signal on ADC map with ADC values measuring 1.4 for the mass & 1.2 for the lymph node denoting metastasis.
MRI findings in cases with lymphoma and sarcoidosis:

Our study involved the evaluation of 13 patients (6 males & 7 females) with mediastinal/hilar lymphadenopathy; 6 patients pathologically proven as sarcoidosis and 7 patients as lymphoma.

The mean age of patients with lymphoma was 35.9±13.9 years (range: 22-60 years) and of patients with sarcoidosis was 36±6.8 years (range: 26-45 years).

Number of total lymph nodes measured = 33; of the 33 lymphadenopathies 17 were lymphoma and 16 were sarcoidosis.

Lymph nodes localized and defined as follows: in the lymphoma group: 2 amalgamated anterior mediastinal mass, 6 retrocaval paratracheal, 5 prevascular, 2 hilar, 1 aorto-pulmonary and 1 posterior mediastinal. Whereas in the sarcoidosis group: 10 hilar, 4 paratracheal, 1 subcarinal and 1 posterior mediastinal.

**ADC analysis:**

The mean ADC for lymphoma was (1.22±0.23) x 10^{-3} mm^2/s and for sarcoidosis was (1.9±0.28) x 10^{-3} mm^2/s (Figs. 2,3).

The ADC value in the lymphoma group was lower than in the sarcoidosis group, and the difference was statistically significant (p-value <0.001) (Table 2) (Chart 1).

**Table (2): Quantitative analysis of DW imaging of lymph nodes in sarcoidosis and lymphoma.**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Lymphoma (n=17)</th>
<th>Sarcoidosis (n=16)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC (x 10^{-3} mm^2/s)</td>
<td>1.22±0.23</td>
<td>1.9±0.28</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Chart (1): Comparison of ADC values between lymphoma & sarcoidosis.** The mean ADC value of lymphoma was lower than those of sarcoidosis.

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**Fig. (2):** A 44 year-old-male patient diagnosed as lymphoma (a) Axial T2WI, (b) Axial DWI, (c) ADC map (d) Coronal T2WI showing enlarged anterior mediastinal prevascular, retrosternal, retrocaval and aorto-pulmonary lymph nodes of intermediate signal on T2 WI, hyperintense on DWI and show low signal on ADC map (restricted diffusion). The mean ADC value was 1.4 x 10^{-3} mm^2/s. coronal T2 showed neoplastic splenic mass lesion.
By using the cut-off value of $1.525 \times 10^{-3}$ mm$^2$/s, ADC had a sensitivity of 100% and specificity of 100% for the differentiation of lymphoma and sarcoidosis.

With the cut-off value of $1.625 \times 10^{-3}$ mm$^2$/s, ADC had a sensitivity of 100% and specificity of 93.7% whereas with the cut-off value of $1.45 \times 10^{-3}$ mm$^2$/s, ADC had a sensitivity of 82.4% and specificity of 100% (Table 3).

Table (3): ADC sensitivity and specificity for differentiating sarcoidosis and lymphoma at different cut off values.

<table>
<thead>
<tr>
<th>ADC cut off value (x $10^{-3}$ mm$^2$/s)</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.450</td>
<td>82.4%</td>
<td>100%</td>
</tr>
<tr>
<td>1.525</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>1.625</td>
<td>100%</td>
<td>93.7%</td>
</tr>
</tbody>
</table>

Associated findings in patients with lymphoma:

Associated MRI findings included:
- Vertebral osseous lesions in 1 case.
- Splenic mass in 1 case.
- Pleural effusion in 1 case.
- Liver deposits in 1 case.

Discussion

This study included evaluation of 23 patients with mediastinal lymphadenopathy by MRI chest with diffusion weighted images; 15 males and 8 females with mean age of $46.1 \pm 16.1$ (range: 22-76 years).

Cases were referred from the Chest and Oncology Departments to Radiology Department in Kasr El-Aini Hospital for MRI assessment.

Our study included 10 cases with metastatic lymph nodes from bronchogenic carcinoma, 7 cases with lymphoma and 6 cases with sarcoidosis.

10 cases presented with central bronchogenic carcinoma and associated mediastinal lymphadenopathy, most of the lymph nodes showed restricted diffusion with mean ADC value $(1.067\pm0.33) \times 10^{-3}$ mm$^2$/s (range 0.6-1.5), whereas only 2 lymph nodes showed facilitated diffusion and were hyperintense on the calculated ADC map.

In their study Hasegawa et al. [10] found that diffusion MR imaging can be used for the diagnosis of metastatic lymph nodes in patients with NSCLC with a high degree of accuracy (95%).

Kosucu et al. [11] found that the ADC value is significantly lower in metastatic nodes $(1.01\pm0.02) \times 10^{-3}$ mm$^2$/s than in benign lymph nodes $(1.51\pm0.07) \times 10^{-3}$ mm$^2$/s.

Whereas Nomori et al. [9] reported that the cut-off ADC value used to differentiate metastatic from non-metastatic lymph nodes in patients with NSCLC is $1.63 \times 10^{-3}$ mm$^2$/s, with an accuracy of 89%.
Differentiation between lymphoma versus sarcoïdosis in the setting of mediastinal-hilar lymphadenopathy is an issue of debate for radiologists. CT has been widely used but is not sufficient for malignant-benign differentiation.

Our study involved the evaluation of 13 patients with mediastinal/hilar lymphadenopathy whose differential diagnosis was lymphoma versus sarcoïdosis; Number of total lymph nodes measured was 33; of the 33 lymphadenopathies 17 were lymphoma and 16 were sarcoïdosis.

We analyzed ADC values and found that the ADC value in the lymphoma group was lower than in the sarcoïdosis group, and the difference was statistically significant ($p$-value <0.001), which is consistent with Gümüstas et al. [5] who reported the same results.

In our study the mean ADC for lymphoma was $(1.22 \pm 0.23) \times 10^{-3}$ mm$^2$/s and for sarcoïdosis was $(1.9 \pm 0.28) \times 10^{-3}$ mm$^2$/s.

Nearly the same results were reported by Gümüstas et al. [8] who reported that the mean ADC for lymphoma was $(1.130 \pm 0.581) \times 10^{-3}$ mm$^2$/s and for sarcoïdosis was $(2.065 \pm 0.518) \times 10^{-3}$ mm$^2$/s.

As for the cut-off value for differentiating lymphoma and sarcoïdosis; we found that at cut-off value of $1.525 \times 10^{-3}$ mm$^2$/s ADC had a sensitivity of 100% and specificity of 100%, at the cut-off value of $1.625 \times 10^{-3}$ mm$^2$/s the sensitivity was 100% and specificity was 93.7% whereas at the cut-off value of $1.45 \times 10^{-3}$ mm$^2$/s ADC had a sensitivity of 82.4% and specificity of 100%.

In their study, Gümüstas et al. [8] reported that by using the cut-off value of $1.266 \times 10^{-3}$ mm$^2$/s, ADC had a sensitivity of 100% and specificity of 81% for the differentiation of lymphoma and sarcoïdosis and with the cut-off value of $1.97 \times 10^{-3}$ mm$^2$/s ADC had a sensitivity of 50% and specificity of 99.4%.

Conclusion:

MRI diffusion can differentiate malignant from reactive or inflammatory mediastinal lymph nodes. It can be used to detect metastatic mediastinal lymph nodes which affect N staging of malignant tumours.

It can be also used to differentiate lymphoma from sarcoïdosis in the setting of mediastinal/hilar lymphadenopathy.

References

دور الرنين المغناطيسي بحاسبة الانتشار
في تقييم القدد اللمفاوية المنصفية

الرنين المغناطيسي بحاسبة الانتشار هو أحد طرق التصوير الطبي في الرنين المغناطيسي والتي تستغرق وقتاً قصيراً (يتراوح من أربع إلى ست دقائق) بدون التعرض إلى اشعة و بدون الحاجة إلى حقن صبعة. من الممكن إدماج الرنين المغناطيسي بحاسبة الانتشار في فحص الرنين الروتيني مما يعني طبيب الإشعة قدرة أكبر على تشخيص أورام المنصف و تقسيمها.

يستطيع الرنين المغناطيسي بحاسبة الانتشار التمييز بين القدد اللمفاوية الحميدة والخبيثة وكذلك التفرقة بين سرطان القدد اللمفاوية ومرض الساركوديد.

اشتملت هذه الدراسة 23 مريضاً (15 ذكور و8 إناث) وتراوحت أعمار المرضى بين 22 إلى 71 سنة. اشتملت هذه الدراسة على 10 حالات مصابة بسرطان الرئة مع ثانياً في القدد اللمفاوية المنصف، 7 حالات سرطان القدد اللمفاوية وال6 حالات ساركوديد.

وقد أمكн التفرقة بين الساركوديد وسرطان القدد اللمفاوية باستخدام خاصية الانتشار في الرنين المغناطيسي.

ويتضح من خلال هذه الدراسة أنه الرنين المغناطيسي بالانتشار يستطيع تقييم القدد اللمفاوية المنصف والتمييز بين الحميدة والخبيثة منها. ويدعى في تحديد مرحلة الأورام الخبيثة وخاصة سرطان الرئة.