ABSTRACT

Background: Characterization of vertebral pathologies as benign or malignant is a commonly encountered problem. Imaging is sufficient for diagnosis of most benign vertebral pathologies with further confirmation on response to therapy. With better understanding of diffusion characteristics of tissues, attempt is being made to assess various imaging characteristics to make a definite diagnosis of malignant lesions as well. In this study we quantified apparent diffusion coefficient (ADC) of lesions in an effort to determine whether ADC values are different for benign or malignant vertebral body lesions.

Methods: We included 32 cases, that is, 22 benign and 10 malignant vertebral lesions, diffusion weighted (DW) MRI sequence was done and ADC values were recorded. Confirmation was done with post treatment follow up or wherever feasible, tissue diagnosis. All malignant cases had histopathology confirmation from the site of primary lesion. Quantitative variables using independent t-test were used for comparison of ADC values between two groups.

Results: The difference in mean ADC values of benign and malignant lesions were statistically significant (P<0.0001). The optimal cutoff of ADC value for differentiating benign from malignant vertebral body lesion was 0.950 x 10^-3 mm/s with sensitivity of 80% and specificity of 95.45%.

Conclusion: In all cases, DWI/ ADC, along with routine MR sequences, were able to characterize the lesion either as benign or malignant except in two cases of tuberculosis infection of spine and one each of spindle cell sarcoma & metastasis from cancer lung where there was overlap of ADC values.

KEYWORDS

Vertebral imaging, Diffusion Weighted Imaging, Apparent Diffusion Coefficient value, Diffusion restriction.

BACKGROUND

Vertebral imaging. Diffusion Weighted Imaging, Apparent Diffusion Coefficient value, Diffusion restriction.

METHODS:

For this cross sectional observational study approved by the Institutional Review Board, consecutive patients who reported to the department of Radiodiagnosis, for evaluation of vertebral lesion by MRI, during 1st November 2017 to 31st March 2019, were included in the study, after informed consent. These patients were clinically suspected to have vertebral lesions or patients with vertebral lesions incidentally diagnosed on MR. Patients having general contraindications for MRI, such as, cardiac pacemaker and non MR compatible implants were excluded. Detailed history with general physical & systemic examination were followed by antero-posterior and lateral radiographs of the spine. MRI was performed on 3.0 T scanner (Siemens Magnetom SKYRA) using sagittal T1WI, T2WI and STIR, axial T1, T2, STIR, DWI & ADC, and wherever indicated, post Gadolinium T1 fat suppressed sagittal and axial MR sequences.

Diffusion weighted fast spin echo, sequence with single shot acquisition was acquired in transverse axis, with standard b values, of lesion with most pronounced signal alteration seen in STIR sequence. For qualitative DWI analysis, the signal intensity of diseased vertebra was categorised as hypo-intense, iso-intense or hyper-intense relative to the areas of presumed normal bone marrow, with correlation of signal intensity on ADC. Areas with diffusion restriction are bright on DWI and dark on ADC. For quantitative assessment, a region of interest (ROI) occupying optimal area in the central part of abnormal signal intensity lesion, excluding the end plates, cortical margins and disc spaces was selected. The ADC values were recorded.

Imaging diagnosis was correlated with clinical and wherever feasible, histo-pathological/ surgical findings. All malignant cases had histopathology confirmation from the site of primary lesion. Analysis of the study was done as per standardized statistical method.

RESULTS

Most infective cases were less than 40 years of age. As the age increased, non-infective cases became common. Two benign lesions, which were restricting, were due to tubercular (TB) infection of the spine causing a fluid collection. Rest of the benign lesions were not restricting on DWI sequence. ADC value of the two malignant lesions, a spindle cell cancer of vertebral body (showed restriction on DWI) and a metastasis from lung cancer (did not show restriction on DWI), above 950.6 x 10^-3 mm/s, the cut off as per current study to differentiate between benign and malignant vertebral lesions. Rest of the malignant lesions were dark on ADC & restricting.

For statistical analysis, lesions were classified as benign or malignant. Malignant tumors were further sub-divided into primary malignant or secondary malignant tumors (metastasis). Quantitative variables were compared using independent t-test. P < 0.05 was considered to be significant.

Table 1: Presence of restriction of diffusion and mean ADC values

<table>
<thead>
<tr>
<th>Type</th>
<th>Diagnosis</th>
<th>Restriction on DWI of Numbers of lesions</th>
<th>Mean ADC values (10^-3 mm/s)</th>
<th>Total ADC values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>present</td>
<td>absent</td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>Pott's spine</td>
<td>2</td>
<td>12</td>
<td>1.33</td>
</tr>
<tr>
<td></td>
<td>Hemangioma</td>
<td>0</td>
<td>6</td>
<td>1.42</td>
</tr>
<tr>
<td></td>
<td>Aneurysmal bone cyst</td>
<td>0</td>
<td>1</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>Simple bone cyst</td>
<td>0</td>
<td>1</td>
<td>1.8</td>
</tr>
</tbody>
</table>

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...differentiate between benign and malignant vertebral lesions. ROC curve for determining the cut off ADC value to...excluded from consideration, at P value = 0.970, as well as when outliers are included for consideration, at P = 0.7849.

**DISCUSSION**

Twenty two out of 32 cases were benign (68.75%); most of these were in the age group of 21-40 years. There were ten malignant lesions (31.25%); most of the patients were in the age group of 60-80 years. Similar proportion of malignant lesions were noted in a previous study. There were 14 infective (43.75%) and eight non-infective benign lesions. A previous study had similar findings. DWI MRI characteristics of different pathologies are detailed below:

- **Hemangioma**: None of the cases of hemangioma had restriction, similar to the findings of a previous study by Matrawy et al. The mean ADC value was 1.5x10^-6 mm²/s, similar to that in the current study and that by Kob, et al. Kim, et al attributed low ADC values in some cases of hemangioma to the fact that hemangioma sometimes contain abnormal tissue and thrombosis in its vascular spaces which reduces the ADC values.

- **TB spine**: Twelve lesions had no restriction. Two had restriction with ADC values of 1.0x10^-6 mm²/s and 0.88x10^-6 mm²/s respectively. In both these cases, fluid collections were present. Hence low ADC might be explained by the presence of inflammatory cells and proteins. Subhawong et al stated in their study that an abscess has restricted diffusion with low ADC value due to high viscosity of its content, caused by pus, inflammatory cells, protein and granulation tissue. Fifty five patients of TB spine, had mean ADC value of 1.47±0.25x10^-6 mm²/s.

- **Simple and aneurysmal bone cysts**: Simple bone cyst and aneurysmal bone cyst were the benign bone tumors that had the highest ADC values in our study. 1.7 x 10^-6 mm²/s and 1.9 x 10^-6 mm²/s, among benign lesions. Our findings were similar to previous studies (Pekcevik et al, Hayashida et al), where ADC values in these cases were in the range of 1.9-2.7 x 10^-6 mm²/s.

- **Ewing's sarcoma**: One case was of Ewing's sarcoma involving C2-C6 vertebrae. The lesion had diffusion restriction with mean ADC value of 0.7x10^-6 mm²/s. Rodalec et al found in their study that primary vertebral Ewing's sarcoma is quite rare and cervical spine is the least affected site. D Beomonte Zobel et al stated that Ewing's sarcoma can be differentiated from benign lesions like osteomyelitis with the help of diffusion weighted MR imaging. Kob Z et al found that diffusion restriction in Ewing's sarcoma has a mean ADC value about 0.7x10^-6 mm²/s. This correlated well with our study.

- **Metastatic vertebral lesions**: Of seven cases of metastatic vertebral lesions; two cases each had lesions in lumbar, thoracic and sacral spine, while one had involvement of multiple levels. Six were restricting with mean ADC value of 0.85x10^-6 mm²/s. One lesion, a metastasis from lung cancer, had mean ADC value of 2.0x10^-5 mm²/s (no restriction).

Filogranà et al reported similar findings. In our study one metastasis was from lung cancer, which did not show diffusion restriction probably due to its osteolytic nature. One study stated that ADC value is higher as osteolytic lesions have increased content of water and cells as compared to osteosclerotic lesions.

In a previous study, the ADC value for malignant lesions was found to range from 0.56 to 2.1x10^-5 mm²/s. The highest ADC values were observed in one case out of 23 of pathologic fractures in a non-small cell lung cancer metastasis. These findings correlate well with our findings.

<table>
<thead>
<tr>
<th>Sub Group</th>
<th>Mean ADC</th>
<th>Standard Deviation</th>
<th>Range of ADC values</th>
</tr>
</thead>
<tbody>
<tr>
<td>All malignant lesions</td>
<td>997.9 x 10^6 mm²/s</td>
<td>388.68 x 10^6 mm²/s</td>
<td>736 to 2042 x 10^6 mm²/s</td>
</tr>
<tr>
<td>Malignant lesions excluding outliers</td>
<td>881.8 x 10^6 mm²/s</td>
<td>135.36 x 10^6 mm²/s</td>
<td>736 to 950.6 x 10^6 mm²/s</td>
</tr>
<tr>
<td>All benign lesions</td>
<td>1400.21 x 10^6 mm²/s</td>
<td>309.34 x 10^6 mm²/s</td>
<td>850 to 2100 x 10^6 mm²/s</td>
</tr>
<tr>
<td>Benign lesions excluding outliers</td>
<td>1424.98 x 10^6 mm²/s</td>
<td>293.78 x 10^6 mm²/s</td>
<td>1080 to 2100 x 10^6 mm²/s</td>
</tr>
<tr>
<td>All metastatic lesions</td>
<td>1012.64 x 10^6 mm²/s</td>
<td>455.54 x 10^6 mm²/s</td>
<td>800 to 2042 x 10^6 mm²/s</td>
</tr>
<tr>
<td>Metastatic lesions excluding outlier</td>
<td>540.95 x 10^6 mm²/s</td>
<td>151.60 x 10^6 mm²/s</td>
<td>800 to 900 x 10^6 mm²/s</td>
</tr>
<tr>
<td>All primary malignant lesions</td>
<td>963.5 x 10^6 mm²/s</td>
<td>234.02 x 10^6 mm²/s</td>
<td>736 to 1203 x 10^6 mm²/s</td>
</tr>
<tr>
<td>Primary malignant lesions</td>
<td>843.4 x 10^6 mm²/s</td>
<td>37.53 x 10^6 mm²/s</td>
<td>736 to 950.6 x 10^6 mm²/s</td>
</tr>
</tbody>
</table>

The mean ADC values as seen in Tables 1 & 2, were significantly different (P<0.0001) for all benign and malignant lesions. The mean ADC values, excluding outliers, for benign and malignant lesions were significantly different (P<0.0001).

From Table 1, it can be seen that ADC value is similar for all malignant lesions, whether primary or secondary in etiology when outliers are excluded from consideration, at P value = 0.970, as well as when outliers are included for consideration, at P = 0.7849.

**Qualitative** analysis based on visual assessment of diffusion restriction appearing bright on DWI and dark on ADC sequences, yielded sensitivity of 90% for identifying malignant lesions, specificity of 90.91%, positive predictive value of 81.82%, and negative predictive value of 95.24%. The diagnostic accuracy was 90.63% (P<0.0001).

**Quantitative** analysis: An ROC (Receiver Operator Curve) curve was used to determine optimal cut off ADC for differentiating between benign and malignant lesions.
Statistical Evaluation: The optimal cutoff for differentiating benign from malignant lesions was $0.95 \times 10^{-3}$ mm/s with sensitivity of 80%, specificity of 95.45%, positive predictive value of 88.9%, negative predictive value of 91.3%, and $P < 0.0001$. Abo Dewan et al., were able to differentiate benign and malignant lesions with sensitivity of 95.12%, specificity of 92.73%, positive predictive value (PPV) of 90.70%, and negative predictive value (NPV) of 96.23% with an optimal cut-off value of $1.21 \times 10^{-3}$ mm/s. Taskin, et al. found the optimal cut-off value of $1.32 \times 10^{-3}$ mm/s for the differentiation of benign and malignant vertebral bone-marrow lesions with sensitivity 96.5%, specificity 95.2%, positive predictive value (PPV) 96.5%, and negative predictive value (NPV) 95.2%. It is possible that the optimal cut off value for ADC needs to be determined for different MR scanners. Perhaps this aspect can be ascertained by studies with a large number of cases on different scanners.

Limitations: The small numbers of cases of individual pathologies is a limitation of the study.

CONCLUSION
Cut-off value of 0.95 x $10^{-3}$ mm/s on ADC map can be used to differentiate benign from malignant cases with sensitivity of 80% and specificity of 95.45%. The results for a few cases of tuberculosis and metastasis, were not uniformly unequivocal. With patient history, examination, routine blood tests, plain radiograph studies, MRI in most cases can significantly narrow the list of differentials, with histopathology needed only in a few cases of primary malignancy of vertebrae. To conclude, DWI/ ADC can be considered as a discriminatory sequence in determining whether a vertebral mass is benign or malignant.

Abbreviations:
- CT: Computerised Tomography;
- MRI: Magnetic Resonance Imaging;
- DWI: Diffusion weighted imaging;
- ADC: Apparent Diffusion Coefficient;
- T2WI-T1 weighted imaging;
- T2WI-T2 weighted imaging;
- STIR: Short-TI Inversion Recovery;
- ROI: region of interest;
- TB: tubercular infection;
- ROC: Receiver Operator Curve;
- PPV: positive predictive value;
- NPV: negative predictive value;

REFERENCES