The Value of Diffusion Weighted Magnetic Resonance Imaging in Differentiating Atypical Vertebral Haemangiomas from Metastatic Lesions

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ABSTRACT:

BACKGROUND:

Atypical vertebral hemangioma and metastatic spinal lesions share many MRI signal intensity and appearance in common ,thats why differentiation between them is crucial. For two decades, diffusion-weighted imaging (DWI) has been applied to the evaluation of intracranial diseases, but DWI technical advancement make it possible to apply for assessment of extra cranial sites, including vertebral column.

OBJECTIVE:

The goal of our study is to assess the value of diffusion weighted MRI imaging in differentiating vertebral atypical hemangiomas from metastatic lesions.

PATIENTS AND METHODS:

A prospective cross-sectional study was employed at AL-Imammain AL-Khadymain Medical city in Baghdad health directorate, (43)patients with total (65) vertebral lesions grouped into three groups Group(A) 10 patients (23.2%)with total (15) lesions of vertebral typical hemangiomas, Group(B) 13 patients (30.3%) with total (13) lesions of vertebral atypical hemangiomas and Group (C) 20 patients(46.5%) with total (37) lesions of spinal vertebral metastases .

MRI was done for all patients (including T1, T2, T1 fat suppression with IV contrast administration (when needed) and DWI). Complementary non contrast CT was also done.

RESULTS:

Total study sample were (43) patients with total (65) lesions, with (29/43) females and (14/43) males with male to female ratio of (1:2), their age range from (28-75 years) and their mean age was (54.2$\pm$ 10.1 years). Atypical hemangioma and malignant lesions were generally low signal in T1 and high or intermediate signal in T2 WI. Restricted diffusion and low ADC values were seen in atypical hemangioma compared with metastasis with mean ADC value were ($1.426\pm0.231.6x10^{-3}mm^2/s$ and $0.6182\pm 0.137x10^{-3}mm^2/s$ respectively).

Complementary CT confirmed the lytic or sclerotic nature of malignant lesions while in haemangiomas, it showed their characteristic striated (polka dot) appearance.

CONCLUSION:

Diffusion weighted Magnetic Resonance Imaging is a valuable tool in differentiation of atypical hemangioma and metastasis of spine with high sensitivity and specificity with the aid of ADC values calculated from the maps obtained by DWI.

KEYWORDS: diffusion weighted magnetic resonance imaging, atypical haemangiomas, metastasis.

INTRODUCTION:

Vertebral haemangiomas are common primary spine tumours [(1)]. They are benign vascular lesions with a hamartomatous proliferation of vascular tissue of endothelial origin with an estimated incidence of 10–12 % in all patients at autopsy [(2)].Vertebral hemangiomas predominantly affecting the lumbar and thoracic spine [(3, 4)]. About 25-30% are multiple, particularly in thoracic spine. Most Haemangiomas affect vertebral body, but about 10-15% may extend in the pedicles and even the

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spinous processes are involved [5]. The majority of lesions are discovered incidentally on spinal imaging done for other reasons [6]. Although most vertebral hemangiomas remain asymptomatic, thoracic hemangiomas produce symptoms more often than lumbar ones [4]. Two types of vertebral haemangiomas exist: Benign, asymptomatic type, and more aggressive, symptomatic ones, with compression of the spinal cord. Aggressive vertebral haemangiomas (AVH) are benign vascular tumours, which breach the posterior cortical wall of affected vertebra, may affect anterior column stability, and compress the spinal cord epidurally [7, 8].

The typical radiographic appearance of a haemangiomas characteristically seen as parallel linear streaks ('jail bar') in a vertebral body of diffuse decreased density, or 'honeycomb' pattern [5]. Transverse CT shows the pattern as multiple dots, also known as 'polka dot' pattern, representing a cross-section of thickened trabeculae. The key features that differentiate haemangiomas from other similar tumours area are hyperintense signal on T1 and T2 [9]. Low signal intensity on T1with vivid contrast enhancement, extra osseous soft tissue extension and pathologic fracture may indicate a more aggressive, atypical lesion with the possibility to compress the spinal cord [5]. Aggressive types are characterized by a prominent soft-tissue component that can invade the epidural space and compress on the spinal cord. Metastatic disease to the spine is the most frequent spinal tumour, past medical history of a primary tumour is generally available to suggest this diagnosis [9], its assumed that spine metastases found in 5-10% of cancer patients [5].

Differentiation between atypical hemangioma and ominous metastatic spine lesion is crucial because of its great impact on patient future life and to avoid unnecessary invasive procedure for diagnoses, here, Diffusion weighted magnetic resonance imaging is an excellent non-invasive sequence to differentiate benign vertebral from malignant lesion, and the presence of iso- or hypo intensity of the vertebral body lesion is suggestive of a benign lesion while hyper intensity is highly suggestive of malignancy. Similarly high signals on ADC are highly suggestive of benign rather than a malignant cause [10].

DWI measurements are rapid to perform (typically 1–5 minutes) and do not require the administration of exogenous contrast medium.

Thus, these imaging sequences can be superadded to existing imaging protocols without a significant increase in the examination time. Furthermore, DWI obtains both qualitative and quantitative information that can assist in tumor assessment [11].

AIM OF THE STUDY:

To assess the value of diffusion weighted MRI sequence in the differentiation between focal vertebral metastases from atypical spinal vertebral hemangiomas.

PATIENTS AND METHODS:

Study sample: A prospective cross-sectional study was conducted at AL-Imammain AL-Khadymain Medical city in Baghdad health directorate, performed from February 2015 to October 2015. A total of 43 patients (29females, 14males), male to female ratio=1:2, mean age were (54.2±10.1years) [range 28–75 years]studied. all patients were presented with back pain of variable severity and the 43 patients had a total of (65) spinal lesions.

The exclusion criteria were:

Diffuse spinal vertebral marrow infiltration, History of traumatic spinal injury, Radiological evidence of spondylodiscites, History of previous operation or radiotherapy & Small lesion below 0.5cm

Methods and protocols:

The 43 patients included in this study subjected to full clinical history and all of them show evidence of focal spinal vertebral lesion (single or multiple) confirmed on conventional MRI study ,(15) patients were referred from AL-Jawad center of oncology at AL-Imammain AL-Khadymain Medical city with known history of primary malignancy. All MRI studies were performed with Avanto 1.5T closed magnet MRI machine (Siemens, Germany) and MRI protocol which used included:

1. Sagittal T2-weighted turbo spin echo sequence done with parameters: slice thickness 4.0 mm; intersection gap 8 mm; 14 sections acquired, field of view, 280 mm; matrix size, 265 _ 256; repetition time 3500msec,echo time 99msec , flip angle 90º ; total acquisition time 54 seconds.
2. Sagittal T1-weighted spin echo sequence done with parameters: slice thickness 4.0 mm; intersection gap 8 mm; 14 sections acquired, field of view, 280 mm; matrix size, 256 _ 256; repetition time 792msec,echo time 9.9msec , flip angle 90º ; total acquisition time 45 seconds. And
3. Sagittal and Axial T1-weighted fat suppression spin echo (SE) after intravenous administration (in cases of metastases and atypical hemangioma only, while in cases of typical

hemangioma no contrast given) of 0.1 mmol/kg of Gad-DTPA (Magnevist, Germany).

4.DW MR Protocol: The diffusion-weighted study done for all patients before contrast administration using spin echo-echo planar imaging (SE-EPI) sagittal diffusion-weighted sequence at b-values of 0, 400 and800 mm2/s , diffusion gradients applied in all three orthogonal directions separately and subsequently averaged to minimize the effects of diffusion anisotropy and the images were obtained post processing in the extended workstation in Sagittal plane. The following DWI parameters were used: Slice orientation=sagittal ,EPI factor = 53, slice thickness 4.0 mm; intersection gap 8 mm; 14 sections acquired, field of view 313 mm; matrix size 192 _ 192; repetition time 4300sec/echo time 93 msec , flip angle 90º ; total acquisition time 240 seconds ,number of averages = 4, receiver bandwidth = 2697 Hz/pixel, number of b-factor=3. Diffusion-weighted images were processed automatically by the machine software to generate trace apparent diffusion coefficient maps for the all patients.ADC maps were derived automatically on a voxel-by-voxel basis with the MR system, Calculated ADC values are expressed in square millimeters per second.

Image analysis: Regions of interest (ROI) as circle of size 0.5 cm² were placed in the center of the lesions. For quantitative measurement of the ADC of spinal lesion, three such ROIs were placed and the mean ADC of these three values was calculated to decrease the chance of error. The ADC values were expressed as mean ± standard deviation in the form of Ax10-3mm²/s.

Complementary non contrast CT scan: using 64 multislice CT unit (Somatom, Siemens, Germany) done for all patients with atypical hemangioma and for patients with metastases to confirm the typical appearance of hemangiomas and the lytic or sclerotic nature of metastases, and we considered this as gold standered reference for differentiation.

Statistical analysis:

The statistical analysis was performed using commercially available software SPSS (statistical package for social sciences) version 22.0; Student's t-test and One way analysis of variance(ANOVA) were used to test the difference in ADC between the different groups, the ROC curve (Receiver Operating Characteristics) was employed for sensitivity, specificity and cut off value calculation. Data are presented as mean ± standard deviation or as numbers and percentages. A probability (P) value of less than 0.05 was considered statistically significant.

RESULTS:

In this study (43) patients with total (65) lesions included, The study sample was divided into three groups:

Group(A):10 patients (23.2%) with total of(15)vertebral lesions of typical hemangiomas, five of them had multiple lesions but largest two were included in the study, their ages range from (43-70 years) and mean age (53.5±10.9 years), from which 8 (80%) patients were females and 2 (20%) were males and their ADC value range were (1.111-1.727 $x10^{-3}$ mm^2/s) with a mean of (1.420± 0.1795 $x10^{-3}$ mm^2/s).

Group(B):13 patients (30.3%) with total of (13)vertebral lesions of atypical hemangiomas with their ages range from (52-75 years), mean age (55.8±8.5 years) from which 7 (53.9 %) patients were female and 6 (46.1%) patients were male and their ADC value range were (1.036-1.81 $x10^{-3}$ mm^2/s) and a mean of (1.426±0.2316 $x10^{-3}$ mm^2/s).

Group (C): 20 patients (46.5%) with total of (37) lesions of spinal vertebral metastases, 9 patients had multiple lesions but maximum three lesions were selected, their ages ranges from (28-65 years), mean age (53.6 ±11years) from which 14 (70%) patients were females and 6 (30%) patients were males, with their ADC value range were (0. 366-0.862 $x10^{-3}$ mm^2/s) with a mean of (0.6182±0.1373 $x10^{-3}mm^2/s$). The mean ADC values of vertebral lesions included in this study are shown in Table (1).

Table 1: The mean ADC value of 65 spinal lesions included in the study.

	No. of patients	No. of lesions	Mean ADC value$x10^{-3}m^2/s$
Typical hemangiomas	10	15	1.420 +0.1795
Atypical hemangiomas	13	13	1.426 +0.2316
Metastases	20	37	0.6182+0.1373
Total	43	65	

The metastatic spinal lesion shows lower ADC values with the mean ADC value for this group (n=37) were ($0.6182\pm0.1373x10^{-3}mm^2/s$), in contrary to the other two groups of typical hemangiomas (n=15) and atypical hemangiomas (n=13) where the mean ADC value were ((1.420 ± 0.1795 and 1.426 ± 0.231) $x10^{-3}mm^2/s$ respectively)). The difference in the mean ADC value between each group of vertebral typical and atypical hemangiomas lesions independently (ADV value (1.420 ± 0.1795 and 1.426 ± 0.2316) $x10^{-3}$ mm^2 /s respectively)) in comparison with metastatic vertebral lesions group (mean ADC value=$0.618.2\pm0.1373x10^{-3}$ mm^2/s) was statistically significant (p=0.0001). In the other hand the relation of mean ADC value between typical and atypical hemangiomas groups were statistically insignificant (p=1.0) as shown in table (2).

Table 2: Comparison of mean ADC value between typical haemangioma, atypical hemangiomas and metastatic lesions in the studied sample.

	Typical hemangiomas	Atypical hemangiomas	Metastases
Mean ADC	1.420 ± 0.1795	1.426 ± 0.2316	0.6182 ± 0.1373
Typical hemangiomas	P=0	P=1.000**	P=0.0001*
Atypical hemangiomas	P=1.000**	P=0	P=0.0001*

*=Significant, **= Non significant.

Data analyzed by using Receiver operating characteristics (ROC) curve for ADC cut-off value to differentiate patients with typical and atypical hemangiomas in one hand and patients with vertebral metastatic lesions in the other hand, revealed a cut-off ADC value of ($1.063 x10^{-3}$ mm^2/s) with AUC of 1.000, SE = 0.000 and sensitivity of 100%, specificity approaching 100%, P value < 0.001 and 95% confidence intervals = (1000–1000) (values below cut-off indicated metastatic disease with specificity 100%), as in figure (1).

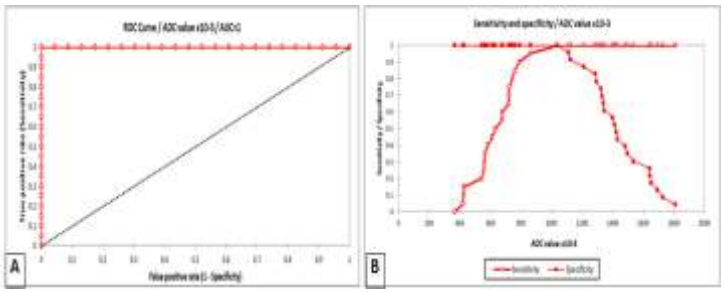

Figure 1: (A) ROC curve, (B) ADC cut value of $1.063x10^{-3}$.

All lesions which were proved to be hemangiomas (28 lesions) by classical MRI sequences with complementary CT scan showed high ADC value above the proposed cut-off point and non were false negative also all patient with metastatic lesion (37 lesions) by classical MRI sequences with complementary CT scan show ADC values below the threshold cut off value and no false positive results detected that give DWI sequence (100% sensitivity and 100% specificity) and excellent positive and negative predictive value. Atypical hemangioma (figure 2), typical hemangioma (figure 3) and metastatic bony lesions of vertebral body (figure 4) shows variable different MRI signals but when diffusion weighted sequence done restricted diffusion was seen in metastasis while in typical and atypical hemangiomas they showed free diffusion, then complementary CT scan done which revealed the lytic or sclerotic nature of metastatic bony lesions while in hemangiomas it showed its characteristic striated (polka dot sign) appearance.

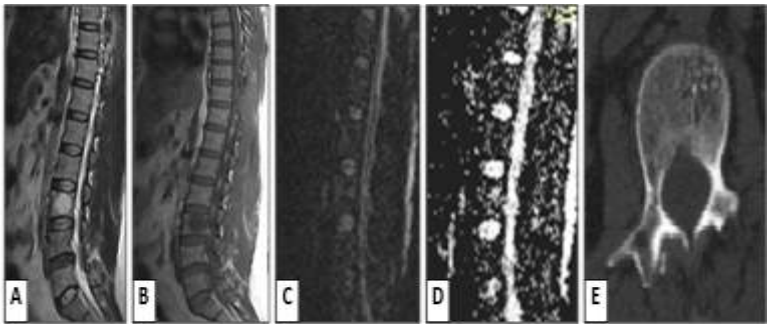

Figure 2: Atypical vertebral hemangioma in 70 years female. A: 3rd lumbar vertebral hypointense lesion onT1sequence, B: hyperintense on T2 MR sequence, C: free diffusion in DWI sequence, D: dark on ADC map and E: polka dot appearance in CT scan.

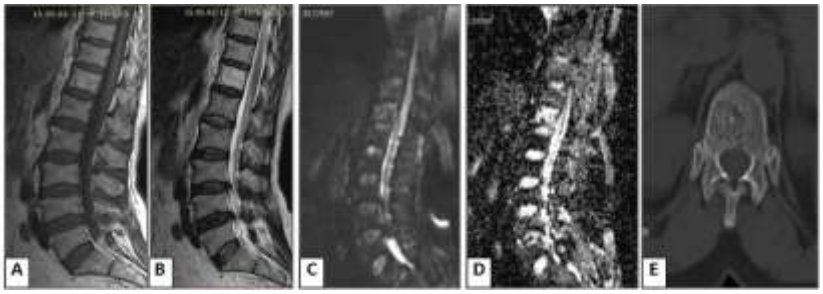

Figure 3:50 years female with spinal typical hemangioma. A: D12 hyperintense lesion in T1 sequence, B: hyperintense in T2sequence, C: intermediate signal in DWI sequence, D: bright ADC map, E: characteristic polka dot seen in CT scan.

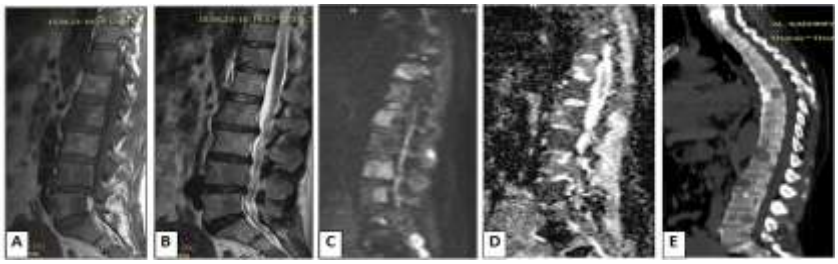

Figure 4: 59 years female with primary breast carcinoma.A: multiple spinal T1 hypointense lesions, B: some lesions are intermediate signal and other are hypointense onT2sequence, C: restriction seen in DWI sequence, D: dark in ADC map, E: mixed (lytic and sclerotic) lesions seen in CT scan.

DISCUSSION:

Over the last decade, DWI MR imaging of the vertebral body has proved its value and has been successfully employed in the differentiation of vertebral benign collapse due to osteoporosis and malignant collapse due to tumor infiltration [(12)]. Interleaved diffusion weighted echo-planar MR imaging of the spine is sufficient for quantitative analysis of diffusion effects, and the ADC calculated from diffusion weighted MR images is a dependable parameter to distinguish vertebral metastases from normal vertebrae [(13)]. Vertebral bone-marrow pathologies could be differentiated with high sensitivity and specificity as benign or malignant with the help of ADC values calculated from maps obtained by DWI [(14)]. Common benign lesions that may be mistaken for metastases include acute osteopenic compression fractures of the spine and atypical hemangiomas. Converse to report by Castillo et al. [(15)], the new technique of using DWI combined with ADC mapping provides more reliable information to differentiate benign spinal lesions from metastases and may obviate need for biopsy when in doubt [(16, 17)].

In malignant disease, there are often multiple lesions. However, uncertainty may occur more often with a single lesion. Metastases usually are well-marginated or round lesions that are not parallel or related to the vertebral end plates. These lesions are hypointense on T1-weighted images, hyperintense on T2-weighted images, and enhanced on T1-weighted, fat-suppressed post-contrast images. Atypical hemangiomas, which may vary in appearance, include those that are hypointense on T1-weighted images but retain the typical characteristics on T2-weighted and fat-suppressed post-contrast images [15].

We report here our finding regarding the value of diffusion weighted Magnetic Resonance Imaging in differentiation of atypical hemangioma and metastasis of spine. It has been found that atypical and typical hemangiomas in our study sample exhibits non restricted diffusion in the form of low signal on DWI, while the metastases showed restricted diffusion in the form of high signal in DWI and low signal in ADC maps. We found significantly low ADC values calculated in metastatic bony lesions compared with typical and atypical hemangioma. These differences were clearly apparent. In our results the mean ADC value of hemangiomas was found as ($1.426\pm0.231 \times 10^{-3}$ mm^2/s).The mean ADC value of metastatic bony lesions was found as($0.6182\pm0.1373 \times 10^{-3}$ mm^2/s). The study results were relatively in agreement with Taskın et al [14] who found that ADC values for atypical hemangiomas were between 1.94 and 2.82 x 10^{-3} mm^2/s. with a mean ADC value of 1.80 $\pm$ 0.37 x 10^{-3} mm^2/s, while the ADC values of malignant lesions were between 0.43 and 1.44 X 10^{-3} mm^2/s with a mean ADC value of 0.94 $\pm$0.34 x 10^{-3} mm^2/s. They reported a statistically proven optimal ADC threshold of 0.96x 10^{-3} mm^2/s that can be used for differentiating malignant from benign vertebral lesions; this is in agreement with our finding of the highest sensitivity and specificity ADC cut value of $1.063x10^{-3}$ mm^2/s.

Also the results of our study were comparable with results obtained from Kh. AL-Matrawy et al [18] who found the mean ADC value of hemangiomas as 1.54 x 10^{-3} mm^2/s and the mean ADC value of metastatic bony lesions as 0.83x 10^{-3} mm^2/s. Also our results were in agreement with Leeds et al [16] who reported that hemangiomas had ADC values higher than those of metastases because of the contribution of water molecules within the vascular spaces. The results of current study were also similar to the results obtained by Chan et al [19] who studied A total of 49 acute vertebral body compression fractures were found in 32 patients. 25 fractures in 18 patients were due to osteoporosis, 18 fractures in 12 patients were histologically proven to be due to malignancy, and 6 fractures in 2 patients were due to tuberculosis). The ADC is useful in differentiating benign from malignant acute vertebral body compression fractures, but there may be overlapping ADC values between malignant fractures and tuberculous spondylitis. Also Wonglaksanapimon et al [20] who studied a total of 39 vertebral fractures, 7 malignant compression fractures and 32 benign compression fractures were evaluated. The difference between ADC values of malignant, benign compression fracture and normal vertebrae were statistically significant ($p < 0.0001$). The accuracy, sensitivity and specificity were 89.7%, 85.7% and 90.6% respectively with the ADC threshold of 0.89 to discriminate malignancy.

CONCLUSION:

Diffusion weighted Magnetic Resonance Imaging is a valuable tool in differentiation of hemangioma (whether it is typical or atypical) and metastasis of spine with high sensitivity and specificity. Malignant spinal lesions show low ADC value when compared to that of typical and atypical haemangiomas. Cut-off ADC value of ($1.063x10^{-3}$ mm^2/s) is suggested to be used to differentiate between malignant spinal lesions from typical and atypical haemangiomas.

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