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ORIGINAL ARTICLE

The Usefulness of the Added Diffusion Weighted-magnetic Resonance Imaging in the Differentiation of Various Bone Tumors and Tumor-like Focal Lesions

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Abstract

Background: **Any imaging method that is now available can be used to diagnose malignancies that originate in the bones. Plain radiography is the imaging modality that is utilized the vast majority of the time in order to arrive at a diagnosis and identify the characteristics of a variety of osseous lesions. The diagnosis of bone cancer can be challenging, but computed tomography scans can provide useful information about the anatomical breadth of the disease. Magnetic resonance imaging (MRI) is the test that is considered to be the gold standard when it comes to diagnosing cancer and anomalies in the skeleton that are similar to tumors.**

Aim and objectives: **To evaluate the utility of adding diffusion weighted-magnetic resonance imaging with ADC value measurements to differentiate between benign and malignant bone lesions, as well as tumor-like localized bone lesions, using histological correlations or a final clinical diagnosis as the reference gold standard.**

Patients and methods: **In a study that was carried out at the Assiut Hospital affiliated with Al-Azhar University, the Radio-Diagnosis Department enlisted the participation of 50 patients who were thought to have a localized bone lesion.**

Results: **The comparison of the average ADC values of malignant and benign lesions revealed a discrepancy that was statistically significant. Concerning the ADC, it was not possible to differentiate between cancerous and benign lesions based on statistical significance. As a result of any disorder that disrupts or replaces the normal microarchitecture of bony trabeculae and fatty marrow, there is an increase in the amount of free water flow, along with a larger ADC when compared with the marrow that is next to the affected area. This is true for BTs of both benign and malignant varieties.**

Keywords: Bone tumors, Diffusion weighted-magnetic resonance imaging, Tumor like focal lesions

1. Introduction

In order to select the most appropriate course of treatment for a bone lesion, it is necessary to do a preoperative classification of the lesion as benign, malignant, or tumor-like.[1]

In spite of the fact that plain film radiography is generally considered to be the gold standard for detecting the etiology of and describing primary bone lesions,[1] it can still be difficult to profile specific sections of the musculoskeletal system due to the existence of overlapping structures. This can make it challenging to diagnose primary bone lesions.

The imaging technique known as computed tomography (CT), which is sometimes referred to as CT in some circles, can shed light on a wide range of

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disorders. These diseases include, but are not limited to, subtle cortical deterioration, soft tissue expansion, matrix mineralization, and endosteal scalloping. When compared with simple radiography and CT scans, magnetic resonance imaging (MRI) is considered to be the gold standard for finding bone cancers. This is due to the fact that MRI is extremely sensitive when evaluating anomalies in the bone marrow as well as the volume of the tumor.

Through the use of MRI, bone tumors can be found, the local extent of a malignant process can be examined for staging, and treatment responses can be determined. In clinical settings, however, robust T2-signal but mild enhancement lesions present a challenge for diagnostic purposes. Certain tumors, both benign and malignant, have peculiar properties that require further investigation.[2] These traits can be seen in both types of tumors.

It has been demonstrated that the utilization of diffusion weighted DW-MRI leads to an improvement in the characterization of bone lesions by MR.[1] DW-MRI is able to do so because it makes use of Brownian motion, which enables it to reveal specifics regarding the physiological context of water within tissues. Specifically, malignancies are defined by changes in the distribution of water inside cells, a reduction in membrane permeability, a rise in cellular density, and a breakdown in cellular membrane depolarization. All of these characteristics can be identified by DWI.[3] Malignancies are also characterized by a breakdown in cellular membrane depolarization.

Because DW-MRI does not require the use of ionizing radiation or extrinsic contrast chemicals, it may be able to provide quantitative assessments of the response of malignant lesions that have not been possible up until now. Then, DW-MRI is being utilized to monitor how effectively a patient is healing from radiation therapy.[4]

It is possible to improve the sensitivity of bone metastasis identification as well as the positive predictive value by employing DW-MRI in addition to T1WI and STIR sequences.[5]

The goal of the research team was to determine whether or not DW-MRI with ADC value measurements might serve as a gold standard when used in conjunction with histological correlations or a definitive clinical diagnosis to differentiate between benign and malignant bone lesions as well as tumor-like localized bone lesions.

2. Patients and methods

The Radio-diagnostic Department of Al-Azhar Assiut University Hospital was the site of this prospective investigation. Patients who have been referred by an orthopedics or clinical oncology clinic. Fifty people who had been diagnosed with a focal bone lesion underwent this procedure. The final diagnosis, whether from histopathology or the clinic, was utilized as the benchmark.

Ethical considerations: include informing participants of the study's goals before they provide any data, obtaining their verbal and written agreement, and protecting the confidentiality of their information.

Inclusion criteria: Patients having a prior history of primary malignancy in a separate part of the body presenting with bone pain, and pre-operative staging of known bone malignancies meet the inclusion criteria.

Individuals with pacemakers, severe claustrophobia, or previous MRI artifacts from bone-fixation surgeries will not be included.

All patients were subject to the followings: full history taken, thorough clinical history, plain radiography examination, conventional MRI examination and DW-MRI examination.

Plain radiography: radiographs were done for tumor containing part in antero-posterior (AP) and/or lateral views with adequate image density and collimations.

2.1. Conventional and diffusion MRI exam

Patient preparation and positioning and Technique and MR imaging data acquisition All of the examinations were carried out on a Philips Achevia 1.5-T machine (Fig. 1), and the postprocessing and analysis were carried out on a Philips Extended MRI workstation. Additionally, all of the patients were subjected to routine conventional MRI planes and pulse sequences, postgadolinium studies were performed if necessary for the characterization of

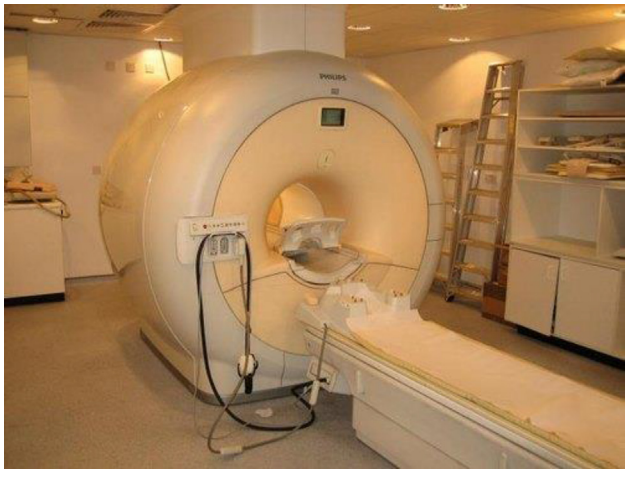


Fig. 1. Philips version Achevia.

Table 1. Demographic characteristics in the study group.

Parameters	Study group ($n = 50$) N (%)
Age (y)	
Mean ± SD	35.33 ± 20.1
Median (IQR)	32.0 (17.5–65.0)
Range	8–80
Children: 2–18 years	12 (24.0%)
Adults: 19–60 years	27 (54.0%)
Old age: >60 years	11 (22.0%)
Sex	
Male	27 (54.0%)
Female	23 (46.0%)

IQR, interquartile range; SD, standard deviation.

Table 2. Distribution of radiography findings in the study group.

Radiographic findings	Study group ($n = 50$) N (%)
Lytic bony lesions	19 (38.0%)
Multiple lytic and sclerotic bony lesions	6 (12.0%)
Permeative and moth-eaten appearance of bone destruction	4 (8.0%)
Sclerotic bony lesions	4 (8.0%)
Endosteal latency	3 (6.0%)
Grid line appearance	2 (4.0%)
Cortical thickening	2 (4.0%)
Bony projection with continuation of cortex and medulla of native bone	2 (4.0%)
Metaphyseal cloudy like bone lesion with sunburst appearance and Codman triangle in lateral view	1 (2.0%)
Bone destruction with soft tissue shadow	1 (2.0%)
Central radio-lucent area at metaphysis and crossing/the nonclosedepiphysis	1 (2.0%)
Thickening and ground glass opacities	1 (2.0%)
Thickening and increased bone density	1 (2.0%)
Trabeculations of vertebral body	1 (2.0%)
Unremarkable	1 (2.0%)
Well defined expansile lesion with narrow zone of transition and multiple fluid levels	1 (2.0%)

lesions in selective cases, and axial diffusion weighted imaging was performed.

2.1.1. Image interpretation

Conventional MR images, DWI-MR images, Biopsy Technique and Final Diagnosis.

2.2. Statistical analysis

Information will be entered into SPSS (Statistical Package for the Social Sciences) 26.0, Microsoft Excel 2016, and MedCalC (19.1) for tabulation and statistical analysis.

The χ^2 test for two-sample inferences was used on qualitative data with two-way design. We considered a P value of less than 0.05 to be statistically significant. The P-value is a statistical indicator of how likely it is that the results of a study could have been produced by random chance alone.

3. Results

Adults aged 19–60 years old accounted for 54% of all cases, whereas those aged 60+ accounted for 22% of all cases. The male to women (M: F) ratio in our research was 1.17 : 1, with 27 (54%) men and 23 (46%) females Table 1).

The most common finding was lytic bony lesion that found in 16 (32%) patients (Table 2).

There was a statistically significant ($P < 0.001$) disparity among the average ADC values of malignant and benign lesions. When comparing malignant and benign lesions, there was no significant difference in normal ADC ($P = 0.343$), with a mean ADC value of 0.37 ± 0.32 103 mm^2/s (Table 3).

Table 3. Comparison among malignant and benign lesions regarding normal and lesion ADC values.

	Total cases ($n = 50$)	Benign cases ($n = 25$)	Malignant cases ($n = 25$)	Test value	P- value
Normal ADC					
Mean ± SD	0.33 ± 0.29	0.37 ± 0.32	0.43 ± 0.35	^{Z}MWU = 0.949	0.343
Median	0.20	0.3	0.40		
Minimum	0.0	0.0	0.0		
Maximum	1.0	1.4	1.40		
Lesion ADC					
Mean ± SD	1.43 ± 0.6	1.11 ± 0.61	0.81 ± 0.44	^{Z}MWU = 4.07	**<0.001**
Median	1.40	0.95	0.70		
Minimum	0.05	0.05	0.30		
Maximum	2.50	2.5	2.20		

P less than or equal to 0.05 is considered statistically significant, P less than or equal to 0.01 is considered high statistically significant. IQR, Interquartile range; SD, standard deviation; ZMWU, Mann–Whitney U test.

Table 4. Validity of diffusion weighted-magnetic resonance imaging in prediction and differentiation between benign and malignant bone lesions.

DW-MRI	
Cutoff value	≤0.7
AUC (95% CI)	0.838 (0.705–0.928)
Sensitivity	66.67%
Specificity	96.0%
PPV	94.34
NPV	74.23
Accuracy	83.8%
P value	<0.001

AUC, Area under curve; CI, confidence index; NPV, Negative Predictive Value; PPV, Positive Predictive Value.

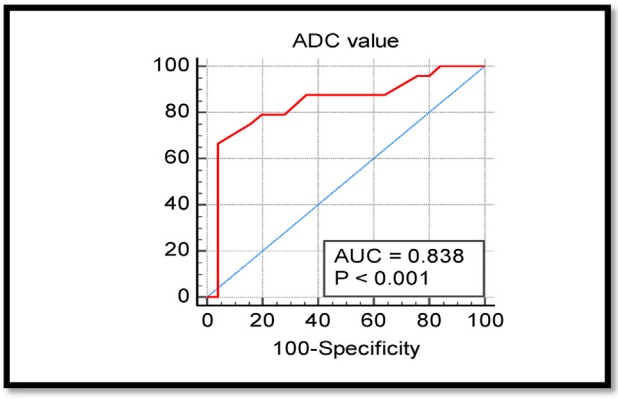


Fig. 2. Receiver operating characteristic curve of diffusion weighted-magnetic resonance imaging in prediction and differentiation among benign and malignant bone lesions.

By using receiver operating characteristic-curve analysis, DW-MRI can differentiate among malignant and benign lesions with cut off value 0.7, good accuracy (83.8%). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) was 66.67, 96.0, 94.34, and 74.23%, respectively ($P < 0.001$) (Table 4 and Fig. 2).

The majority of cases (28%) were diagnosed to have metastasis from other types of malignant tumors, 8% had Ewing's sarcoma, osteosarcoma and hemangioma (Fig. 3).

Osteosarcoma was found in 4 cases with two age peaks 8–22 years and 48–63 years. Pain was found in all cases. The mean ADC value in these cases was $(0.88 \pm 0.51) \times 10^{-3}$ mm^2/s (Table 5).

4. Case presentation

4.1. Case No (1)

4.1.1. Clinical history

A 66 years old female case with history of diabetes mellitus, right hip pain, swelling and fever.

4.1.2. Radiographic examination

Plain radiography and MRI of the right hip region.

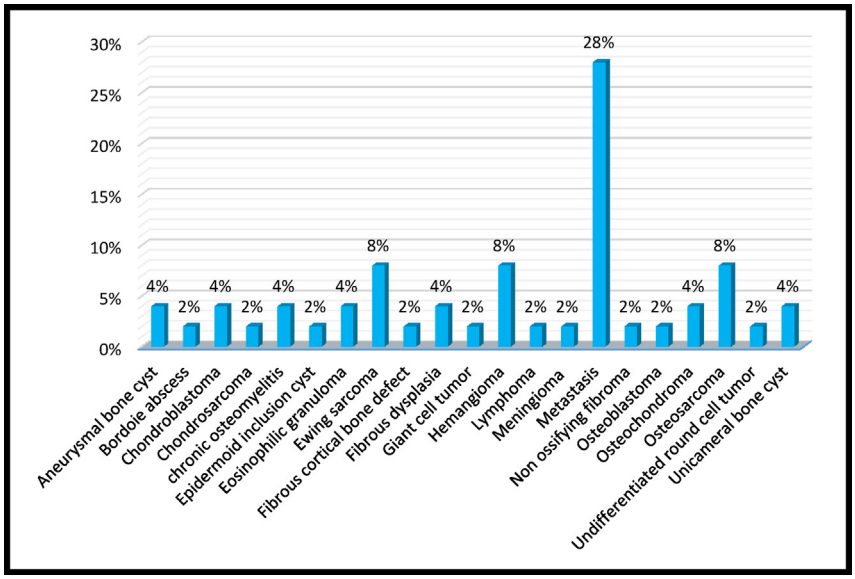
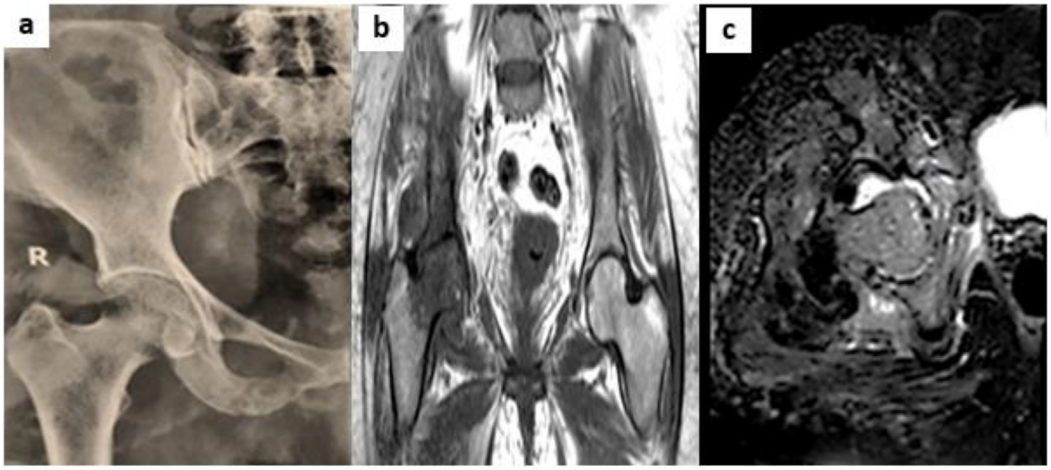


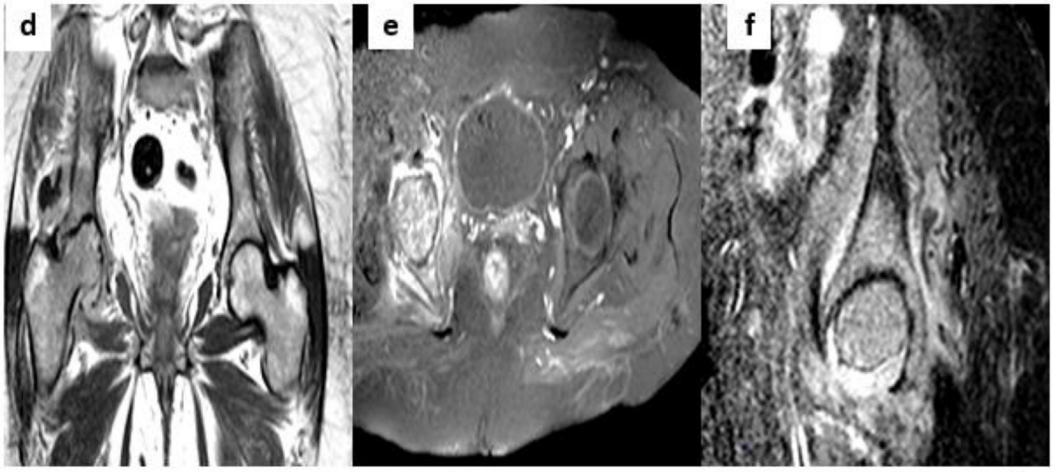
Fig. 3. Bar chart showing distribution of pathology findings in the study group.

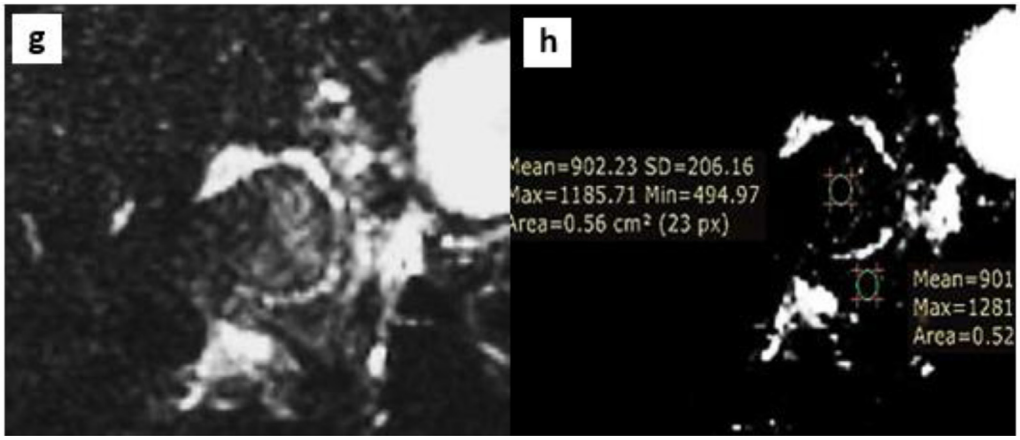
Table 5. Osteosarcoma findings in our research.

Osteosarcoma	Number of cases No. (%)	Age (y)	Clinical picture	ADC value
	4 (16)	8-22 and 48–63 years	Pain 4	0.88 ± 0.51



Plain radiography right hip joint AP a) showing irregular flattened head of right femur with sclerosis of the inferior ischial ramus and acetabulum, pelvis MRI in coronal T1WI showed low signals at acetabulum, ischium, head and neck of right femur b) and axial STIR showed high signals at the acetabulum, ischium, head and neck of right femur with joint effusion and para-ostial fluid loculi c) axial pelvis in DWI showed restricted diffusion in the form of high signals g) and ADC map showed corresponding low ADC signals and mean ADC value $= 0.9 \times 10^3$ mm^2/s h).





4.1.3. Radiological diagnosis

Collectively diagnosed as benign featuring likely inflammatory process osteomyelitis with septic arthritis and soft tissue abscess formation.

4.1.4. Final diagnosis

Osteomyelitis with septic arthritis with aspirate staphylococcus pneumoniae from abscess.

4.2. Case No (2)

4.2.1. Present history

A 35 years old women case is suffering from swelling and pain in left thigh.

Examined part: left knee and femur.

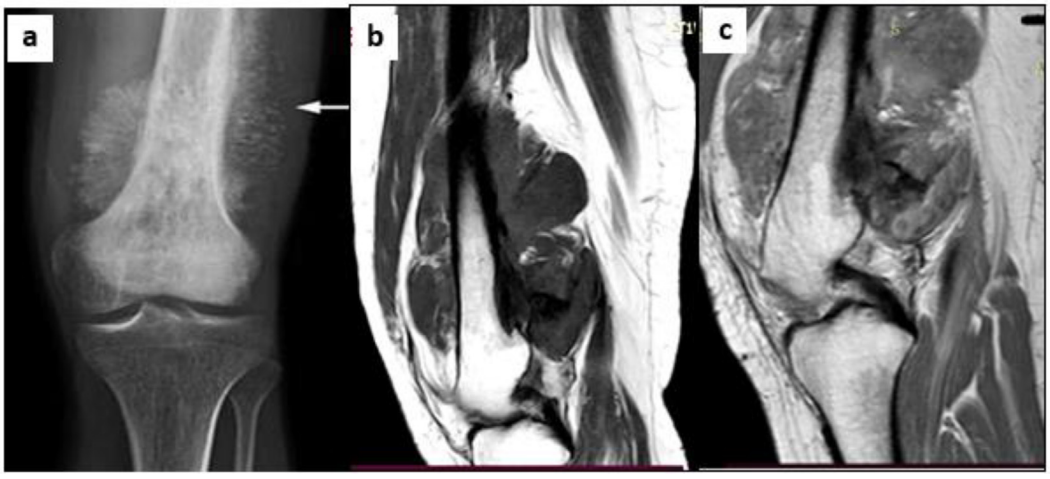
4.2.2. Radiographic examination

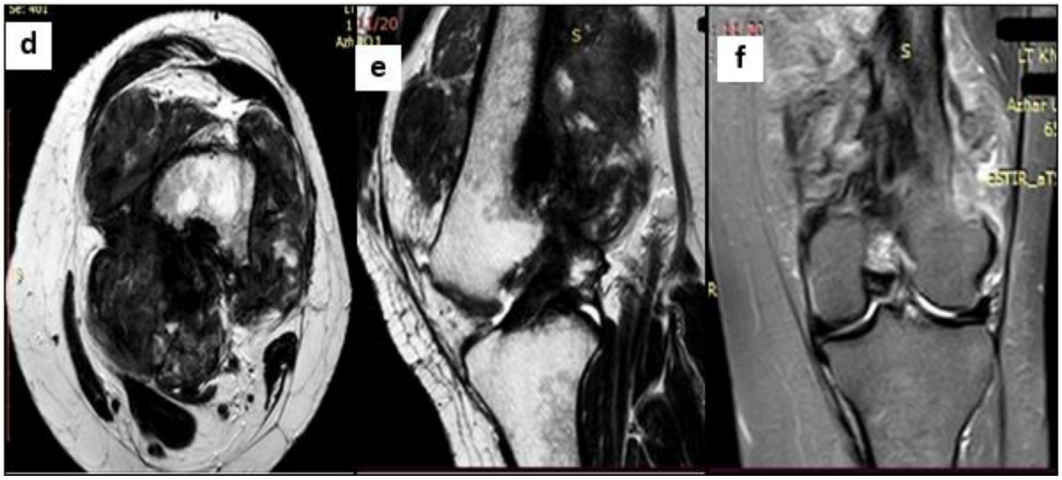
Radiography and MRI examination of left femur:

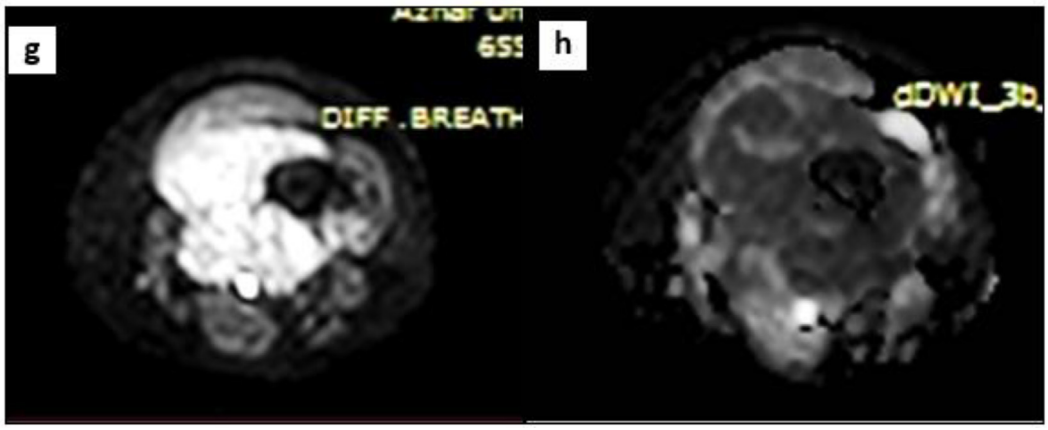
A simple radiography of the left knee joint taken in AP view (a) reveals a bony lesion of the distal femur. This lesion has cortical disruption and periosteal response (arrows), giving it the appearance of a sunburst. MRI: sagittal T1WI picture (b) and PD image (c) of the left femur demonstrating aberrant mixed signals (primarily isointense to muscle) soft tissue lesion with cortical disruption.

MRI T2WIs in axial (d), sagittal views (e) and coronal STIR (f) images of left femur showing abnormal mixed signals soft tissue lesion (mainly hyper intense signals) with small area of cystic changes and cortical destruction, no line of cleavage from inner most related muscles and neurovascular bundle.

DWI (g) and ADC map (h), axial images of left femur showed restricted diffusion in the form of high signal in DWI, corresponding at ADC map low ADC signals and ADC values 0.8×10^{-3} mm^2/s.







4.2.3. Radiological diagnosis

The radiographic features are suggestive of malignant lesion with destructing bony lesion of left femur and para-ostial soft tissue component, MRI features of para-ostial osteosarcoma, it was done to demonstrate extent of lesion, skip lesion and associated soft tissue component that is seen inseparable from the surrounding structures so case underwent radiotherapy before surgical excision.

4.2.4. Final diagnosis

High grade osteosarcoma of left femur on true cut biopsy and histopathology.

5. Discussion

In order to improve the therapy and outcome of bone cancers, diagnostic methods that can reliably and noninvasively distinguish among benign & malignant lesions must be developed. DWI is a relatively new technique that complements standard MR sequences. DWI offers both quantitative and qualitative insights into the cellular water transport processes.[6]

The research found the following as its primary outcomes:

Cases' ages were found to range from 8 to 80 years old, with a mean ± SD = 35.33 ± 20.1 years and a median of 32 years old, according to the present data. The age range of 20–39 years accounted for 34% of all cases, followed by 8–19 years (28%), 60–80 years (22%), and 40–59 years (16%). The male to female (M: F) ratio in our research was 1.17 : 1, with 27 (54%) males and 23 (46%) women.

Consistent with our findings, R. Setiawati *et al.*[7] assumed that cases among the ages of 11–20 accounted for the largest proportion 31 (36.49%) cases of benign and malignant bone cancers. A further 18 (21.4%) cases occurred among the ages of 51–60. Ages 0–10 had the fewest occurrences (1.2% each), while those over 60 had the highest (1.3% each), however the average age was only 32 years and 702 days. The study found that there were 44 males affected (or 52.3% of the total) and 40 females affected (or 47.6% of the total), for a male-to-female ratio of 1.1 : 1.

However, the 62 cases (37 men and 25 women) with bone lesions in the research by Mansour *et al.*[8] were treated differently. Sixty-two (67.7%) cases were younger than 40 years old, whereas 20 (32.2%) cases were older.

The radiography taken of our research population revealed that the most prevalent anomaly was a lytic bone lesion, which was present in 19 cases, or 38% of the total. After that, six cases, or twelve percent, showed signs of having both lytic and sclerotic bone lesions simultaneously. When compared with the gold standard of pathology, radiography were successful in correctly diagnosing bone abnormalities in 19 out of 30 cases (true positives). We were able to attain a sensitivity of 76%, specificity of 68%, accuracy of 60%, a PPV of 65.52%, and NPV of 71.4%.

According to Hamaoka *et al.*[9] radiography of bone lesions may show up as sclerotic lesions or rims (osteoblastic), areas of feeble or nonexistent density (osteolytic), or disruption of the trabecular structure. All of these manifestations are caused by osteoblastic activity. Recommend XR for evaluating 'suspicious' lesions on SS or symptomatic lesions, but do not recommend it for screening due to its limited sensitivity (44–50% according to level II-III evidence), as well as the fact that osteolytic lesions in the lumbar vertebrae do not become apparent on XR until 30–75% of the normal bone mineral content has been lost.

In contrast, a sample of 30 cases found that radiographic diagnosis of bone cancers correlated well with histopathology, with a sensitivity of 92.9%,

specificity of 87.5%, PPV of 86.7%, and NPV of 93.3%.

Due to the limited sensitivity and specificity of radiography findings, MRI with additional DWI and post-gadolinium was performed in 9 cases to distinguish solid from cystic lesions, stage the disease, and identify the para-ostial soft tissue component.

T1WI and CEMRI can faithfully portray the original lesion's extension, since their precise locations aid in surgical planning, as stated by D. Nascimento *et al*.[10] CEMRI can be used to distinguish among hyperintense solid lesions and fluid-filled lesions. In contrast to liquid, solid, non-necrotic surfaces will exhibit diffuse amplification. Helps differentiate among edema and a healthy tumor, and permits precise measurement of vascularization. We divided cases into two groups, one with benign and inflammatory lesions accounting for 44% and 6% of group (1), and another with malignant lesions accounting for 50% of group (2), based on our pathology findings.

Study comprises total of 30 cases of bone lesions, of which 28 were bone tumors (93.33%) and 2 (6.66%) were non-neoplastic lesions, similar to Kharolkar V *et al*.[11] There were 28 occurrences of bone tumors, with 14 (50%) being benign and 14 (50%) being malignant.

Using receiver operating characteristic-curve analysis, DW-MRI has a high rate of success (83.8%) in distinguishing between malignant and benign lesions using a cut off value less than or equal to 0.7. ($P < 0.001$). The results showed a sensitivity of 66.67%, specificity of 100%, positive predictive value of 94.34%, and negative predictive value of 74.2%.

At a mean threshold ADC value less than or equal to 0.84×10^3 mm^2/s, Mansour *et al*.[8] found that malignant and benign bony lesions could be differentiated with a sensitivity of 88.89%, specificity of 88.57%, PPV of 91.2%, NPV of 88.71, accuracy of 0.912, and area under the curve (AUC) of 0.912.

One incidence of osteoblastoma was discovered in a 16-year-old girl, and the presenting symptom was discomfort. $1.5 \times 10 (-3)$ mm^2/s is the average ADC value.

In addition, one case of osteoblastoma affecting an 11-year-old was reported in Ahlawat in 2015,[12] with an average ADC value of 1.1×10^3 mm^2/s.

5.1. Conclusion

To begin, it is essential to keep in mind that the aqueous dissolution rates, also known as ADCs, of BTs (regardless of whether they originate from a benign or malignant source) are often higher than those of normal yellow marrow. This is due to the fact that any disorder that disturbs or replaces the normal microarchitecture of bone trabeculae and fatty marrow generates enhanced free water flow, along with a larger ADC compared with the marrow that is next to the affected area.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

Conflicts of interest

The authors declared that there were NO conflicts of Interest.

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