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Research Article

MR SPECTROSCOPY: A KEY TO DIFFERENTIATE BENIGN AND MALIGNANT SOFT TISSUE LESIONS

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ABSTRACT

Objectives- To evaluate soft tissue lesions on 1.5T MR to determine the usefulness of MRS in differentiating benign and malignant lesions.

Materials and methods- Contrast enhanced MRI and proton MR spectroscopy was performed on 20 patients on a 1.5T magnet system after initial evaluation of the lesion by radiography. MR examination was performed with a surface coil, either a flex body or extremity coil, appropriate for the location and size of the lesion. Multivoxel spectroscopy was performed at a TR/TE of 700/135. Area of interest was positioned within the lesion in the solid part excluding the necrotic region. Presence of choline peak was noted. The results of MR spectroscopy were compared with histology results obtained by either surgical biopsy in 4 cases, fine needle aspiration cytology in 11 cases, one case of leprosy was diagnosed by skin biopsy. No histological tests were done in a case of myositis ossificans, ruptured cysticercosis and two tubercular abscesess. The infective cases were followed up and showed improvement with antihelminthic/ antitubercular treatment respectively while the patient with myositis also was followed up.

Results- On MRS choline was detected in 9/11 malignant lesions and 1/9 benign lesion. This benign lesion was a case of tubercular soft tissue abscess. MRS had a sensitivity of 81.8 % and a specificity of 88.9% in characterizing the lesions as benign and malignant on the basis of choline peak.

Conclusion- Detection of choline in the tumour has high sensitivity and specificity for diagnosing malignancy and can be helpful in aiding the differential diagnosis of benign from malignant soft tissue masses on MRI.

INTRODUCTION

MRI is the most sensitive imaging investigation for detecting soft tissue lesions due to its high contrast resolution. It gives excellent definition of the tumour extension, assessment of bony involvement and infiltration into the neurovascular structures[1,2,3,4]. However MR morphological features are insufficient to define the benign versus malignant nature of soft tissue lesions in a large number of cases[5,6,7]. As benign lesions are encountered more commonly than the malignant lesions, an improved means of differentiating benign from malignant lesions may obviate biopsy reducing patient anxiety and management costs[8,9,10]. In recent years proton MRS has been applied to musculoskeletal lesions with the aforementioned aim[11,12]. MRS provides information about pathological changes at the molecular level. Choline is an important component of the tumour cell membrane, with higher cell turn over, higher concentrations of choline can be detected by proton MRS[13,14]. Thus it has been suggested and various authors have shown that choline elevation is noted in malignant lesions of brain, liver, prostate, breast etc[15,16,17,18]. The presence of choline has also been used a biomarker and to predict the outcome of therapy and monitor treatment. Studies have shown that MRS at 1.5T and 3T is capable of differentiating benign from malignant soft tissue lesions[19,20,21,22,23]. In this study we sought to evaluate utility of proton MRS at 1.5T in characterizing benign and malignant soft tissue lesions

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MATERIALS AND METHODS

Twenty consecutive patients referred for MR exam of soft tissue masses or swelling were included in the study. The study group included 11 males and 9 females. An informed consent was obtained from all the patients. Approval for the study was also obtained from the institutional review board. An initial radiograph of the area of interest was obtained. MRI was performed for all patients on a 1.5T (Siemens Sonata, Erlangen, Germany) MR unit. Depending on the size and site of the lesion, either a surface flex or extremity coil was used for examination. All the studies included T1W turbo spin echo, T2 W turbo spin echo and STIR /T2 fat suppressed sequences. Images were obtained in axial, coronal and/or sagittal planes. Fat suppressed T1 weighted images were obtained after contrast administration of 0.1 mmol/kg of gadopentate dimeglumine intravenously. The lesions were evaluated for location, size, signal intensity, margins, involvement of joint and neurovascular bundles, contrast enhancement and presence of necrosis on MRI. Multivoxel spectroscopy was done using 3D CSI (PRESS) at a TR of 700ms and TE of 135 after manual shimming to optimize field homogeneity. Water suppression was done by an automated routine provided by the manufacturer using CHESS pulse. The grid was placed over the solid component of the lesion, avoiding fat and cortical bone as far as possible. Appropriately placed six to eight saturation bands were used with the CSI grid to obtain outer voxel signal suppression. Spectral analysis was done using commercially available software supplied with the system. The presence or absence of a discrete choline peak within each spectrum was recorded. The criterion for determining whether choline was present was the presence of clearly identifiable peak at 3.2ppm.

The results of MR spectroscopy were compared with histology results obtained by either surgical biopsy in 4 cases, fine needle aspiration cytology in 11 cases. The case of leprosy was diagnosed be skin biopsy. No histological tests were done in a case of myositis ossificans, ruptured cysticercosis and two tubercular abscesess. The two tubercular abscesses showed positivity on PCR. The infective cases were followed up and showed improvement with antihelminthic/antitubercular treatment respectively while the patient with myositis also was followed up.

RESULTS

The study group included 11 patients with malignant and 9 with benign masses. The histopathological findings are summarised in table 1

Table 1 Spectrum of soft tissue lesions evaluated.

	Malignant Soft Tissue Masses	Male	Female	
1	Synovial sarcoma	1		
2	Alveolar soft part sarcoma		1	
3	Malignant peripheral nerve sheath tumour		1	
4	Clear cell sarcoma	1		
5	Extraskeletal Ewing's tumour (Fig-1 (A-F))		1	11
6	Malignant fibrous histiocytoma	1		
7	Spindle cell sarcoma	1	1	
8	Extraskeletalchondrosarcoma	1		
9	Rhabdomyosarcoma	1		
10	Mesenchymal tumour	1		
	Benign Soft Tissue Lesion			
1	Benign fibrous tumour		1	
2	Myositis ossificans	1		
3	Benign spindle cell tumour	1		
4	Neurogenic tumour (Fig-3 (A-I))	1	1	9
5	Lepromatous ulnar nerve thickening	1		
6	Tubercular abscess		2	
7	Ruptured cysticercosis		1	

On plain radiographs, soft tissue calcification was seen in four patients, one of which was a case of myositis ossificans while three were malignant lesions. One of these malignant lesions showed characteristic chondroid calcification and was proven to be a case of extra skeletal chondrosarcoma. The other two malignant lesions showing calcification were of spindle cell sarcoma and synovial sarcoma. A lytic lesion of the upper end tibia was seen is one case with alveolar soft part sarcoma with osseous metastasis (Fig -2(A-F)).

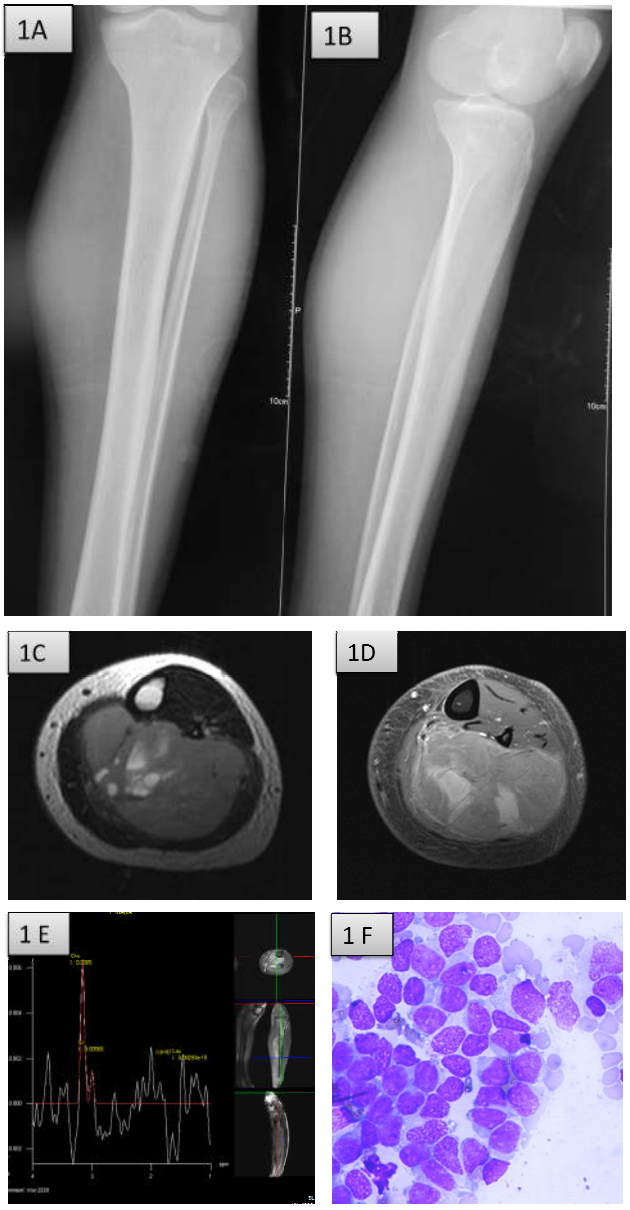

Fig 1 (A-F) Ewing's Sarcoma

Anteroposterior and lateral radiographs of the leg (A), of a 21 year old reveals soft tissue swelling in the region of calf with no obvious bony involvement. T2 axial (C) and post contrast axial images (D) reveal large soft tissue mass in the posterolateral aspect of the calf appearing heterogenously hyperintense on T2, showing heterogenous enhancement on post gado images. The lesion is closely abutting the fibula, however the marrow signal and cortical outline are maintained. MR spectroscopy from the lesion revealing a prominent choline peak (E). FNAC from the lesion was suggestive of Ewing's sarcoma (F)

MRI findings of benign and malignant soft tissue lesions is given in table 2 55.56% of the benign soft tissue lesions had a well-defined margin while 81.81% of the malignant lesions

showed well defined margins on MR. In our study, majority of benign lesions (66.66%) were less than 5cm in size while all of malignant lesions were more than 5cm in size. Most of the benign, malignant and infective lesions were hypointense on T1WI. On T2W and STIR sequences, all the benign and malignant lesions were hyperintense. T2W heterogeneity was seen in 72.7% of malignant lesions but only in 1/9 (11.11%) of benign lesions.

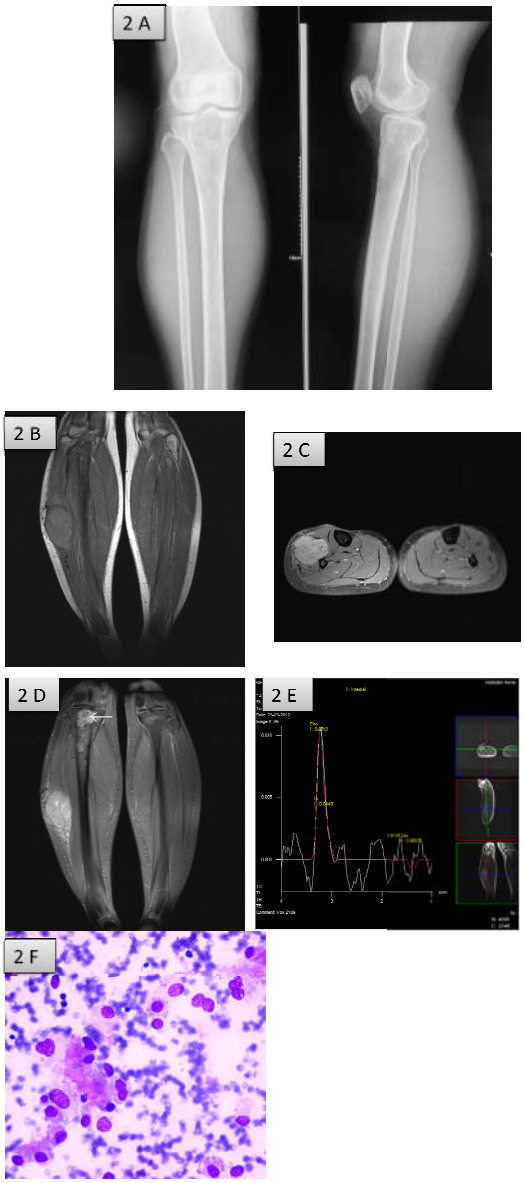

Fig 2 A F Alveolar Soft Part Sarcoma (CALF)

AP and Lateral radiograph of the leg with knee joint (A) reveals well defined lytic lesions in the epiphysis and proximal metaphysis of the tibia due to metastasis. No obvious soft tissue swelling is seen in the calf. T1W coronal image (B) reveals a well defined iso to hypointense soft tissue mass within the muscles in the anterolateral aspect of the leg. On T2 W fat saturated axial image (C) the lesion appears homogeneously hyperintense with well demarcated margin. Overlying soft tissues appear normal. No cortical erosion of the underlying bone is noted. Post contrast fat suppressed T1 coronal images (D) reveal a homogenously enhancing soft tissue mass lesion. The bony lesion within the epimetaphysis (arrow) is also shows homogenous post contrast enhancement. MR spectroscopy (E) revealed a definite choline peak at 3.2ppm. FNAC (F) was suggestive of alveolar soft part sarcoma confirmed on immunohistochemistry (not shown)

Bone involvement was seen in 36.3% and neurovascular involvement was seen in 45.45% of malignant masses and in none of the benign masses and infections. Most of the lesions whether benign, malignant or infective showed heterogeneous enhancement. On MRS, none of the benign soft tissue masses showed evidence of choline peak. But one of the infective lesions showed a choline peak, this was a case of tubercular abscess showing peripheral rim enhancement pattern on post contrast images.

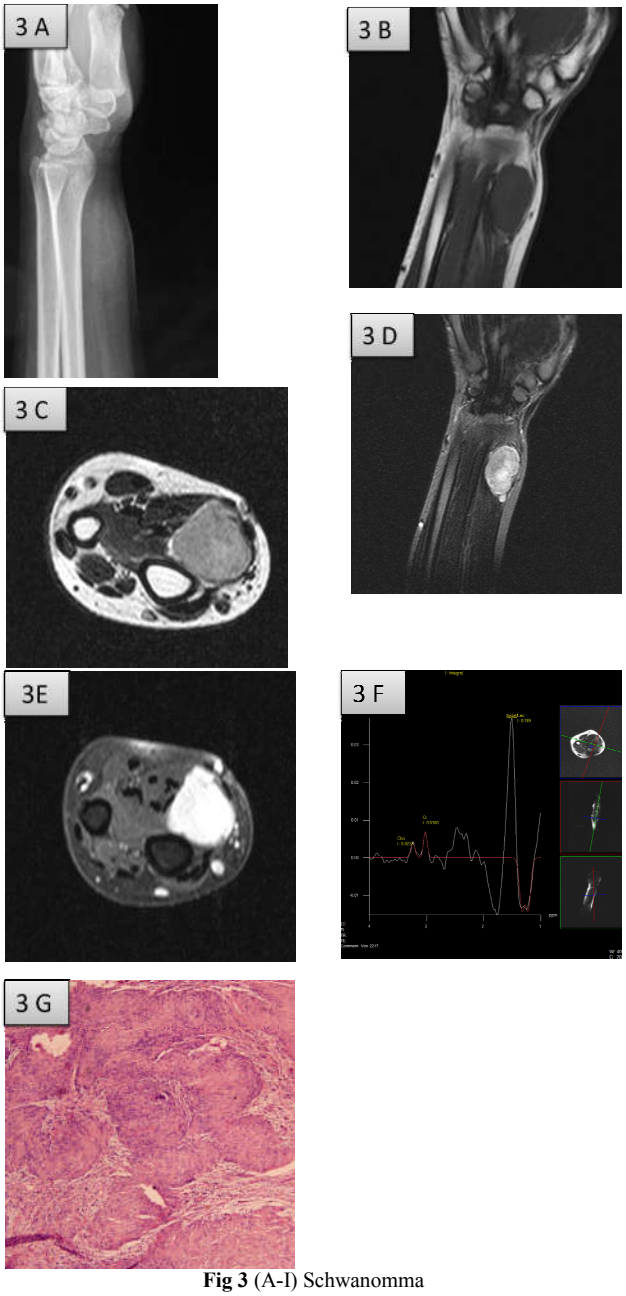

Fig 3 (A-I) Schwanomma

(A)- Lateral radiograph of the forearm reveals a relatively well defined soft tissue swelling in the volar aspect of the forearm near the distal metaphysis . No evidence of any bony lesion is noted. T1W coronal (B) and T2W axial (C) and STIR coronal images (D) of the wrist reveal a well defined lesion abutting the cortex of the distal end of radius with no associated bony abnormality, appearing hypointense on T1 and hyperintense on T2WI. Post contrast axial image (E) demonstrates intense homogenous enhnacement . MR spectroscopy (F) reveals lipid peak but no choline. Histopathological examination (G) of the lesion was suggestive of schwannoma

Thus overall choline was seen in 11.11% of benign cases. Of the malignant soft tissue masses, choline was seen in 81.81% cases. In two cases only noise was identifiable. These included a case of synovial chondrosarcoma and a spindle cell sarcoma.

Thus, of the twenty soft tissue lesions studied by MRS, 10 showed presence of a choline peak, of which 9 were confirmed to malignant on histopathology while one of the benign soft tissue lesions, which was a case of isolated soft tissue tubercular abscess also showed a choline peak. Two malignant lesions did not show choline peak due to excessive noise in the spectrum. Hence, the sensitivity and specificity of choline peak to predict malignancy was 81.8% and 88.9% respectively.

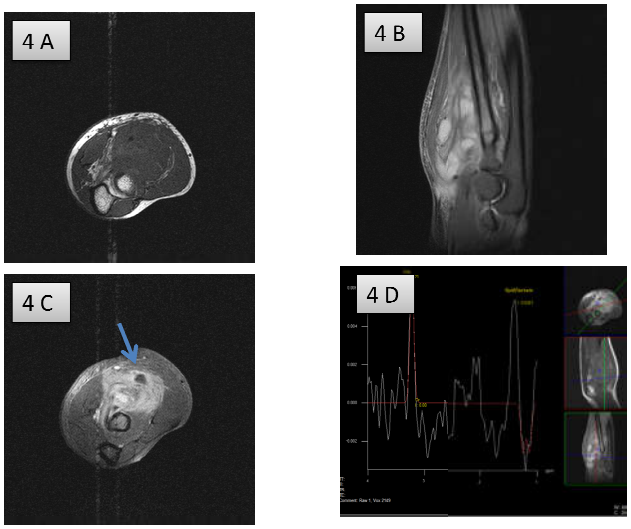

Fig 4 A-E Tubercular Abscess

T1W (axial), STIR sagittal (B) images reveal bulky flexor compartment muscles appearing hypointense on T1W, heterogenously hyperintense on STIR. Adjacent humerus shows some marrow edema on STIR. Post contrast axial images (C) reveals heterogenous enhancement of the same with few non enhancing areas within (arrow). On MRS (D) a distinct choline peak is noted at 3.2ppm along with a prominent lipid peak.

Table 2 Comparison of Benign and Malignant Lesions

	Characteristic		Benign Lesions (n=9)	Malignant Lesions (n=11)
MRI	Margins	Well defined	5 (55.56%)	9 (81.8%)
		Ill defined	4	2
	Size (cm)	<5	6	
		>5	3	11
	T1WI	Hypo	7*	11
		Iso	1	
	T2WI/STIR	Hetero	1	8 (72.7%)
		Hypo	0	1
		Hyper	8 (~89%)	2
	Bone involvement			4
	Joint involvement			3
	Neurovascular			5
	Enhancement	Hetero	7	8
		Homo	1	2
		Rim	1	1
MRS	Presence of choline peak		1	9

DISCUSSION

The differentiation of benign and malignant soft tissue neoplasms is important for prognostication. MRI is currently the imaging technique of choice for detection of soft tissue lesions; however characterization of such lesions is not definitely possible by routine MRI[5,6].

In our study 55.56% benign and 81.8% malignant lesions had a well-defined margin. Most of these lesions showed heterogeneous or rim enhancement (~89% of benign and 82% of malignant lesions), thus these features were not found to be useful in distinguishing benign from malignant masses. Heterogeneously hyperintense signal was noted in 72.72% malignant lesions in our study, whereas most of the benign lesions were homogeneously hyperintense on T2WI. Some previous studies have reported that T2 heterogeneity may favour malignant etiology[24,25,26] while the other features may overlap. Involvement of bone and neurovascular bundle was seen only in malignant lesion in our study. However osseous involvement can occur in benign infective lesions like osteomyelitis too.

MRS has been applied to musculoskeletal lesions in an attempt to increase the specificity of the diagnosis. Most authors have used single[19,23,27] and few others multivoxel[12,28] spectroscopy for the evaluation of musculoskeletal lesions. The advantage of using multivoxel spectroscopy is the ability to obtain spectra over a large field of view. It can also be helpful in delineating the boundaries of the lesion, invasion into surrounding structures and also to know areas of necrosis within the lesion[12,28]. However the limitations of this method are complexity of the procedure, need for manual shimming and longer scan time[29,30,31]. In comparison a single voxel technique provides information only a small part of lesion that is being analysed but is simpler to execute.

On MR spectrum, the main peak evaluated is the choline peak seen at 3.2ppm which consists of three metabolites like glycerophosphocholine, phosphocholine and free choline, the chemical shift of which cannot be resolved separately on 1.5T in vivo[32]. Choline is precursor of acetylcholine and participates in phospholipid metabolism of cell membranes. The levels of choline vary with disorders affecting membrane turnover like increase in number of cells or increased membrane synthesis[23,30,32,33], both of which are seen in malignant disorders. Thus choline levels usually increase in malignant tumours[34,35]. The absence of choline peak has been found to be highly predictive of benign lesions, it may however be seen in some benign lesions which have a high proliferative rate[12,19].

In our study malignant lesions showed presence of choline. False negative findings were noted due to noisy spectrum in one case each of extraskeletal chondrosarcoma and spindle cell sarcoma. These lesions also showed presence of calcification in plain radiographs. Low proton levels and susceptibility effects due to mineralization have been suggested to be responsible for this finding[19]. Other studies have also attributed low mitotic index and low grade malignancies to show absence of choline peak[36].

Out of the nine benign lesions include in the study, one lesion did show a choline peak. This lesion with a choline peak was a case of tubercular abscess (Fig-4 (A-E)). Choline peak has been previously described in abscesses as well and is attributed to increased tissue metabolism and abundance of inflammatory cells produced in response to inflammatory process[19,37,38,39,40]. Presence of choline peak has also been reported in few other benign lesions including desmoid tumour, myositis ossificans,

eccrine spiroadenoma and giant cell tumour. High cellular density of the lesion, hypervascularity, metabolically active lesions increased cell turnover were the contributing factors for the presence of choline in these lesions[12,27,19].

Since choline peak was noted in one benign lesion i.e 11.11% in our study and has also been reported by previous authors, one should not diagnose a lesion as malignant just on the basis of presence of choline peak without taking into account the other MR and clinical features.

The sensitivity of choline peak to predict malignancy in our study was 81.8% and specificity was 88.9%. These findings are in agreement with the studies done by Russo *et al*, Doganay *et al* and Zhang *et al* who reported a sensitivity and specificity of 95% & 83%, 72.2% & 83.3% and 76% and 88% respectively[29,34,41]. These authors used single voxel spectroscopy at TE ranging from 40 to 270ms. Agarwal S *et al* have found a specificity of 93.33%, however with a relatively low sensitivity of 60% for predicting malignancy in musculoskeletal mass lesions using single voxel spectroscopy[42]. Multivoxel spectroscopy has also been used in a study done by Fayad *et al* conducted on a 3T system[43].

Our study shows that multivoxel proton MR spectroscopy can be done in majority of soft tissue masses on 1.5T magnet system and can be used to detect choline in soft tissue lesions. Presence of calcium may however hinder spectroscopy, information obtained by MRI and MRS can be complementary to each other for characterization of soft tissue masses.

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