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Magnetic resonance imaging versus radiological skeletal survey of the lumbosacral spine in patients with advanced multiple myeloma: A single-institute experience

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Abstract:

BACKGROUND: Multiple myeloma (MM) is a plasma cell malignancy in the bone marrow (BM), where imaging is an essential tool in its management.

OBJECTIVE: The aim of this study was to compare the sensitivity of radiological skeletal survey (RSS) with magnetic resonance imaging (MRI) of the lumbosacral spine (LSS) in advanced MM patients.

PATIENTS AND METHODS: We retrospectively reviewed the RSS and MRI of the LSS for 33 patients with a new diagnosis of symptomatic MM. Chi-squire test was used for comparing the results.

RESULTS: Of 33 patients, 20 (60%) were male and 13 (40%) female, with a mean age of 61 years. Characteristic findings on RSS were osteopenia (86%), compression fractures (60.5%), multiple lytic lesions (39.5%), solitary focal lesion (6.06%), and normal findings (9.3%), The commonest findings on the MRI were combined diffuse and focal lesions (27.27%), multiple focal lesions of macronodular pattern (18.2%) and variegated (micronodular) pattern (15.15%), The other finding on MRI were diffuse homogeneous infiltration with SI> adjacent disc (12.12%) while SI ≤ adjacent disc (6.06%), solitary focal lesions (6.06%), and normal findings (15.15%). A majority (58.1%) of patients presented with an advanced stage and the pathological compression fracture found in 60% of cases. Focal lesions were detected in five patients (15.15%) whose radiographs were negative, and more lesions were detected in 11 patients (33.33%) with positive radiographs. Diffuse infiltration pattern was found in eight cases (24%) on MRI imaging when radiographs showed only osteopenia and in one patient (3%) in whom radiographs were normal.

CONCLUSIONS: MRI had higher sensitivity in the detection of diffuse BM involvement and discovery of focal spinal lesions compared to conventional radiographs with a positive *P* value.

Keywords:

Magnetic resonance imaging, multiple myeloma, radiological skeletal imaging

Introduction

Multiple myeloma (MM) is a type of hematological malignancy that occurs as a result of the proliferation of abnormal malignant plasma cells in the bone marrow (BM) and other tissues.[1] Malignant plasma cells produce abnormal monoclonal para-proteins called M-protein in the serum and urine (light chains) that lead to the development of bone lesions.[2] Plasma cell disorders include monoclonal gammopathy of undetermined significance, smoldering

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multiple myeloma, and symptomatic myeloma with features of end-organ damage.[3,4]

According to the International Myeloma Working Group, the diagnosis of MM depends on the presence of marrow plasmacytosis, M-protein in the serum and urine, and the presence of myeloma-associated end-organ damage. The myeloma-associated end-organ damage includes anemia, hypercalcemia, bone lesion, and renal impairment.[5-7]

For the staging of MM, we have been using Durie and Salmon Staging System since 1975 that relied on conventional radiological skeletal survey (RSS).[8,9] In 2003, the Durie and Salmon Staging System was revised and named Durie Salmon Plus. The Durie and Salmon Plus Staging System now includes whole-body magnetic resonance imaging (MRI) or fluoro-2-deoxyglucose positron emission tomography-computed tomography, compared to the original order, which relied on the RSS. Radiologists now use the revised scheme to stage these patients [Table 1].[10-12]

RSS is used as the standard in the detection of bone lesions in myeloma, despite its limited sensitivity, since it needs more than 30% bone replacement to become identified, in addition to radiation risk.[13,14]

The classical appearances of MM on RSS are punched out <20 mm round/oval lytic bone lesions; diffuse spinal osteopenia; and rarely osteoblastic or mixed lesions.[15,16] In symptomatic MM patients, RSS may be normal initially in 10%–20%. RSS has limited specificity in differentiating other more common causes of osteopenia, rather than MM as early osteoporosis, steroid use, and excessive alcohol intake. Conventional radiography shows 30%–70% false-positive results compared to MRI.[17]

Spinal MRI findings in MM are classified into mild, moderate, and diffuse on T1-weighted images (T1 WI); mild is defined as "salt-and-pepper" pattern or minimal infiltration; moderate is vertebral signal intensity lower than normal but still brighter than adjacent disc; while the severe diffuse disease is vertebral signal isointense or hypointense to disc signal.[10-12]

MRI is highly sensitive and specific for detecting BM infiltration. Vertebral fractures in MM patients occur in 55%–70% in which may be due to diffuse osteopenia (66%) or tumor infiltration (33%). MRI is used for differentiating benign versus malignant vertebral collapse. The appearance of MRI may predict some prognostic values, in which those with diffuse involvement will have a more unsatisfactory outcome than those with a healthy appearance.[18] The aim of our study was to compare the sensitivity of RSS with MRI of the lumbosacral spine (LSS) in advanced MM patients.

Patients and Methods

This is a retrospective study conducted on 33 patients diagnosed with symptomatic MM. This study done on myeloma patients, who attended the Hematology Outpatient Clinic of Hiwa Hospital in Sulaymaniyah province from January 1, 2018, to April, 2018. The questionnaire data were filled from the files of the patients. The questionnaire form included a brief, relevant history, RSS findings, and MRI findings. RSS and MRI of the LSS studies at the time of diagnosis were reviewed retrospectively in patients with MM. The staging was done using the "Durie/Salmon Plus" Staging System. Sociodemographic data included name, gender, age, and compliant of patients at the time of diagnosis. The study was approved by the ethical committee at the Kurdistan board of medical Specialties in Erbil, Iraq.

All selected patients were subjected to both RSS and MRI of the LSS. RSS was done by computed radiography machines, including X-rays of the vertebrae anteroposterior and lateral view. The MRI performed by MAGNETOM AERA 1.5 Tesla Siemens MRI machine. All the MRI studies had at least T1 W sagittal, T2 W sagittal, STIR sagittal, and T1 W T2 W axial images. Data entry and analysis were done using SPSS program Version 25 (Armonk, NY: IBM Corp, USA). Chi-squire test was used for comparing the results, and $P < 0.05$ was regarded as statistically significant.

Results

The demographic characteristics of the patients are illustrated in Table 2. The study sample is composed of

Table 1: The Durie and Salmon PLUS staging system

Stage	Definition
Stage IA*	Normal skeletal survey or a single lesion ≥5mm
Stage IB*	up to five focal lesions or mild diffuse spinal disease
Stage IIA/B	5 to 20 focal lesions or moderately diffuse spinal disease
Stage IIIA/B	More than 20 focal lesions or severe diffuse spinal disease

*Subclasses A refer to normal renal function while B is abnormal renal function

Table 2: Demographic characteristic of patients

Age groups	No.	Percentage
40-49	5	15.15
50-59	10	30.3
60-69	10	30.3
70-79	6	18.18
80-89	2	6.06
Male / female	1.52:1	
Total	33	100.0

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33 adults with MM; 20 (60%) were male and 13 (40%) were female. The male-to-female ratio was 1.5:1. The age range at diagnosis was between 44 and 87 years, with a mean of 61.06 (±10.9 standard deviation) years. Backache was the primary presentation at diagnosis found in 16 (48.5%) of the patients. beside that bone pain represented in 10 (30.3%) of cases, pallor in 5 (15.15%), and generalized body aches in 2 (6.06%) [Table 3].

Regarding the X-ray of the LSS, the majority of the study group had osteopenia and compression vertebral fracture pattern as seen in 9 (27.27%) of cases, while osteopenia, compression fracture, and lytic lesion together were also seen in 9 (27.27%) [Table 4]. Osteopenia was the most common radiological feature on the X-ray of the LSS (26, 86%), followed by compression fractures (60.5%), multiple lytic lesions (39.5%), and solitary focal lesions (2, 6.06%). X-ray of the LSS was normal in 3 (9.3%) [Figure 1].

MRI of the LSS (including lower dorsal spines) showed that combined diffuse and focal lesion pattern was found in 9(27.27%) patients followed by multiple focal lesions (macronodular) 6(18.2%), variegated (micronodular) pattern 5(15.2%), diffuse homogenous infiltration (SI > adjacent disc) 4(12.1%), diffuse homogenous infiltration (SI ≤ adjacent disc) 2(6.06%), and solitary focal lesions 2(6.06%), and 15.2% of the MRI studies were normal [Table 5].

Regarding the staging of MM, we found that the majority of our patients were in Stage III at the time of diagnosis 19 (57.6%), while Stage IA was found in 5 (15.1%), Stage IB in 9 (6.06%), and Stage II in 7 (21.2%) [Table 6]. Complications were compression vertebral fracture in 60% of the patients and pathological (due to underlying myeloma lesion) long bone fracture in 3% of the patients [Table 7].

Among those who had compression fractures, 20 patients had MRI for which benign and malignant features evaluated. From the former, 75% had malignant characteristics and 25% were benign fractures. MRI of the LSS showed osteolytic bone lesions in 23 (69.7%) patients of the study group while only 18 (54.54%) patients showed osteolytic lesions using RSS of the LSS of the same patients. We found a statistically significant *P* value of 0.046, indicating that MRI is more sensitive than RSS [Figure 2].

Discussion

The present study provides the first data, in our region, which we analyzed the radiological features on RSS and MRI of the LSS in MM cases in Sulaymaniyah City.

The percentage of male patients was higher than female patients; the male: female ratio among the study group was 1.52:1 [Table 2]. This ratio was close to a study done by Lecouvet *et al*.[19] but was slightly lower than that reported in other studies in the literature,[20,21] which was said to be close to 2:1, although this might be related to small sample size.

The mean age at the time of diagnosis in our study was 61 years, with the peak age groups of 50–69 years; the minimum age was 44 years. These were close to what mentioned in the literature[21,22] and similar to what reported by Khoshnaw *et al*.[23]

The majority of our patients presented with backache (48.5%) and other bone pain (30.3%); our findings were close to another study[20] in which the majority (88%) complained of bone pain.

Multiple lytic lesions followed by diffuse osteopenia were the most frequent radiographic pattern on RSS of the lumbar spine (39.9%) and (18.6%) respectively. The previous results were lower than those reported

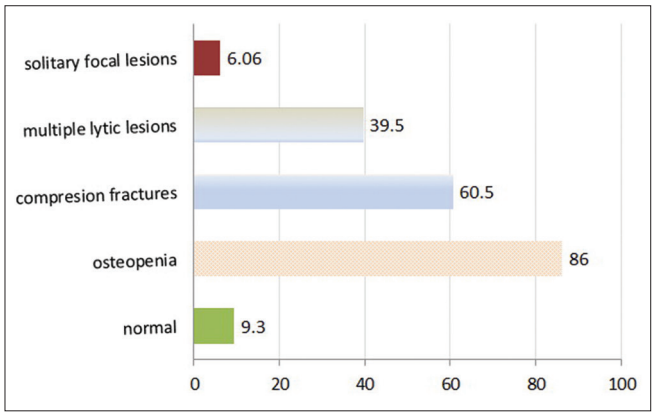

Figure 1: Distribution of radiological features on X-ray of the lumbosacral spine

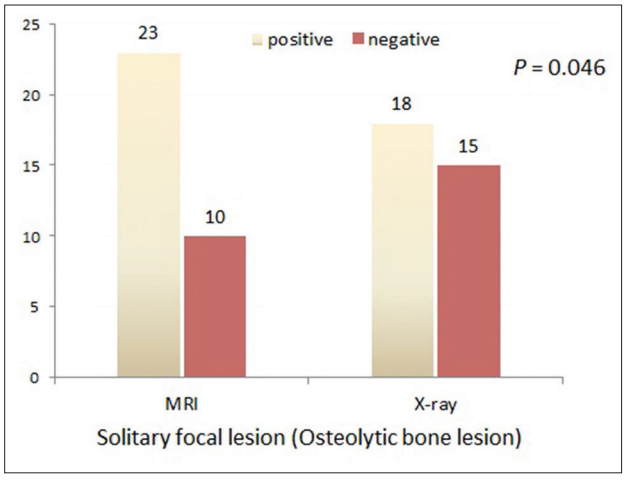

Figure 2: Magnetic resonance imaging versus radiological skeletal survey in detecting focal osteolytic bone lesion in lumbosacral imaging

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by Lecouvet *et al*.,[19] in which RSS showed 86.5%, while comparable to another study done by Smith *et al*.,[24] in which diffuse osteopenia was 15%.

In our research, plasmacytoma was present only in two cases (6.06%), consistent with what mentioned in the literature,[12] which is <5%. Finally, only one case (3.03%) was normal. However, it was found that up to 20% of the radiographs and MRI could be normal in another study,[19] while in another study,[24] 10% was normal.

Osteopenia was the most frequent radiographic feature on LSS (86%), consistent to what is mentioned in the literature,[11] although it is not possible to differentiate between osteopenia due to senile osteoporosis and postmenopausal osteoporosis from osteopenia caused by myelomatosis.

MRI patterns in a study done by Schreiman *et al*.[20] showed combined diffuse and focal lesions in 50% while in our study showed 27.3%. In the previous survey, multiple focal lesions (macronodular) and variegated (micronodular) lesions were noted in 20% and 7%, respectively; however, in our research, they were noted in 18.2% and 15.2%, respectively. In their study, MRI was done for the whole spine, pelvis, and extremities, while in our study, only MRI of the LSS was analyzed because MRI of the LSS was the most regular examination available in this retrospective study.

In our study, about 15.2% of the cases had normal MRI examinations, and this was close to the figures found in other studies in which up to 20% of the MRI examinations were unremarkable despite a significant BM infiltration.[25]

MRI has higher sensitivity for focal lesion detection as focal lesions were detected in five patients (15%) with negative radiographs and more lesions were detected in 11 patients (33%) with positive radiographs. The diffuse infiltration pattern was found in 8 cases (24%) when radiographs showed only osteopenia and in 1 case (3.03%) when radiographs were normal. MRI was normal in four cases (12.12%) having radiographs showing osteopenia. In one example, there was a lytic lesion on X-ray, while MRI showed a moderate diffuse pattern without focal lesions. Two cases (6.06%) showed a single lesion (plasmacytoma) on both X-ray and MRI of the LSS. In one fact (3%), both MRI and X-ray were normal. In general, LSS MRI findings, when combined with RSS in our study, lead to upstaging in five cases (15%).

The disadvantage of conventional radiography is its low sensitivity, which is explained by the fact that lytic lesions are only detectable if more than 30% of the trabecular bone destroyed. Further, conventional radiography cannot detect a diffuse BM infiltration.[26,27] Moreover, conventional radiography fails to differentiate benign reasons for focal lucent bone lesions, it has a relatively high interobserver variability, and certain regions cannot be depicted free from superposition.[27]

The majority of our patients were in Stage III when diagnosed (57.6%), this might be due to delay in seeking medical help, while Stage II was (21.2%), Stage IA (15.1%), and Stage IB (6.06%).

Bone fractures are common in MM; in our study, the most common complication was vertebral compression

Table 3: Clinical features at presentation in study group

Chief complaint	No.	Percentage
Back pain	16	48.48
Other bone pain	10	30.3
Pallor	5	15.15
Generalized body ache and weakness	2	6.06
Total	33	100.0

Table 4: Distribution of x-ray patterns on x-ray of LSS

LSS x-ray finding pattern	No.	Percentage
Normal	3	9.09
Osteopenia	6	18.18
Osteopenia and compression fracture	9	27.27
Osteopenia, lytic lesions and compression fracture	9	27.27
Osteopenia and lytic lesions	4	12.12
Solitary focal lesion and compression fracture	2	6.06
Total	33	100

Table 5: Distribution of MRI patterns on MRI of LSS including lower dorsal spines

MRI Patterns	Number of patients	Percentage
Normal	5	15.15
Solitary focal lesion	2	6.06
Multiple focal lesions (macronodular)	6	18.18
Salt and pepper (variegated) (micronodular) or minimal infiltration	5	15.15
Diffuse homogenous infiltration (SI >adjacent disc)	4	12.12
Diffuse homogenous infiltration (SI <or equal to adjacent disc)	2	6.06
Combined mild to moderate diffuse infiltration and multiple focal lesions	9	27.27
Total	33	100

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Table 6: Radiological staging among the study group

Radiologic Staging	No.	Percentage
IA	5	15.15
IB	2	6.06
II	7	21.21
III	19	57.57
Total	33	100.0

Table 7: Distribution of bone complications on x ray

Complications	No.	Percentage
Vertebral compression fracture	20	60.06
Long bone fracture	1	3.03
None	12	36.36
Total	33	100.0

fractures, found in 20 patients (60.6%) (one or more compression fractures). Only one patient had a long bone fracture (3.03%). About 75% of the fractures had one or more features of malignant cause. One study showed that vertebral fractures in MM occur in 55%–70% of cases and may be either benign, due to diffuse osteopenia in 66%, or pathological, due to tumor infiltration in 33%.[15] We found a significant *P* value (<0.05) in comparing MRI with RSS on LSS at the time of presentation of patients with symptomatic myeloma.

Conclusions

Conventional radiography still is standard for diagnosis of MM due to its full availability and low costs. However, it has limitations in complex anatomical areas such as the spine, because of existing natural artifacts.

MRI has higher sensitivity for the detection of diffuse BM involvement and focal lesions in the spine than radiographs. MRI of the whole spine (if feasible whole-body MRI) should be considered in all patients with negative conventional radiography and all patients with apparently solitary plasmacytoma.

Further prospective studies with a large sample size need to be done using MRI of the whole spine, to declare more radiological abnormalities in patients with MM that presentation.

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Conflicts of interest
There are no conflicts of interest.

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