Skeletal Involvement in Multiple Myeloma: The Radiological Point of View

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Abstract: Multiple myeloma is one of the most common hematologic malignancies.

Bone marrow is typically involved and characterization of osseous lesions, in terms of number, size and localization, is necessary for disease staging and post-treatment assessment.

Different imaging modalities can be performed in multiple myeloma evaluation, with a consequential number of information achievable.

The aim of this work is to provide a general overview of multiple myeloma radiological findings detectable at X-ray, CT-scan and MRI, with relative advantages and drawbacks for each technique.

Keywords: Multiple myeloma, X-ray, Computed tomography, Magnetic resonance imaging.

INTRODUCTION

Multiple Myeloma (MM) is the second most common hematologic malignancy after lymphoma, typically occurring in the sixth or seventh decade [1, 2].

It is caused by an abnormal proliferation of malignant plasma B cells within the bone marrow and consequent overproduction of monoclonal proteins that can be found in serum and urine [2-4].

Bony infiltration by myeloma cells mainly determines osteolysis, through the release of osteoclastic-promoting cytokines [2, 5].

Although occasionally asymptomatic, the typical clinical picture includes fatigue with weight loss, anemia, recurrent infections, renal impairment due to extensive excretion of monoclonal light chains, hypercalcaemia with bone demineralization and risk of pathologic fractures and vertebral collapses [3-6].

Extramedullary localization of MM (*i.e*. hepatic, renal, pancreatic, lymphnodal, etc.) may occur in a small percentage of patients (10%-16%) [2].

The final diagnosis is reached through different examinations, such as blood count, serum biochemistry, serum and urine electrophoresis and bone marrow biopsy [7].

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Nevertheless, radiological imaging has a pivotal role in identification and quantification of bone lesions.

Different techniques, with related different outcomes, have been employed in this field.

Although x-ray was the first one performed and still represents the most widespread, the greater availability of Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) have significantly improved the diagnostic assessment as well as the prognostic estimation.

Therefore, imaging findings are considered mandatory for the correct patient staging in the same way of laboratory parameters [8].

The aim of this work is to provide a general overview of MM radiological findings detectable at x-ray, CT-scan and MRI.

X-RAY

Due to its high availability and low healthcare costs, X-ray plain films are usually the first imaging approach in MM skeletal assessment.

The spine (65%), the ribs (45%), the skull (40%) and the shoulder (40%) are the most common anatomical sites involved [3].

Within plate bones, MM localizations appear as round-shaped lytic lesions, generally without a sclerotic rim (Figure **1**). Conversely, within long bones, a "moth-eaten" appearance and the scalloping of the inner cortical bone can be displayed [2, 3].

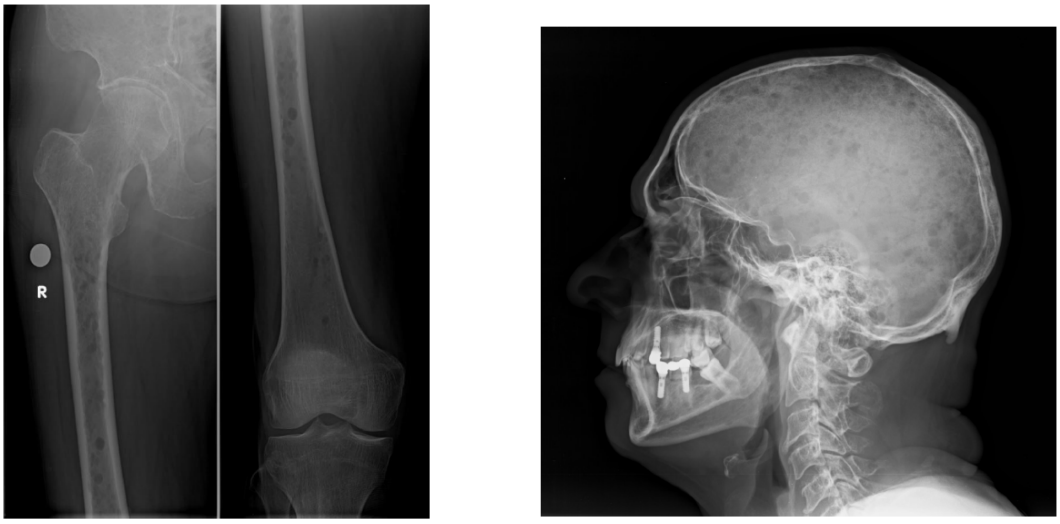

Figure 1: 60 years old male patient. X-ray typical appearance of osteolytic bone involvement of the right femur (**a**) and the skull (**b**), the latter with a “salt and pepper” appearance.

Diffuse bone marrow involvement lead to general osteopenia, focal compression and vertebral collapses [3].

On the other hand, conventional radiology is impaired by several limitations.

First, although it provides an exhaustive evaluation of the bone structures, the patient has to take different and often uncomfortable positions and the examination-time is consequentially elevated.

Moreover, considering the severe and diffuse bone rehash, the sensitivity of this imaging modality is low

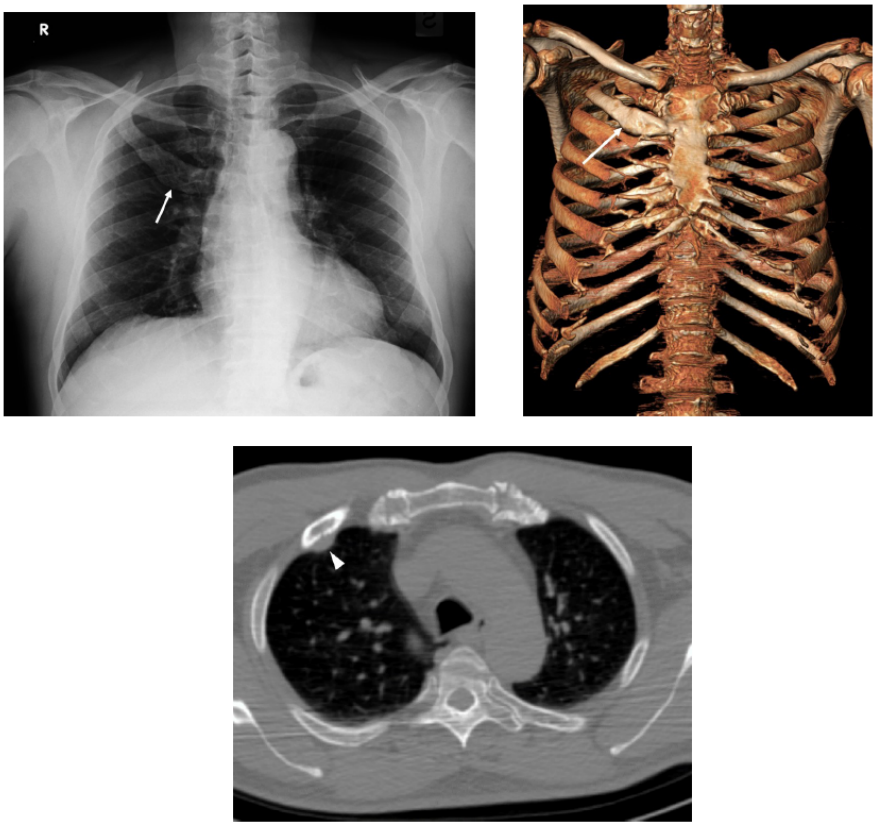

Figure 2: 66 years old male patient. Chest X-ray (**a**) shows an enlargement with diffuse alteration of the anterior arch of the second right rib (arrow). CT-scan confirmed the MM bone lesion, as visible on volume-rendering reconstruction (**b**), and further showed an extra-osseous extension (arrowhead) on the axial plane (**c**).

and therefore MM lesions can be undetectable in a large amount of patients (from 20 to 70%) [3, 4, 7].

The final limit is clearly represented by radiation exposure [9].

COMPUTED TOMOGRAPHY

In less than one minute, CT-scan is capable to provide a three-dimensional and comprehensive evaluation of the whole body, including skeletal and soft-tissues structures.

This results in greater comfort for the patient and possibility to detect intraosseous as well as extramedullary lesions (Figure **2**).

Nevertheless, CT-scan has demonstrated a higher sensitivity over x-ray in detecting bone lesions, especially if small (< 5 mm) or placed within diffuse bone alteration areas (*i.e*. demineralization, fractures, vertebral collapses, etc.) (Figures **3** and **4**).

Moreover, skeletal evaluation does not need the injection of intravenous contrast agent, which is also

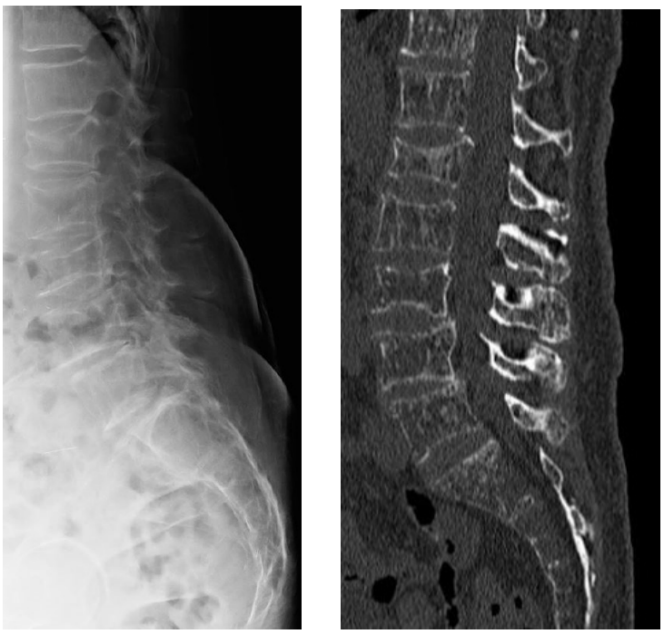

Figure 3: 73 years old female patient. Spine assessment can be challenging in case of severe MM involvement, with diffuse demineralization and vertebral collapses at X-ray plain film (**a**). CT-scan (**b**) represents a faster and more accurate alternative.

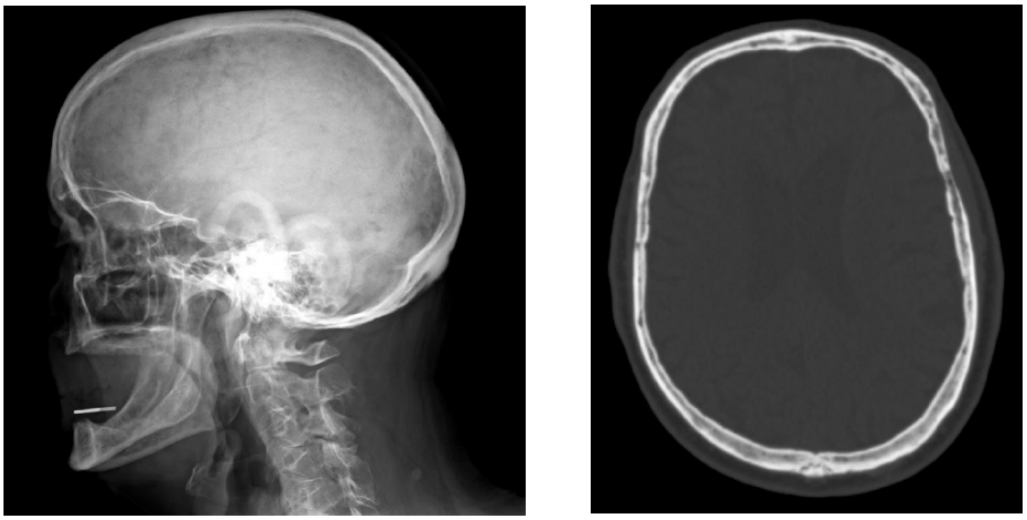

Figure 4: 67 years old male patient. Skull x-ray demonstrates a diffuse shaded osseous alteration due to the presence of several osteolytic foci, as confirmed by CT-scan (**b**), mainly detectable within the left frontal bone.

inappropriate in subjects suffering from proteinuria and/or renal failure, such as MM patients [7, 10].

The main drawback of this technique is radiation exposure, which can be higher up to three-times than plain x-ray [3].

Over the last years, this limit was partly overcome by low-dose protocols, albeit at the cost of lower contrast resolution. In this sense, a further improvement has come from the recent introduction of iterative reconstructions, that allowed a significant improvement of image quality [2, 9].

MAGNETIC RESONANCE IMAGING

Considering its high sensitivity, superior than both radiography and CT, the wide evaluation of body tissues and the lack of ionizing radiations, MRI have become of paramount importance for MM evaluation and therefore it is considered by many as the gold standard imaging modality (Figure **5**) [3, 9].

As a general rule, MM lesions appear hypointense on T1-weighted images and hyperintense on T2-weighted scans, due to the low amount of fat and the high water content and cellular density.

In particular, T2-weighted short-tau inversion recovery (STIR), a sequence that magnify the fluid intensity signal with a simultaneous drop of the adipose one, is generally recognized as the most sensitive acquisition in detecting MM lesions.

Bone lesions are also generally characterized by contrast enhancement [7].

Up to five different patterns of bone marrow involvement can be recognized at MR: normal, focal and/or diffuse and “salt and pepper” infiltration.

MRI has also demonstrated its importance for response assessment, revealing with high accuracy number or size changes of bone marrow lesions after treatment [4].

MRI can also take advantage from the so-called “functional” techniques, such as perfusion MRI (p-MRI) and diffusion weighted imaging (DWI).

P-MRI is based on a seamless series of fast gradient echo T1-weighted acquisition with fat-saturation, obtained before, during and after administration of intravenous contrast medium.

This technique allows quantifying the ongoing contrast distribution of contrast enhancement, which mainly reflects neoangiogenesis phenomenons, and calculating time-intensity-curves (TIC).

MM bone marrow lesions are generally associated with a steep slope of enhancement followed by wash out or persistent/progressive late enhancement [4, 11].

On the other hand, DWI is based on randomized Brownian motion of extracellular water molecules, thus reflecting cellular density of a certain tissue. Apparent diffusion coefficient (ADC) maps represent a further advise in DWI evaluation through the removal of the T2-weighting effects [12].

The lesions are generally characterized by elevated intensity signal on DWI on high b-value images (usually b1000) and high ADC values rather than healthy bone

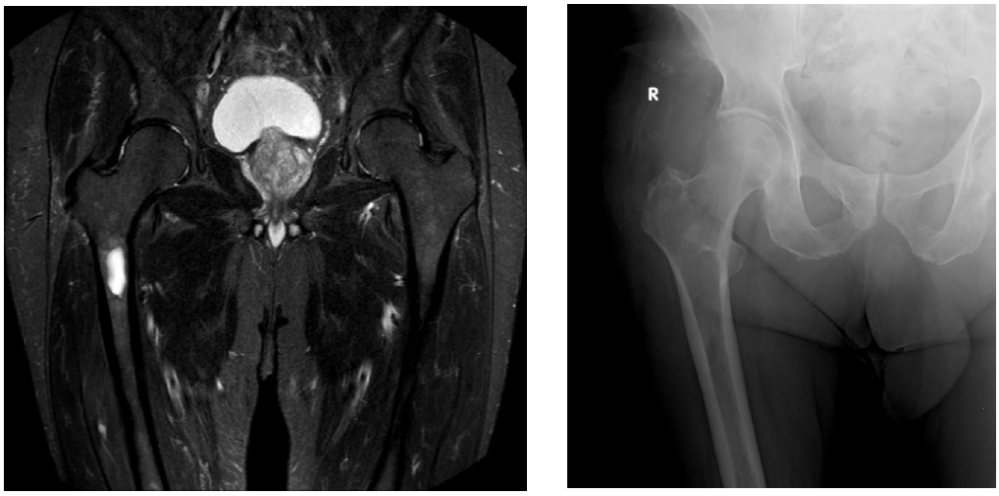

Figure 5: 70 years old male patient. Coronal T2-w STIR image (**a**) clearly demonstrates a MM lesion placed within the right femur, barely visible at X-ray plain film (**b**).

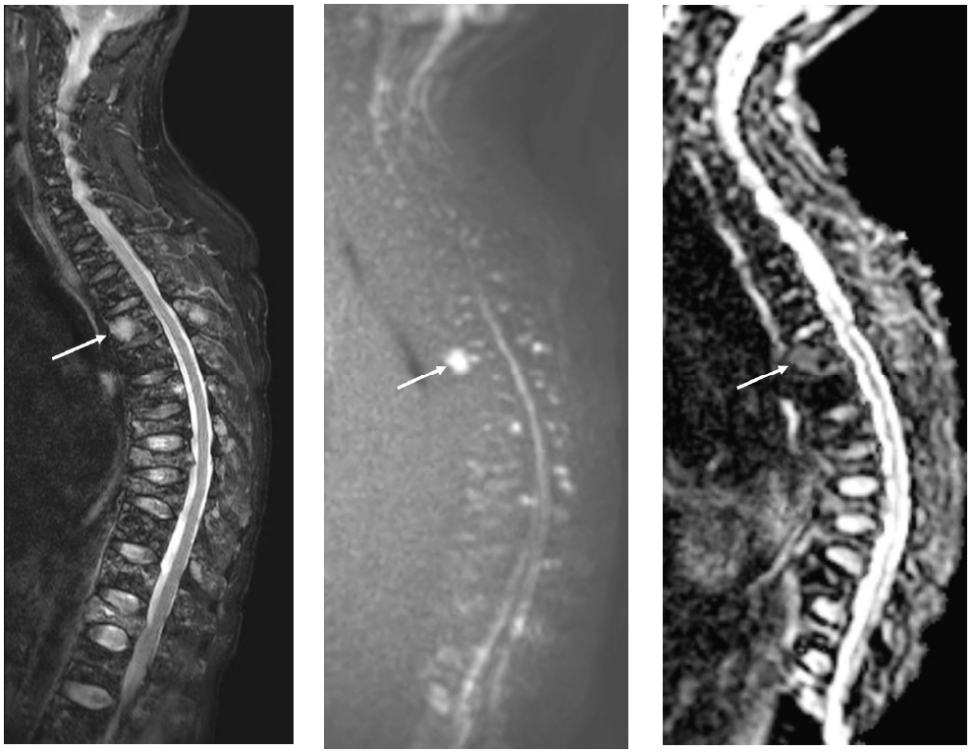

Figure 6: 69 years old male patient. Sagittal T2-STIR (**a**), DWI (**b**), and ADC map (**c**) show a number of MM high-intensity lesions of vertebral bodies and spinous processes, the large one within the vertebral body of D4 (arrow). Diffuse infiltration of the spine and several vertebral collapses.

marrow, due to the high cellular density occupying the interstitial space (Figure **6**) [4].

Chemical shift sequences can also help in recognizing MM lesions and differentiating them from reconversion phenomena or edema [13].

However, MRI limitations have to be reminded.

Beyond the high healthcare costs, whole-body MRI needs a prolonged scan time, considering that a simple morphological evaluation can lasts up to 30-45 minutes and an additional functional assessment can reach or exceed one hour [14].

The forced position, without any possibility of movement for such a long time could be hardly tolerable by the patient that often already suffers from back pain.

DWI evaluation can be impaired by the local bone alterations, with a mixture of hematopoietic cells, plasmacellular infiltrates and fat deposits placed in the interstitial space [10].

General MRI contraindications (*i.e*. metal implants, claustrophobia, etc.) have to be kept in mind as well [4].

CONCLUSIONS

Imaging has a well-established role in the framework of MM.

Radiological findings are important not only for initial staging, but also for disease course assessment and treatment response.

Nowadays, radiologists and clinicians can rely on different techniques with a related high amount of information achievable.

A fair knowledge of the advantages and the drawbacks of each technique currently available is helpful in the daily clinical practice and mandatory for the correct patient management.

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