A voluminous mass as an initial clinical symptom of multiple myeloma: A case report

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Abstract. Extramedullary multiple myeloma (EMM) is a type of multiple myeloma (MM) that is defined by the presence of extraskeletal (soft tissue or visceral) clonal plasma cell infiltrates, which may be present at the time of initial diagnosis or at the time of relapse. Although extramedullary lesions may be present with other clinical features at the time of diagnosis, the onset of a solid formation as a first clinical symptom of MM is unusual. The present study reports the case of a 77-year-old male who was admitted to the Hematology Unit of the National Cancer Research Center, Istituto Tumori 'Giovanni Paolo II' (Bari, Italy) with a mass protruding from the right side of his lower back. Serum immunofixation revealed positivity for monoclonal protein (M-protein) and Bence Jones proteinuria was positive. In addition, a computed tomography scan of the abdomen, which was confirmed by magnetic resonance imaging, revealed a voluminous solid formation resembling a sarcoma. M-protein is known to be present in numerous diseases encountered in clinical practice, including hematological or other diseases; thus, a Tru-Cut biopsy of the lesion was performed, which revealed an infiltration of plasma cells. In addition, a bone marrow biopsy revealed the presence of 70% plasma cells, and a diagnosis of primary EMM was established. In conclusion, EMM should be included in the differential diagnosis of a mass, particularly in patients where M-protein is detected in the blood and/or urine.

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Abbreviations: MM, multiple myeloma; EMM, extramedullary multiple myeloma; CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography

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Introduction

Multiple myeloma (MM) is a malignancy that is characterized by the proliferation of clonal plasma cells and the overproduction of structurally homogeneous immunoglobulins. The disease comprises ~1% of all malignant diseases and 10% of hematological malignancies (1). MM is most commonly observed in elderly individuals, with a median age at diagnosis of 65 years (2). Furthermore, the increase in the median age at diagnosis in western countries has resulted in an increase in the incidence of this disease. However, the etiology of MM remains unclear (3). MM is most frequently restricted to the bone marrow; however, there is a subset of patients with extramedullary disease in whom pathogenic plasma cells are located at distant anatomical sites, including the liver, kidney, pleura, breast, testes, skin and meninges. Synthetically, extramedullary multiple myeloma (EMM) is a type of MM that is defined by the presence of extraskeletal (soft tissue or visceral) clonal plasma cell infiltrates (4). EMM may be present at the point of the initial diagnosis (primary EMM) or at the time of relapse (secondary EMM) (5), and is typically associated with an unfavorable prognosis relative to MM with marrow-only disease. Although plain radiographs of the skeleton, positron emission tomography (PET), computed tomography (CT) and magnetic resonance imaging (MRI) are used currently in patients with MM and EMM for the detection of disease extension, none of the radiological features of the various imaging techniques are specific for EMM. Thus, a needle biopsy is mandatory to achieve a confirmed diagnosis. Although extramedullary lesions may present with other clinical factors at the time of diagnosis, the onset of a solid formation as a first clinical feature of MM is unusual.

Case report

A 77-year-old Caucasian male with no history of trauma was admitted to the Hematology Unit of the National Cancer Research Center of the Istituto Tumori 'Giovanni Paolo II' hospital (Bari, Italy) in June 2013 with a painful mass protruding from the right side of his lower back. The patient reported that the mass had been growing incrementally. Physical examination revealed a solid, non-tender mass that was localized in the upper region of the pelvis. The mass was fixed and not reducible with manual compression. The renal

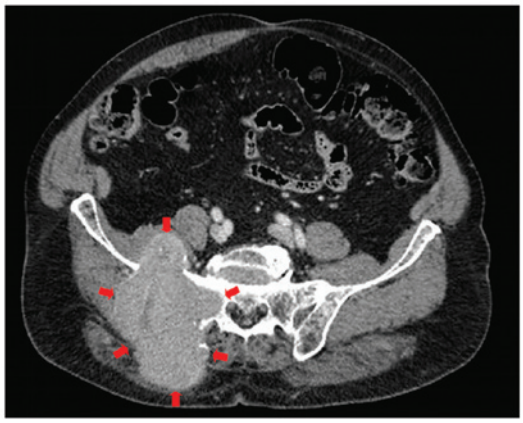

Figure 1. Computed tomography image of the abdomen (axial section) showing a voluminous solid formation in the area of the right large and medium gluteal muscles, extending partially into the small gluteal muscle (arrows) and eroding the right iliac wing.

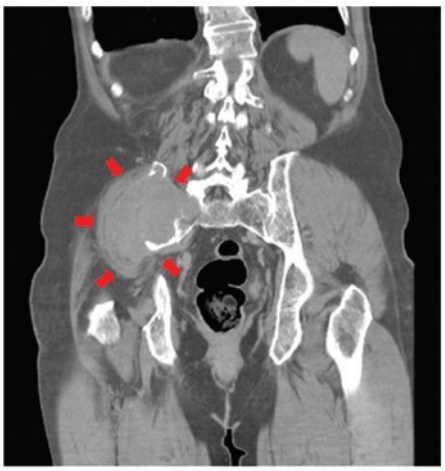

Figure 2. Computed tomography multiplanar reconstruction of the neoplasm (arrows).

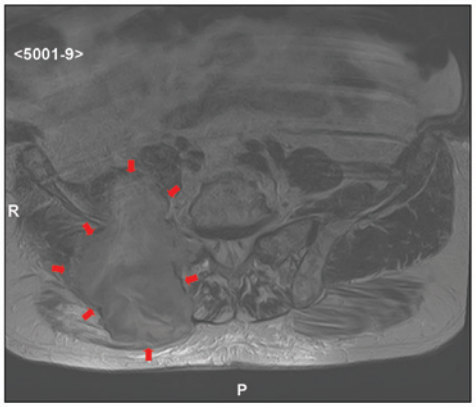

Figure 3. Magnetic resonance image showing formation of the neoplasm (arrows).

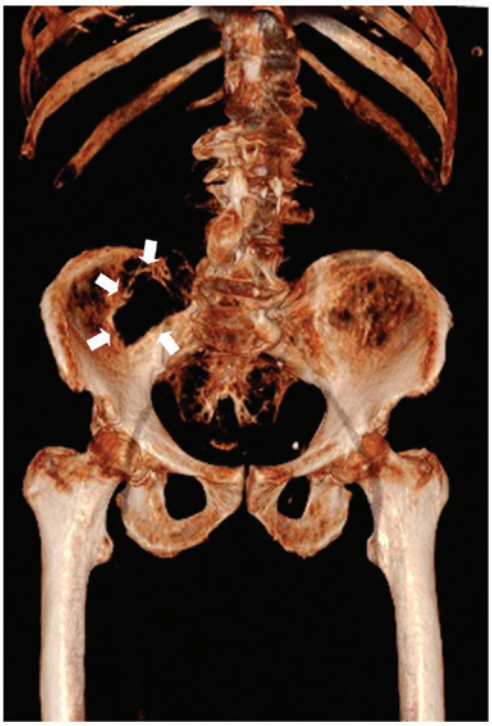

Figure 4. Three-dimensional computed tomography reconstruction of the bone showing erosion of the right iliac wing (arrows).

function of the patient, in addition to the levels of electrolytes (sodium, potassium and calcium) and the hemoglobin level, were all normal. However, serum electrophoresis revealed an increase in β-globulin, and serum immunofixation analysis indicated positivity for IgA-κ (1.19 g/dl); Bence Jones proteinuria was positive for monoclonal light κ chains. M-protein is known to be present in numerous diseases (hematological or other) encountered in clinical practice. CT examinations of the abdomen (Figs. 1 and 2, arrows), which were confirmed by MRI (Fig. 3, arrows), revealed a voluminous solid formation with a maximum dimension of 9.3x12 cm in the area of the right large and medium gluteal muscles, which extended partially into the small gluteal muscle. Contrast medium highlighted limited areas of colliquative necrosis. In addition, erosion of the right iliac wing, as a result of the solid formation, was clearly evident in a three-dimensional CT reconstruction of the bone (Fig. 4, arrows), and the iliac muscle was also shown to be involved. Furthermore, the solid formation was observed to result in the erosion of the sacrum and spinal muscles on the same side. These imaging features led to a hypothesis of a sarcoma. With the exception of the sacrum and right iliac wing, no other bone lesion was evident during the skeletal survey. A Tru-Cut biopsy of the lesions was performed, which revealed an infiltration of plasma cells ($CD38^+$, $CD138^+$ and κ $chains^+$). In addition, a bone marrow biopsy revealed the presence of 70% plasma cells ($CD38^+$, $CD138^+$ and κ $chains^+$). Fluorescence *in situ* hybridization analysis was performed on the marrow cells, and revealed monosomy of chromosome 13. Therefore, a diagnosis of primary EMM was established and the patient underwent nine 6-week cycles of treatment with melphalan (9 mg per square meter of body-surface area) and prednisone (60 mg per square meter) on days 1-4. In addition, the patient received bortezomib (1.3 mg per square meter) on days 1, 8, 22 and 29 during cycles 1-9. After nine cycles of therapy a reduction of M-protein of 80% and of solid formation of 40% was observed. Written informed patient consent was obtained.

Discussion

MM is a plasma cell neoplasm that is associated with the presence of M-protein in the serum and/or urine, which can be detected by electrophoresis. The diagnosis of MM requires the presence of ≥10% bone marrow clonal plasma cells of nucleated cells in the marrow or the plasmacytoma (6). Distinguishing between asymptomatic (smoldering) MM and symptomatic MM is possible, since the latter is defined by the presence of end-organ damage (hypercalcemia, renal insufficiency, anemia and bone lesions). In order of frequency, the clinical features of MM are lytic bone lesions (>80%), anemia (75-80%), bone pain (65-75%), fatigue (35-45%), an increase in the serum creatinine level (25-30%) and hypercalcemia (15-20%). Therefore, a conclusive evaluation is based on a combination of pathological, radiological and clinical features.

Extraskeletal clonal plasma cell infiltrates may be present at the time of the initial diagnosis (primary EMM); however, the onset of a solid formation as a first clinical feature of MM is unusual.

Clinically, three types of EMM can be described: i) Tumor mass adjacent to the bone and extending into the soft tissues; ii) soft tissue or visceral tumor that is not connected to the bone; or iii) diffuse infiltration of organs by plasma cells without any evident focal lesion (7). However, the majority of studies do not discriminate among these three types of EMM lesions (7). Primary EMM is identified in 4-16% of MM patients at the time of diagnosis, while secondary EMM is found in 6-20% of patients during the further disease course of MM (8). However, the precise pathogenic mechanisms that contribute to the extramedullary spread of clonal plasma cells remain poorly understood. In addition, the prognosis of EMM patients is generally poor, and an effective treatment strategy is yet to be established (9).

Various imaging techniques are used currently in patients with MM and EMM for the detection of disease extension. A traditional skeletal survey forms part of the standard of care for the staging and follow-up of bone lesions in patients with MM (10), and enables the identification of osteolytic lesions. In addition, CT examinations are commonly used to visualize the areas that are unable to be observed well on conventional radiographs, and may also be used to characterize soft tissue involvement (11). However, CT observations for MM are non-specific; thus, CT examinations may be used to guide a needle biopsy for histological diagnosis.

MRI has been demonstrated to have a high sensitivity and specificity for the detection of diffuse and focal forms of MM in the spine and extra-axial skeleton (12). In T1-weighted imaging, bone myeloma lesions appear hypointense, while the lesions are visualized as hyperintense on T2-weighted imaging. Furthermore, bone myeloma lesions appear hyperintense in short T1 inversion recovery imaging and enhanced on post-contrast T1 sequences (11). PET is a non-invasive functional imaging technique that enables whole-body screening in a single procedure. PET imaging is sensitive for the detection of early bone marrow involvement, prior to any identifiable bone changes (13).

In conclusion, all the imaging techniques discussed are useful for the detection of an extension of MM; however, none of the radiological features of the various imaging techniques are specific for EMM. Thus, a needle biopsy is mandatory to achieve a confirmed diagnosis. The occurrence of a mass as an initial symptom in MM is uncommon, and may result in a delayed diagnosis. In addition, considering that M-protein is present in numerous conditions encountered in clinical practice, there are no specific radiological features of EMM, and EMM can resemble other neoplasms, including sarcoma, EMM should be included in the differential diagnosis of a mass, particularly in patients where M-protein is detected in the blood and/or urine.

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