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^{18}F-FDG PET/CT in Myeloma with Presumed Solitary Plasmocytoma of Bone

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Abstract. *Aim: To evaluate the value of ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography with computed tomography (PET/CT) in myeloma in patients presenting with a solitary plasmacytoma of bone (SPB). Patients and Methods: Fourteen consecutive patients studied since 2006, all having a diagnosis of SPB before PET/CT imaging took part in this study. In 3 patients PET/CT was performed for staging while in the remaining 11 it was used to monitor therapy. PET/CT was performed using a dedicated tomograph 60-90 minutes after intravenous injection of 5.3 MBq/kg of ^{18}F-FDG and the results were compared to other diagnostic procedures [radiographs and magnetic resonance imaging (MRI)], biopsy, and other available follow-up data. Results: In 8/14 patients, PET/CT scans showed previously unsuspected sites of increased FDG accumulation. In 6/8 patients, FDG uptake was considered pathologic, depicting myeloma involvement in bone, while in the remaining cases, findings were considered incidental and not related to myeloma. PET findings attributed to myeloma were confirmed (i.e. true positives) in 6/6 cases (100%) and in all patients with findings reported as non-pathologic, myeloma was excluded (100% true negatives). Conclusion: Our preliminary data in a small number of cases suggests that there are a group of patients with SPB (local disease) in whom FDG PET/CT may detect other unsuspected sites of bone involvement, upstaging the extent of the disease. In these cases, SPB may be a local manifestation of multiple myeloma where other sites of involvement have eluded detection by other less sensitive imaging modalities (i.e. skeletal surveys) or anatomically restricted imaging (i.e., less than total body MR or CT). Finding other sites of involvement have significant implications for appropriate treatment of myeloma.*

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Multiple myeloma (MM) is a disease characterized by accumulation of plasma cells, generally derived from a single clone, representing about 10% of all haematological malignancies (1, 2). Manifestations of MM usually include lytic bone lesions, monoclonal proteins detected in blood or urine, and plasma cell infiltration in bone marrow. The bone involvement in myeloma frequently affects multiple bones, causing diffuse and often severe bone pain and pathological fractures (3, 8). Despite the systemic nature of the disease, a small number of patients (~3% of all patients with MM) will present with a single bone lesion, a solitary plasmacytoma of bone (SPB) (9). Although of identical pathology to MM, SPB differs from the more frequent systemic MM presentation in the approach to therapy as solitary lesions are treated with local radiation therapy and thus it follows that a correct assessment of the extent of disease in MM is a critical consideration in planning therapy. Anatomic imaging studies have been used to evaluate the site(s) and extent of myeloma involvement, including conventional skeletal radiography, computed tomography (CT) and magnetic resonance imaging (MRI) (10, 14). These imaging methods, and especially MR, when applied to MM have demonstrated useful contributions to the initial staging of SPB (15). Scintigraphy has also played a role in the evaluation of MM with bone seeking tracer (*e.g.* ^{99}Tc-methylene diphosphonate and ^{99}Tc-hydroxyethylene diphosphonate), and other cellular radiopharmaceuticals (^{99}Tc-MIBI, ^{67}gallium and ^{201}thallium) (16, 20). More recently, positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose (FDG) has been used to identify

Table I. *Clinical details of patients and the results of PET/CT and other imaging procedures in single plasmocytoma of bone.*

ID	Gender and age	Localization of plasmacytoma	Disease status	PET-CT findings	MRI findings	CRSS findings
1	M 59	Sacrum	Post therapy	Negative	Sacrum	Negative
2	M 54	Sacrum	Post therapy	Negative	Sacrum	-
3	M 50	Left pelvis	Post therapy	Negative	-	-
4	F 65	Right sacrum	Post therapy	Right sacrum	Right sacrum	Right sacrum
5	M 50	Left pelvis	Post therapy	Left pelvis and D11, D12, L1, L3, L4	Negative	-
6	M 47	Right pubis	Post therapy	Right pubis, right femur, left pubis, both sacro-iliac joints, one rib, left scapula, D6, D7, D11, L1, L2, L3, L4.	Inconclusive	Rib, right pubis
7	F 61	Left pelvis	Post therapy	Skull, sternum, 14 vertebrae, right rib, left pelvis	Left pelvis, L3	Left pelvis
8	M 31	Left pelvis	Post therapy	Left pelvis, D7	Left pelvis	-
9	F 64	Left pelvis	Post therapy	Right breast	-	-
10	M 57	Sacrum	Post therapy	Sacrum and D8	-	-
11	M 50	Sacrum	Staging	Sacrum	Sacrum	Sacrum
12	M 52	Right scapula	Staging	Right scapula	-	-
13	M 59	L4	Staging	L4, thyroid	L4	L4
14	M 66	Right femur	Post therapy	Right rib, sternum, D8, D10, D11, left pelvis	Right femur, left pelvis	Right femur

MRI, magnetic resonance imaging; CRSS, conventional radiographic skeletal survey.

unsuspected sites of medullary and extra medullary disease in MM and other metastatic disease spread to bone (21-23). The recent combination of PET with CT has demonstrated better anatomic localization of lesions that include metastases to bone, resulting in a significant increase of diagnostic accuracy in cancer. Preliminary data indicate a useful role of FDG PET-CT in evaluating MM (24, 26). The principal aim of this study was to evaluate the extent of disease using FDG PET-CT in patients with myeloma presenting with an SPB.

Patients and Methods

Inclusion criteria. All FDG PET/CT scans performed at our institutions (Policlinico S. Orsola-Malpighi, Bologna, and S. Maria della Misericordia Hospital, Rovigo, Italy) in patients with SPB during the interval 2005 to 2007 were retrospectively evalueted. All patients had a diagnosis of SPB, according to the criteria defined by Durie and Salmon, at the time of PET/CT imaging (27). Fourteen consecutive patients were included, where 3 patients were studied with PET/CT for disease staging, while 11 were studied to monitor therapy. The basic clinical characteristics of patients are detailed in Table I.

FDG PET/CT imaging. Each patient received 5.3 MBq/kg of ^{18}F-FDG intravenously and PET/CT was performed 60-90 minutes after tracer administration. ^{18}F-FDG was produced in our radiopharmacy using standard synthetic techniques (28).

PET/CT scans were carried out on a dedicated PET/CT tomograph (Discovery LS scanner, GE Medical System, Waukesha, WI, USA). PET emission images were collected for 4 minutes for each bed position from the vertex of the skull to the thighs with the inclusion of the upper extremities and CT was used to perform non-uniform attenuation correction. Parameters of CT acquisition were: 140 kV, 90 mA, 0.8 s tube rotation, 5 mm thickness. To optimize FDG uptake in normal and neoplastic tissues, patients were asked to fast for at least 6 hours and were encouraged to void in order to minimize activity in the bladder before PET/CT examinations and none of the patients had a history of diabetes.

PET/CT interpretation. PET/CT images were interpreted by three experienced analyst and in all cases consensus was obtained for each patient. Scans were interpreted as negative when no abnormal tracer uptake was seen on FDG PET/CT or there was FDG uptake at sites of known physiological accumulation, including the kidneys, ureters, bladder, and musculoskeletal areas exhibiting symmetric FDG uptake. Collections of focal uptake within the skeleton were interpreted as positive for myeloma when significantly greater than accumulation in other bone tissues, and generally when a standardized uptake value $(SUV)_{max}$ region of interest created around the abnormal focus of uptake in bone exceeded 3.0. Increased FDG accumulation in the gastrointestinal tract was also considered non-pathological and other sites outside of the skeleton were attributed to a previously identified or possible cause that in some cases included extramedullary myeloma.

Other diagnostic imaging procedures. All patients had a complete evaluation according to standard clinical guidelines for MM including: conventional radiographic skeletal surveys (CRSS), with radiographs of the skull, ribs, spine, pelvis, femurs and humeris; CRSS were always obtained at diagnosis and within 1 month before PET/CT execution. All patients were also studied with MRI of the spine and pelvis within 1 month of PET/CT and in 10 cases MRI was performed before PET. MRI was performed using a 1.0 Tesla magnet with a spinal coil. Sagittal images included a T1-weighted spin echo sequence and a fat-suppressed T2-weighted fast spin echo sequence. If a finding was ambiguous, the T1-weighted images were repeated after the intravenous injection of gadolinium chelate. MRI studies were reviewed by two radiologists and myeloma was

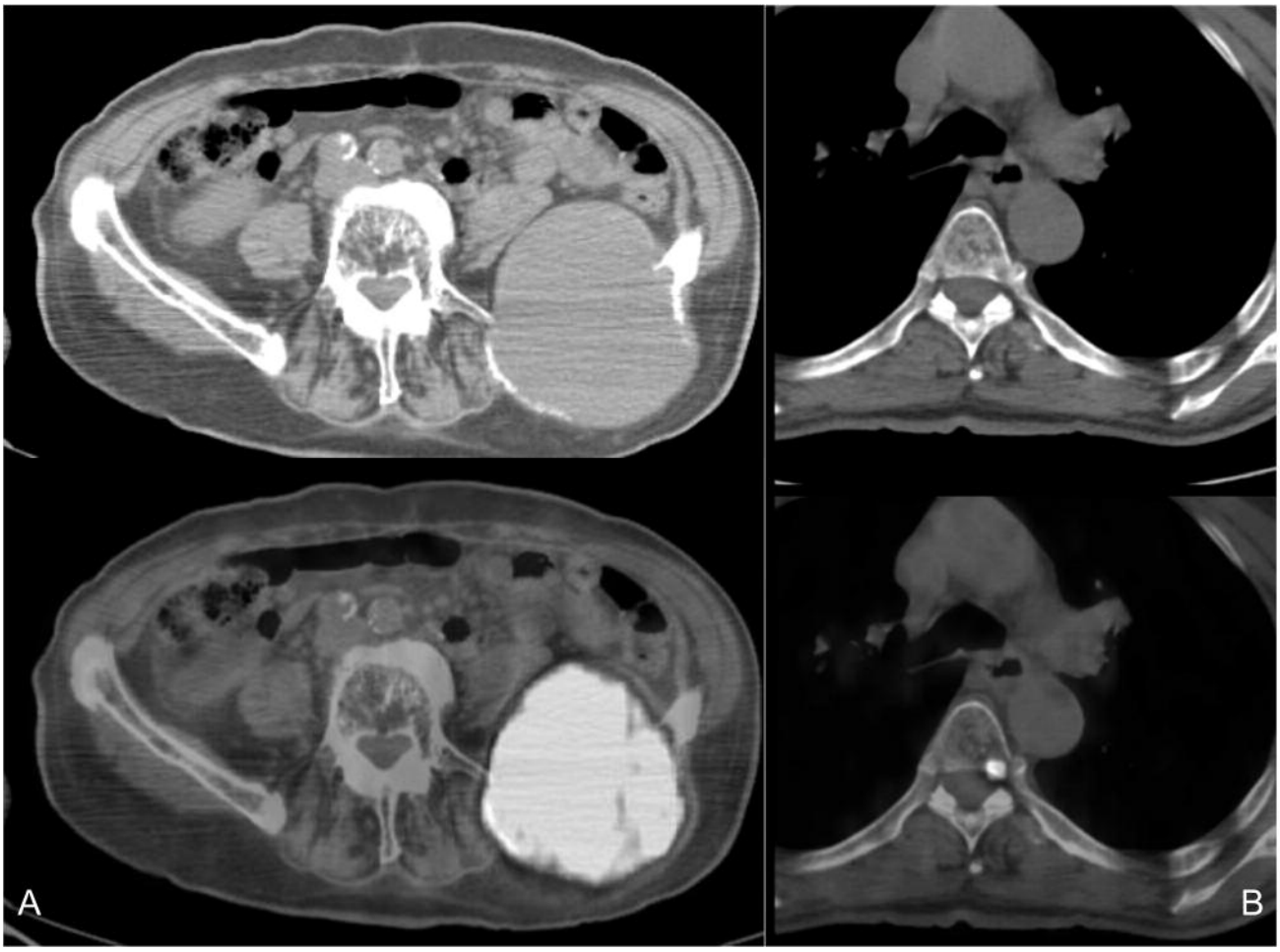

Figure 1. *^{18}F-FDG PET/CT of patient no. 8. The image shows increased uptake in the left pelvis lesion (A) and an early tiny hypermetabolic focal lesion in D7, with no morphological changes at CT (B).*

classified into three categories according to MRI patterns of spinal bone involvement that include a normal pattern, focal pattern and diffuse pattern (30), although no cases of a diffuse pattern were seen in our patient group.

Final assessment of findings. To assess the significance of PET/CT findings, all other available data were collected for each patient, including biopsy, other diagnostic imaging procedures and clinical follow-up for a minimum follow-up of 8 months. Final diagnosis in all cases was established by haematologists aware of the clinical, laboratory and diagnostic imaging data on each of these patients.

Results

Unsuspected sites of increased FDG uptake were seen in 8 out of the 14 patients, and in 6 out of 8 patients FDG uptake was considered to be indicative of myeloma bone disease, while in the remaining 2 patients the scan findings were not considered to be related to myeloma. PET/CT findings attributed to myeloma were subsequently confirmed at follow-up in all cases (100%). The results of imaging in SPB are shown in Table I.

In 2 out of the 14 patients, PET/CT detected extraskeletal, hypermetabolic lesions located in the thyroid and breast, respectively. Both patients were further evaluated with fine-needle aspiration of these lesions, which subsequently proved to be papillary thyroid cancer and breast cancer respectual.

Discussion

SPB is a hematological disease presenting as a single lytic bone lesion without evidence of involvement elsewhere and as such is considered a local pathological process and typically treated with local radiation therapy to that anatomic site. However, in 80% of the patients treated for SPB, MM subsequently evolves, with a median time of disease progression of 2 years, suggesting that SPB is in reality not

a localized disease at all, but the earliest manifestation of MM, a systemic disease (16). Whole body plain radiography is traditionally used to depict and stage bone involvement in MM, according to the Durie and Salmon staging system (27). This imaging method is, however, insensitive for small bone lesions and for lesions located in marrow that have not resulted in local bone lysis; thus limiting sensitivity. MRI is a very sensitive technique to correctly identify early bone lesions and marrow involvement in MM. The major limitations to MRI are difficulties in performing whole body studies, especially those involving extremities. In addition, MRI has been less useful in distinguishing active from fibrotic bone marrow lesions and it has not been used routinely to monitor therapy response. FDG PET/CT is a sensitive imaging technique which in a variety of other types cancer has improved staging and post therapy restaging as a result of high spatial resolution and the ability to recognize early lesions, not yet associated with alterations in organ or tissue contour or anatomy (21, 30).

In the present study, PET/CT disclosed unsuspected lesions not evident on routine plain radiography or MRI screening in a significant number of patients (8/14, 57%) and in 6 of 8 patients with unanticipated lesions (43% of our population) changing an initial diagnosis of SPB to MM. Our results are similar to those reported by Schirrmeister et al in 2003, who found additional bone lesions in 33% of patients studied with FDG PET with SPB (9). In the present study, unanticipated lesions were detected in 43% of patients with FDG PET/CT and this increase in detection may be related to the improved anatomic localization afforded by the use of hybrid tomography. Although preliminary and albeit in a small number of patients, our data do suggest that in a subset of patients, SPB may be MM presenting as a single lesion recognized with conventional imaging techniques, but accompanied by other tumor deposits that are either too early in their development, too remote or too small to be identified with conventional imaging techniques. This may explain why 80% of patients with SPB develop a MM over a short interval of time. PET/CT may prove to be of value in assessing potential sites and the extent of tumor burden in multiple myeloma and may play a significant role in the correct choice of therapy, local radiation or systemic chemotherapy.

Conclusion

FDG PET/CT may have added value to conventional imaging techniques in patients with SPB as in this preliminary study almost half of a small group of patients had unanticipated myeloma deposits detected either during additional staging procedures or in the follow-up of therapy, upstaging their diagnosis from SPB to MM. Larger, prospective studies will be necessary to confirm these results to further determine the role that PET/CT will play in the evaluation of SPB and MM.

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