INCIDENTAL PAGET'S DISEASE DISGUISED AS BONE METASTASIS IN A PATIENT WITH ENDOMETRIUM CARCINOMA

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Abstract

Paget's disease is a disorder of aging bone which occurs in the setting of accelerated bone remodelling. In the presented case we discuss the difficulties in the diagnosis of Paget's disease in a 77 year old patient with coexisting endometrium carcinoma. The patient was initially diagnosed with metastatic bone disease due to endometrium adenocarcinoma when she was admitted to oncology clinic with pelvic pain. Bone scintigraphy with Tc99 and (18) F fluorodeoxyglucose positron emission tomography/CT revealed an increased uptake on the bone lesions which were reported as metastatic bone involvement. Although the (18) F-FDG uptake was much higher than the levels that would generally be anticipated in a case with Paget's disease, high levels of bone turnover markers indicated further evaluation in the differential diagnosis and the definitive diagnosis of Paget's disease was established with the pathological evaluation of bone biopsy.

Key words: Paget's Disease, Endometrium carcinoma, Bone metastasis.

INTRODUCTION

Paget's disease of bone (PDB) is characterised with an accelerated bone turnover resulting in disorganisation of the bone structure and thickening of the trabecular compartment. The most common sites that are effected are skull, lumbar vertebrae, pelvis and long bones of the lower extremities. Patients are generally asymptomatic and the diagnosis is usually based on incidental findings in imaging studies or elevated serum alkaline phosphatase (ALP) levels during routine laboratory screening tests. The most common symptom of a pagetic lesion is pain in the related skeletal region (1). The incidence of PDB is high in some areas of northern Europe, but it is rare in the middle east region in general and there is no current study regarding PDB prevalence in Turkish population (2).

PDB is often attributed to the aging bone and it is generally present in the elderly population which also has a more predilection to malignant disorders. However, coexistence of malignancy generates difficulties in the diagnosis of PDB due to confusing findings in the imaging studies that may be interpreted as bone metastasis. We hereby present a challenging case of inoperable endometrium carcinoma complicated with presence of PDB in the pelvic region which was initially considered as bone metastasis during the imaging studies.

CASE

A 77 year-old woman was admitted to our hospital with severe pelvic pain. She had been diagnosed with inoperable endometrium adenocarcinoma a year ago. Pain was localized in the pelvic region and metastatic bone disease was considered as initial diagnosis. Plain sacroiliac X ray and computed tomography (CT) indicated presence of lytic lesions on the sacrum, lumbar vertebra (L5) and pubis ischiadicum. Bone scintigraphy with Tc99 revealed increased uptake on the same lesions which were reported as metastatic bone involvement. However, PDB was also considered in the differential diagnosis. An (18) fluorodeoxyglucose positron emission tomography/CT [(18)F-FDG PET/CT] was ordered. On the (18)F-FDG PET/CT, osteolytic and osteosclerotic lesion areas showed heterogeneous FDG uptake in early (SUV max:7.4) and late images (SUV max:8.7), and the fused images showed moderate FDG uptake on osteosclerotic lesions (SUV max:3.7) as well, which could also be compatible with Paget's disease (Fig. 1). Based on these findings the patient was referred to our endocrinology department for a differential diagnosis of PDB. On admission patient's laboratory results were as follows: BUN: 24 mg/dL (n: 8–22 mg/dL), creatinine: 2.3 mg/dL (n: 0.7–1.4 mg/dL), serum corrected calcium:

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Figure 1. PET-CT fusion images demonstrating moderate FDG uptake on osteosclerotic lesions.

Figure 3. Histological section of bone biopsy. Trabecular bone showing osteoblastic and osteoclastic activity, pathognomonic mosaic pattern in trabecular bone, widening of vascular structures and fibrosis between bone trabeculae, without evidence of tumoral invasion. HEx200.

9.6 mg/dL, PTH: 80 pg/mL (n: 15–65 pg/mL), β -CTX: 1.2 ng/mL (<1 ng/mL), ALP: 120 U/L (n: 35–105 U/L). Bone biopsy was performed for the differential diagnosis of PDB and metastatic endometrium carcinoma. Histopathological evaluation revealed osteoblastic and osteoclastic activity, increased vascularity and fibrosis in the trabecular compartment and mosaic pattern which were pathognomonic for presence of PDB with no evident focus of tumoral infiltration indicating metastasis of endometrium carcinoma (Fig. 2). Although bisphosphonates are the primary agents in the treatment of PDB, calcitonin (s.c.) was used in the initial treatment

Figure 2. Axial CT of the pelvis. Bone enlargement as well as trabecular and cortical thickening with presence of lytic lesions in the sacrum and pubis ischiadicum.

as the patient's glomerular filtration rate (eGFR) was calculated as 24.3 mL/min/1.73m².

DISCUSSION

PDB proceeds in three stages; the initial lytic phase involves increased osteoclastic activity and bone resorption with high bone turnover markers. Second phase is the mixed lytic-sclerotic phase in which osteoblasts begin to produce new bone formation with ineffective mineralization and the third sclerotic phase is characterised with dense cortical and trabecular bone deposition (3). In the early period of PDB, plain radiographies demonstrate lytic lesions due to increased resorption by osteoclasts (1). Radionuclide bone scanning (Tc99) is more sensitive than plain radiography particularly in early disease and also helpful in determining the extent of disease. Enhanced radionuclide uptake indicates increased bone remodelling and blood flow. When malignancy is of concern, the mixed lytic sclerotic characteristics of PDB make it difficult to distinguish the presence of malignancy based on plain radiographical imaging studies and computed tomography (CT) or magnetic resonance imaging (MRI) are recommended in the evaluation of suspicious bone lesions (4).

Although Technetium scan is more useful and cost effective in the diagnosis of PDB in our case the diagnosis was established incidentally based on high uptake in FDG-PET imaging which was performed due to the presence of malignancy (18). F-FDG PET/CT imaging may be helpful in the differential

diagnosis of bone metastasis and PDB in patients with malignancy (5). As the 18F-FDG enters the osteoblasts proportional with increased bone mineralisation and enhanced glycolysis, PDB demonstrates a variable FDG uptake pattern in the osseous lesions for any individual patient, possibly due to the differences in the rate of bone remodelling. Thus FDG uptake in PET imaging is correlated with ongoing disease activity (6). However, the majority of patients with PDB do not demonstrate a high 18F-FDG uptake and low to moderate uptake is generally attributed to increased disease activity (6, 7). This provides the availability of PET/CT imaging in monitoring for sarcomatous changes in PD and in the differentiation of benign PDB from metastatic bone lesions (1, 8). Marked 18F-FDG uptake is rare in PDB and implicates further investigation for presence of malignancy especially in the elderly population (9). On the other hand this also leads to the possibility of false positive PET results (with high 18F-FDG uptake) for malignancy in patients with active pagetic lesions (9).

Malignant bone lesions are characterised with higher levels in the FDG uptake compared with benign conditions. Several previous studies have suggested variable cut off levels for maximum SUV (standardized uptake value) in differentiating between benign and malignant bone lesions. Shin *et al.* defined a cut off point as 3.4 with sensitivity 91% and specificity 78%; Shulte *et al.* defined a cut off point as 3.0 with sensitivity of 93% and specificity of 66.7% and Tien *et al.* defined the cut off point as 2.5 with sensitivity of 96% and specificity of 44% (10-12). According to these suggestions the FDG uptake in our patient's PET imaging was as high as the FDG uptake that would be anticipated for presence of metastatic malignancy.

High FDG uptake is even rarer in the PET/CT fusion images compared with PET only imaging studies. Hence the fusion techniques are considered to be useful in the differential diagnosis of PDB and malignancy (4). A previous report demonstrated a high FDG uptake on PET only images which later resolved in the PET/CT fusion images (13). However, our case demonstrates an increased FDG uptake which persisted in the later PET/CT fusion images, generating a suspicion for bone metastasis in a patient with coexisting endometrium carcinoma. It is also previously suggested that the exact FDG uptake location might be important in the differential diagnosis of benign and malignant bone lesions. Cortical FDG uptake is more likely to be seen in PD, whereas metastatic bone lesions generally demonstrate medullary FDG uptake (4). In our patient PET/CT fusion images revealed medullary uptake

which was also confusing for presence of malignancy.

As the ALP levels were only moderately elevated despite high activity uptake in imaging studies, in order to reach a definitive diagnosis, bone biopsy was performed and diagnosis was confirmed with histological findings pathognomonic for PDB with no evidence of tumoral invasion in the bone structure. It is reported that a normal plasma ALP can be seen in patients with an isolated pelvic lesion, with several vertebral bodies involved, or with end-stage sclerotic disease (14). In the final sclerotic phase of PDB, dense cortical and trabecular bone deposition is the characteristic feature (3) and evident plain X-ray and CT findings are generally associated with the third sclerotic stage (15). In our case relatively lower levels of serum ALP levels may be related with presence of sclerotic phase demonstrated also with presence of increased fibrosis in the bone biopsy specimens. Furthermore low plasma bone ALP levels in active PDB are also previously reported in the literature (15).

In conclusion, although Paget's disease is generally characterised with normal or mildly elevated FDG uptake, severe disease activity may occasionally lead to high FDG uptake levels mimicking presence of malignancy or metastasis. When the imaging studies fail, the definitive diagnosis may be confirmed with the pathognomonic findings of PDB in the pathological evaluation of these lesions especially in patients with coexisting malignancies.

Conflict of interest

The authors declare that they have no conflict of interest concerning this article.

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