

Paget bone disease demonstrated on 18F-fluorocholine PET/CT: a case report

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Abstract

Paget disease (PD) is a chronic disorder resulting in enlarged and misshapen bones, caused by disorganized bone remodeling. This case involves a 64-year-old man with prostatic adenocarcinoma and PD of some skeletal areas with increased uptake shown on 18 F-fluoro-methyl-choline (FMC) positron emission tomography/computed tomography (PET/CT) performed for cancer restaging. Besides this feature, Paget disease may mimic metastases on PET/CT using various radiotracers, including 18 F-FMC PET/CT. In particular, this case highlights the potential of multiparametric disease characterization on PET. Therefore, in suspected cases, in which differential diagnosis is difficult, histology can be a helpful tool for diagnostic purposes.

Introduction

Paget's disease (PD) consists of 3 phases.¹ The first phase is called *osteolytic* and is characterized by intense bone resorption

and hypervascularization. The second phase is mixed, both osteoblastic and osteolytic, and is characterized at the same time by an increased production of new bone matrix by numerous osteoblasts and by bone resorption by osteoclasts. However, mineralization of the new bone matrix is ineffective. Accordingly, normal lamellar bone is replaced with haphazard (woven) bone. The third phase is sclerotic with progressively diminished bone resorption, which leaves a dense, sclerotic, disorganized bone that is weaker than normal. All 3 phases may be present simultaneously at different skeletal sites.¹ Conventional radiographs and computed tomography (CT) remain the best imaging tools to diagnose PD, and its appearance depends on the disease phase (lytic, mixed lytic/sclerotic, or sclerotic). The mixed phase exhibits the most characteristic findings, which show whole bone involvement or extension to the end of long bones, trabecular coarsening, cortical thickening, and osseous enlargement on both CT and radiographs. Maintenance of intramedullary fat attenuation or signal intensity on CT or magnetic resonance imaging (MRI), respectively, is also characteristic and is useful for the purpose of differential diagnosis.² When pagetic lesions are active, bone scintigraphy shows a moderately intense uptake of lesions and is useful to assess the distribution and extent of disease.³ Also, 18 fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT show an increased metabolic activity of PD; so pagetic lesion can simulate prostate cancer skeletal metastases on staging or follow up.^{4,5} More recently, PD was shown to increase uptake of 68 Ga PSMA and increased uptake of 18 F fluorocholine in patients undergoing prostate-specific membrane antigen (PSMA) or PET PET/CT for prostate cancer evaluation, simulating skeletal metastases.⁶ After radical prostatectomy for prostate cancer (PCa), prostate specific antigen (PSA) is a sensitive biomarker indicating the presence of recurrent disease. To recognize the sites of recurrent disease and to plan the correct treatment, it is necessary to perform an imaging test such as PET/CT with a choline tracer radiolabeled with either 11 C (11C-choline) or 18 F (18 F-choline).⁷ The rate of detection by choline PET/CT may vary according to the PSA level. Accuracy is higher for PSA levels greater than 1 ng/ mL.^{8,9} However, the European Association of Urology guidelines recently suggested the use of choline PET/CT in patients with biochemical relapse (BR) and PSA levels of 1- 2 ng/ mL.¹⁰

We report the case of a 64-year-old patient with prostate cancer who displayed some areas skeletal uptake of 18 F FMC on a restaging PET/CT, which was attributed to pagetic bone disease.

Case Report

A 64-year-old man with a history of prostate adenocarcinoma came under our clinical observation. He was also affected by au-

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toimmune hypothyroidism. In June 2019, he underwent radical prostatectomy for a recently-diagnosed prostatic adenocarcinoma. At the time of staging in June 2019, an hypercaptant structural alteration was detected in the right iliac wing. In particular, the total body bone scan with ^{99m}Tc Technetium-HDP revealed the presence of focal hyper-fixation of the radionuclide in the area located between the right anterior superior iliac spine, the left iliac wing near synchondrosis and the posterolateral tract of the right IV rib. These findings required further investigation, since an oncological genesis could not be excluded (Figure 1). In July 2019 a subsequent pelvis computed tomography (Figure 2) showed in the middle third of the right iliac wing an osteostructural alteration, primarily lytic, with a diameter of about 30 mm and a cortical bone thinning, which could indicate a suspected secondary localization of disease. Another similar lithic alteration with a diameter of 11 mm was visible at the level of the ipsilateral sacral wing. Blood tests showed normal renal function, calcaemia (9.21 mg/dL), phosphoremia (2.16 mg/dL), total alkaline phosphatase and bone isoenzyme within the normal range, serum beta-cross-laps within the normal range, vitamin D 25 OH (16 ng/mL) PTH was normal. Since prostatic antigen PSA was equal to 0 after prostatectomy, in September 2019 the patient performed an ^{18}F -fluoro-methyl-choline (FMC) positron emission tomography/computed tomography (PET/CT) (Figure 3) that showed an hypercaptant structural alteration in correspondence with the middle third of the right iliac wing. This area corresponded to the osteostructural alteration reported to the computed tomography of July 2019 and it was suspected for oncological alteration. The medical examination showed that the patient did not have pain in the peritrochanteric site or at the level of the right iliac wing and had no synovitis. Suspecting a secondary injury, the orthopedist suggested a bone biopsy which led to a histological finding of bone Paget (immunohistochemical staining performed CK AE1/AE3 negative). On the basis of histology, a diagnosis of lithic variant Paget bone disease in the right iliac wing was confirmed in a patient subjected to radical prostatectomy for adenocarcinoma. A single infusion of zoledronic acid 5 mg iv was scheduled and was well tolerated.

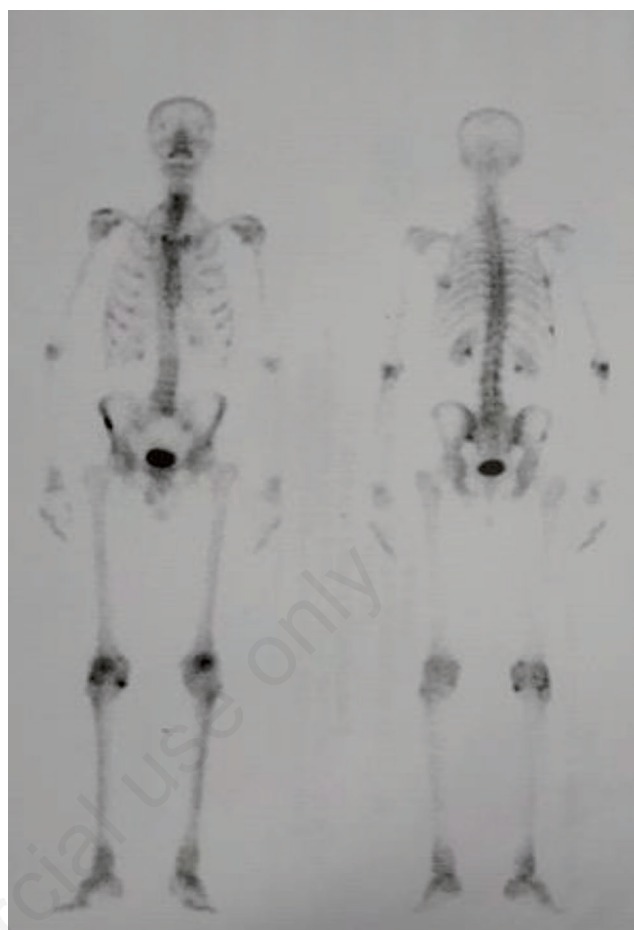


Figure 1. Total Body Bone Scan with ^{99m}Tc Technetium-HDP: a focal hyperfixation of the radiopharmaceutical is present in the area between the right anterior superior iliac spine, the left iliac wing near synchondrosis and the posterolateral tract of the right IV rib.

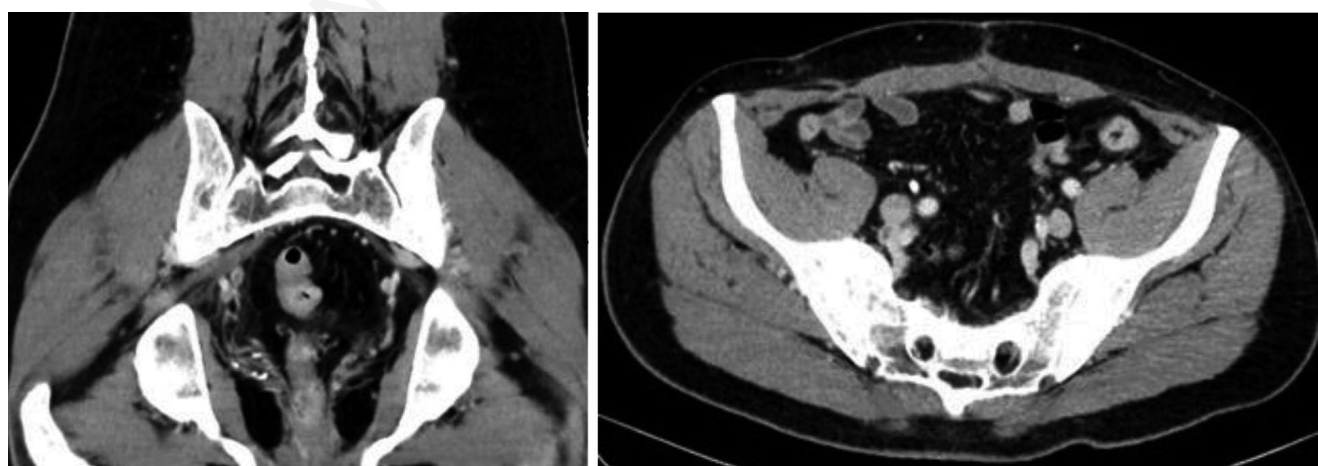


Figure 2. A) Pelvis computed tomography, coronal scan of the middle third of the right iliac wing which shows an alteration of the bone structure oval-shaped with a diameter of about 30 mm and thinning of the cortical bone which may be a suspected secondary localization of disease. B) Another similar lithic alteration with a diameter of 11 mm is visible at the level of the ipsilateral sacral wing.

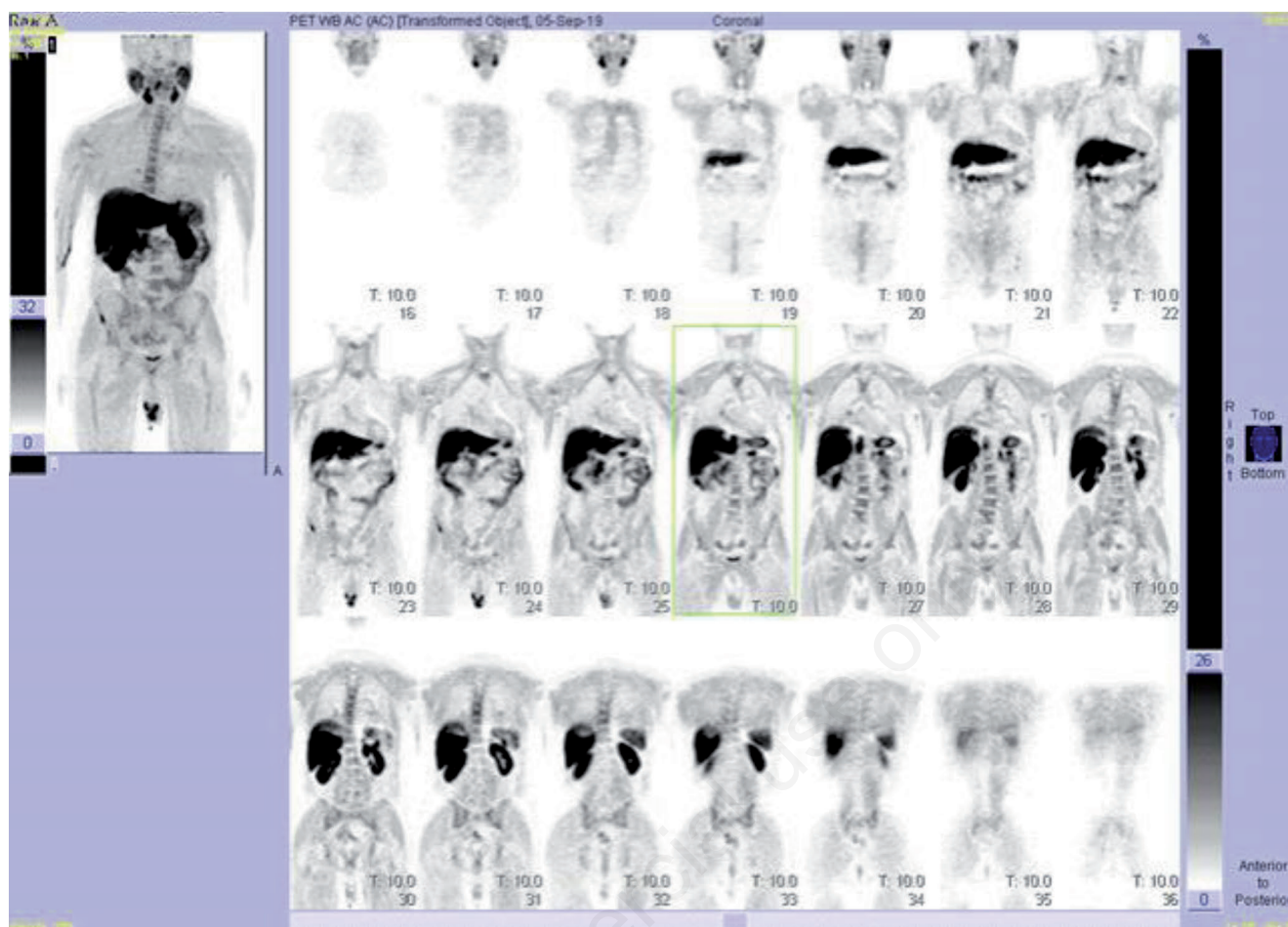


Figure 3. 18 F-Fluoro-Methyl-Choline (FMC) positron emission tomography/computed tomography (PET/CT): there is an increased fixation of the tracer which initially orientates for oncological genesis in the middle third of the right iliac wing.

Discussion

Paget's disease (osteitis deformans) is a benign focal disorder with accelerated skeletal remodeling. Its approximate prevalence is 1.1% in pelvic bones in patients above the age of 40. Pagetic disease can affect a single bone segment (monostotic) or multiple bone segments (polyostotic) leading to bone hypertrophy, cortical expansion, and abnormal bone architecture.^{11,12} Clinical symptoms include bone pain, bone deformity, and skeletal fragility. Complications of Paget's disease involve bones (deformity, fracture, and neoplastic degeneration), joints (osteoarthritis), the nervous and the vascular system.¹³ When Paget disease is suspected, an initial biochemical evaluation should be done with serum total alkaline phosphatase (ALP) or a more specific marker of bone formation such as serum cross-linked C-telopeptide (CTX) and conventional radiographs.¹³ Treatment with a bisphosphonate is recommended for most patients with active Paget's disease who are at risk of further skeletal and extra-skeletal complications. A single dose of 5 mg i.v. zoledronate as the treatment of choice in patients without contraindications is suggested.¹³ It is known that skeletal Paget disease can be associated with prostate cancer. Bone scintigraphy can differentiate between these 2 conditions.¹⁴ It is clear that PD may show an uptake on PET with several different radionuclides,

including 18F FDG, 68Ga PSMA, 18F NaF, 18F fluorocholine and 11C choline PET/CT.¹⁵⁻²⁰ As 11C choline is important in cell membrane synthesis, the increased C-11 choline uptake in PD is related to the increased rate of bone turnover, and therefore cell formation. It is unclear why choline uptake varies so widely and is apparently unrelated to the stage of disease activity, since it is not associated with the serum ALP level and there is no correlation between the uptake on 11C choline PET/CT and 99mTc MDP skeletal scintigraphy. Because of increased uptake of prostate cancer lesions to 11C choline PET/CT, it is important to recognize Paget's disease as a potential pitfall on 11C choline PET/CT. In particular, and when it is difficult to differentiate PD from bone metastases in prostate cancer, it is mandatory to perform a bone biopsy.

Conclusions

The possibility of 18F-FMC PET/CT uptake in pagetic bone should be kept in mind when interpreting PET/CT findings in patients with prostate cancer. Therefore, the histological examination remains the goal standard in cases of suspected Paget's bone in patients with a history of prostate cancer.

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