False-negative Bone Scan and Choline PET/CT Study in a Case of Prostate Cancer: The Pitfall of the Small Cell Prostate Carcinoma Variant

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Abstract

We present a rare variant of prostate carcinoma. The patient is a 45-year-old male with elevated prostate-specific antigen levels at screening. Magnetic resonance imaging revealed hyperenhancing lesions throughout the axial skeleton. The fluorine-18 fluorocholine (FCH) positron emission tomography/computed tomography (PET/CT) scan showed no abnormal bone findings. Subsequently, a technetium-99 methydiphosphonate (Tc99m-MDP) bone scan was performed, with additional correlative single-photon emission computed tomography (SPECT)/CT imaging of the pelvis and the results were essentially normal. A percutaneous core biopsy of one of the bone lesions in L5 was performed and histology confirmed small cell (neuroendocrine) variant of prostate cancer. Our case illustrates a possible pitfall in molecular imaging of prostate carcinomas, whereby both bone scintigraphy and FCH PET/CT scans showed no definite bone lesions to correlate with marrow signal abnormalities seen on MR imaging. This highlights the need for caution in the diagnostic evaluation of prostate cancers with known small cell variants.

Key words: Fluorocholine, positron emission tomography, prostate carcinoma, small cell cancer

Introduction

Prostate gland can be involved by many unusual types of neoplasm including small cell carcinoma, mucinous cystadenocarcinoma, neuroendocrine cancer, lymphoma, spindle cell neoplasm, squamous cell carcinoma, and transitional cell carcinoma. Bone metastases is the second common site after lymph nodes in prostate cancer.[1] The work-up for bone metastases in prostate cancer is bone scan and MRI scan, but they show limited sensitivity and specificity. Many positron emission tomography tracers were tried to evaluate bone metastases including (FCH).

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Case Report

We report the case of a patient who presented with a rare variant of prostate carcinoma. The patient is a 45-year-old male who was found to have elevated prostate-specific antigen (PSA) levels (143 ng/ml) at screening. Cystoscopy revealed a hard irregular prostatic lesion, and transrectal ultrasound (TRUS) guided biopsy of the prostate initially revealed Gleason 3 + 4 adenocarcinoma of the prostate. Magnetic resonance imaging (MRI) for local staging of the prostate cancer incidentally detected multiple pelvic bone lesions suspicious for metastases. Dedicated imaging of the spine revealed additional hyperenhancing lesions throughout the axial skeleton [Figure 1].

The patient underwent a fluorine-18 fluorocholine (FCH) Positron Emission Tomography/Computed Tomography (PET/CT) scan, which showed heterogeneously increased tracer uptake in the prostate, in keeping with known histological findings. No abnormal bone lesions were detected [Figure 2].

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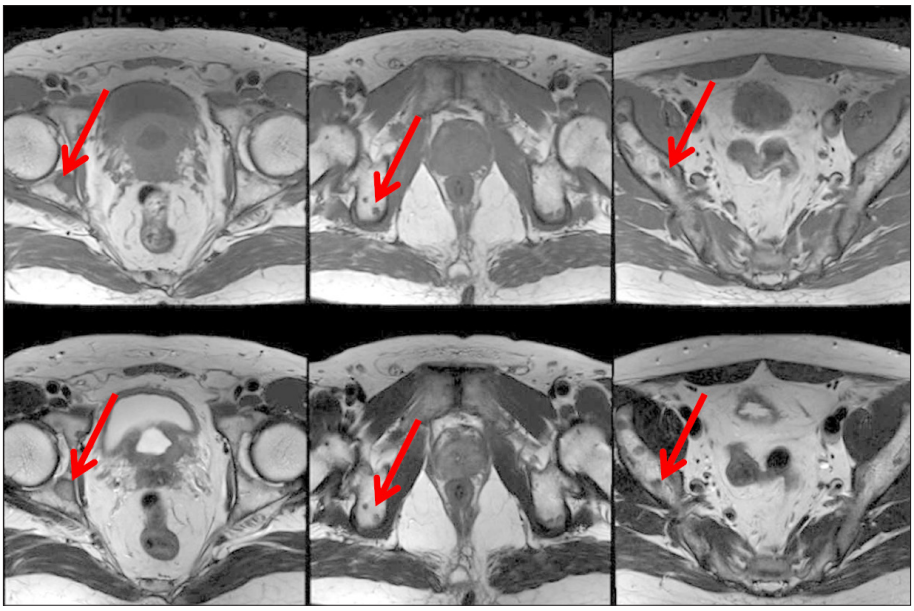

Figure 1: Axial T1- and T2-weighted MRI of the pelvis reveals multiple discrete hypointense lesions scattered in the bony pelvis (red arrows), suspicious for metastatic deposits

Subsequently, a technetium-99 methydiphosphate (Tc99m-MDP) bone scan was performed, with additional correlative Single-Photon Emission Computed Tomography (SPECT)/CT imaging of the pelvis. No abnormal scintigraphic or CT changes were detected in the bones [Figure 3].

There was a discrepancy in the results obtained by different imaging modalities, and the bone lesions were suspected to be either early non-sclerotic bony metastases or due to an underlying hematological disorder (e.g. multiple myeloma).

He subsequently underwent a channel transurethral resection of prostate (TURP) and gold seed brachytherapy. Follow-up assessment revealed complete biochemical response (PSA < 0.03 ng/ml). However, as the diagnosis of metastasis was still in doubt, a repeat MRI spine was performed, and this again showed persistent diffuse marrow abnormalities as noted in the cervical and thoracic spine as well as the posterior ribs showing mild patchy enhancement.

A percutaneous core biopsy of one of the bone lesions in L5 was performed. Histology showed presence of a 0.2-mm nest of cells that marked positive for kertain (AE1/3 MNF116) and synaptophysin. Negative staining was seen with PSA and prostate-specific acid phosphatase (PSAP. Histopathologic features were consistent with small cell (neuroendocrine) variant of prostate cancer [Figure 4a and b].

Discussion

Unusual neoplasms involving the prostate have been described in recent years, including mucinous cystadenocarcinoma, neuroendocrine cancer, lymphoma, spindle cell neoplasm, squamous cell carcinoma, and transitional cell carcinoma. While radiological findings among these uncommon subtypes of prostate carcinoma generally overlap, knowledge of how they may appear different from adenocarcinoma of the prostate can improve diagnosis.

The small cell (neuroendocrine) variant of prostate carcinoma is a rare subset of prostate cancer. It accounts for between 0.5% and 2% of all prostatic carcinomas.[2] However, recent autopsy studies suggest development of hormone-refractory disease in up to 10%–20% of such cases.[3] Progressive small cell (neuroendocrine) prostate carcinoma is characterized by the presence of visceral metastases, a high proportion of lytic bone disease, and contrary to adenocarcinoma of the prostate, low serum PSA.[4]

Molecular imaging modalities such as bone scintigraphy and, more recently, FCH PET/CT are used in the evaluation of prostate carcinomas. Bone scintigraphy is a sensitive modality for detecting prostate cancer bone metastases, and is used routinely in the staging and prognostication of prostate cancers.[5] Choline is a compound of phosphatidylcholine, which is a major component of cell membranes. Malignant tumors are associated with high cellular proliferation and increased cell membrane metabolism, and FCH PET/CT has been used in several centers to image and stage prostate adenocarcinomas, with reported sensitivities of between 86% and 89%.[6,7]

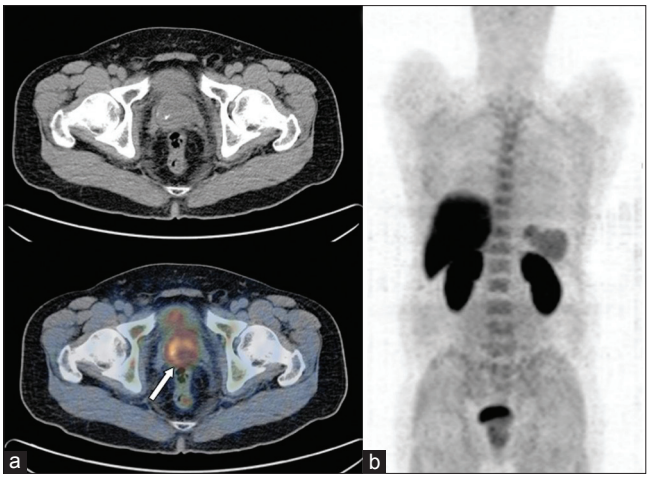

Figure 2: (a) Axial fused (upper) and unfused (lower) FCH PET/CT of the pelvis shows heterogeneously increased choline uptake in the prostate (white arrow). (b) Coronal whole-body PET shows essentially homogeneous tracer uptake in the axial skeleton with no abnormal tracer focus detected

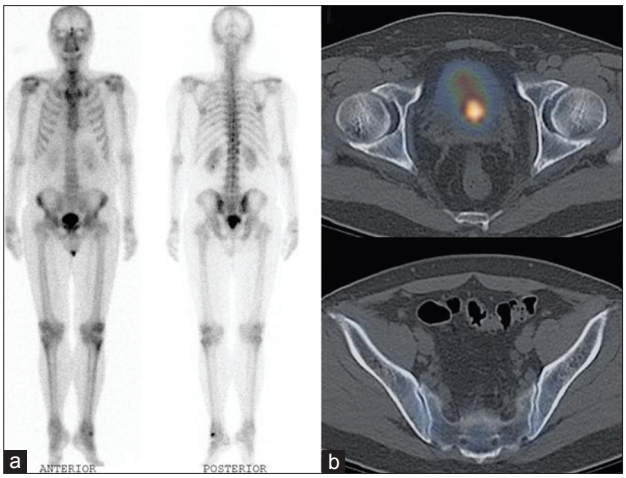

Figure 3: (a) Coronal Tc99m-MDP anterior and posterior whole-body views show essentially symmetrical and homogeneous tracer uptake. No focal osteoblastic lesions were detected. (b) Axial fused SPECT/CT sections of the pelvis show no abnormal tracer focus or CT bone changes for corresponding lesions seen on the MRI pelvis depicted in Figure 1

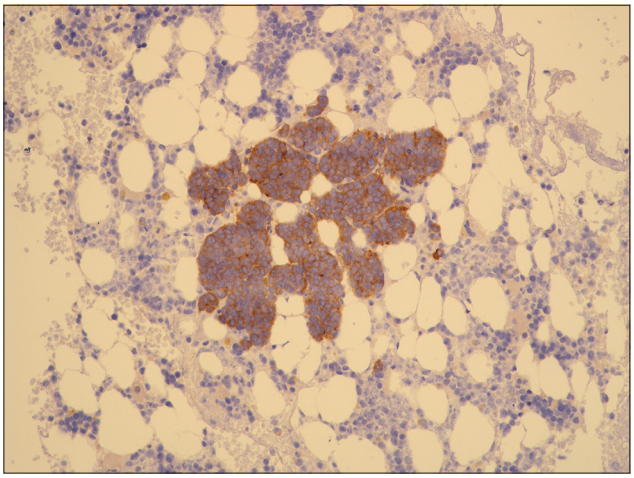

Figure 4a: H and E stain. Curetting from bone marrow, showing a small group of tumor cells. Tumor cells are small with hyperchromatic nuclei and scanty fragile cytoplasm (×40)

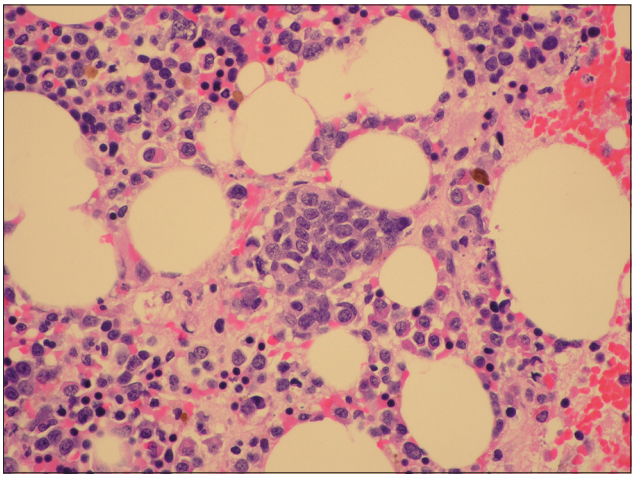

Figure 4b: Immunoperoxidase stain of the same group of cells showing positive reaction with synaptophysin (×40)

Our case illustrates a possible pitfall in molecular imaging of prostate cancer, whereby both bone scanning and FCH PET/CT scans showed no definite bone lesions to correlate with marrow signal abnormalities seen on MR imaging. Interestingly, molecular imaging findings corroborated well with the biochemical marker (PSA) which indicated biochemical response (<0.03 ng/ml). This study highlights the need for caution in the diagnostic evaluation of prostate cancers with known small cell variants, and possibly in patients with hormone refractory disease in view of the significant reported percentage of such variants.[2] Although not performed in our patient, tumor markers such as carcinoembryonic antigen, CA 19-9, CA 15-3, and CA 125 have been found to be elevated in this small subset of patients,[4] and may be useful for screening and response assessment.[8]

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