Case Report

Prostate cancer and sarcoma: Challenges of synchronous malignancies

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Abstract

Synchronous primary malignancies are a rare finding which can be difficult to diagnose. We present the case of a 57-year-old patient with a high prostate specific antigen who was found to have prostate cancer on subsequent magnetic resonance imaging. A skeletal metastasis was also identified at the time, although no osteoblastic activity or sclerosis was identified on skeletal scintigraphy or computed tomography, respectively. The patient was started on hormonal therapy and follow-up imaging revealed the prostate cancer to have reduced in volume. Despite this, the skeletal metastasis appeared unchanged on magnetic resonance imaging and an F18-choline positron emission tomography study was negative. A computed tomography guided bone biopsy was organized and this demonstrated metastatic leiomyosarcoma. As a result, an F18-fluorodeoxyglucose positron emission tomography study was performed to find the primary lesion which demonstrated a large malignant tumor within the calf. Subsequently, the patient was referred to a tertiary sarcoma unit. This case highlights the challenges involved in diagnosing and managing synchronous malignancies.

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Introduction

Prostate cancer is among the most common malignancies in men [1]. Synchronous malignancies are a rare finding with a reported incidence of approximately 2%-17% depending on the definition used [2]. These cases can be diagnostically challenging, both clinically and in terms of imaging findings, and they often require full multidisciplinary involvement. Particular imaging clues include differential responses to therapy and atypical patterns of disease spread. In these situations, whole body PET studies can play a key role in identifying primary sites of disease and any occult malignant lesions.

This report describes a challenging, histologically rare prostate cancer with a synchronous sarcomatous lesion of the
left leg. Arriving at the eventual diagnosis required a combination of MRI, CT, and PET studies, as well as histopathological correlation.

**Case Report**

A 57-year-old male presented to his GP following a single episode of hematuria and worsening lower urinary tract symptoms. The GP performed a digital rectal examination which demonstrated an abnormal, enlarged prostate gland. The patient’s prostate specific antigen (PSA) was measured and found to be raised at 10.1 μg/L. Given the high suspicion of prostate cancer, the GP requested an urgent 2-week-wait prostate MRI. Biparametric prostate MRI study (Fig. 1) demonstrated high-grade disease with involvement of almost the entire peripheral zone and evidence of bony metastatic disease, most notably, within the left iliac crest. No abnormally enlarged lymph nodes by size criteria were identified but an unusual rounded mesorectal lymph node (Fig. 1C) was noted. The case was referred to the local urology multidisciplinary team meeting where transperineal template biopsy, Tc⁹⁹m MDP bone scintigraphy, and a staging CT of the chest, abdomen, and pelvis was recommended (Figs. 2 and 3). Both the CT study and bone scan did not identify any suspicious bony or locoregional disease. The left iliac wing metastatic deposit was occult on both CT and bone scintigraphy. Incidentally, both modalities also identified a severely obstructed left kidney, possibly due to impacted calculi within the pelviureteric junction.

Transperineal template prostate biopsy was performed and 10 cores were obtained. Core biopsy results confirmed high-grade disease, corresponding to a Gleason score of 5+5. Although the overall histopathological classification was in keeping with adenocarcinoma, tumor PSAP, and synaptophysin were positive, indicating the presence of a rare, neuroendocrine small cell component. Overall, the clinicopathological scenario represented a poorly differentiated prostate cancer with minimal PSA secretion. Under the care of the oncology team, the patient was subsequently started on a luteinizing hormone-releasing hormone analogue. This was in the form of 3-monthly intramuscular Zolodex injections.

Follow-up imaging in the form of an F18-choline PET scan was performed after 2 months (Fig. 4). The primary malignancy was weakly positive which may, in part, have been due to its atypical cell type. The mesorectal lymph node appeared unchanged on interval imaging and adjacent thickening within the rectosigmoid junction was suspicious for a synchronous primary in the form of a high rectal cancer. Direct visualization via flexible sigmoidoscopy was recommended. The left iliac wing metastasis could not be appreciated on the low-dose CT component of the PET study and did not demonstrate any uptake. As a result, another prostate MRI study was performed which demonstrated interval decrease in the burden of prostate cancer. However, the metastatic deposit in the
Fig 3 – Whole body Tc\(^{99m}\) MDP bone scintigram. No osteoblastic metastatic disease is seen. Incidental obstruction of the left kidney is identified.

Fig 4 – Images from the F18-choline PET study. (A) Axial image showing mild uptake within the prostate gland. (B) Axial image demonstrating no uptake at the site of left iliac wing metastasis. (C) Mild uptake within the mesorectal lymph node is noted on axial imaging.
left iliac wing had not responded to therapy (Fig. 5). Again, the question of a synchronous tumor was raised and speculated to be possibly rectal or myelomatous in origin.

Further discussion in the urology multidisciplinary team meeting led to the organization of a CT-guided bone biopsy, a few weeks after the F18-choline PET study. The histology was difficult to accurately characterize and the results were surprising. Rather than containing malignant adenomatous or neuroendocrine cells, the skeletal metastasis was composed of malignant spindle cells and likely represented metastatic leiomyosarcoma. As a result, an F18-FDG PET was performed to help identify the primary site of the iliac wing deposit. Images were acquired from the vertex to the feet which identified a large intramuscular necrotic mass within the left calf (Fig. 6). This was almost certainly malignant in nature and it was presumed to be sarcomatous in origin. The patient was subsequently referred to a tertiary centre sarcoma unit and is currently awaiting clinical review. The mesorectal lymph node had markedly reduced in size and was not seen on the F18-FDG PET study; it may have been an entirely incidental finding. The prostate cancer itself responded well to hormone therapy with a reduction in the patient’s PSA levels from 10.1 μg/L to 0.3 μg/L during recent follow-up. The patient is not for curative treatment due to the presence of two different primary malignancies with evidence of metastatic disease. However, he is relatively symptom free at present.

Discussion

Prostate cancer is the most common malignancy in men over the age of 55 years with the vast majority of cancers being adenocarcinomas [3]. Neuroendocrine small cell prostate can-
cancer is rare, representing less than 1% of all cases [4]. They are more aggressive with early metastatic involvement of the lung and relatively limited PSA secretion in relation to the extent of disease [5]. This was the case in our patient with extensive involvement of the peripheral zone which was not reflected in the PSA value. Due to limited evidence, the most effective treatment has yet to be determined [5]. Our patient was started on hormonal therapy which was effective in reducing the volume of prostate cancer and the PSA value.

Regardless of subtype, the overwhelming majority of skeletal metastatic disease in prostate cancer is sclerotic in nature, with only isolated cases of osteolytic lesions being mentioned in the literature [6]. The left iliac wing metastasis proved to be challenging to accurately characterize in our case. It was not visible or sclerotic on CT imaging, which is highly unusual for prostate malignancies. However, it persistently showed up on MRI studies. It was eventually found to be F18-FDG avid on PET with a similar SUV as the synchronous sarcomatous malignancy within the left calf muscle. Atypical presentations of bony metastatic disease should prompt further investigations to rule out a synchronous primary, as was the case in our patient. Of course, rare histopathological subtypes can present in unusual ways, such as osteoblastic metastases in sarcomatoid renal cell carcinoma [7].

Furthermore, abnormal sites of lymphadenopathy can also suggest a secondary malignant process. The prostate is typically drained through the iliac lymph node chains [8]. Mesorectal involvement is less common, but it can occur in aggressive tumors, such as in our case. In more indolent neoplastic processes, atypical or distant lymphadenopathy should raise suspicion and may warrant further investigation.

PET CT could be useful in the evaluation of a suspected synchronous malignancy or in unusual primary presentations such as osteolytic metastasis in the context of prostate cancer. The whole-body nature of PET-CT allows for structural and functional assessment of distant organ systems, including the appendicular limbs. A retrospective study by Chun-Sing et al. demonstrated how PET-CT was crucial in identifying an unknown synchronous malignancy [9]. However, PET-CT has a number of disadvantages, not least the potential of the tumor to be non-avid to the given radiotracer. This limitation was evident in our case with the leiomyosarcoma bone metastasis appearing non-avid to F18-choline but highly avid to F18-FDG.

In summary, this case highlighted the challenges associated with correctly identifying synchronous malignancies, especially when the secondary tumor is rare and in an unusual location. Key to the diagnosis was having a high index of suspicion due to the atypical presentation of the prostate cancer and close clinical and histopathological collaboration.

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