Case Report

Primary Neuroendocrine Tumor of Prostate in a Case of Metastatic Adenocarcinoma of Lung: Rare Entity with Histopathological and Gallium 68 DOTANOC Positron Emission Tomography Correlation

Abstract

Neuroendocrine tumor (NET) of the prostate is an extremely rare entity which represents <1% of the prostatic cancers, but with increasing incidence. Its spectrum encompasses several histological variants ranging from well-differentiated tumor which are often indolent in nature; to aggressive neuroendocrine carcinoma which portends aggressive management. Hence, such rare entities are to be characterized and treated accordingly. We report an unusual case of well-differentiated NET of prostate which was flagged on fluorodeoxyglucose positron emission tomography computed tomography (PET/CT) performed for other indication and confirmed on Gallium-68 DOTANOC PET/CT. Histopathology and immunohistochemistry confirmed the findings subsequently.

Keywords: *DOTANOC, fluorodeoxyglucose, neuroendocrine tumor, positron emission tomography computed tomography, prostate*

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Introduction

Neuroendocrine tumors (NET) arise from neural crest cells and can metastasize to any part of the body. Neuroendocrine differentiation of underlying adenocarcinoma of prostate is an aggressive variant with increasing incidence. Androgen deprivation therapy is thought to be the underlying possible cause for such transformation. However, *de novo* NET of prostate is extremely rare which represents <1% of total prevalence. Clinically, these often manifest as metastatic disease, a disproportionately low serum prostate-specific antigen (PSA) level with loss of androgen receptor expression. We report one rare incidentally detected case of NET of prostate serendipitously detected in a coexisting metastatic adenocarcinoma of the lung.

Case Report

A 62-year-old-male, presented with sudden onset of the right upper limb weakness and loss of consciousness. Magnetic resonance imaging revealed well-defined space-occupying lesion involving the left parietal lobe. Wide local excision was done. As shown in Figure 1, microphotographs of (a) parietal brain tumor showing a tumor with glandular and papillary pattern, high-grade nuclei with prominent nucleoli, and frequent mitosis (×200). This tumor was diffusely positive for CK7 (b) and thyroid transcription factor 1 (TTF1) (c) Which was suggestive of metastatic adenocarcinoma. The patient was referred for whole-body fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET/CT) for the detection of primary and other metastatic sites. Maximum intensity projection [MIP - Figure 2a, Blue arrow] revealed the focus of increased tracer uptake in the mediastinum. Corresponding fused transverse images revealed metastatic prevascular node [Figure 2b]. CT window revealed a consolidative patch with low-grade FDG uptake seen in the left lung [Figure 2c, blue arrow]. Surprisingly, also seen was a large enhancing soft tissue mass with no FDG uptake appearing to arise from prostate and seminal vesicle [Figure 2d and e, white arrows]. Considering the pathophysiology & spread pattern of lung adenocarcinoma, the possibility of this being metastatic deposit was less favored. Low grade FDG uptake in a well-defined enhancing mass arising from prostate raised suspicion of aggressive histology of primary prostatic origin Hence,

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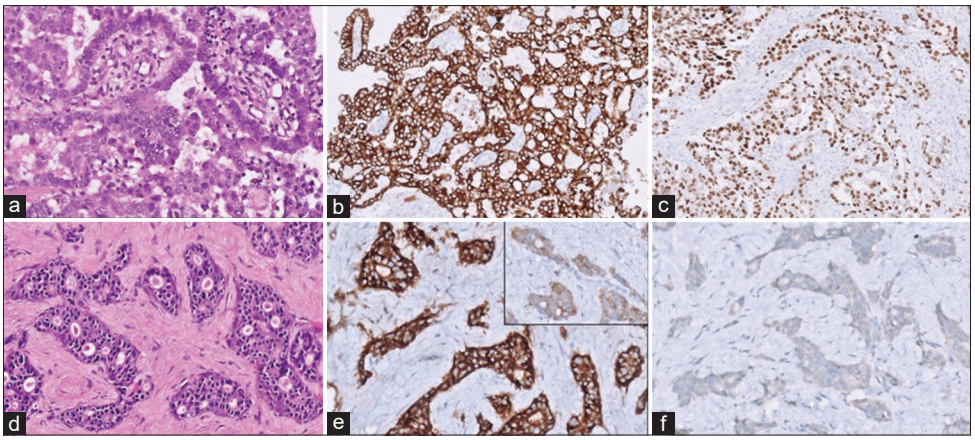

Figure 1: Microphotographs of (a) parietal brain tumor showing a tumor with glandular and papillary pattern, high-grade nuclei with prominent nucleoli and frequent mitosis (×200). This tumor was diffusely positive for CK7 (b) and thyroid transcription factor 1 (c). Biopsy from pelvic mass showed (d) tumor composed of cribriform nests, with uniform round hyperchromatic nuclei, without mitotic activity (×200). This tumor was strongly and diffusely positive for chromogranin (e), weakly for AE1/AE3 (e, inset), and negative for thyroid transcription factor 1 (f)

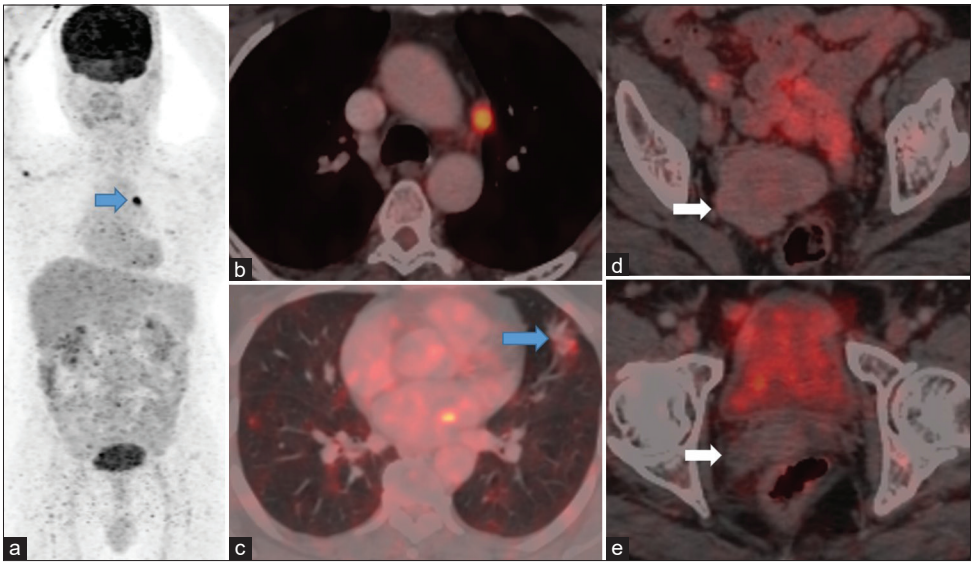

Figure 2: ^{18}F-Fluorodeoxyglucose positron emission tomography computed tomography: Maximum intensity projection (a) Focal fluorodeoxyglucose uptake in mediastinum. Fused transverse images (b and c) focal increased fluorodeoxyglucose uptake in prevascular node and consolidation involving left lung. Large enhancing soft-tissue mass with no fluorodeoxyglucose uptake seen involving prostate (d and e)

a biopsy from prostatic lesion and Gallium-68 (Ga-68) DOTANOC PET/CT (DOTA PET) was performed. MIP revealed solitary soft-tissue lesion involving prostate with strong somatostatin receptors (SSTR) expression [Figure 3a, red arrow]. Corresponding fused transverse and coronal images revealed large intensely enhancing prostatic soft tissue mass with strong SSTR expression [Figures 3b and 2c]. This was suggestive of neuroendocrine origin. Histopathology showed [Figure 1d] tumor composed of cribriform nests, with uniform round hyperchromatic nuclei, without mitotic activity (×200). This tumor was strongly and diffusely positive for chromogranin [Figure 1e] and negative for TTF1 [Figure 1f] suggestive of a primary prostatic NET. Serum PSA level was 0.3 ng/ml. The patient is on routine follow-up, with imaging suggested every 6 months over the next 1 year.

Discussion

The differential diagnosis for primary prostatic masses can range from benign hyperplasia to conventional adenocarcinoma, later being the most common in elderly patients.[1] These tumors are usually confined to the peripheral zone of prostate gland and involve adjacent structures such as the seminal vesicle and bladder only in the setting of locally advanced disease.[2] The diagnosis is often straightforward with distinct radiological features and sensitive tumor markers. However, the diagnostic dilemma arises if there is a clinicoradiological mismatch.[3] Since in our case, the initial diagnosis was adenocarcinoma of lung, possibility prostatic mass being the second primary was favored over metastasis; considering the spread pattern of lung adenocarcinoma. However, intense enhancement in a well-defined soft-tissue mass arising from the prostate

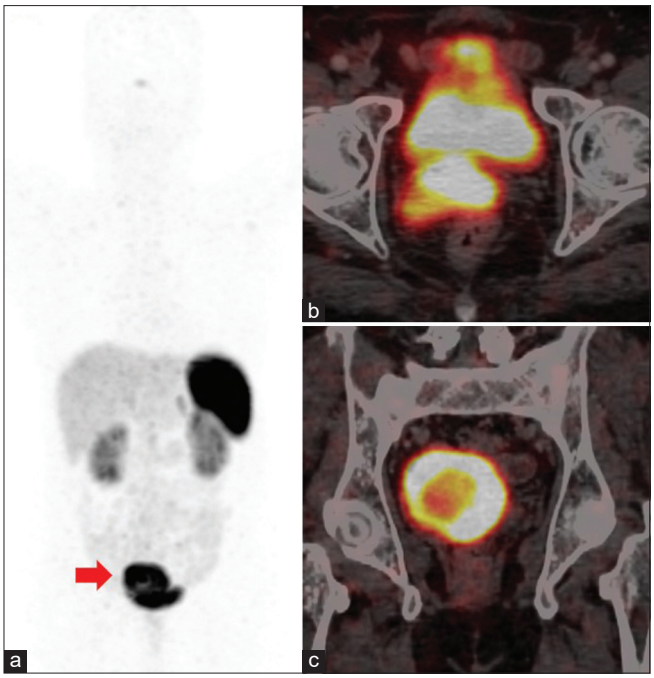

Figure 3: Ga-68- DOTANOC PET/CT: MIP shows intense SSTR uptake in pelvic region (a). Corresponding fused transverse and coronal images show large soft tissue mass involving prostate & seminal vesicle with intense SSTR expression (b,c)

with no locoregional nodal involvement and normal serum PSA values raised a suspicion of neuroendocrine differentiation.[4,5] Hence, the patient was referred for Ga-68 DOTANOC PET/CT which revealed intense SSTR expression in prostatic mass with no areas of SSTR uptake elsewhere in the whole-body scan. Final histopathological and IHC were suggestive of well-differentiated NET of prostate.

Neuroendocrine differentiation of primary prostatic adenocarcinoma represents a subset of prostatic cancer phenotypes (10%–15%) which are associated with resistance androgen receptor-directed therapies and with poor prognosis. However, the primary NET of prostate and seminal vesicles is an extremely rare tumor with incidence <1%.[6,7] Most of the literature includes few case reports and short series.[8-11] Its clinical features include a rapid progression of the metastatic disease and no response to treatment. Hence, these rare entities should be kept in mind, typically when there is a clinicoradiological mismatch or there is no response to conventional line of treatment.

Our case is unique as it was incidentally detected on routine FDG PET/CT done for staging workup, findings of which were later confirmed with SSTR imaging and histopathology.

Conclusion

Primary NET of prostate, though rare entity should be suspected in primary prostatic masses with equivocal features on conventional imaging. Ga-68 DOTANOC PET/CT can help in further characterizing such tumors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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