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Detection and Implications of Increased PSMA Uptake in Thyroid Nodule Following Lu-177 PSMA Therapy: A Case of Hürthle Cell Variant Thyroid Papillary Carcinoma Identified by Ga-68 PSMA PET/CT

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Abstract

Background: Prostate-specific membrane antigen (PSMA) imaging is increasingly used in the evaluation and management of prostate cancer. However, PSMA expression can also occur in non-prostatic malignancies and benign tissues, presenting diagnostic challenges.

Case presentation: We report a 70-year-old male with metastatic prostate adenocarcinoma who underwent serial Ga-68 PSMA PET/CT imaging before and after six cycles of Lu-177 PSMA therapy. While initial imaging revealed multiple PSMA-avid lesions in the prostate and skeletal system and a mildly PSMA-avid thyroid nodule, post-therapy PET/CT demonstrated resolution of most metastatic sites with notable increase in PSMA uptake in the left thyroid nodule. Fine-needle aspiration biopsy of the thyroid lesion revealed papillary carcinoma, Hürthle cell variant. Total thyroidectomy was performed, and histopathology confirmed the diagnosis. The patient subsequently received radioiodine therapy for residual thyroid tissue.

Discussion: This case highlights a rare but clinically significant scenario of increased PSMA uptake in a thyroid nodule following Lu-177 PSMA therapy, leading to the diagnosis of Hürthle cell variant papillary thyroid carcinoma. PSMA expression in thyroid neoplasms is uncommon but should be recognized as a potential pitfall during PSMA-targeted imaging in prostate cancer patients. The findings also suggest a possible influence of Lu-177 PSMA therapy on subsequent PSMA expression in non-prostatic tissues.

Conclusion: Increased PSMA uptake in thyroid nodules after Lu-177 PSMA therapy can indicate underlying malignancy, as in this rare case of Hürthle cell variant papillary carcinoma. Awareness of this potential finding is essential to avoid misinterpretation and to ensure prompt and accurate diagnosis.

Keywords: Ga-68 PSMA PET/CT, Lu-177 PSMA therapy, thyroid nodule, Hürthle cell variant, papillary thyroid carcinoma, prostate cancer.

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Introduction

Thyroid nodules are characterized as lesions that are clearly differentiated from the parenchyma of the thyroid gland (1). They are quite common both globally and nationally. They have a prevalence of 2–6% by palpation in clinical examinations, 19–35% by ultrasonography, and 8–65% in autopsy studies. The increased use of advanced imaging techniques has increased the incidental detection rate of these nodules (2). Early diagnosis and appropriate therapeutic intervention can significantly improve patient survival rates, so early detection of these lesions is of critical importance.

Prostate-specific membrane antigen (PSMA) was initially thought to be a type II transmembrane glycoprotein found only in prostate tissue (3). However, recent studies have shown that PSMA can also be found in the cell membrane of vascular endothelial cells during the neovascularization process. Therefore, PSMA antigen can also be detected in cancerous and non-cancerous tissues other than prostate (4). Thyroid malignant nodules are one of the rare cancers that may show PSMA expression in some cases. This indicates the presence of focal PSMA expression in the thyroid gland and such a finding warrants further investigation. Therefore, further investigation and research such as fine needle aspiration biopsy (FNA) are needed to determine the exact cause and clinical significance of PSMA expression in thyroid nodules (5).

Case Presentation

A 70-year-old patient with prostate adenocarcinoma (Gleason score: 4 + 5 = 9 and PSA: 89) was referred to our clinic for Ga-68 PSMA PET/CT whole body scan for staging. All images acquired 60 min after injection of 185 MBq (5 mCi) Ga-68 PSMA; slice thickness 3 mm; window width/level optimized for soft-tissue contrast. In the Ga-68 PET/CT images obtained for staging, we found multiple focal lesions in the prostate gland and PSMA expression in multiple areas and numbers in the skeletal system. In addition, nodules with mild PSMA expression were observed in the thyroid gland. The prostate cancer patient developed recurrence after chemotherapy and Lu-177 PSMA treatment was administered in 6 doses of 200 mCi each. As a result of Ga-68 PSMA PET/CT performed for treatment response, PSMA expressions previously observed in the prostate gland and skeletal system almost completely disappeared in the scan, while increased PSMA expression was observed in the nodule in the left lobe of the thyroid, which previously showed mild PSMA expression (Figure 1).

Given the increased PSMA expression observed in the nodule, FNA was recommended to exclude primary thyroid malignancy. FNA of the thyroid lesion demonstrated papillary thyroid carcinoma with Hürthle cell features, a finding subsequently confirmed as the Hürthle cell variant on total thyroidectomy. The largest tumor diameter was 4×3×1 cm. Lymphovascular invasion and perineural invasion were not observed and extrathyroidal spread was not detected. The patient was then treated with 100 mCi radioactive iodine for the remaining residual thyroid tissues.

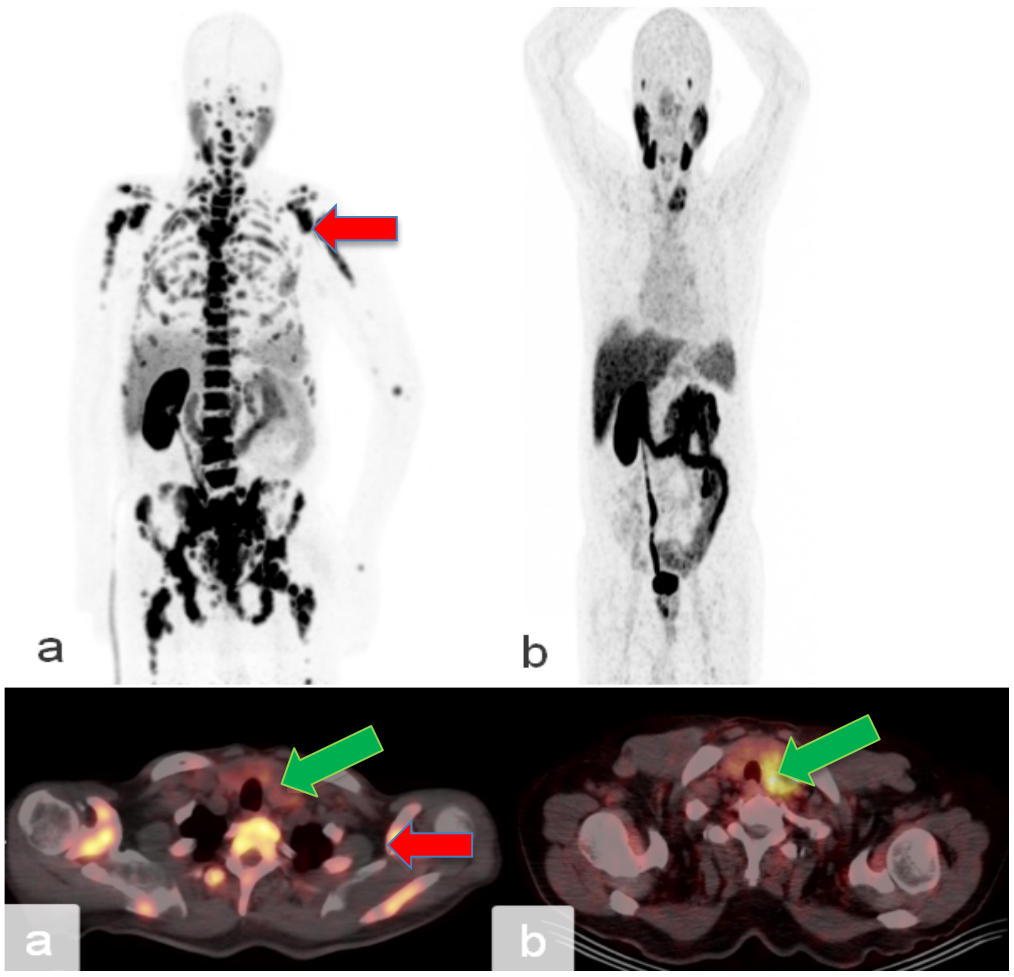

Figure 1. *Ga-68 PSMA PET/CT image.*

(a) Baseline maximum-intensity projection (MIP) and axial PET/CT fusion showing multiple PSMA-avid prostate and bone metastases (red arrows) and a mildly PSMA-avid left thyroid lobe nodule (green arrow; SUV_{max} 3.2).

(b) Post–Lu-177 PSMA therapy MIP and axial fusion images: near-complete resolution of prior metastatic lesions and increased PSMA uptake in the left thyroid nodule (green arrow; SUV_{max} 7.8).

Discussion

This case highlights the identification of a thyroid nodule as thyroid papillary carcinoma Hürthle cell variant discovered during Ga-68 PSMA PET/CT scan during prostate cancer treatment. Thyroid papillary carcinoma Hürthle cell variant is a rare variant of thyroid cancer. This rare case also highlights the fact that PSMA may be involved in cancers other than prostate (6). Increased PSMA uptake in thyroid cancer patients has also been reported in several case reports and some small prospective studies (7,8). These findings emphasize the utility of PSMA as a potential target in the diagnosis and treatment of cancers other than prostate cancer.

Furthermore, this case draws attention to the possibility of increased PSMA expression in a previously observed nodule in the thyroid gland after Lu-177 PSMA treatment. Lu-177 PSMA treatment is a radioactive treatment method used in the treatment of prostate cancer, and increased PSMA expression in the thyroid gland after treatment is considered a rare side effect that may occur due to this treatment (9). Studies have shown that PSMA expression levels may be associated with tumor aggressiveness (10,11). Another study shows that increased PSMA expression is associated with poor prognostic factors and is associated with a lower progression-free survival (12). PSMA can accumulate in benign neovessels—such as those seen in inflammatory processes or follicular hyperplasia—and this

physiologic uptake must be distinguished from malignant lesions to avoid false-positive interpretations (13).

This case is important as it demonstrates both the potential role of PSMA in different cancer types and that PSMA expression may increase in thyroid nodules after Lu-177 PSMA treatment. Therefore, more large-scale studies investigating the future use of PSMA expression in cancer diagnosis and treatment are needed.

Conclusion

This case report presents a rare case example of a thyroid nodule incidentally detected during prostate cancer treatment and identified as a Hürthle cell variant of thyroid papillary carcinoma. It also demonstrates that PSMA expression can be seen in cancers other than prostate cancer and that PSMA expression may increase in thyroid nodules after Lu-177 PSMA treatment.

Ethical Approval: *All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.*

Conflict of Interests: *The authors declare that there is no conflict of interest in the study.*

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Informed Consent: *Informed consent was obtained from all individuals participants included in the study.*

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