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CASE REPORT

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Bilateral Renal Metastasis of Hürthle Cell Thyroid Cancer with Discordant Uptake Between I-131 Sodium Iodide and F-18 FDG

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Abstract Renal metastasis of thyroid cancer is extremely rare. We report the case of a 62-year-old woman with Hürthle cell thyroid cancer (HCTC) with lungs, bones, and bilateral kidneys metastases. The renal metastatic lesions were clearly demonstrated by ^{131}I whole body scan (WBS) with SPECT/CT. However, they exhibited false-negative results in ^{18}F-FDG PET/CT, kidney ultrasonography, and contrast-enhanced CT scan. The findings imply that tumors have low glucose metabolism and are able to accumulate radioiodine, which is not commonly found in the relatively aggressive nature of HCTC. The patient received two sessions of 200 mCi ^{131}I therapy within 6 months duration. There was complete treatment response as evaluated by the second post-therapeutic ^{131}I SPECT/CT and serum thyroglobulin. To our knowledge, renal metastasis from HCTC with positive ^{131}I but negative ^{18}F-FDG uptake has not been reported in the literature. This case suggests that ^{131}I SPECT/CT is useful for lesion localization and prediction of ^{131}I therapy response.

Keywords F-18 FDG PET/CT · Hürthle cell thyroid cancer · I-131 whole-body scan · Renal metastasis · Discordant uptake

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Introduction

Thyroid cancer is a common endocrine cancer. Well-differentiated thyroid cancer includes papillary and follicular carcinomas. Hürthle (oxyphilic) cell thyroid carcinoma (HCTC) is a variant of follicular thyroid carcinoma (FTC). HCTC is rare, accounts for about 3% of all thyroid malignancies, and shows an overall survival similar to that of FTC in the same stages [1]. However, rate of distant metastasis was found to be highest in HCTC (33%) compared to other subtypes [2].

Renal metastasis of thyroid cancer is extremely rare and tends to be overlooked or misdiagnosed [3]. Conventional radiological imaging such as ultrasonography and computed tomography (CT) are not specific to indicate thyroid cancer in origin for metastasis. Both ^{131}I whole-body scan (WBS) and ^{18}F-FDG PET/CT may have important roles for the diagnosis and follow-up of this disease entity. Radioiodine scan is specific for well-differentiated thyroid cancer, however, there is a tendency to disregard abnormal uptake lesion in kidney regions due to superimposed intestinal activity or radioactive urine retention in collecting systems. This shortcoming may simply be overcome by using the SPECT/CT for localization of the suspicious radioactivity. Sensitivity of ^{131}I scan is limited in aggressive and dedifferentiated thyroid cancer, including HCTC. Whereas ^{18}F-FDG PET/CT is an alternating tool to detect these tumors with high sensitivity.

Here, we present a case of renal metastasis from HCTC with discordant ^{131}I and ^{18}F-FDG uptake. To the best of our knowledge, this is the first case report of renal metastasis from HCTC that showed positive ^{131}I scan but negative ^{18}F-FDG PET/CT. The patient showed complete treatment response after the first high dose radioiodine therapy. In this case, ^{131}I SPECT/CT played a key role in the differential diagnosis and follow-up.

Case Report

A 62-year-old woman was found with multiple small pulmonary nodules from her routine check-up chest CT scan. She underwent lung biopsy from another hospital, which revealed Hürthle cell neoplasm. The patient was referred to our hospital for further investigation and treatment. She disclosed the history of left thyroid lobectomy 20 years ago and post radiofrequency ablation of right thyroid nodule 8 years ago from local hospital. However, the previous pathological reports could not be obtained. On physical examination, there was no palpable thyroid nodule or cervical lymphadenopathy. Neck ultrasonography revealed a 2.2 x 1.2 x 2.2 cm isoechoic nodule in the remaining right thyroid lobe. Needle biopsy from the thyroid nodule reported indeterminate result. Pathological evaluation from subsequent gun biopsy showed microfollicular proliferative lesion with nuclear atypia, oncocytic change, and suspicious of capsular invasion, which is suggestive of Hürthle cell neoplasm.

^{18}F-FDG PET/CT was performed for staging (Fig. 1). The study showed intense hypermetabolic tumor in the right thyroid lobe with maximal standard uptake value (SUV_{max}) of 40.0. There was mild hypermetabolism in bilateral small lung nodules (SUV_{max} of 1.9). The regions elsewhere, including kidneys, were unremarkable. PET/CT findings suggested thyroid cancer with multiple lung metastases.

The patient received completion thyroidectomy. Pathological report revealed Hürthle cell adenoma, 2.1 x 2.0 x 1.5 cm in size, free resection margin, and no tumor embolus. Further immunohistochemical and DNA analysis revealed negative HBME-1, cytokeratin 19, galectin-3, and BRAF mutation.

Postoperatively, thyroid function was evaluated, which showed a TSH level of 0.09 uIU/ml, thyroglobulin (Tg) level of 54.92 ng/ml, and a low level of thyroglobulin antibody (TgAb; 27 U/ml). The patient, therefore, received radioiodine therapy (RIT) with 7400 MBq (200 mCi) of ^{131}I. Her serum level of TSH was 53.53 uIU/ml after the administration of recombinant human TSH, Tg was 224 ng/ml, and TgAb was 25 U/ml. Whole-body scan (WBS) was imaged at 4 days after ^{131}I administration and revealed multiple hot spots which is consistent with residual thyroid tissue at right thyroid bed and metastasis to cervical lymph nodes, lungs, skull, and vertebrae (Fig. 2). Abnormal hot spots were also noted at both upper abdomen, more clearly seen in the posterior view. Therefore, SPECT/CT imaging was performed and located them in bilateral renal cortices without anatomical abnormality seen from the low-dose CT. Contrast-enhanced CT imaging was ordered subsequently and revealed a 0.6 cm nodule with slight radioopacity and no definite contrast enhancement, located in the posterior midpole of the left kidney.

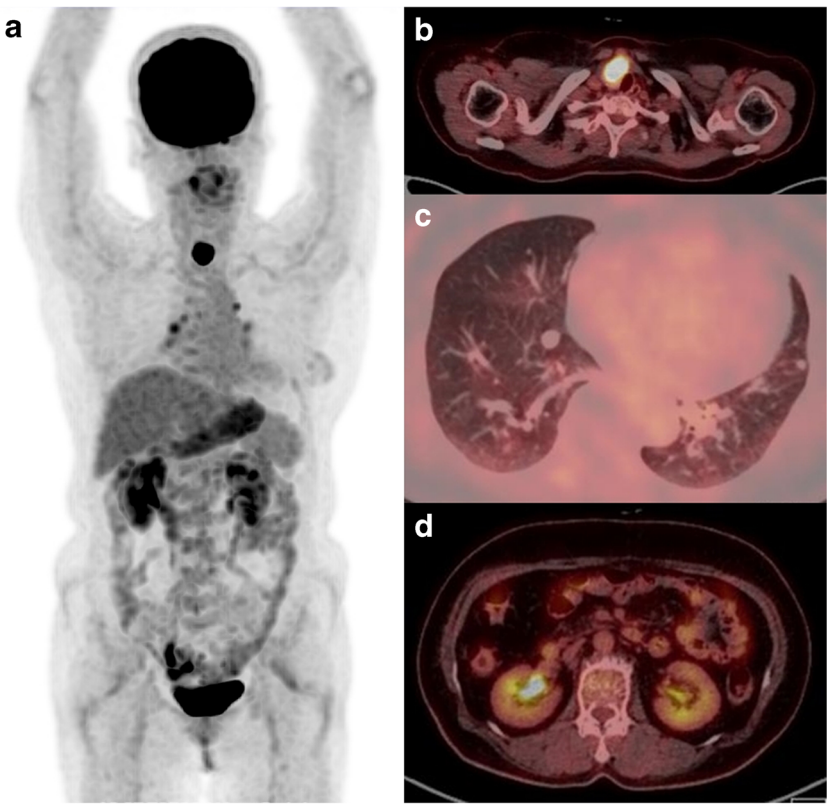

Fig. 1 ^{18}F-FDG PET/CT images performed for staging. Maximal-intensity projection image (**a**) shows intense hypermetabolism in lower neck region. Transaxial images of fusion PET/CT show hypermetabolic right thyroid nodule (**b**) and mild hypermetabolism in multiple pulmonary nodules (**c**), without abnormality in both kidneys (**d**)

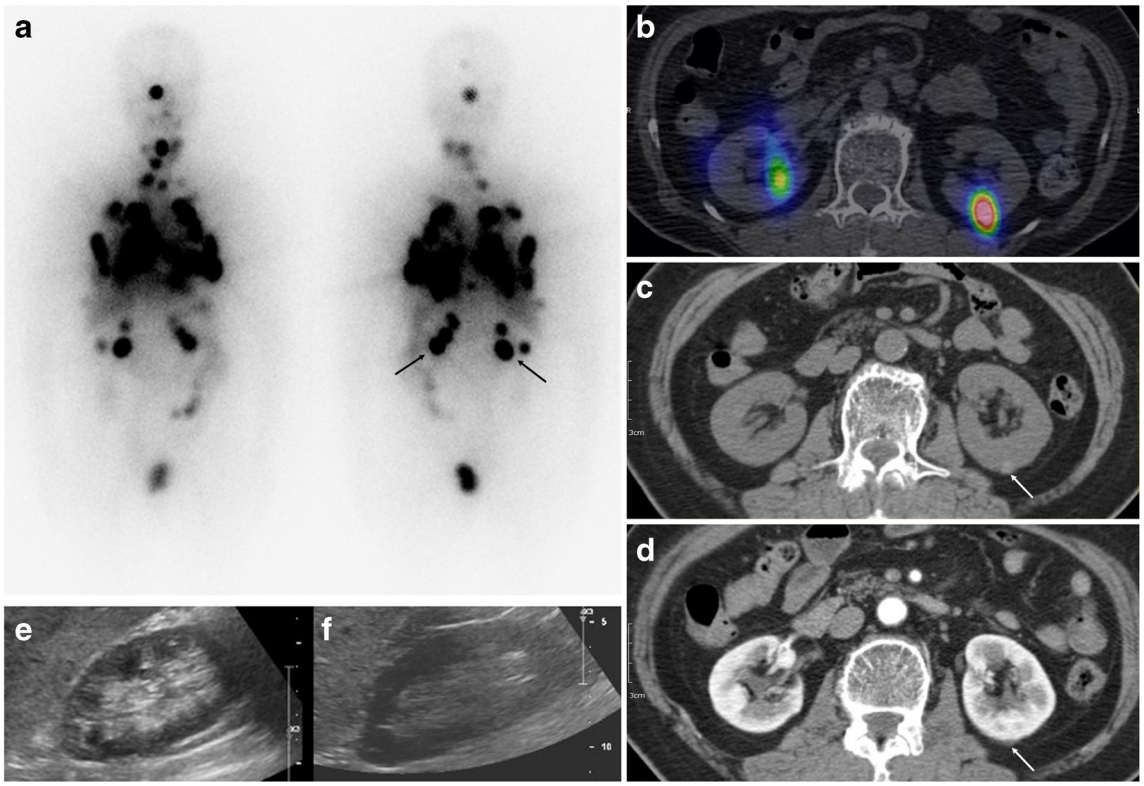

Fig. 2 Anterior and posterior planar images from the first radioiodine therapy (7400 MBq) shows multiple increased ^{131}I uptake foci at thyroid bed, lungs, bones (skull base and vertebrae), and bilateral renal regions *(arrows)*, (**a**). SPECT/CT image localizes the uptake foci in bilateral renal parenchyma, not in the collecting systems (**b**). Non-contrast enhanced CT image reveals a 0.6 cm, slightly radioopaque nodule *(arrow)* in the posterior aspect of the left kidney (**c**) without contrast-enhancement (**d**). The other renal lesions are not visualized. Ultrasonography images of the left (**e**) and the right kidneys (**f**) show no abnormality

The CT lesion was in the corresponding area of that seen in the ^{131}I SPECT/CT images. Other ^{131}I uptake lesions were not discernible in the diagnostic CT, probably due to their small sizes. Transabdominal ultrasonography detected no abnormality in the kidneys. She had neither urinary symptoms nor abnormal findings on her urine analysis. In this case, pathological confirmation of renal lesions could not be obtained owing to their small size limited the utility of either ultrasonography or non-contrast enhanced CT for guiding the biopsy location. Also, pathological confirmation might neither provide benefit to the patient nor alter the treatment plan. The conclusion of renal metastasis of thyroid cancer was made based on ^{131}I SPECT/CT findings as well as by exclusion of potential false-positive causes such as urinary retention in collecting systems or ^{131}I accumulation in renal cyst.

After RIT, the patient received L-thyroxine for TSH suppression. Blood tests at 2 months post-RIT revealed TSH level of less than 0.05 uIU/ml and Tg of 2.75 ng/ml. The second RIT (7400 MBq of ^{131}I) was administered at the 6 months after the first RIT. Post-therapeutic WBS and SPECT/CT showed no discernible ^{131}I uptake throughout the body (Fig. 3). Serum Tg was decreased to 0.89 ng/ml and TSH was 35.76 uIU/ml. These results indicated complete remission status.

Discussion

Kidney is a rare site for metastasis of thyroid cancer. Renal metastasis usually occurs in the setting of extensive multiple organ metastases [4]. Diagnosis of renal metastasis of thyroid cancer may be late or missed because patients may not have urinary symptoms and conventional imaging findings are also non-specific. It has a potential to be misdiagnosed as the relatively more common diseases, including primary renal tumors or metastasis from other cancers. The best treatment for renal metastasis of thyroid cancer remains unclear. However, for small size ^{131}I avid renal metastatic lesions, RIT is the treatment of choice [5].

In general, the diagnosis of renal metastasis should be made based on tissue pathology. However, for tiny lesion that were incapable to biopsy, diagnosis based on multimodality imaging was also acceptable [6]. It is reasonable to make a conclusion of renal metastasis from thyroid cancer for focal ^{131}I uptake lesion(s) in renal parenchyma, after careful exclusion of potentially false positive causes such as urinary radioactivity in dilated collecting systems and renal cyst(s). In the study of Bakheet et al., they reported 2.2% prevalence of renal uptake in radioiodine scan, 44% of which were unilateral. To evaluate the nature of uptake lesion(s) in renal bed, they

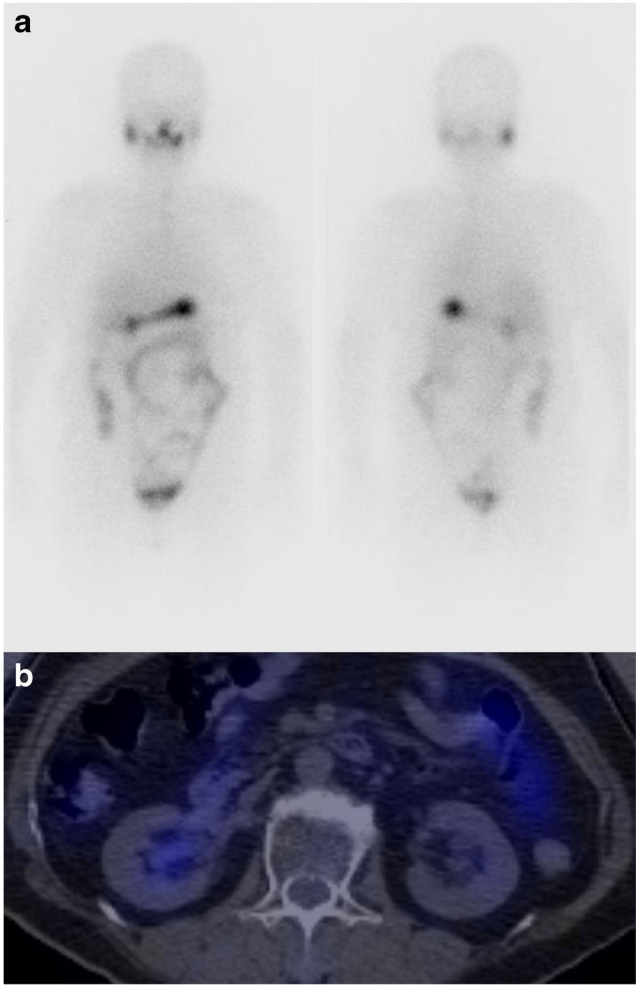

Fig. 3 Anterior and posterior planar images from the second radioiodine therapy (7400 MBq) shows no abnormal increased ^{131}I uptake throughout the body (**a**). SPECT/CT image shows disappearance of previously noted bilateral renal uptake foci (**b**)

suggested the careful review of bilaterality, pattern (focal, patchy, etc.), clearance after delay imaging, and anatomical imaging findings such as pelvocalyceal system dilatation or diverticulum, renal cyst (that may have connection with collecting system or able to accumulate iodine) [7, 8]. In our case, the uptake lesions located in renal parenchyma and there is no evidence of renal cyst or pelvocalyceal abnormality that may accumulate radioactive iodine. Also, the intensity of focal uptake lesions were far higher than that of urinary activity in either renal pelvis or urinary bladder. By this approach, exclusion of false-positive renal uptake was made in our case.

Both ^{131}I scan and ^{18}F-FDG PET/CT scan play an important role in the diagnosis and management of metastatic thyroid cancer. However, detection sensitivity may be limited for renal metastatic lesions according to superimpose intestinal activity of ^{131}I and urinary excretion of ^{18}F-FDG. The present case demonstrated higher detection sensitivity of ^{131}I scan than other conventional radiological imaging modalities, as well as the advantage of using SPECT/CT for lesion localization and diagnosis. In contrast, ^{18}F-FDG PET/CT exhibited a false-negative result. Such discordant uptake between ^{131}I and ^{18}F-FDG was called the flip-flop phenomenon.

Degree of tumor differentiation can be evaluated by comparing the uptake intensity of ^{131}I and ^{18}F-FDG. Upregulation of glucose transporters 1 (GLUT1) and reduced expression of sodium iodide symporter (NIS) can be observed during the dedifferentiation process and usually found in aggressive tumor subtype such as HCTC. A previous report showed low sensitivity (about 10%) of ^{131}I scan to detect HCTC metastases [9]. In contrast, false-negative results of ^{18}F-FDG PET/CT do not often present in metastatic HCTC [10] because it usually expresses a high level of (GLUT1) on the cell surfaces [11]. In the previous case report of a HCTC patient that underwent both ^{131}I WBS (150 mCi) and ^{18}F-FDG PET/CT scan showed only equivocal faint ^{131}I uptake in cervical node region, while there was intense ^{18}F-FDG avidity in multiple metastatic lesions at cervical nodes, bones, and kidney [12]. In the previous study of 44 patients with HCTC who underwent ^{18}F-FDG PET/CT, there was only one false-negative PET in a patient with lung and chest wall metastases. The rest of the patients showed ^{18}F-FDG avidity in primary tumors and metastases, including the cervical lymph nodes and bones that was missed by CT. Overall survival of the HCTC patients was significantly related with FDG avidity, using SUV_{max} cutoff at 10. They concluded the usefulness of ^{18}F-FDG PET for prognostication and its excellent diagnostic accuracy for evaluation of HCTC patients with overall sensitivity and specificity of 95.8% and 95%, respectively [13].

There were several case reports that described the image findings of renal metastasis of thyroid cancer evaluated from ^{131}I WBS and ^{18}F-FDG PET/CT [5, 6, 12, 14–16]. Only one of these reports was HCTC subtype, which showed negative ^{131}I but positive ^{18}F-FDG uptakes in the renal metastatic lesion [12]. Our case is the first to show renal metastasis form HCTC with positive ^{131}I but negative ^{18}F-FDG uptake, which is an uncommon findings for HCTC. Findings in our patient indicate well-differentiation of tumors and predict the excellent response to RIT in spite of widespread metastasis.

In conclusion, we report a rare case of renal metastasis from HCTC detected by ^{131}I SPECT/CT but missed by ^{18}F-FDG PET/CT and other conventional imaging modalities. The findings indicate well-differentiation of tumors and excellent response to RIT.

Compliance with Ethical Standards

Conflict of Interest Apichaya Claimon, Minseok Suh, Gi Jeong Cheon, Dong Soo Lee, E. Edmund Kim, and June-Key Chung declare that they have no conflict of interest.

Ethical Statement This study was approved by the Institutional Review Board at Seoul National University Hospital (IRB No. 1602-151-747) and performed in accordance with the ethical standards of the

responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000. Acquisition of informed consent was exempted by the board because of the retrospective nature of the study. Details that might disclose the identity of the subject were omitted.

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