Renal Metastasis and Dual (^{18}F-Fluorodeoxyglucose and ^{131}I) Avid Skeletal Metastasis in a Patient with Papillary Thyroid Cancer

Abstract

Differentiated thyroid carcinoma (DTC) though usually behaves in an indolent manner, can have unusual metastatic presentation. Initial presentation of metastatic disease has been reported in 1–12% of DTC being less frequent in papillary (~2%) than in follicular (~10%) thyroid carcinoma. Renal metastasis from DTC is very rare. To our knowledge, only about 30 cases have been reported in the English literature to date. To make clinicians aware that management of such high-risk thyroid cancer frequently requires novel multimodality imaging and therapeutic techniques. A 72-year-old female is described who presented with abdominal pain and bilateral lower limbs swelling. Initial contrast enhanced computed tomography (CT) scan of abdomen showed a well-encapsulated mass in the upper pole of right kidney favoring a renal cell carcinoma. Postright sided radical nephrectomy, histopathology, and immunohistochemistry reports suggested metastatic deposits from thyroid malignancy. ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography-CT demonstrated hypermetabolic nodule in the left lobe of thyroid and a lytic lesion involving left acetabulum suggestive of skeletal metastasis. Subsequently, ultrasound-guided fine needle aspiration cytology of the thyroid nodules in bilateral lobes confirmed thyroid malignancy (Bethesda 6/6). Total thyroidectomy revealed papillary thyroid cancer (PTC) (follicular variant-PTC [FV-PTC]). After surgery, ^{131}I-whole body scan showed iodine avid lytic lesion in the left acetabulum. The present case is a rare scenario of a renal metastasis as the presenting feature of an FV-PTC. Dual avidity in metastatic thyroid cancers (iodine and FDG) is rare and based on the degree of dedifferentiation of the DTC.

Keywords: *^{131}I-whole body scan, ^{18}F-fluorodeoxyglucose-positron emission tomography, follicular variant, papillary thyroid carcinoma, renal metastasis*

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Introduction

Differentiated thyroid carcinoma (DTC) is the most common endocrine malignancy and accounts for < 1% of malignant neoplasms in humans.[1,2] Papillary and follicular carcinomas of the thyroid gland are often referred together as DTC. They are characterized by an indolent course with a 10-year survival rate as high as 80–95%.[3] DTC can sometimes have unusual metastatic presentation. Initial presentation of metastatic disease has been reported in 1–12% of DTC being less frequent in papillary (~2%) than in follicular (~10%) thyroid carcinoma.[1] Distant metastases are seen in a minority of patients and the reported rates of occurrence range from 4% to15%.[4] The major sites of distant metastases from DTC are the lungs and bones while minor sites include the brain, liver, skin, and muscle. In contrast, renal metastases from DTC are extremely rare. Ahmed *et al*. reported only one case of DTC metastasizing to the kidney among 3500 patients at their institution from December 1975 to September 2005.[5] To the best of our knowledge, only about 30 cases have been reported in the English literature to date. The overall prevalence of renal metastasis from DTC is only 0.47%.[6] Here, we report an interesting case of follicular variant papillary thyroid cancer (FV-PTC) presenting as primary renal neoplasm.

Case Report

A 72-year-old female, with previous history of hypertension and hypothyroidism, initially presented with abdominal pain and bilateral lower limbs swelling. She was on regular treatment with 50 mcg of thyroxine daily. On evaluation, contrast

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enhanced computed tomography (CT) scan of abdomen showed 5.5 cm × 4.4 cm sized well-encapsulated mass in the upper pole of right kidney [Figure 1]. The mass showed inhomogeneous contrast enhancement with central areas of necrosis suggestive of renal cell carcinoma. The patient underwent right laparoscopic radical nephrectomy. Gross examination of the right kidney specimen revealed a well circumscribed gray tan homogenous tumor measuring 4.5 cm × 4.5 cm × 3 cm in the upper pole. Microscopic examination offered a differential diagnosis of metastatic deposits from thyroid malignancy or a primary thyroid-like follicular carcinoma of the kidney) [Figure 2]. Immunohistochemistry performed showed that the cells were strongly positive for pan-cytokeratin, thyroid transcription factor-1 and thyroglobulin [Figure 2], suggesting metastatic deposits from thyroid malignancy. Clinical examination of patient's neck at this point revealed palpable thyroid nodules in the both lobes. Ultrasonography (USG) of the neck showed 2.1 cm × 1.7 cm × 1.5 cm (R) and 2 cm × 1.5 cm × 1.6 cm (L) hypoechoic nodules with peripheral eggshell calcification with interruptions [Figure 3]. There were no suspicious appearing lymph nodes in the central or lateral compartment of the neck. USG guided fine needle aspiration cytology of nodules in bilateral lobes was then performed. Cytology smears showed varying sheets of follicular cell groups with nuclear irregularity, fine chromatin, occasional nuclear grooves, and intracytoplasmic inclusions suspicious for papillary thyroid carcinoma (Bethesda 6/6). A positron emission tomography-CT (PET-CT) was performed after injection of 10 mCi of ^{18}F-fluorodeoxyglucose (FDG). ^{18}F-FDG PET-CT maximum intensity projection image showed a hypermetabolic lesion in the left thyroid region [Figure 4]. Intense uptake was noted in a calcified nodule in the left lobe measuring 1.8 cm × 1.6 cm with maximum standardized uptake value (SUVmax) of 12.6, suggestive of neoplastic etiology [Figure 4]. Hypermetabolic lytic lesion with soft tissue component was seen in left anterior acetabular margin extending up to the left pubic bone with an SUVmax of 9.5 suggesting of skeletal metastasis [Figure 4]. Total thyroidectomy was performed. Histopathology report of the thyroidectomy specimen revealed a 3 cm × 2.5 cm × 1 cm

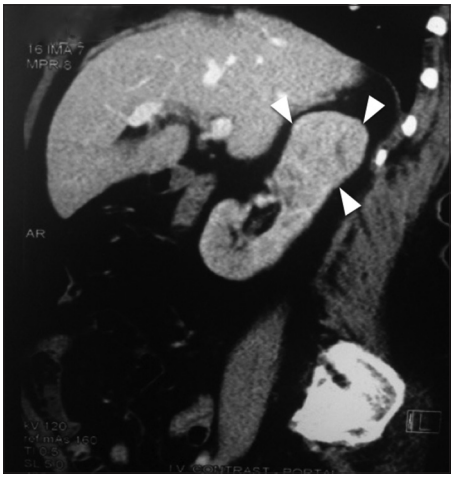

Figure 1: Contrast enhanced computed tomography image of the abdomen: 5.5 cm × 4.4 cm sized well encapsulated inhomogeneous mass (arrow heads) with central areas of necrosis in the upper pole of right kidney

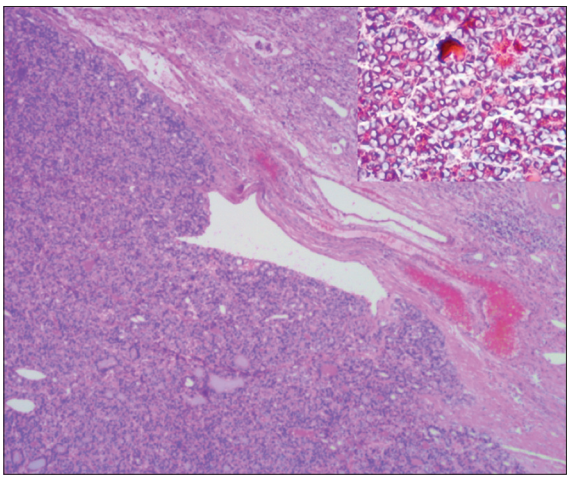

Figure 2: Microscopic examination of right nephrectomy specimen follicular cells suggesting metastatic deposits from thyroid malignancy or a rare primary renal tumor (thyroid like follicular carcinoma of the kidney) inset: Immunohistochemistry performed showed that the cells were strongly positive for pan-cytokeratin, thyroid transcription factor-1, thyroglobulin (as shown in figure), suggesting metastatic deposits from thyroid malignancy

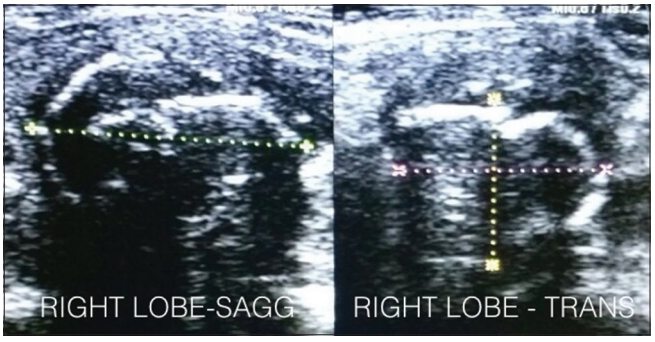

Figure 3: Ultrasound of neck revealed bilateral hypoechoic nodules with peripheral rim of egg-shell calcifications (left lobe nodule is shown)

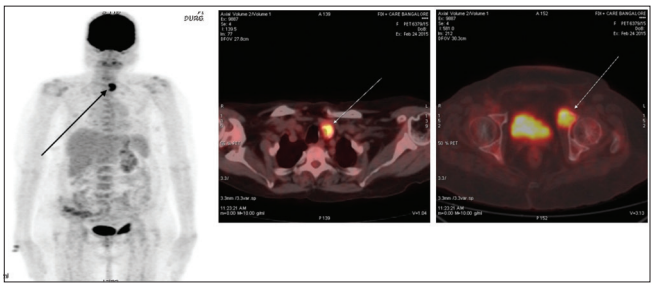

Figure 4: Fluorodeoxyglucose positron emission tomography-computed tomography maximum intensity projection image shows a hypermetabolic lesion in the thyroid and left acetabular region. Transaxial fused ^{18}F-fluorodeoxyglucose positron emission tomography-computed tomography image shows hypermetabolic calcified nodule (black arrow) in the left lobe of thyroid gland with maximum standardized uptake value of 12.6 (arrow) and hypermetabolic lytic lesion in left acetabulum with maximum standardized uptake value of 9.5 (arrow)

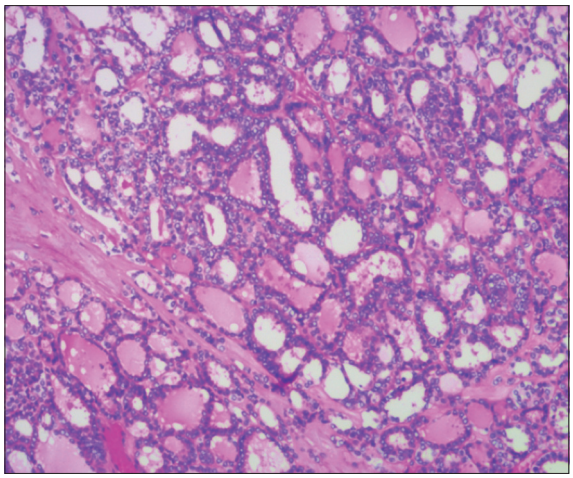

Figure 5: Histopathology image of thyroidectomy specimen revealed features consistent with follicular variant of papillary thyroid carcinoma with vascular invasion

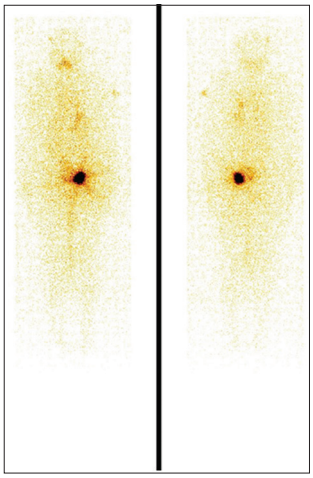

Figure 6: Postthyroidectomy iodine whole body scan image shows increased focal tracer uptake in the left acetabular region corresponding to the metastatic lytic lesion. No tracer uptake seen in the region of thyroid bed

nodule with areas of calcification and microscopic features were consistent with FV of PTC with vascular invasion in the left lobe and nodule in the right lobe revealed encapsulated variant of PTC, with no vascular or tumour capsular invasion [Figure 5]. Postoperative iodine whole body scan (WBS) showed increased focal tracer uptake in the lytic lesion in the left acetabulum and no evidence of tracer uptake in the region of thyroid bed [Figure 6]. High dose radioactive iodine therapy was advised for the patient.

Discussion

The presence of distant metastases reflects advanced clinical presentation, associated with higher mortality rate, especially in elderly patients. The primary sources of metastases to the kidney in decreasing order of frequency are breast, lung, intestine, contralateral kidney, stomach, ovary, cervix, pancreas, uterus, and prostate. Metastasis from thyroid is very rare. Metastases to the kidney from papillary and follicular thyroid cancer are found in 2.8–3.8% and 6–20% of cases, respectively.[7] Follicular thyroid carcinoma spreads through hematogenous route hence metastasis to kidney is relatively more common. FV of PTC metastasizing to kidney has been reported in just ~ 10 cases in literature. Diagnosis of the kidney metastasis preceding the knowledge of the primary thyroid neoplasm has been reported in very few cases. Due to the rare occurrence of renal metastases from DTC, the best management for this condition is unclear. If the renal metastasis is the only metastatic site, it may be reasonable to perform nephrectomy in appropriate cases. Renal metastases of PTC may retain adequate levels of sodium iodide symporter expression, and hence, ^{131}I therapy can be a feasible and effective treatment, particularly in those with multiple metastatic sites. However, there are no data showing the efficacy of ^{131}I for the treatment of renal metastases. Sorafenib, a tyrosine kinase inhibitor that targets several molecular signals involved in the pathogenesis of DTC, can be used in the treatment of advanced or metastatic ^{131}I-refractory DTC.[5]

Most metastases of well-differentiated thyroid cancer alternatively accumulate either ^{131}I or ^{18}F-FDG, according to tumor differentiation ("flip-flop" pattern).[8] Hence, tumors that take up radioactive iodine are less likely to yield positive ^{18}F-FDG PET-CT scans. Patients with larger volumes of FDG-avid disease or higher SUV's are less likely to respond to radio-iodine and have a higher mortality over a 3-year follow-up compared with the patients with no FDG uptake. Only a few metastases exhibit simultaneous ^{131}I or ^{18}F-FDG uptake indicating a mixed population of well-differentiated and dedifferentiated cells.[9,10] Metastatic lesion involving left acetabulum, in this case, was both iodine and FDG avid, which is a rare occurrence and likely indicates varying stages of dedifferentiation.

Conclusion

DTC can have unusual metastatic presentation. PTC metastasizing to the kidney is rare with about 30 case reports in the English literature. It is important to clarify if the renal tumor is a primary thyroid-like follicular carcinoma of the kidney or a secondary deposit of the DTC. Management options include surgery, radioiodine ablation, and chemotherapy. We also report dual avidity (^{18}F-FDG-PET and ^{131}I-WBS) of skeletal metastasis in PTC indicative of varying stages of de-differentiation that PTC and emphasizing the importance of multimodal imaging techniques that need to be used in staging of DTC during the treatment course.

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Conflicts of interest

There are no conflicts of interest.

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