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CASE REPORT

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Metastasis of Renal Clear Cell Carcinoma to Thyroid Gland Mimicking Adenomatous Goiter

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Summary

Background: Renal cell carcinoma is an interesting tumor due to its unpredictable behavior. Common metastatic sites of renal cell carcinoma are the lungs, lymph nodes, bones and liver. Concurrent thyroid metastasis of clear cell carcinoma is uncommon but it can appear as a rapidly growing cervical, painless nodular mass.

Case Report: We report a case of a 56-year-old male patient with clear cell renal carcinoma confirmed on a histopathological examination. The patient noticed a rapidly growing mass in the thyroid region when receiving medical anticancer therapy. Because of that, gray-scale thyroid ultrasonography and a fine-needle aspiration biopsy were performed. The histopathological examinationof the biopsy specimen revealed a lesion composed of malignant epithelial cells compatible with metastasis of renal carcinoma.

Conclusions: In patients with with a history of RCC, both past and present, a thyroid mass, especially co-existing with an adenomatous goiter, should prompt a work-up for thyroid metastasis.

MeSH Keywords: Carcinoma, Renal Cell • Goiter • Neoplasm Metastasis • Thyroid Nodule

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Background

Renal cell carcinoma (RCC) is the most frequent renal malignancy and comprises approximately 3% of all malignancies [1]. Metastases of RCC usually occur in the lymph nodes, lungs and bones [2]. Thyroid metastasis is an uncommon entity. Despite its rich vascular supply, metastatic thyroid nodules comprise only 2–3% of all thyroid malignancies [1,3]. Metastases in the thyroid gland occur more frequently in follicular adenomas than in the normal thyroid tissue [4]. They can occur many years after initial diagnosis but are extremely rare in clinical practice. In autopsy series, the incidence of metastasis to the thyroid gland ranges from 0.5% to 24% in high-stage malignancies [5]. Thyroid metastases of RCC usually occur after nephrectomy, but in some cases they can be found before the primary malignancy [6]. Herein, we presented radiologic and cytopathologic findings of a patient diagnosed with RCC who had ametastatic thyroid nodule.

Case Report

A 56-year-old man was referred to our hospital because of weight loss and left flank pain. A left renal mass was found on ultrasound imaging. On abdominal magnetic resonance imagining (MRI), there was an exophytic, hypervascular, solid mass, measuring 83×83×97 mm, with a heterogeneous signal in the middle-lower zone of the left kidney. There were also high signal areas in T2-weighted images, suggesting necrosis in the center of the mass, and an extension to the renal sinus with sparing of the renal vessels. The MRI findings were compatible with a malignant renal tumor. In the right adrenal gland, there was a mass with similar signal characteristics as the renal mass, measuring 48×78×76 mm (Figure 1A, 1B). Two weeks later, the patient underwent left total nephrectomy and right adrenalectomy. The histopathological examination reported clear cell renal carcinoma with Fuhrman grade 4 and adrenal metastasis without infiltration of the Gerato capsule,

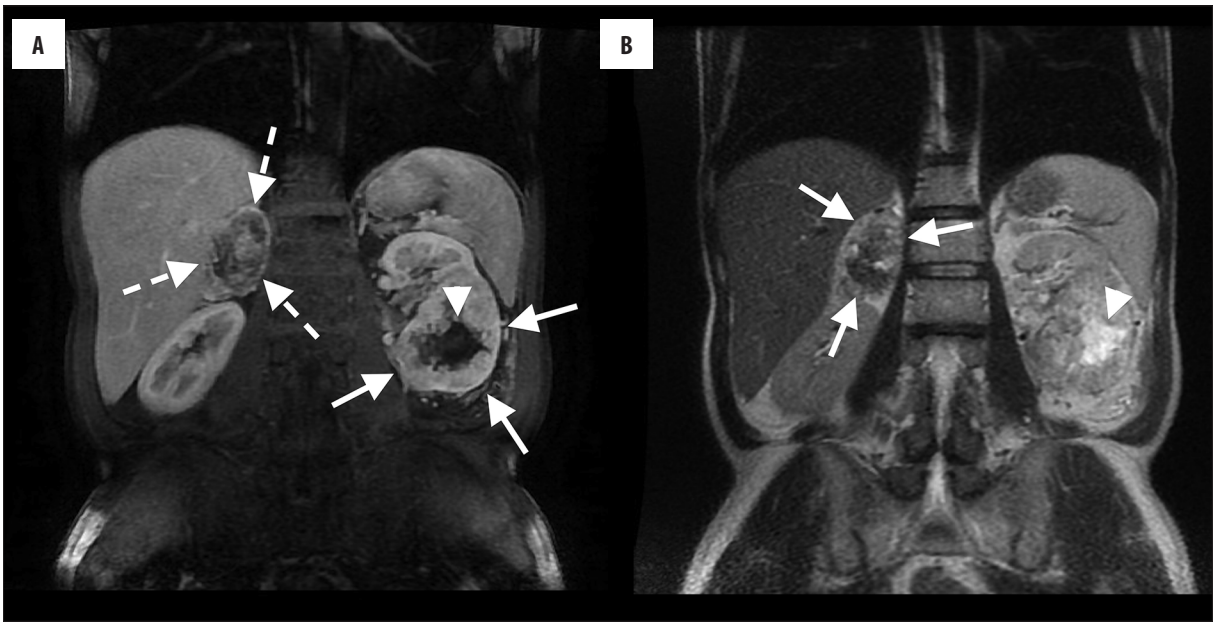

Figure 1. (**A**) Coronal abdominal magnetic resonance imaging. Post-contrast T1-weighted imaging (WI) demonstrated a mass originating from the middle and lower zone of the left kidney (arrows), with irregular contours and 83×97 mm in size. The mass enhanced post-contrast except for necrotic areas (arrow head) similarly to another mass in the right adrenal with heterogeneous enhancement (dashed arrow). (**B**) On T2WI, the central area of the mass is hyperintense due to necrosis (arrow head). Another mass in the right adrenal gland (arrows), 48×76 mm in size, whose signal characteristics are similar to those of the renal mass.

perirenal fat, renal artery/vein, ureter and no involvement of the surgical border (Figure 2A). After the surgery, a Positron Emission Tomography/Computed Tomography (PET/CT) study was performed for the purpose of re-staging. On PET/CT, there were metabolically active areas in the thyroid right lobe and in upper abdominal lymph nodes. Because of metabolically active areas in the thyroid gland, an ultrasound imagining was performed and a hypoechoic, round-shaped, solid nodule with macrolobulated contours, measuring 30×22 mm, was found along with multiple oval-shaped, hypoechoic, solid nodules (Figure 3). Subsequently, a fine-needle aspiration biopsy (FNAB) was performed from the nodule that was metabolically active on PET/CT and from the round-shaped, hypoechoic nodule found on ultrasound imaging. The FNAB reported atypical epithelial cells that had eosinophilic or clear cytoplasm, with large nuclei and nucleoli (Figure 2B). Follicular cells were not seen in the specimen. Additionally, colloidal material was not seen in the background. The results confirmed that the nodule was a metastatic lesion containing malignant epithelial cells in both cytology and cell blocks. Clinical and pathological data, together with immunostaining carried out in cell blocks and cytospin slides (negativeness of tyroglobulin, TTF-1, Calsitonin and positiveness Vimentin, Pax8 and EMA) confirmed the diagnosis of metastatic renal clear cell carcinoma (Figure 2C).

Discussion

Metastases from non-thyroid malignancies to the thyroid gland have been reported to have a wide range of prevalence, from 1.9% to 24%, in autopsy studies. The low frequency of metastasis to the thyroid can be explained by high iodine and oxygen concentrations as well as a high intrathyroidal vascular flow [7]. Because of these reasons, the thyroid is not a likely site for malignant metastatic cells. Iodine concentrations in the adenomatous goiter are lower than in the normal thyroid tissue and therefore patients with malignant diseases who have an adenomatous goiter have a greater risk of thyroid metastases [4]. Based on a recent review of the literature, the most common non-thyroid malignancies that metastasize to the thyroid gland are renal cell (48.1%), colorectal cancer (10.4%), lung cancer (8.3%), breast carcinomas (7.8%), and sarcomas (4.0%) [8].

Renal cell carcinoma can develop late and/or as a solitary metastasis. Although metastatic foci are present in about 25% of RCCs at the time of diagnosis of the primary malignancy (synchronous), metastatic disease can develop after many years of dormancy (metachronous). Moreover, solitary metastasis from RCC occurs with an incidence rate of about 1–4%, of which about 1% occur in the thyroid gland [9].

It is reported that metastasis of RCC can be seen even 10–20 years after diagnosis [10]. Our patient had a left radical nephrectomy 2 weeks before the metastasis to the thyroid gland was seen. The usual symptoms of metastatic RCC to the thyroid gland include enlarged solitary or multiple neck swellings, painless palpable thyroid nodules, shortness of breath, vocal changes, wheezing and difficulty in swallowing, but most secondary metastases of the thyroid are asymptomatic. Moreover, we may not be able to differentiate them with radiological studies as both types of these lesions appear as "cold" nodules on radioiodine uptake studies or as "inhomogeneous, hypoechoic" masses on ultrasound. They also show non-specific metabolic activity on PET/CT scans, as was seen in our patient.

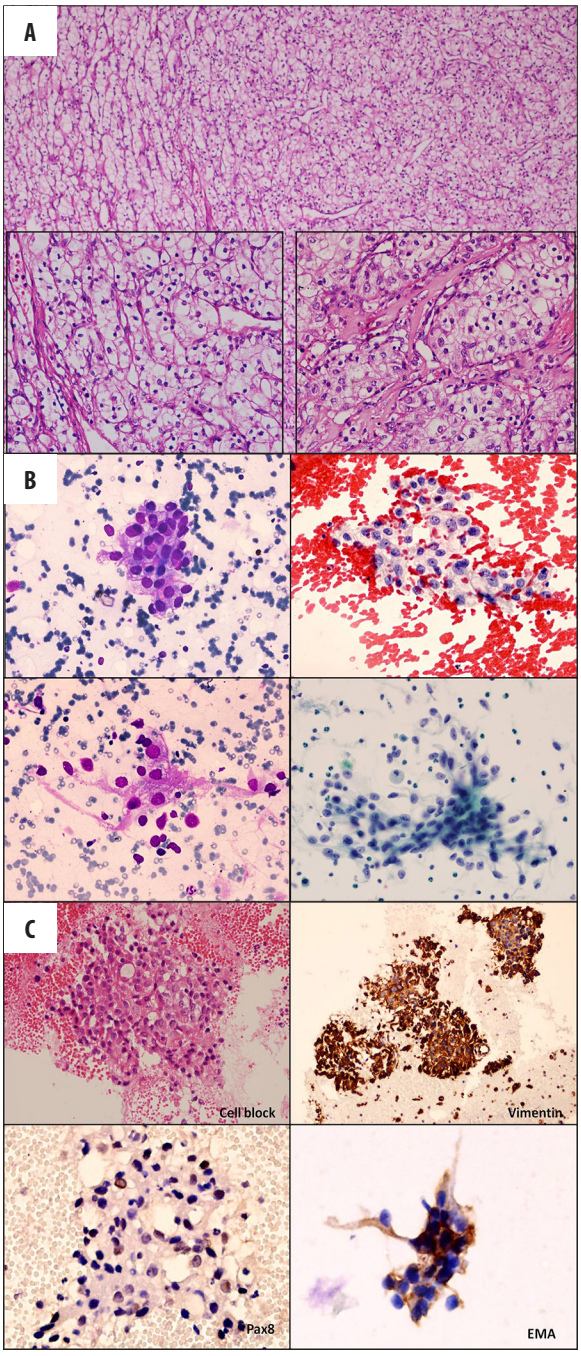

Figure 2. (**A**) Clear cell RCC; Fuhrman nuclear grade 2 (left side) and 4 (right side) (Nephrectomy specimen, Haematoxylin & Eosin ×40, ×200). (**B**) Fine needle aspiration biopsy from the thyroid nodule; atypical epithelial cells with abundant clear or vacuolated cytoplasm, vesicular nucleui and concipious nuclei in the background of scant or no colloid (MGG left side, PAP right side ×400). (**C**) Cell block preparation; tumoral cells showed positive immunostaining for Vimentin, Pax8 and EMA.

Kobayashi et al. reported that metastasis from RCC has some characteristic ultrasonographic finding, such as prominent, chaotic, intra-tumoral vascularity and tumor thrombi [11]. They also stated that these findings are not specific to this disease. Therefore, all patients in whom

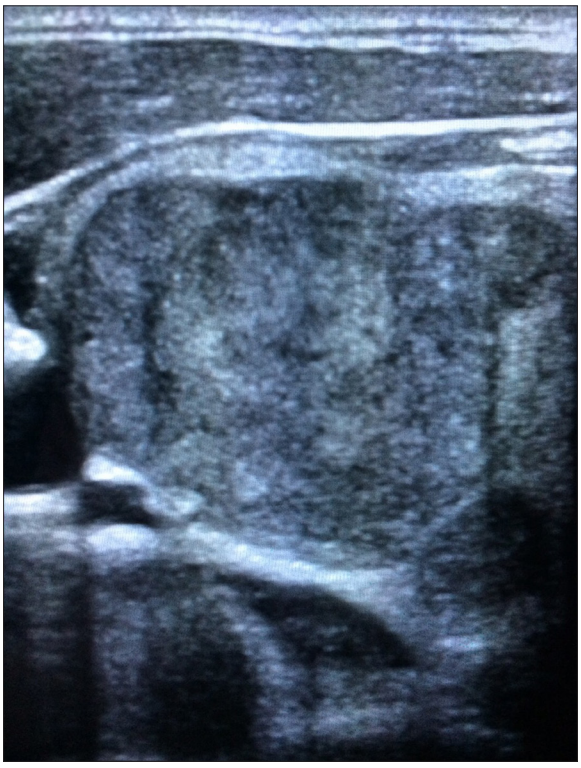

Figure 3. Ultrasound imaging showed a hypoechoic, nodular, solid mass in the thyroid gland, 30×22 mm in size, with microcalcifications and macrolobulated contours.

there is clinical or radiologic evidence of a mass in the thyroid gland require a FNAB or a core-needle biopsy of the mass. FNAB is useful in the diagnosis of metastatic RCC to the thyroid. In FNAB, distinctive features differentiate between benign follicular nodules and metastatic nodules such as poor colloid matrix and absence of follicular cells. Metastatic nodules contain atypical epithelial cells with clear cytoplasm and large nuclei, which helps to differentiate them from well-differentiated primary thyroid carcinomas such as follicular carcinoma or papillary carcinoma. Moreover, differentiation between clear type variants of the primary thyroid carcinomas and metastatic nodules can be done with clinical history and immunohistochemistry (negative thyroglobulin, TTF-1 and calcitonin). Clusters of cells with sharp borders, abundant clear cytoplasm and large, oval, moderately hyperchromatic nuclei with visible nucleoli should raise the suspicion of a metastatic RCC.

Our patient had thyroid gland enlargement due to both metastatic RCC and multinodular goiter. In such patients, attempts to establish diagnosis with FNAB may yield false-negative results if a benign nodule is sampled. In our patient, detection of the dominant nodule with distinctive features differentiating it from other nodules in the thyroid as well as the use of sonography-guided FNAB helped us reach the final diagnosis. In some cases, FNAB may not be helpful in differentiating primary tumors from metastases. However, if the pathologist is aware of the oncologic history of the patient, the tumor pathology may be revealed by immunohistochemical techniques.

Conclusions

In patients with with a history of RCC, both past and present, a thyroid mass, especially co-existing with adenomatous goiter, should prompt a work-up for thyroid metastasis.

Conflict of interest statement

The authors of this paper have no conflicts of interest, including specific financial interests, relationships and affiliations relevant to the subject matter or materials included.

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