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Case Report
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Renal Cell Carcinoma with Thyroid and Bilateral Adrenal Gland Metastases

Tiroid ve Bilateral Adrenal Gland Metastazı olan Renal Hücreli Karsinom

[1]Bartu Badak, [1]İbrahim Kısalar, [1]Arda Şakir Yılmaz, [2]Emel Yaldır

[1]Department of General Surgery, Eskisehir Osmangazi University, Faculty of Medicine, Eskisehir, Türkiye
[2]Department of Pathology, Eskisehir Osmangazi University, Faculty of Medicine, Eskisehir, Türkiye

BB. 0000-0003-3465-8719
İK. 0009-0002-2316-0093
ASY. 0000-0003-1269-0814
EY. 0000-0001-7297-9869

Correspondence / Sorumlu yazar:
Arda Şakir YILMAZ

Department of General Surgery, Eskisehir Osmangazi University, Faculty of Medicine, Eskisehir, Türkiye

e-mail: dr.ardayilmaz@hotmail.com

Abstract: Renal cell carcinoma is the most common type of malignant kidney disease, representing more than 90% of cases. It frequently metastasizes to the lungs, bones, liver and brain. Thyroid and adrenal metastases are rare. In this case report, we present a 64-year-old man with renal cell carcinoma who developed bilateral adrenal metastases three years after right radical nephrectomy and thyroid metastases five years later. Renal cell carcinoma has a high metastasis rate and requires careful follow-up. The increasing use of non-invasive imaging modalities has increased the detection rates of rare adrenal and thyroid metastases. Due to the rarity of such cases, standard treatment protocols are not well defined, emphasizing the need for careful follow-up even years after surgery..
Keywords: Renal cell carcinoma, thyroid, adrenal, metastasis

Özet: Renal hücreli karsinom, vakaların %90'ından fazlasını temsil eden en yaygın malign böbrek hastalığı türüdür. Sıklıkla akciğerlere, kemiklere, karaciğere ve beyne metastaz yapar. Tiroid ve adrenal metastazlar nadirdir. Bu vaka raporunda, sağ radikal nefrektomiden üç yıl sonra iki taraflı adrenal metastaz ve beş yıl sonra tiroid metastazı gelişen renal hücreli karsinomlu 64 yaşındaki bir erkek hasta sunduk. Renal hücreli karsinomun yüksek metastaz oranı vardır ve dikkatli takip gerektirir. Non-invaziv görüntüleme yöntemlerinin artan kullanımı ile nadir görülen adrenal ve tiroid metastazlarının da tespit oranlarını artırmıştır. Bu tür vakaların nadir olması nedeniyle standart tedavi protokolleri iyi tanımlanmamıştır; bu da ameliyattan yıllar sonra bile dikkatli bir izlemenin gerekliliğini vurgulamaktadır.
Anahtar Kelimeler: Renal hücreli karsinom, tiroid, adrenal, metastaz

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1. Introduction

Renal cell carcinoma (RCC) is the most common form of malignant kidney disease, accounting for over 90% of all malignant kidney cases. RCC ranks as the sixth most frequent cancer type in men and the tenth in women (1). Men are generally more affected, with a male-to-female ratio of 1.5:1. The incidence rate is highest among patients aged 60 to 70 years (2). RCC has several histological variants, with clear cell RCC (75%), papillary RCC (10-15%), and chromophobe RCC (5%) being the most prevalent forms, collectively representing 90% of RCC cases (3). The bones, liver, and lungs are the most common sites of metastasis in RCC, with thyroid metastases typically emerging around ten years after initial diagnosis (4). In recent years, RCC diagnoses have increased due to incidental discoveries during diagnostic investigations conducted for other purposes (2). Ipsilateral adrenal metastasis occurs in 7-23% of RCC cases, whereas bilateral adrenal metastasis is quite rare (5). The thyroid gland and the head and neck region are also uncommon sites for metastasis (4).

In our case, we aim to present a patient who developed bilateral adrenal metastasis three years after right radical nephrectomy and thyroid metastasis observed in the fifth year, in light of the literature.

2. Case Report

A 64-year-old male patient, under follow-up for known RCC, presented to our clinic due to thyroid nodules detected during his 5-year follow-up. The patient had undergone a right radical nephrectomy for RCC five years earlier and subsequently received treatment with the tyrosine kinase inhibitor sunitinib. During the patient's 3-year follow-up, a computed tomography (CT) scan revealed suspicious areas in both adrenal glands. A subsequent dynamic adrenal CT scan showed hypervascular lesions in the axial sections, with precontrast high densities and 70% absolute washout values, indicative of metastases. These lesions measured 4 cm in the right adrenal gland and 4.2 cm in the left adrenal gland. Percutaneous biopsy of these newly developed lesions confirmed RCC metastasis. The patient continued oncological treatment, and at the 5-year follow-up, a control thoracic CT scan revealed hypodense, nodular lesions with calcified foci in both thyroid glands (Figure 1). Consequently, the patient was referred to our clinic.

Upon reevaluation, we requested a thyroid ultrasound. The ultrasound revealed a cystic nodular lesion measuring 11x9x15 mm in the right thyroid lobe and a hypoechoic lesion with calcified foci measuring 9x10x15 mm in the left lobe. Fine-needle aspiration biopsy from the left thyroid lobe showed atypical epithelial cells with clear cytoplasm, nuclear enlargement, and prominent nucleoli forming papilla-like structures in Papanicolaou-Giemsa-stained cytocentrifuge smears and cytoblock sections (Figure 2). Immunohistochemistry revealed positivity for PAX2 and CD10, weak focal positivity for RCC, and negativity for thyroid transcription factor-1 (TTF-1) and thyroglobulin (Figures 3-5). Based on these cytopathological findings and the patient's history, the diagnosis was determined to be RCC metastasis. The patient was subsequently evaluated by the oncology council and referred to the medical oncology clinic for further oncological follow-up.

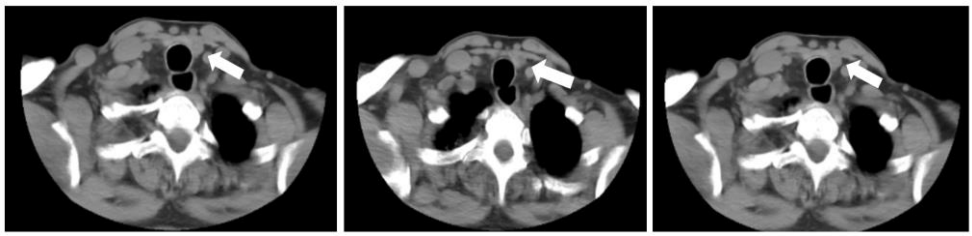

Figure 1. A nodule thought to be metastatic was observed in the left thyroid lobe.

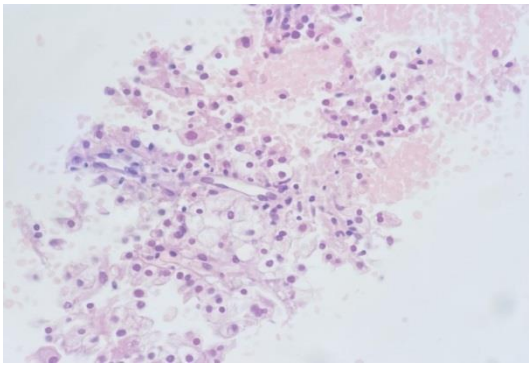

Figure 2. Tumoral cells with clear cytoplasm and pleomorphic nuclei in the cell block, along with features consistent with tumor necrosis, H&E stain.

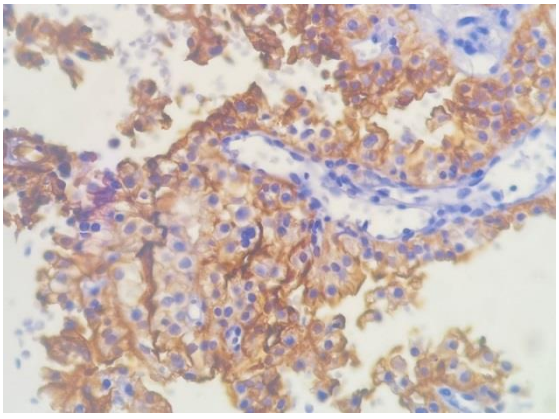

Figure 3. CD10 positivity, immunohistochemical staining.

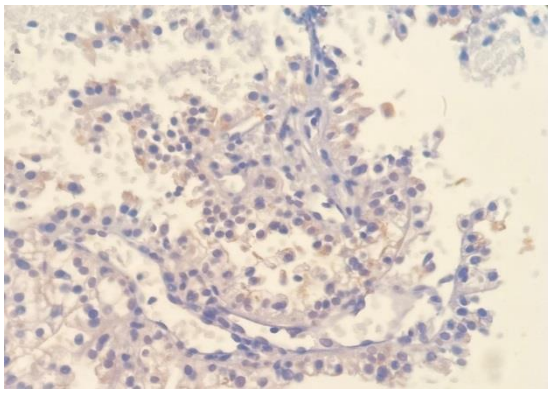

Figure 4. Weak focal positivity for RCC, immunohistochemical staining.

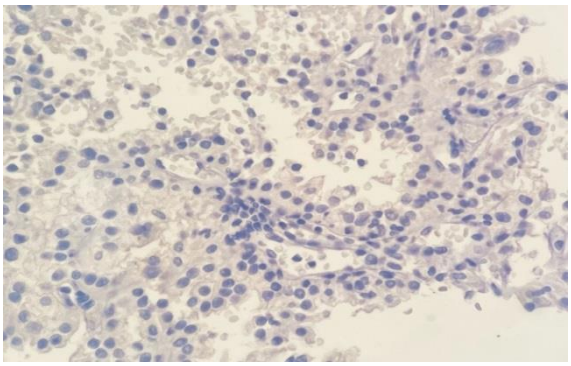

Figure 5. TTF-1 negativity, immunohistochemical staining.

3. Discussion

Approximately 25-30% of patients diagnosed with RCC present with metastatic disease at the time of diagnosis. Furthermore, 20-40% of patients with initially localized disease may develop metastases after surgical treatment. Therefore, the frequency of metastasis in RCC is quite high, necessitating close monitoring of these patients. RCC most commonly metastasizes to the lungs, but bones, liver, and brain are also frequent sites of metastasis. Less commonly, metastases can occur in the adrenal glands, lymph nodes, and other organs.

Thyroid metastasis from RCC is rare and often presents as a rapidly growing, painless cervical mass during follow-up after nephrectomy. Similar to primary thyroid tumors, thyroid metastasis can manifest with symptoms such as hoarseness, dysphagia, dyspnea, neck pain, cough, and epistaxis. The diagnostic algorithm for thyroid metastasis from RCC is not significantly different from that for primary thyroid tumors. Fine-needle aspiration biopsy can establish the diagnosis (6). Markers used to identify primary thyroid malignancies, such as TTF-1 and calcitonin, are negative, whereas immunohistochemical markers such as cytokeratin, vimentin, and CD-10 are positive for metastatic renal cell tumors (7).

Despite the rarity of thyroid metastasis from RCC, RCC is the most common malignancy metastasizing to the thyroid, accounting for 48.1% of such cases (8-9). Other common malignancies metastasizing to the thyroid include colorectal cancer (10.4%), lung cancer (8.3%), breast cancer (7.8%), and sarcomas (4.0%) (10).

The likelihood of adrenal metastasis from RCC is relatively low. Among patients undergoing nephrectomy, the incidence of isolated ipsilateral and contralateral adrenal metastasis is 3-5% and 0.7%, respectively. The literature reports the rate of bilateral adrenal metastasis to be less than 0.5% (11-12).

The widespread use of non-invasive radiological imaging methods, such as ultrasonography and CT, has led to an increase in the diagnosis of such lesions. In our case, the diagnosis was made during routine CT follow-up in the absence of any symptoms and was confirmed by ultrasound and histopathological examination.

Surgery for thyroid metastases is intended as palliative therapy and local control of metastatic disease and should be part of a broader systematic and multidisciplinary approach (13). Whether there is a difference between total and subtotal thyroidectomy is a controversial issue. Many studies suggest that there is no difference in survival between the two operations. Beutner et al. found that 5-year survival was better with total thyroidectomy than with non-total thyroidectomy, but the results were not statistically significant (P=0.49) and suggested that there was no improvement in survival when compared with total thyroidectomy and partial thyroidectomy (14). Another retrospective study from Europe showed that 5-year overall survival with thyroid metastasectomy was 51% (15).

The decision regarding the choice of treatment for metastatic renal cell carcinoma depends on different factors, including the extent of disease, sites of metastatic involvement, and prognostic risk factors such as time from diagnosis to treatment and laboratory findings. Due to the limited number of cases in the literature, it is impossible to establish a standard treatment protocol or gain definitive prognostic information for RCC patients with thyroid and bilateral adrenal metastases. Therefore, it is crucial to be vigilant for metastases in the follow-up of RCC patients, even years after radical nephrectomy.

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