Internist's Tumour into Thyroid: A Case Report

Abstract

Renal cell carcinoma (RCC) is well known for its unpredictable and diverse behaviour, with tendency to cause synchronous or metachronous metastasis to unusual site, which is why it is called the "internist's tumour." Although thyroid gland is an infrequent site for metastasis of different primary malignancies, metastatic RCC is one of the most common secondary thyroid malignancies. Diagnosis relies on a high index of suspicion in patients with prior RCC, combined with cross-sectional imaging and biopsy. A case of secondary thyroid neoplasm from RCC after 13 years of radical nephrectomy is described with clinicopathological features and literature review.

Keywords: *Hemithyroidectomy, nephrectomy, renal cancer, secondary thyroid malignancy, sorafenib*

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Case Presentation

We present an 87-year-old man who underwent left radical nephrectomy in 2008 for Grade 3 pT3b Renal Cell Cancer. His past medical history includes transient ischaemic attack and hypertension. He was discharged after cancer-free surveillance for 10 years and he also had completed "SORCE" (A phase III randomised double-blind study comparing sorafenib with placebo in patients with resected primary renal cell carcinoma at high or intermediate risk of relapse) study immunotherapy with Sorafenib within this timeframe (placebo vs. sorafenib as adjuvant treatment).

He was subsequently referred by his general practitioner to Ear, Nose, Throat (ENT) services in December 2020 with a gradually enlarging, painless right-sided thyroid lump without compressive symptoms or symptoms of over/underactive thyroid. There was no history of neck radiation therapy. General examinations including vital parameters did not show any significant abnormality. Loco-regional evaluation revealed a 4 cm, right-sided firm thyroid nodule, and subsequent flexible endoscopy showed bilateral mobile vocal cords.

A thyroid ultrasound (USS) in December 2020 demonstrated right-sided U3 (intermediate) nodule without lymphadenopathy. Thyroid function test was normal. Later on, he underwent a USS-guided thyroid biopsy, which was inconclusive (Thy 1). His follow-up appointment with ENT organised due to inability to reach a definitive diagnosis showed the lump had increased by more than 1 cm in size in a year without any retrosternal extension or cervical lymphadenopathy. He, hence, underwent right hemithyroidectomy in October 2022 and the final histopathology report showed metastatic clear renal cell carcinoma (RCC) [Figure 1], confirmed with positive immunohistochemistry (IHC) for Vimentin, CD10, and PAX8 [Figures 2-4] but negative for CK7, CK20, and thyroid transcription factor-1 [Figure 5].

Patient had staging chest, abdomen, and pelvic computed tomography (CT) and fluorodeoxyglucose-positron emission tomography in November 2022, which showed an 18-mm indeterminate right renal cortical nodule without any other definitive metastasis. This finding was not present in previous imagings. He was discussed in a multidisciplinary team meeting, and the consensus was to repeat CT in 6 months to evaluate the malignant potential of the newly diagnosed renal lesion.

Discussion

Introduction

RCC accounts for 3% of all cancer cases globally[1] and is the most common urological cancer (accounts for approximately 90% of all kidney malignancies). Approximately one-third of patients will have metastatic

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disease at diagnosis. Most common sites of metastases are lung (71%), lymph nodes (49%), bone (36%), liver (21%), adrenal (9%), and thyroid (0.6%).[2]

Primary origin and pathophysiology of secondary neoplasm of thyroid

In a clinical series of 62 cases of secondary neoplasm of thyroid gland reported by Pusztaszeri *et al*., the kidney was the most common primary tumour site (39%), followed by the lung (26%), breast (22%), and colon (3%).[3]

Metastatic deposits have a predilection for hypervascular organs. Despite the extensive vascularity of the thyroid gland, it is an uncommon site for secondary metastasis.

The widely accepted hypothesis postulated by Willis[4] described the glandular microenvironment including its unique feature of rapid arterial blood flow and high agglomeration of oxygen and iodine as potential inhibiting factor, which washes off circulating tumour cells preventing their anchorage and secondary growth. Heffess *et al*.[5] suggested that alteration of this environment due to concomitant presence of non-malignant thyroid abnormalities might lead to the development of metastatic lesions.

Szymańsk *et al*.[6] found alteration in thyroid hormone metabolism and glandular environment up to 1/4th of patients with RCC treated with a tyrosine kinase inhibitor (TKI). Could there be any interlink between thyroid metastasis and TKI-related thyroid dysfunction as our patient was treated with Sorafenib?—this is difficult to ascertain.[6]

Period of latency

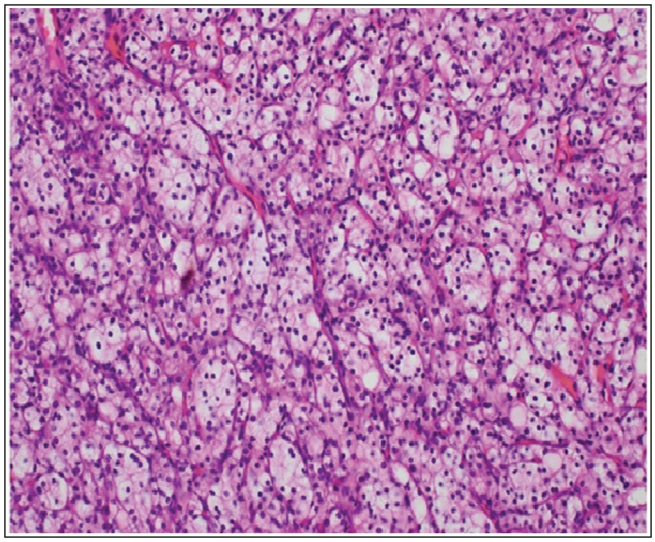

Figure 1: Clear tumour cell nests with sinusoidal vasculature

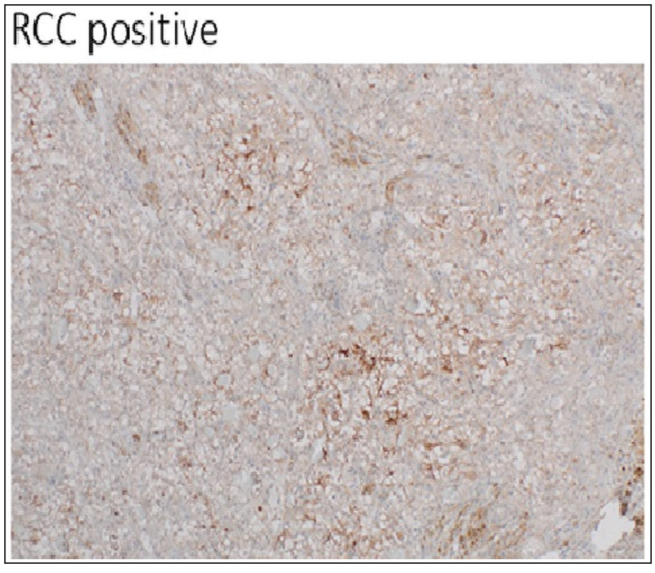

Figure 2: IHC stain—RCC marker carbonic anhydrase IX positive. IHC: immunohistochemistry

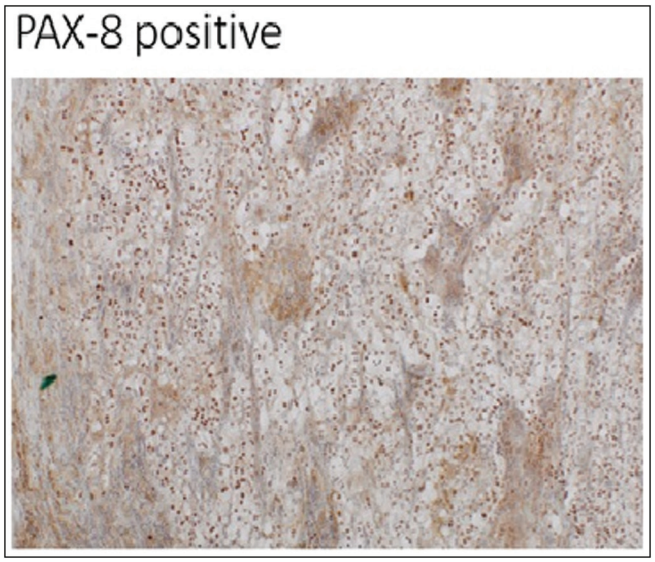

Figure 3: IHC stain—strong nuclear positivity in tumour cells for PAX 8. IHC: immunohistochemistry

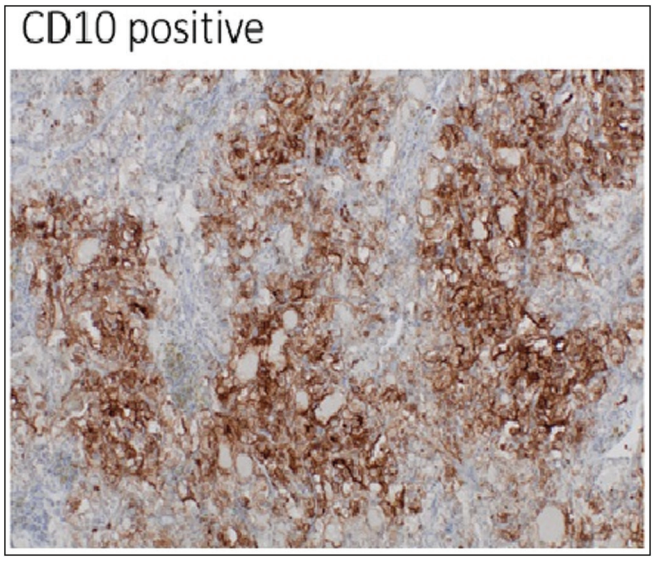

Figure 4: IHC stain—luminal and membrane positivity for CD10. IHC: immunohistochemistry

A retrospective clinical case series of 158 patients showed evidence of metastasis within 3 years of radical nephrectomy in 85% of cases.[7] However, solitary RCC metastasis to the thyroid can present even after 20 years of RCC diagnosis. The median interval between primary RCC diagnosis and thyroid metastasis was 106 months.[8] Our patient was diagnosed with metastatic spread of RCC to thyroid after 13 years of nephrectomy.

Preoperative work-up

Symptomatology of many patients with thyroid metastasis can be hardly distinguishable from those with primary thyroid disease. The patients may present with palpable, painless neck mass, or compressing symptoms within the central neck. Some patients can be asymptomatic and are diagnosed incidentally. Thyroid hormone profile usually stays within normal ranges.

In our case report, the patient was evaluated as per American Thyroid Association's revised guideline (2015). The diagnostic algorithm began with USS detecting thyroid nodule with intermediate malignant potential. Fine needle aspiration cytology, which remains the gold standard diagnostic tool for histopathological confirmation of thyroid malignancy, could not confirm thyroid malignancy in our case report. Hence, a clinical decision was made to offer right hemithyroidectomy based on clinical finding of rapid growth of thyroid lump, which finally brought out the rare finding of secondary deposit of RCC to thyroid validating importance of clinical insight inspite of the advancement of investigative tools.

Therapeutic modalities

Decision about the choice of treatment in metastatic RCC should be weighed individually and against disease factors including the bulk of the disease load, metastatic sites of concern/involvement, Kornofsky performance status, and patient's wish.

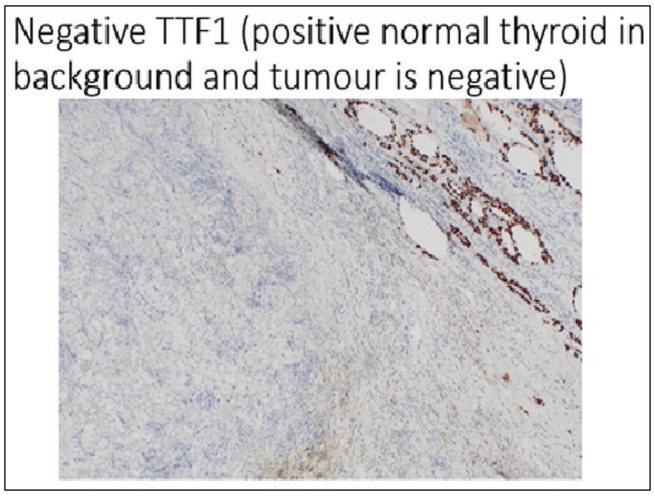

Figure 5: IHC stain—negative thyroid transcription factor-1. IHC: immunohistochemistry

Patient with unilateral disease in the absence of extrathyroidal metastasis and locally recurrent disease can be suitable candidate for hemithyroidectomy. However, the presence of bilobar or multifocal metastasis may warrant total thyroidectomy.

There is no evidence to support administering neoadjuvant targeted immunotherapy before thyroidectomy or adjuvant radiotherapy till date

Prognosis

Jackson *et al*.[9] opined following systematic review of six papers including 77 patients that median survival after secondary spread of RCC to the thyroid was 3.8 years (95% confidence interval: 2.0–5.2). As our patient is yet to have his first post-operative follow-up with us, it is too early to comment on his prognosis.

Conclusion

We hope our case report highlights the importance of maintaining low threshold to initiate investigations for patients presenting with unexplained thyroid mass with previous RCC, even if treated many years ago. Moreover, further studies should be designed to analyse the potential of the development of thyroid malignancy in patients treated with TKI

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Mr. Theokli performed hemithyroidectomy and followed up the patients for secondary thyroid malignancy.

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Authors' contribution

PKS researched literature and conceived the study. EN-J provided histology pictures as she did histology report for the patient. ME provided radiological images. SK was incharge for the case report. All authors reviewed and edited the manuscript and approved the final version of the manuscript

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of interest

There are no conflicts of interest.

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