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# A single thyroid nodule revealing early metastases from clear cell renal carcinoma: case report and review of literature

Marino Di Furia[a,*], Andrea Della Penna[a], Andrea Salvatorelli[a], Marco Clementi[b], Stefano Guadagni[a]

[a] Department of Applied Clinical Science and Biotechnology, University of L'Aquila, Via Vetoio, 67100 L'Aquila, AQ, Italy
[b] Department of Medicine, Health and Life, University of L'Aquila, Piazza S. Tommasi, 67100 L'Aquila, AQ, Italy

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ABSTRACT

*INTRODUCTION:* We report the case of an incidental solitary renal cancer cell (RCC) thyroid metastatic nodule treated by thyroidectomy.
*PRESENTATION OF CASE:* A 53 year male presented with a solitary, asymptomatic thyroid nodule. He was treated with left nephrectomy 1 year before for a RCC. Radiological standard follow-up was negative for secondary lesions but ultrasound (US) 12 months after surgery revealed a 1.5 cm solid nodule in the right lobe of the gland. Fine needle aspiration biopsy (FNAB) was inadequate and the patient was submitted to total thyroidectomy. Histology showed the presence of solitary metastasis from RCC. At 2 years follow-up, no evidence of recurrence has been found.
*DISCUSSION:* Solitary RCC metastasis to the thyroid usually occurs late from nephrectomy and have no specific US pattern. When FNAB provides an uncertain cytological results, the patient received thyroidectomy for primary thyroid tumors and diagnosis of metastases from RCC was incidentally made.
*CONCLUSION:* Thyroid nodules in a patient with history of malignancy can pose a diagnostic challenge. The presence of a solitary thyroid nodule in a patient with history of RCC should be carefully suspected for metastasis. We suggest to extend at neck the thorax and abdomen CT scan routinely recommended during the follow-up in high-risk cases. Thyroidectomy may result in prolonged survival in selected cases of isolated thyroid metastasis from RCC.



## 1. Introduction

Intra-thyroid Metastases (ITM) are very rare, approximately representing 1–2.4% of all malignant nodules [1].

Autopsy studies in patient who die for cancer suggest that these tumors are underdiagnosed with frequency up to 24.4% [2].

About half of these non-thyroid malignancies arise from RCC [3].

These metastases have not a typical symptomatology and show a late presentation from nephrectomy, making often impossible an early different diagnosis from primary thyroid tumors. Routine diagnostic techniques (US and CT scan) are unable to distinguish primary from secondary thyroid tumours. Cytological exam by fine FNAB has been shown to achieve an accuracy of over 90% for thyroid methastasis [4].

Appropriate management of ITM is controversial but thyroidectomy for RCC solitary metastases is a reasonable option to improve outcome and increase survival in selected patients.

We present a case of ITM from RCC unexpectedly detected after total thyroidectomy for a solitary nodule preoperatively classified as primitive thyroid tumour.

The work has been reported in line with the SCARE criteria [19].

## 2. Case report

A 53-years-old male underwent surgical visit for a single and palpable thyroid nodule. The patient was submitted to left nephrectomy for RCC (pT1c N0 Mx – G3) 1 year before. Follow-up showed no metastasis or locoregional recurrence with thorax/abdomen CT scan at 6 and 12 months performed according to ESMO Guidelines [5].

He referred no symptoms linked to thyroid hyperfunction and blood exams where unremarkable (FT3: 2.32 pg/mL, n.v. 1.8–4.6 pg/mL; FT4: 1.23 ng/dL, n.v. 0.9–1.7 ng/dL; TSH 1.76 μUI/mL, n.v. 0.3–4.2 μUI/mL). Clinical examination revealed a little asymptomatic nodule in the right lobe of the gland. No regional lymph node was detected with palpation. Thyroid US confirmed a 1.5 cm solid, hypoechoic nodule with intranodular vascularization in the right thyroid lobe, highly suspected for neoplasm. FNAB was inadequate. Therefore, the patient accepted

* Corresponding author.
*E-mail address:* marinodifuria@gmail.com (M. Di Furia).

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the surgical approach and a total thyroidectomy was performed with no early or late complication. Histology showed the presence of a single, white, partly capsulated nodule in the right thyroid lobe characterised by RCC+, CD10+, Vimentin +, TTF1− and Thyroglobulin−. This report, as suggested by immunohistochemistry and clinical history, was highly suggestive for metastasis from RCC. Two years after surgery no evidence of other site of tumor recurrence has been found.

## 3. Discussion

ITM represent less than 2.5% of all thyroid malignances [1]. Despite metastases are of diverse histogenesis and include a variety of carcinomas as well as sarcomas, melanomas, and hematologic malignancies, quite half of ITM rise from RCC [3].

Generally RCC diffuses in an unpredictable manner and can show a late recurrence as a notable feature. Clinical presentation of ITM is nonspecific and tumors are often unsuspected especially when metastases develop many years after the primary diagnosis. Recently it has been reported that in 67% of ITM, indication to thyroidectomy was for suspected primary thyroid malignancies or nodular goiter [6]. Also in our case, ITM was the first metastatic site during follow-up for RCC removed 1 years before and it was misinterpreted as a primary thyroid tumor.

In patients treated for RCC with radical nephrectomy, follow-up is carefully managed to establish local recurrence and/or the presence of metastases. This is stressed by the high incidence of recurrence of neoplasm that appear in almost 60% of the patients in the first year from diagnosis [7]. The recurrence of the neoplasm has to be identified as soon as possible because the possibility to obtain a radical resection decreases with increasing delay of diagnosis [8]. In literature, there are no current prospective randomized trials that help to evaluate the correct timing and/or which patients should be strictly evaluated for high risk of recurrence. However, important clinical and molecular factors, identified at primary diagnosis, emerge from long-term follow-up, showing which patients have an increased risk of recurrence and therefore have to be strictly followed [9]. According to these data, CT scans of thorax and abdomen are routinely carried out, with time intervals depending on risk factors. It is recommended to perform CT scans every 3–6 months in high-risk patients for the first 2 years, while a yearly CT scan is probably sufficient in low-risk patients [5]. Timing and duration of follow-up is controversy in literature for clinical and cost-effectiveness reasons.

In retrospective studies [10] it has been reported that thyroid metastases usually present in the context of widespread metastatic disease, more rarely they appear as a single mass. The reported interval of presentation for metachronous isolated ITM is very wide ranging from 68 to 130 months [11]. Our case represent an exception because ITM has been detected only 1 year after nephrectomy; this may be linked to the physical shape of the patient, who was very thin and immediately noted the nodule in the neck. Interestingly, the thorax/abdomen CT scans at 6 and 12 months after surgery did not target the ITM. The rarity of ITM do not allow to propose a routinely US or CT study of the neck. Our experience suggests that CT-scan proposed in ESMO follow-up should be extended to the neck without a significant increase of cost.

When ITM appears as single non-functioning nodule, often several years after nephrectomy, metastatic RCC may be misinterpreted as a primary thyroid tumor. US distinction between primary versus secondary thyroid neoplasm is almost impossible [12]. The commonly known US features of thyroid metastasis are nonspecific findings including nonhomogeneous hypoechogenicity, noncircumscribed margins, no calcifications, and increased vascularity [3]. The true metastatic nature of the tumor is recognized only after tumor sampling. FNAB has become an important tool in diagnosis of the thyroid nodules but in case of ITM, an accuracy ranging from 70% to 90% has been recently reported [3,11], and the most common primary tumor sites for which FNAB did not make the correct diagnosis were kidney and lung [3,11]. Noncontributory FNAB can result from inadequate sampling or interpretation difficulties. Increased vascularity, like showed in metastatic nodules from RCC, may be the most plausible reason for the low diagnostic yield of FNAB in relation to high blood contamination, which makes cytologic examinations more difficult [13]. Immunohistochemistry (HIC) can be able to differentiate between primary and secondary thyroid malignancies but it cannot be performed with FNAB specimens [3]. Another potential source of confusion in cytologic interpretation is the difficulty of distinguishing primary anaplastic thyroid carcinoma from metastatic high-grade malignancy. Positive immunostaining for thyroglobulin suggests a primary thyroid malignancy [12] remembering that only 20% to 30% of anaplastic carcinomas stain for thyroglobulin [14].

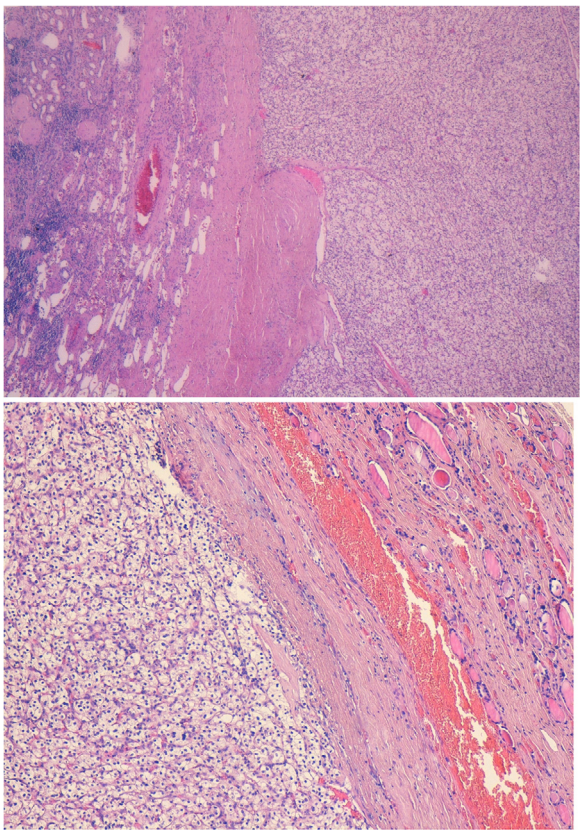

**Fig. 1.** Upper image: Primitive tumor (RCC), H-H, 4×. Lower image: Intra-thyroid Metastases (ITM) from RCC, H-H, 10×.

In our case, thyroid was the first metastatic site of a RCC diagnosed and removed 12 months earlier. US revealed a solid lesion suggestive of a neoplastic nodule but cytological examination after FNAB was inadequate. The patient was submitted to total thyroidectomy for suspected primary thyroid carcinoma according to the standard treatment of the thyroid neoplasm adopted in our institute. The metastatic nature of the thyroid nodule was then unexpected. The histological examination with immunohistochemistry (Thyroglobulin and TTF-1 negative with CD10 and Vimentin positive) *(Figure)* and the patient's history of previous RCC provided definitive diagnosis (Figs. 1 and 2).

Although 35–80% of patients with thyroid involvement from different malignancies present with multi-organ metastases [15], overall prognosis appears to be most closely linked to the innate