CASE REPORT

Unveiling the enigma: Thyroid-like follicular carcinoma of the left kidney

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Abstract

Thyroid-like follicular carcinoma of the kidney (TLFCK) is a rare renal cancer, not aligning with established renal cell carcinoma subtypes. Histologically akin to primary thyroid follicular carcinoma, TLFC poses diagnostic challenges due to absent thyroid immunohistochemistry markers. This case details a 40-year-old army personal, previously hypertension-free, presenting with bilateral flank pain and severe haematuria. Imaging revealed a 5.5 × 5 cm calcified lesion in the left kidney, suggestive of renal cell carcinoma (T3aN0Mx). Immunohistochemistry confirmed the diagnosis, with positive Paired box gene 8 (PAX8), Cytokeratin 7 (CK7) and Carbonic anhydrase IX (CAIX) and negative Cluster of differentiation 10 (CD10), Alpha-methyl acyl-CoA racemase (AMACR), Cluster of differentiation 117(CD117), Thyroid transcription factor 1 (TTF1) and thyroglobulin. The tumour was confined to the kidney, with clear margins. Subsequently, signs of metastasis prompted systemic treatment initiation with immunotherapy and tyrosine kinase inhibitors, emphasizing diagnostic intricacies and therapeutic complexities associated with TLFC.

Keywords: Thyroid-like follicular carcinoma of the kidney; Renal cell carcinoma; Metastatic follicular carcinoma of the thyroid; WHO classification.

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Introduction

Renal cell carcinoma (RCC) has a subtype known as Thyroid-like follicular carcinoma of the kidney (TLFCK), which is incredibly uncommon and unique, with a limited potential for malignancy.[1] It is distinct from other thyroid follicular neoplasms due to its strong histological similarity. To differentiate it from kidney hybridization and metastatic thyroid follicular cancer, TLFCK is defined by the absence of thyroid immunohistochemistry markers, particularly thyroid transcription factor-1 (TTF-1) and thyroglobulin (TG). Notably, TLFCK has yet to be included in the World Health Organization's (WHO) 2004 classification of renal tumours, despite its unique characteristics. Additionally, the International Society of Urological Pathology (ISUP) has not yet suggested adding TLFCK as a separate histological classification. The first reports of TLFCK were made in 2004, marking the beginning of investigation into this rare kidney tumour subtype.[1] Subsequently, 26 more cases have been documented in medical literature, enhancing our understanding of this unusual condition.[2] This case represents the 27th documented instance of TLFCK, contributing to the study of TLFC diagnosis and treatment complexities.

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Case Report

A 40-year-old man, weighing 80 kg and measuring 168 cm in height (BMI ≈29.407, classified as overweight), presented with bilateral flank pain at the Urology Department of Pakistan Kidney and Liver Institute and Research Centre, Lahore, Pakistan, on 2nd May 2023. He had no history of hypertension and was an army personal with no pertinent family or social history. A non-contrast CT scan revealed a calcified, heterogeneously enhancing exophytic lesion in the lower pole of his left kidney, measuring approximately 5.5 x 5 cm. The lesion extended into the renal sinus fat but did not breach Gerota's fascia, and the left renal vein remained patent. This imaging suggested a left renal mass indicative of renal cell carcinoma (T3aN0Mx). Additionally, small hypodensities in the liver's segments II and VI, with the larger one measuring 9 x 9 mm, were identified,

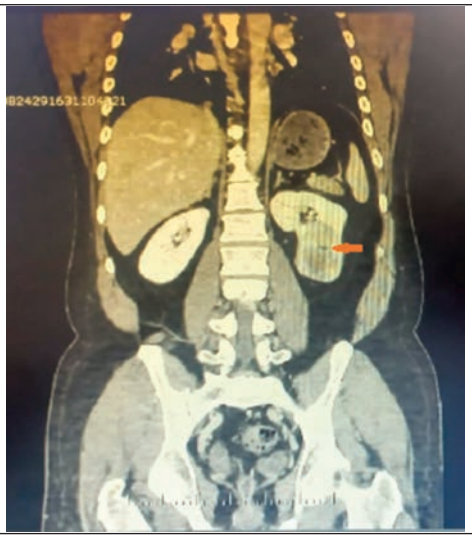

Figure-1: Non-contrast CT scan: Red arrow revealed left renal mass with calcifications, no Gerota's fascia breach—T3aN0Mx renal cell carcinoma.

although too small to characterise definitively. A chest X-ray ruled out metastasis (Figure 1).

To address the suspicion of renal cell carcinoma, a left-sided robotic radical nephrectomy, lasting 3 hours and 30 minutes, was performed in May 2023. The radical nephrectomy specimen, which included a 6.0 cm-long attached ureter, measured 12x9.0x7.0 cm. A well-circumscribed, grey-white, solid tumour was found in the mid-interpolar region, measuring 7.0x6.0x5.0 cm without invading the renal sinus.

Microscopic examination revealed a unifocal primary thyroid-like follicular carcinoma measuring 7 cm in its greatest dimension, with additional dimensions of 6x5 cm. Classified as G2, it exhibited conspicuous nucleoli and eosinophilia at 400x magnification, lacking sarcomatous and rhabdoid features with absent tumour necrosis. Limited to the kidney, all margins were uninvolved by invasive carcinoma, including perinephric fat, renal sinus soft tissue, renal vein, and ureteral margins. No lymphovascular invasion or regional lymph nodes were identified or submitted. The primary tumour was categorized as pT1b, confined to the kidney and lacking distant metastasis (pMx), with regional lymph node status designated as pN not assigned due to absence of submitted or found lymph nodes.

In addition to the renal tumour, the patient had a history of nephrolithiasis. Immunohistochemistry showed positivity for PAX8, CK7, and CAIX in tumour cells, while CD10, AMACR, CD117, and TTF1 were negative. These results, including PAX 8 and CK7 positivity and TTF1 and thyroglobulin negativity, supported the diagnosis of primary thyroid-like follicular carcinoma (Figure 2).

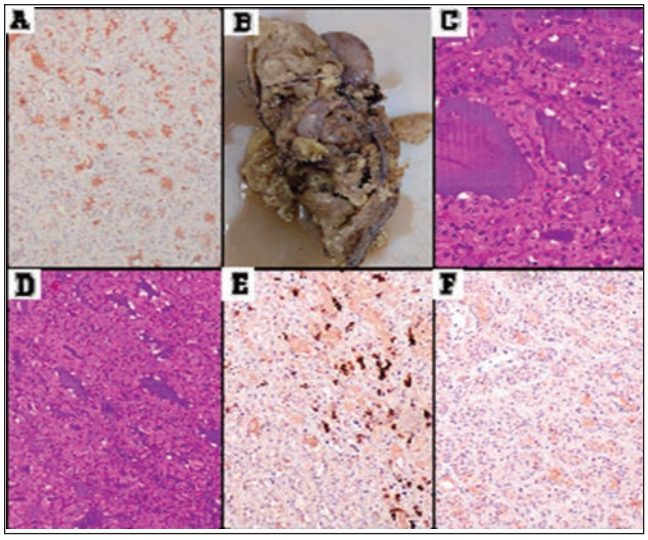

Figure-2: Histopathology: A: AMACR negative, B: Gross, C: Tumour, D: Tumour with follicular like growth pattern, E: CK7 Focal positive, F: TTF1 negative.

Four months postoperatively, the patient reported lower backache and developed a lump in his right forearm. Laboratory results showed a creatinine level of 0.7 mg/dL and an estimated glomerular filtration rate (eGFR) of 170 ml/min. A follow-up CT scan indicated postoperative changes in the left nephrectomy site. The left renal bed was clear, and no significant abdomino-pelvic lymph nodes were observed. However, multiple small hepatic nodules were present, including the largest one in segment IV, showing venous enhancement, raising suspicion of hepatic metastasis given the patient's history of left renal cell carcinoma. A multidisciplinary team opted for systemic treatment with immunotherapy (IO) and tyrosine kinase inhibitor (TKI) combinations.

Discussion

In this thoughtful discourse, a summary of primary thyroid-like follicular carcinoma of the kidney (TLFCK), an incredibly rare and poorly understood renal cancer, was provided. The lack of thyroid-specific markers in TLFCK makes it challenging to identify despite its striking microscopic resemblance to well-differentiated thyroid follicular carcinoma.[3]

Radiological tests such as MRI, CT scan, or ultrasound can reveal the presence of the tumour, but they cannot differentiate it from other differential diagnoses and thus are not valid diagnostics for TLFCKs. However, the best way to locate and characterise this tumour is by using a CT scan.

TLFCKs are typically found in the right kidney, and most cases are unilateral. These tumours are often found in the lower pole of the kidney, but in this case, they were found in the middle pole and the peripheral area.[4]

Amongst the 26 published instances, this case report stands out since the tumour was unintentionally found and manifested as bilateral flank discomfort, illustrating the variety of clinical manifestations of TLFCK. Additionally, the tumour, in our case, measured 7 cm in its greatest dimension, larger than the average size of 4.75 cm.[5]

Histologically, TLFCK is characterised by follicles lined by cells exhibiting uncommon nucleoli, eosinophilic cytoplasm, and sometimes pseudo inclusions or grooves. These cells resemble thyroid follicular carcinoma in that they generate micro and/or macro follicles packed with eosinophilic material. CD10, Vimentin, CK7, AE1/AE3, PAX-2, and CAM 5.2 are examples of positive markers commonly found by immunohistochemistry; negative markers include TG, RCC, and TTF-1.[6]

Thyroid tissue (struma ovary) metastasis from an ovarian teratoma, persistent pyelonephritis, and primary thyroid cancer metastasis are some of the differential diagnoses for

TLFCK. Thyroidisation is a benign disorder that typically affects both kidneys in people with pyelonephritis and end-stage renal disease.[7]

With only 16 cases documented, kidney metastasis from a primary thyroid tumour is incredibly uncommon. The presence of TTF-1 and thyroglobulin markers might be used to make a differential diagnosis. Only 16% of cases of primary thyroid metastasis are in the traditional papillary type, with the remaining 50% being follicular carcinoma and 34% being papillary with a follicular variation. Of the instances, 21% have a bilateral incidence.[2]

Despite TLFCK's benign nature, two occurrences of metastases—one localised to the lung, the other to the peri-hilar lymph node and lung—have been documented. Both were verified by biopsy. Nonetheless, no deaths directly linked to TLFCK have been reported.[8,9]

Due to the possibility of significant malignancy, nephrectomy—partial or total—remains the recommended course of action for all TLFCK cases currently. Even though TLFCK is a benign condition, nephrectomy is advised to reduce the chance of cancer.[10]

In summary, this discussion emphasises the unique diagnostic challenges associated with TLFCK while highlighting the rare occurrence and variety of clinical presentations of this kidney cancer. Relentless reporting of occurrences, along with precise diagnosis and treatment, is essential to further our understanding of this extremely rare entity.

Conclusion

This case highlights the extreme rarity of thyroid-like follicular carcinoma of the kidney (TLFC) and the challenges in its diagnosis. Absence of thyroid immunohistochemistry markers complicates identification. Our thorough histological, clinical, and immuno-histochemical analysis adds to scant literature on this tumour subtype. Additionally, it underscores TLFC's role in differential diagnosis of renal masses and potential systemic treatment with tyrosine kinase inhibitors and immunotherapy for suspected metastasis. Ongoing research and reporting are crucial for better understanding and management.

Patient consent: Written consent was obtained from the patient for publishing his case.

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Author Contribution:
NZ, SI, SM, NBN, AUR: Design, performed experiments and data curation.
SI: Data curation, literature data, writing and editing.