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Case Report

Thyroid-like follicular carcinoma of kidney with lung metastasis: a case report and review of literature

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Abstract: Thyroid-like follicular carcinoma of the kidney (TLFCK), an extremely rare entity of renal carcinoma, is morphologically similar to well-differentiated thyroid follicular neoplasm. To date, only 24 cases of TLFCK have been reported in detail in the English literature. Herein, we reported an additional case of TLFCK arising in a 47-year-old man, who presented with a 2 days history of gross hematuria. The patient received a right radical nephrectomy. However, chest CT scan revealed lung metastasis of the patient after 12 months of postoperative follow-up. Subsequently, the patient underwent thoracoscopic partial pulmonary lobectomy. The patient was still regularly followed up so far, and there was no evidence of local recurrence or new metastasis at 26 months after thoracoscopic surgery.

Keywords: Thyroid-like follicular carcinoma of kidney, renal cell carcinoma, diagnosis, prognosis

Introduction

Thyroid-like follicular carcinoma of the kidney (TLFCK) is a rare primary renal carcinoma, currently classified as a provisional entity according to the International Society of Urological Pathology [1]. In addition, TLFCK is an unusual histologic type of renal neoplasm with low malignant potential, which has a great resemblance to primary thyroid follicular carcinoma. In this article, we reported a new case of TLFCK in a man with lung metastasis to improve the awareness of this rare entity and also provided a review of the literature.

Case report

A 47-year-old man with no relevant family or social history was referred to our hospital because of a 2 days history of gross hematuria in May 2013, without fever, general malaise, fatigue, weight loss, abdominal and back pain. Physical examination of the thyroid, chest, abdomen and pelvis was unremarkable. Vital signs including temperature, pulse, respiratory and blood pressure were not noteworthy. Laboratory data, such as routine blood count, blood catecholamine, serum electrolytes, liver function and thyroid function tests were within the normal ranges. An abdominal ultrasound examination showed a solid mass in the right kidney. Abdomen computed tomography (CT) revealed a round mass measuring 4.0 cm in the upper pole of right kidney (**Figure 1A**). No other tumors, metastatic lesions, lymph node enlargement or renal vein involvement was revealed by systematic clinical examinations, including magnetic resonance imaging (MRI) of the head, neck, chest, abdomen and pelvis. Subsequently, the patient underwent a right radical nephrectomy as a renal cell carcinoma (RCC) was suspected.

Grossly, the nephrectomy specimen measured 15.0 cm×7.5 cm×7.0 cm, with the mass measuring 3.9 cm×3.5 cm×3.5 cm, located in the upper pole. On the cut surface, the lesion was red-gray to whitish, with well-defined margin and focal hemorrhagic zones. Microscopically, the arrangement of the tumor cells showed a notable morphology similar to thyroid follicles and the follicular lumens were filled with pink colloid-like material which mimicked follicular carcinoma of the thyroid. The follicles were irregular and lined by cuboidal cells with moderate amount of amphophilic to eosinophilic cyto-

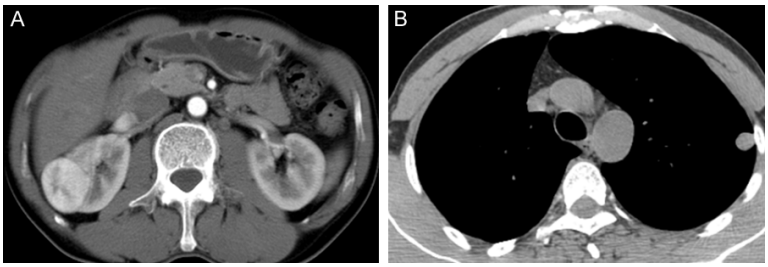

Figure 1. CT scan showed a heterogeneous solid mass with well-defined border in the upper pole of the right kidney (A) and an ovoid solid mass with clear border in the upper lobe of left lung after 12 months of postoperative follow-up (B).

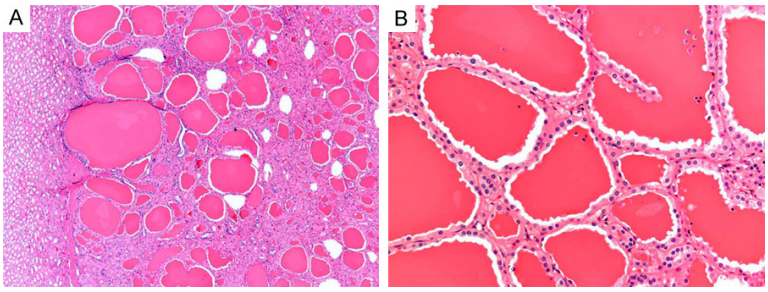

Figure 2. Histopathological analysis. A. Tumor cells showed a notable morphology similar to thyroid follicles and the follicular lumens were filled with pink colloid-like material (40×). B. The follicles were irregular and lined by cuboidal cells with moderate amount of amphophilic to eosinophilic cytoplasm (200×).

plasm. Nuclei of the tumor cells were round to oval with fine chromatin and inconspicuous nucleoli. No mitotic activity was observed (**Figure 2**). Immunohistochemically, the tumors exhibited positive for AE1/AE3, CK7 and Vimentin, and partially positive for PAX8, whereas negative for thyroid transcription factor-1 (TTF-1), thyroglobulin (TG), CK19, CK20, PAX2, HBME-1, galectin-3, CD10, CD56, CD34, synaptophysin (Syn), chromogranin (CgA), neuron-specific enolase (NSE), Wilms tumor-1 (WT-1), RCC marker, carcinoembryonic antigen (CEA) and S-100. The Ki-67 labeling index was approximately 6% (**Figure 3**). Therefore, based on the morphologic and immunophenotypic features, a diagnosis of TLFCK was confirmed.

The patient recovered well from right nephrectomy and remained asymptomatic after a follow-up of 12 months. However, in May 2014, a chest CT scan showed an ovoid solid mass with clear border in the superior lobe of left lung during his regular clinical follow-up visit, and the patient exhibited no obvious clinical symptoms (**Figure 1B**). No other mass was demonstrated except for the nodule in superior lobe of left lung by subsequent systematic examinations including whole body positron emission tomography/computed tomography (PET/CT) scan. After a discussion of the patient's condition by a multidisciplinary team including the pathology, imaging and thoracic surgery experts of our hospital, thoracoscopic partial pulmonary lobectomy was recommended. The operation was performed as planned, and his immediate postoperative course was uneventful. Postoperative pathological displayed that the mass in superior lobe of left lung exhibited similar histology and immunohistochemical features to the renal primary tumor. Of note, the tumor in the left lung was also positive for AE1/AE3, CK7, Vimentin and PAX8 (partially), but negative for TTF-1, TG, CK19, CK20, PAX2, HBME-1, galectin-3, CD10, CD56, CD34, Syn, CgA, NSE, WT-1, RCC marker, CEA and S-100. A pathological diagnosis of TLFCK with lung metastasis was confirmed based on the patient history, imaging findings, histomorphologic and immunophenotypic features. Nevertheless, the patient refused further systemic treatment including chemotherapy and radiotherapy, and was followed without any therapy. The patient was followed up regularly and there was no evidence of local recurrence or new metastasis at 26 months after thoracoscopic surgery.

Discussion

TLFCK was first described by Jung *et al* in 2006 [2]. Since then, only 24 cases have been presented in detail in the English literature [2-16]. The clinicopathogical features of the 25 cases including our case were summarized in **Table 1**, including 15 female and 10 male patients, with the mean age of 44.4 years old and median age of 41 years old (ranged 19-83 years). As shown in **Table 1**, TLFCK occurred mainly in adults in the third to fourth decades of life, with

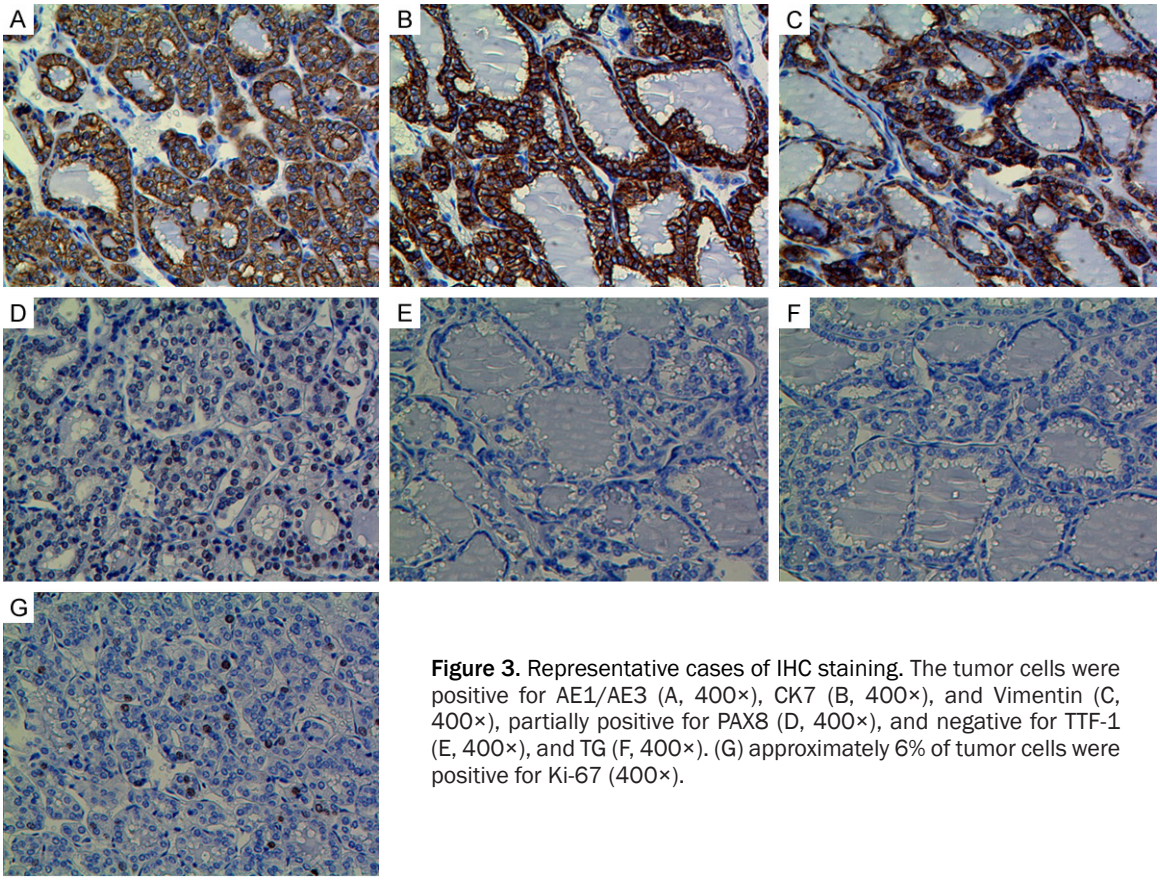

Figure 3. Representative cases of IHC staining. The tumor cells were positive for AE1/AE3 (A, 400×), CK7 (B, 400×), and Vimentin (C, 400×), partially positive for PAX8 (D, 400×), and negative for TTF-1 (E, 400×), and TG (F, 400×). (G) approximately 6% of tumor cells were positive for Ki-67 (400×).

a wide age distribution (19-83 years). There is a slight gender predilection with a female to male ratio of 1.5:1. It is worth noting that common RCC usually occurs in the elderly, predominantly in the seventh decade of life, with a male to female ratio of 2:1, which is different from TLFCK in term of epidemiology [16].

Among 25 cases, six patients were reported with medical history of a previous malignancy, including osteosarcoma of the rib in a 53-year-old female [4], adenocarcinoma of the colon in a 83-year-old male [4], adenocarcinoma of the prostate in a 76-year-old male [7], Hodgkin lymphoma in a 41-year-old female [7], T-cell acute lymphoblastic leukemia (T-ALL) in a 19-year-old female [11], and papillary urothelial carcinoma of the bladder in a 68-year-old female [15]. The relationship between TLFCK and other malignancies remains unclear currently due to the limited number of reported cases. In addition, the tumor was an incidental finding in 14 patients (14/25, 56%). However, other 11 patients were symptomatic (11/25, 44%), such as abdominal/flank pain (4/25, 16%), hematuria (2/25, 8%), and abdominal/flank pain accompanied by hematuria (3/25, 12%). Other symptoms including weight loss (1/25, 4%) [6] and relapsing urinary infection (1/25, 4%) [12] have also been described.

Up to now, all the primary tumors are unilateral and solitary renal diseases, with 56% (14/25) located in the right renal and 44% (11/25) located in the left side. The mean tumor size was 4.3 cm (median size of 4 cm, ranged 1.1-11.8 cm), but there was no significant correlation between tumor size and metastasis. Moreover, the majority of cases showed low grade malignant potential with indolent clinical course. Nevertheless, metastatic disease has been observed in five cases including our case. One 29-year-old female patient presented with lung metastasis 2 months after left nephrectomy [3], a 45-year-old male presented with renal hilar lymph node metastasis at initial diagnosis [4], a 34-year-old female was found to have retroperitoneal lymph node and lung metastases at presentation [5], and another 68-year-old female was identified to skull and meningeal

Table 1. Clinicopathogical features of 25 TLFCK cases

Reference	Age (y)/Sex	Clinical features	Location	Size (cm)	IHC		Treatment	Follow-up
					Positive	Negative		
2	32/F	Incidental	Middle-lower pole of right kidney	11.8	AE1/AE3, CD10, CK35βH11 (F), Vimentin (F)	TTF-1, TG, CK7, CK19, CK20, 34βE12, CEA, EMA, CD15	Radical nephrectomy	ANED after 6 months
3	29/F	Incidental	Middle-polar of left kidney	5.0	CK7, CK20, CAM5.2, Vimentin	TTF-1, TG, CD10, CD117	Radical nephrectomy	Lung metastatis at 2 months, ANED after 5 years
4	53/F	Incidental	Middle-polar of right kidney	2.1	CK7 (1 case)	TTF-1, TG, Pax-2, RCC, CD10, WT1, Ksp-cadherin, AMACR, Vimentin, CD56, CD57	Nephrectomy	ANED after 54 months
4	29/F	Incidental	Upper pole of right kidney	1.9			Nephrectomy	ANED after 84 months
4	45/M	Incidental	Lower pole of right kidney	3.5			Nephrectomy	With renal hilar lymph node metastasis, ANED after 17 months
4	83/M	Incidental	Lower pole of left kidney	2.1			Nephrectomy	ANED after 48 months
4	35/M	Incidental	Middle-polar of right kidney	3.0			Nephrectomy	ANED after 20 months
4	50/F	Incidental	Middle-polar of right kidney	4.0			Nephrectomy	ANED after 7 months
5	34/F	Gross hematuria and right flank pain	Middle-polar of right kidney	6.2	PAX2, PAX8, CK5, CK7, EMA, Vimentin, N-cadherin (focal)	TTF-1, TG, CEA, CK20, CD10, RCC, CD117, WT1, P63, AMACR	Radical nephrectomy, preoprative chemotherapy	Alive 3 months after surgery
6	31/F	Gross hematuria, weight loss and left flank pain	Upper-middle pole of left kidney	4.0	AE1/AE3, CK7, CK19, Vimentin, RCC, PAX2, galectin-3, HBME-1	TTF-1, TG, CD10, CK20, AMACR	Radical nephrectomy	ANED after 21 months
7	76/M	Gross hematuria	Upper pole of left kidney	4.5	CK7, CK19, Vimentin, EMA, 34βE12 (focal), E-cadherin (focal)	TTF-1, TG, CK20, HBME-1, galectin-3, CD56, Syn, CgA, NSE, WT1, CD10, RCC, CEA, Ulex	Radical nephrectomy	ANED after 11 months
7	41/F	Incidental	Lower pole of right kidney	4.3			Partial nephrectomy	ANED after 4 months
8	34/M	Left flank pain	Lower pole of left kidney	5.5	CAM5.2, P504S, Vimentin, CK7, 34βE12, EMA, AE1/AE3	TTF-1, TG, RCC, CD10, CD15, CD56, CD117, CEA, CK20, TFE3, WT1	Radical nephrectomy	ANED after 6 months
9	29/F	Left-sided abdominal pain	Lower pole of left kidney	6.5	EMA, Vimentin, CK7 (focal), CD10 (focal)	TTF-1, TG, CD117, CK20	Radical nephrectomy	ANED after 4 months
10	34/M	Left flank pain	Left kidney	2.8	PAX8	TTF-1, TG	Partial nephrectomy	Not described
11	19/F	right-sided abdominal pain	Lower pole of right kidney	2.0	CK7, AE1/AE3, EMA, PAX2, PAX8, Ki-67 (5%)	TTF-1, TG, CD10, CD56, WT1, SMMHC, CEA, S-100	Partial nephrectomy	ANED after 21 months
12	68/F	Relapsing urinary infection	Middle-polar of right kidney	1.1	EMA, CK7 (focal), CK19, AE1/AE3 (focal), 34βE12 (focal), Vimentin, CD117	TTF-1, TG, CD10, P504S	Partial nephrectomy	ANED after 6 months
13	65/M	Hematuria and right back pain	Middle-lower pole of right kidney	8.0	Vimentin, CK, CK19, EMA, CK7, NSE, Ki-67 (30%)	TTF-1, TG, 34βE12, Syn, CK20, CD56, CD10, WT1, CD34, CD57, P53, CD99, CD15	Radical nephrectomy	ANED after 15 months
13	59/M	Incidental	Middle-lower pole of left kidney	5.2	Vimentin, EMA, CK7, CK20, Ki-67 (20%)	TTF-1, TG, CD56, CD10, WT1, CD34, CD57, P53, CD117, CD15, CD99, CgA, Syn	Radical nephrectomy	ANED after 1 month
14	49/F	Incidental	Left kidney	2.4	CK7, PAX2, PAX8, Vimentin, EMA, CK19	TTF-1, TG, CD10, RCC, HBME-1	Partial nephrectomy	ANED after 10 months
15	68/F	Incidental	Lower pole of right kidney	5.0	Vimentin, CK7, CK19	TTF-1, TG, TPO, RCC, 34βE12, CK8, CD10, CD57, AMACR, VHL, WT1, CHG	Radical nephrectomy	Skull and meningeal metastases after 3 years, ANED after 24 months
16	35/F	Incidental	Lower-middle pole of left kidney	3.0	CK, CK18, CK19, Vimentin	TTF-1, TG, CK117, CgA, Syn	Partial nephrectomy	ANED after 14 months
16	41/M	Gross hematuria and left flank pain	Upper-middle pole of left kidney	6.0	CK7	TTF-1, TG	Radical nephrectomy	ANED after 17 months
16	25/F	Incidental	Upper pole of right kidney	2.5	CK7, CK20, Vimentin, EMA	TTF-1, TG	Partial nephrectomy	ANED after 24 months
Our case	47/M	Gross hematuria	Upper pole of right kidney	3.9	AE1/AE3, CK7, Vimentin, PAX8 (focal), Ki-67 (6%)	TTF-1, TG, CK19, CK20, PAX2, HBME-1, galectin-3, CD56, CD34, Syn, CgA, NSE, WT1, CD10, RCC, CEA, S-100	Radical nephrectomy	Lung metastatis at 12 months, ANED after 28 months

F, female; M, male; ANED, alive with no evidence of disease; AMACR, α-methyl-CoA racemase; SMMHC, smooth muscle myosin heavy chain.

metastases 3 years after initial diagnosis [15]. Our patient presented with lung metastasis 12 months after right nephrectomy.

To date, surgical resection is the major treatment method for TLFCK of the kidney. As summarized in **Table 1**, eighteen patients underwent radical nephrectomy and seven patients received partial nephrectomy. In addition, 24 patients with TLFCK have survived without evidence of disease, with a mean follow-up time of 23 months (ranged 1-84 months). Follow-up information was not described in one patient [10]. Limited data indicates that the biologic behavior of this tumor appears to be low grade and patients may have a good prognosis. Although our patient presented with lung metastasis 12 months after right radical nephrectomy and only underwent a partial pulmonary lobectomy, there is no clinical evidence of local recurrence or new metastasis at 26 months after thoracoscopic surgery and the patient is still in follow-up currently.

The most significant morphological feature of TLFCK is the striking resemblance to the well differentiated follicular carcinoma of the thyroid. Furthermore, TLFCK of the kidney has an interesting immunohistochemical profile as summarized in **Table 1**: usually positive for AE1/AE3, CK7, CK19, CAM5.2, EMA, PAX8, and Vimentin; variable positive for 34βE12, CK20, PAX2, RCC, AMACR, CD10, CD15, CD56, CD99, HBME-1, galectin-3, NSE, and WT-1; but negative for TTF-1, TG, CD117, CD57, CEA, CgA, Syn, and Ksp-cadherin. The Ki-67 proliferation index has been described in only four cases including our case, and so far, its significance is uncertain. In our case, the primary and metastatic tumor cells were positive for AE1/AE3, CK7, Vimentin, and PAX8 (partially), whereas negative for TTF-1, TG, CK19, CK20, PAX2, HBME-1, galectin-3, CD10, CD56, CD34, Syn, CgA, NSE, WT-1, RCC marker, CEA, and S-100. Furthermore, the most important factor of TLFCK immunophenotype is consistent negativity for the thyroid-specific markers, including TTF-1 and TG. The immunophenotype of our case is consistent with the previous reported cases. Though extremely rare, confirmed pathological diagnosis for TLFCK of the kidney is often not difficult based on systematic clinical examinations, morphological and immunohistochemical features. However, it is essential that TLFCK should be distinguished from metastatic follicular carcinoma of the thyroid before performing diagnosis of TLFCK. Besides a careful examination of the thyroid gland, TLFCK were negative for TTF-1 and TG, ruling out the possibility of metastasis from thyroid tumors and supporting a diagnosis of TLFCK.

In summary, TLFCK of the kidney is an extremely rare RCC with a low malignant behavior and the majority of patients have a good prognosis. Even metastasis might occur in the minority of patients, such as the present case, long-term survival also could be achieved by appropriate treatment. Whereas, it is important to recognize this rare type of renal tumor to avoid misdiagnosis. Additionally, more cases and long-term follow-ups should be documented for further recognition of this rare tumor.

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Disclosure of conflict of interest

None.

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