

## Original Article

# Synchronous primary triple carcinoma of thyroid and kidney accompanied by solitary fibrous tumor of the kidney: a unique case report

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**Abstract:** Thyroid cancers coexisted with kidney cancer in a patient is an unusual event. Here, we described a case of 35-year-old woman with synchronous occurrence of primary papillary carcinoma and follicular carcinoma of the thyroid, accompanied by renal cell carcinoma and solitary fibrous tumor of the kidney, which has not been reported in literature to our best knowledge. Its clinical and pathological features, as well as the possible pathogenic factors were discussed.

**Keywords:** Follicular carcinoma, papillary carcinoma, renal cell carcinoma, thyroid, kidney, solitary fibrous tumor

## Introduction

Thyroid cancer accounts for about 1% of all cancers. Papillary carcinoma is the most common histological type of thyroid malignancy, and it coexists with follicular carcinoma occasionally. The simultaneous occurrence of different types of thyroid carcinomas and primary cancer of other organ in a single patient was an unusual event. In this paper, we reported a rare case of papillary carcinoma coexist with follicular carcinoma of the thyroid accompanied by renal cell carcinoma and solitary fibrous tumor (SFT) of the kidney, which was the first report in literature to our best knowledge.

## Case history

A 35-year-old woman complained of pain in her left hip after a sprain in March 2007, leading to slight tenderness in the left groin and slight limping. The pain in her left hip aggravated in December 2007, and the x-ray image showed egg-sized bone destruction in the left iliac bone above the acetabulum with a coarse edge. Bone biopsy in the left iliac was then obtained and the pathologic diagnosis was “metastatic neuroendocrine carcinoma, suspicious of follicular thyroid carcinoma”. Subsequently, a computed tomography suggested malignancy

of the left iliac bone and a mass of the right thyroid. The patient had undergone three times of chemotherapy between January and March 2008 in other hospital.

The patient was taken examinations in April 2008 after submission in our hospital as follows. The thyroid was bulging. A mass measuring 3 cm × 2 cm was found with unclear boundary in the right thyroid. Otherwise, two masses measuring 1.3 cm × 0.6 cm and 1.0 cm × 0.6 cm were found in isthmus and left thyroid respectively by ultrasound examination. A mass measuring 0.8 cm × 0.8 cm can be touched in the left upper quadrant extramammary. Abdominal computed tomography showed a left renal mass, revealing a possibility of renal cell carcinoma. The patient underwent the right thyroid radical surgery and the left thyroid hysterectomy at the same time, and then underwent left renal hysterectomy after a few days. Now, she has taken adjuvant radioiodine treatment after surgical management and still in follow-up.

## Pathology findings

**Gross findings:** 1. A grey-white firm mass measuring 0.6 cm in diameter with irregular border and hard texture was found in the isthmus of

## Synchronous carcinoma and solitary fibrous tumor

**Table 1.** Antibodies for immunohistochemical analysis

Antibody	Clone number	Source	Dilution
CK19	A53/BA2	Zymed	1:200
CgA	LK2H10	Zymed	1:100
Syn	27G12	Novocastra	1:100
Calcitonin	Polyclonal	Dako	1:800
CD10	56C6	Novocastra	1:60
CD34	QBEnd10	Dako	1:100
CD99	12E7	Dako	1:200
CD117	Polyclonal	Dako	1:100
Bcl-2	124	Dako	1:80
Desmin	ZC18	Zymed	1:100
Ki-67	SP6	Zymed	1:200
S100	Polyclonal	Dako	1:2000
SMA	1A4	Dako	1:500
TG	2H11+6E1	Neomarkers	1:400
Vimentin	V9	Zymed	1:400

thyroid. The left thyroid tissue sized 2.5 cm × 0.8 cm × 0.5 cm. 2. The right thyroid tissue measured 5 cm × 2.5 cm × 2.5 cm, and a grey-white mass measuring 3 cm × 2 cm × 1 cm with clear margin was found. 3. The left renal sized 12 cm × 7 cm × 6 cm. A mass measuring 3 cm × 3 cm × 2.5 cm with colorful appearance and a clear boundary was found in the middle of the renal near the hilum. Besides, a grey-white mass measuring 0.4 cm in diameter with clear margin was found 0.2 cm away from the big mass of the same kidney.

The specimen was fixed in neutral, buffered formalin, routinely processed, with tissue sections embedded in paraffin. The sections were cut 4 µm thick and were stained with hematoxylin and eosin. Immunostaining using polymer technique (EnVision, Dako, Denmark) was performed with antigen retrieval being effected by pressure-cooking for 2.5 min in 1 mmol/L EDTA buffer pH 8.0. Immunohistochemical stains were performed with the antibodies listed in **Table 1**.

**Microscopic findings:** Histologically, the tumor in isthmus of the thyroid grows in an infiltrative pattern. The tumor cells were arranged in papillae and follicular structure. The papillary architecture was typically complex branching covered by epithelium with up and down arrangement. The irregular nuclei typically showed a ground glass appearance with numerous grooves. Nuclear pseudoinclusions were occa-

sionally seen. Samomabodies were seen in some areas. Focal invasion of the left thyroid tumor was found (**Figure 1A**).

The mass in the right thyroid was encapsulated with focal capsular invasion. The tumor cells were arranged from colloid-containing follicles to solid or trabecular growth patterns. Tumor cells were polygonal with round deeply stained nuclear (**Figure 1B**).

The large mass of the kidney showed solid nests, alveolar and acinar growth patterns with a plenty of small thin-walled blood vessels. Tumor cells were round or polygonal with clear cytoplasm and a distinct cell membrane (**Figure 1C**). The nuclei were round and small, and nucleoli were seen in some tumor cells.

The small mass of the kidney had a clear margin without a fibrous capsule. The tumor cells were spindly with fascicular arrangement, which were mild and mitosis was not found (**Figure 2A**).

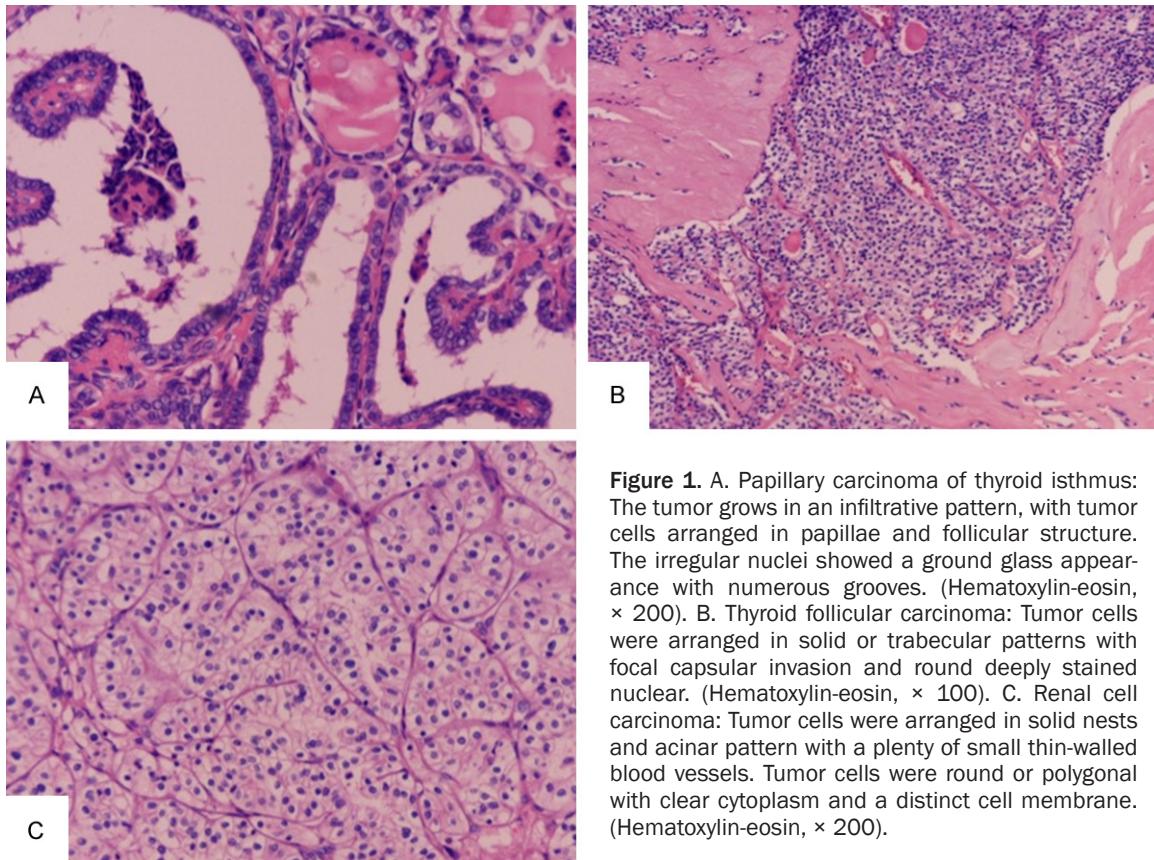
**Immunohistochemical observations:** Immunohistochemically, tumor cells of the isthmus of the thyroid were positive for CK19 and TG, but negative for CgA, Syn, and calcitonin. Tumor cells of right thyroid were positive for TG, but negative for CgA, Syn, and calcitonin. Tumor cells of the large mass of the kidney were positive for CD10 and Vim, but not CD117. Tumor cells of the small mass of the kidney were positive for CD34 (**Figure 2B**), bcl2, CD99 and Vim, but not CD117, desmin, SMA, S100, and Ki67 expression was very low (< 1%).

**Pathological diagnosis:** 1. Follicular carcinoma of the right thyroid. 2. Papillary carcinoma of thyroid isthmus, with involvement of the left thyroid. 3. Clear cell carcinoma of the left kidney (grade II). 4. SFT of the left kidney. 5. Adenosis of the left breast.

**Follow up:** The patient was further treated with a course of <sup>131</sup>iodine radiotherapy 6 months later after thyroid hysterectomy and left renal hysterectomy with definite diagnosis. The patient has remained stable for 15 months without recurrence of any tumor.

### Discussion

This was a rare sporadic case with multiple synchronous carcinomas of papillary carcinoma



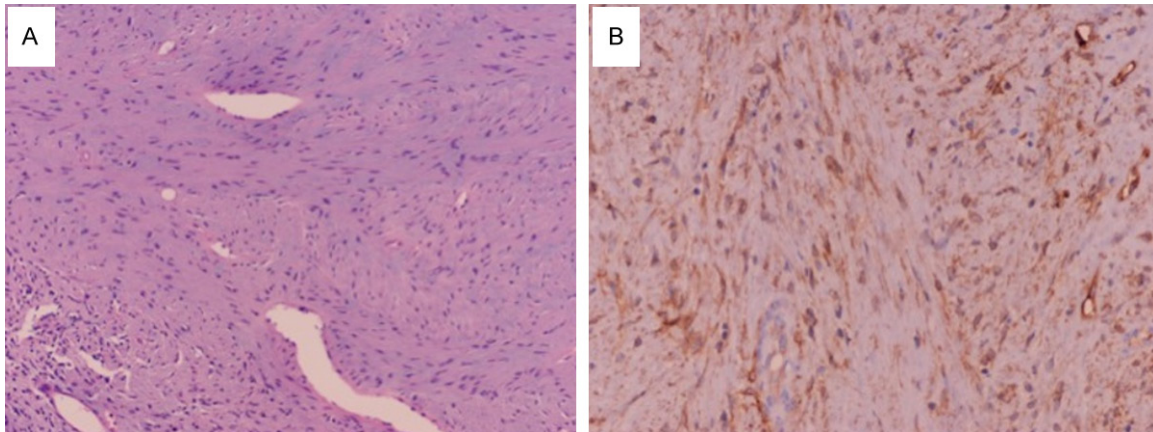
**Figure 1.** A. Papillary carcinoma of thyroid isthmus: The tumor grows in an infiltrative pattern, with tumor cells arranged in papillae and follicular structure. The irregular nuclei showed a ground glass appearance with numerous grooves. (Hematoxylin-eosin,  $\times 200$ ). B. Thyroid follicular carcinoma: Tumor cells were arranged in solid or trabecular patterns with focal capsular invasion and round deeply stained nuclear. (Hematoxylin-eosin,  $\times 100$ ). C. Renal cell carcinoma: Tumor cells were arranged in solid nests and acinar pattern with a plenty of small thin-walled blood vessels. Tumor cells were round or polygonal with clear cytoplasm and a distinct cell membrane. (Hematoxylin-eosin,  $\times 200$ ).

and follicular carcinoma of the thyroid, clear cell renal carcinoma and solitary fibrous tumor of the kidney. The patient denied tumor history in his immediate family members. Papillary carcinoma and follicular carcinoma are the most common thyroid malignancy. The coexistence of different types of thyroid carcinomas in a single patient is unusual. Rare cases of combination of three [1, 2] or four [3] different types of thyroid cancer has been reported. Most thyroid cancers are sporadic, some are associated with heredity such as Gardner syndrome and Cowden disease. The traditional risk factors associated with thyroid cancer include ionizing radiation and hormonal and genetic factors. Thyroid cancer is a heterogeneous disorder characterized by gene mutations. Several genes and gene mutations which are involved in the tumorigenesis of each type of thyroid cancer have been identified. Somatic rearrangements of *RET/PTC* as well as *TRK* and *BRAF* mutations were found in more than 70 percent of papillary carcinomas. Most frequent alterations including *RAS* mutations and *PAX8-PPAR $\gamma$*  rearrangement were found in follicular carcinomas [4].

Clear cell carcinoma was the most common subtype of renal cell carcinoma (RCC). Most cases of RCC are sporadic; up to 4% of patients have an inherited predisposition for this disease, including families with von Hippel-Lindau (VHL) disease, hereditary papillary renal cancer (HPRC), hereditary leiomyomatosis and renal cancer (HLRCC), and Birt-Hogg-Dubé (BHD) syndrome. *VHL* gene was found to act as a loss-of-function tumour-suppressor gene and was mutated or underwent methylation in a high proportion of tumours from patients with sporadic forms of clear-cell RCC [5].

Some studies showed that thyroid cancer has a significant correlation with cancers originated from other organs, such as renal cell carcinoma and breast cancer. An investigation including data from 13 population-based cancer registries in Europe, Canada, Australia, and Singapore showed that increasing incidence and improved prognosis of thyroid cancer have led to concern about the development of second primary cancers, especially after radioiodine treatment. This study has shown that in people with a primary thyroid cancer, there is a 30%





**Figure 2.** A. SFT of the kidney: Tumor cells were spindly with fascicular arrangement. (Hematoxylin-eosin,  $\times 200$ ). B. SFT of the kidney by immunostaining: Neoplastic spindle cells were positive for CD34. (EnVision,  $\times 200$ ).

increased risk of developing a second primary cancer in comparison with the general population. In addition, there is an increased risk of thyroid cancer developing after many other types of primary cancers [6]. Canchola *et al.* [7] demonstrated a fourfold increased incidence of kidney cancer among papillary thyroid cancer patients, supposing both of the two types of cancer may probably share one or more common etiologic factors, such as obesity and vegetable consumption. Recent studies, however, have implicated possible genetic links between thyroid cancer and kidney cancer. Malchoff *et al.* [8] identified a distinct inherited tumor syndrome characterized as the familial association of papillary thyroid cancer, nodular thyroid disease, and papillary renal neoplasia. A genome-wide screening and an investigation of specific candidate genes demonstrated that the family PTC/PRN phenotype was linked to 1q21. Mutations in *CHEK2* gene, which plays a role in DNA repair in many cell types, were found to be associated with thyroid, breast, and kidney cancers by Cybulski *et al.* [9]. Kamiya *et al.* [10] discovered an association between mutations in thyroid hormone nuclear receptor genes and renal clear cell carcinoma. These results offer promising leads for finally understanding the persistent epidemiologic association between the two cancers. However, the synchronous coexistence of primary thyroid cancer and renal cell carcinoma is rare. This case reported herein with primary triple carcinoma of the thyroid and kidney was absence of a clear family history of tumor, suggesting that it was a rare sporadic case. The epidemiologic association

between the synchronous occurrence of primary thyroid cancers and renal cell carcinoma may be related with possible genetic links in these tumors.

SFT is an unusual spindle cell neoplasm of adults that usually occurs in the pleura. This type of tumor has recently been described in diverse extrapleural sites. To our best knowledge, only 20 cases of SFT of the kidney have been reported [11-25]. Grossly, the renal SFTs reported in the literature ranged from 2 to 25 cm (mean, 8.75 cm). Most of the lesions were described as well-circumscribed or pseudocapsulated, lobulated, rubbery or firm masses with a homogeneous, gray or tan-white cut surface. The tumor was characterized by spindle cell proliferation showing a patternless architecture with a combination of alternating hypocellular and hypercellular areas separated from each other by thick bands of hyalinized, somewhat keloidal collagen and branching hemangiopericytoma-like vessels. Immunohistochemical study is the key to diagnosing SFT. CD34 immunoreactivity has been shown to be strongly and diffusely expressed in many of these tumors, and although it is not specific for SFT, strong CD34 reactivity is currently regarded as characteristic and an indispensable finding in the diagnosis of SFT. The tumor cells are immunoreactive for CD99 (70%). 20 to 35% of them are also variably positive for epithelial membrane antigen, Bcl2 and smooth muscle actin. Focal and limited reactivity for S100 protein, cytokeratins and/or desmin has also occasionally been reported. The tumor cells in our report

were bland spindly with fascicular arrangement and mitosis was not found. Mesenchymal tumors that should be differentiated from SFT in our report include renomedullary interstitial cell tumour, leiomyoma, schwannoma and extra-gastrointestinal stromal tumor. The immunostaining of tumor cells are positive for CD34 and Bcl-2, while negative for CD117, SMA and S-100 protein confirms the diagnosis of SFT.

Overall, we reported a unique rare case of synchronous occurrence of primary papillary carcinoma and follicular carcinoma of the thyroid, accompanied by renal cell carcinoma (clear cell carcinoma) and SFT of the kidney, which has not been reported in literature.

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## Disclosure of conflict of interest

None.

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