Published in final edited form as:

Hum Pathol. 2011 January ; 42(1): 146–150. doi:10.1016/j.humpath.2010.01.026.

Thyroid-like follicular carcinoma of the kidney with metastases to the lungs and retroperitoneal lymph nodes

Jasreman Dhillon, MD^a, Nizar M. Tannir, MD^b, Surena F. Matin, MD^c, Pheroze Tamboli, MD^a, Bogdan A. Czerniak, MD, PhD^a, and Charles C. Guo, MD^{a,*}

^aDepartment of Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas

^bDepartment of Genitourinary Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas

^cDepartment of Urology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas

Summary

Thyroid-like follicular carcinoma of the kidney is an extremely rare variant of renal cell carcinoma. Most previously reported cases presented as incidental small tumors confined to the kidney. Here we report a unique case in which the patient presented with flank pain and hematuria. Imaging studies demonstrated a large tumor in the right kidney and metastases to the lungs and retroperitoneal lymph nodes. Both the renal tumor and the sampled lung metastasis were composed almost entirely of follicles with dense, colloid-like material resembling thyroid follicular carcinoma. However, no lesion was found in the thyroid gland, and the patient's thyroid function tests were normal. The tumor cells were immunoreactive for PAX2 and PAX8 but lacked reactivity for thyroglobulin and thyroid transcription factor-1. To our knowledge, this is the first case of thyroid-like follicular carcinoma of the kidney to be initially associated with marked symptoms and widespread metastases, providing evidence that this rare variant of renal cell carcinoma can be clinically aggressive.

Keywords

Kidney; thyroid-like follicular carcinoma; renal cell carcinoma; metastasis

1. Introduction

Thyroid-like follicular carcinoma of the kidney (TLFCK) is a recently described histologic type of renal cell carcinoma (RCC) (1-3) that is not included in the current WHO classification (4). This unique histologic type of RCC exhibits morphologic features that

© 2010 Elsevier Inc. All rights reserved.

*Corresponding author: Charles C. Guo, MD, Department of Pathology, Unit 85, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030-4009. ccguo@mdanderson.org. Tel: (713) 792-3104; Fax: (713) 792-4049.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

strikingly resemble follicular carcinoma of the thyroid, raising the possibility of a metastasis from a primary thyroid tumor. TLFCCK is extremely rare, with only 8 cases reported in the literature (1-3). All reported TLFCCKs were incidentally discovered during a routine medical checkup or radiographic workup for other diseases, and most tumors were small and confined to the kidney. Here we report a unique case of TLFCCK in which the patient initially presented with marked symptoms and widespread metastases to the lungs and retroperitoneal lymph nodes.

2. Case report

The patient was a 34-year-old woman who presented with intermittent gross hematuria and right flank pain. A computed tomography scan demonstrated a 6.3-cm mass in the middle of the right kidney and multiple nodules in both lungs. The largest nodules in the left and right lungs were 2.1 cm and 3.4 cm, respectively. The patient underwent a computed tomography-guided biopsy of the largest nodule in the right lung, which showed features of thyroid-like follicular carcinoma (see Section 4.1). However, physical examination did not reveal any mass lesion in the thyroid gland, and her thyroid function tests were normal. The patient received systemic therapy for one year. She responded well to the treatment with no disease progression. Consolidation therapy for the primary and locoregional disease consisted of a cytoreductive radical nephrectomy with extensive retroperitoneal (paracaval, retrocaval, and interaortocaval) lymph node dissection. The patient recovered well from the surgery and was alive 3 months after the surgery.

3. Methods

The lung biopsy and radical nephrectomy specimens were routinely fixed in 10% buffered formalin, embedded in paraffin, and serially sectioned into 4- μ m-thick sections. Routine staining with hematoxylin and eosin was performed. Immunohistochemical staining was performed using the avidin-biotin-peroxidase complex method in a Dako Autostainer (Dako, Carpinteria, CA), as previously described (5). The primary antibodies included those for PAX2, PAX8, low- and high-molecular-weight cytokeratins, cytokeratin 5, cytokeratin 7, epithelial membrane antigen, vimentin, N-cadherin, thyroglobulin, thyroid transcription factor-1 (TTF-1), carcinoembryonic antigen, cytokeratin 20, CD10, RCC antigen, CD117, Wilms tumor-1 (WT-1), p63, and alpha-methylacyl-coenzyme A racemase (AMACR). Appropriate positive and negative controls were used for each antibody.

4. Results

4.1. Biopsy of lung nodule

The needle biopsy of the right lung nodule showed a striking follicular architecture, which largely replaced the lung parenchyma. The follicles varied in size and contained dense, pink, colloid-like material (Fig. 1A). The follicles were lined with cuboidal to columnar tumor cells containing scant to moderate amounts of eosinophilic cytoplasm (Fig. 1B). The nuclei were round to oval with evenly distributed chromatin and inconspicuous nucleoli.

Extensive immunohistochemical staining was performed on the lung nodule biopsy specimen. The tumor cells were positive for PAX2 (Fig. 1C), PAX8, low- and high-

molecular-weight cytokeratin, cytokeratin 5, cytokeratin 7, epithelial membrane antigen, and vimentin; focally positive for N-cadherin; and negative for thyroglobulin (Fig. 1D), TTF-1, carcinoembryonic antigen, cytokeratin 20, CD10, RCC antigen, CD117, WT -1, p63, and AMACR.

4.2. Radical nephrectomy specimen

Sections of the radical nephrectomy specimen revealed a $6.2 \times 5.2 \times 5.0$ -cm circumscribed tumor in the middle of the kidney (Fig. 2A). The tumor was red-tan and soft with extensive necrosis and fibrosis; it abutted the renal sinus but did not invade the renal vein or perinephric adipose tissue.

Like the lung nodule, the renal tumor showed a predominantly follicular architecture with pink colloid-like material (Fig. 2B). The follicles varied in size and contained dense, pink, colloid-like material (Fig. 2C). In some areas, the colloid-like material extravasated out of the follicles into the stroma (Fig. 2D). The nucleoli were inconspicuous and the chromatin was evenly distributed; these features are characteristic of Fuhrman nuclear grade 2. Mitotic figures were rare. Approximately 70% of the tumor was necrotic as a result of the preoperative chemotherapy. The tumor also showed focal areas of metaplastic bone formation. Seventeen locoregional lymph nodes from the retrocaval, paracaval, and interaortocaval areas were dissected; metastatic carcinoma was present in 2 lymph nodes with extranodal extension. Interestingly, the metastases in the lymph nodes also exhibited distinct features of thyroid-like follicular carcinoma similar to the primary renal tumor (Fig. 2E). In the non-neoplastic renal tissue, there were focal areas of thyroidization of the tubules, which were characterized by atrophic tubular epithelium and dense colloid-like material in the lumens (Fig. 2F).

Selective immunohistochemical staining was performed on the nephrectomy specimen. The tumor cells were immunoreactive for PAX2, vimentin, and cytokeratin 7 and lacked immunoreactivity for thyroglobulin, TTF-1, CD10, and AMACR.

5. Discussion

In the previously reported cases of TFLCK (1-3), the patients included 5 women and 3 men with a mean age of 44.5 years (range, 29-83). All the tumors showed histologic features that strikingly resembled follicular carcinoma of the thyroid, raising the possibility of metastatic thyroid follicular carcinoma; however, physical examinations and radiographic studies disclosed no thyroid lesions in any patient. Furthermore, the tumor cells lacked immunoreactivity for the thyroid-specific markers thyroglobulin and TTF-1. Therefore, the renal tumors were unlikely to represent metastases from primary thyroid follicular carcinoma. All 6 patients described by Amin et al (1) were alive with no evidence of disease at a mean follow-up of 47 months after nephrectomy, including 1 patient who was found to have metastasis to the renal hilar lymph nodes at the time of nephrectomy. These findings indicated that TFLCK has a low malignant potential.

Like the tumors in previous reports (1-3), the tumor in our case showed features typical of TFLCK. The renal origin of our patient's tumor is further supported by its immunoreactivity

for the renal-specific makers PAX2 and PAX8 (6). Unlike the previously reported cases (1-3), the patient in our case presented with symptoms (intermittent gross hematuria and flank pain) and widespread disease, indicating that TFLCK can be clinically aggressive.

It is critical to exclude metastasis, particularly metastatic follicular carcinoma of the thyroid, before making the diagnosis of TFLCK. Thyroid follicular carcinomas rarely metastasize to the kidney, and only a few cases have been reported (8,9). In most reported cases, a primary tumor was present in the thyroid gland and the metastasis was widespread, involving multiple organs. Struma ovarii, an ovarian teratoma composed of predominantly thyroid tissue, may also be considered in the differential diagnosis. Although struma ovarii may become malignant and metastatic, to our knowledge there are no reports of metastatic struma ovarii to the kidney (10). Metastatic carcinoma cells from either thyroid follicular carcinoma or struma ovarii are usually immunoreactive for thyroglobulin and TTF-1 (11), but in all reported cases of TFLCK, including ours, the carcinoma cells lacked immunoreactivity for TTF-1 and thyroglobulin. Furthermore, in our patient and the others diagnosed with TFLCK, no lesions were found in the thyroid glands or ovaries and the thyroid function tests were normal. Therefore, TFLCK is unlikely to represent a metastasis from thyroid follicular carcinoma or struma ovarii.

Non-neoplastic kidney tissue, particularly in patients with chronic pyelonephritis and obstructive nephropathy, may also demonstrate thyroid-like appearance (12). The thyroidization of the kidney is characterized by atrophic distal tubules or collective ducts with colloid-like hyaline casts. While thyroidization of the kidney typically is widespread and bilateral, TFLCK presents as an encapsulated mass. Despite its similar appearance, the colloid material in the renal follicles is different from that in the thyroid follicles. While the former is composed of Tamm-Horsfall glycoprotein, the most abundant protein in normal urine (12), the latter is composed of mostly thyroglobulin. Furthermore, a thyroid-like appearance may occasionally be observed in other types of RCC, renal oncocytoma, and metanephric adenoma; however this appearance is usually focal. In contrast, TFLCK is composed almost entirely of follicular structures with dense, colloid-like material.

Genetic analyses have shown variable genetic alterations in TFLCK (1-3). Using the CGH analysis, Jung et al found gains of chromosomes 7q36, 8q24, 12, 16, 17p11-q11, 17q24, 19q, 20q13, 21q22.3, and Xp and losses of chromosomes 1p36, 3, and 9q21-33 in this tumor (2). Using FISH analysis, William et al reported losses of chromosomes 1, 3, 7, 9p21, 12, 17, and X in their case (3). Amin et al compared the gene expression profiles of TFLCK to clear cell and chromophobe RCCs, and they found that TFLCK overexpressed 135 genes and underexpressed 46 genes (1). In particular, the expression of the mixed lineage leukemia (*MLL*) gene was increased 2.5 fold in TFLCK. The *MLL* gene encodes a transcriptional factor involved in the oncogenesis of some hematologic malignancies, particularly acute leukemia (7). The enhanced expression of the *MLL* gene may suggest a potential role of the *MLL* gene in TFLCK, although additional study is needed.

In summary, TFLCK is a rare variant of renal cell carcinoma with unique morphologic and immunohistochemical features. Although all previously reported TFLCKs presented as incidental small tumors confined to the kidney, the TFLCK in our case presented with

marked symptoms and widespread metastases, demonstrating this cancer's potential for aggressive behavior.

References

1. Amin MB, Gupta R, Ondrej H, et al. Primary thyroid-like follicular carcinoma of the kidney: report of 6 cases of a histologically distinctive adult renal epithelial neoplasm. *Am J Surg Pathol.* 2009; 33:393–400. [PubMed: 19047894]
2. Jung SJ, Chung JI, Park SH, et al. Thyroid follicular carcinoma-like tumor of kidney: a case report with morphologic, immunohistochemical, and genetic analysis. *Am J Surg Pathol.* 2006; 30:411–5. [PubMed: 16538064]
3. William S, Irmgard V, Michael G, et al. Thyroid follicular carcinoma-like renal tumor: a case report with morphologic, immunophenotypic, cytogenetic, and scintigraphic studies. *Virchows Arch.* 2008; 452:91–5. [PubMed: 17704942]
4. Eble JN.; Sauter, G.; Epstein, JI., et al. World Health Organization Classification of Tumours. Lyon, France: IARC Press; 2004. Pathology and genetics of tumours of the urinary system and male genital organs; p. 9-88.
5. Guo CC, Gomez E, Tamboli P, et al. Squamous cell carcinoma of the urinary bladder: a clinicopathologic and immunohistochemical study of 16 cases. *Hum Pathol.* 2009; 40:1448–52. [PubMed: 19454359]
6. Bouchard M, Souabni A, Mandler M, et al. Nephric lineage specification by Pax2 and Pax8. *Genes Dev.* 2002; 16:2958–70. [PubMed: 12435636]
7. Slany RK. The molecular biology of mixed lineage leukemia. *Haematologica.* 2009; 94:984–93. [PubMed: 19535349]
8. Abe K, Hasegawa T, Onodera S, Oishi Y, Suzuki M. Renal metastasis of thyroid carcinoma. *Int J Urol.* 2002; 9:656–8. [PubMed: 12534914]
9. Garcia-Sanchis L, Lopez-Aznar D, Oltra A, Rivas A, Alonso J, Montalar J, Mateo A. Metastatic follicular thyroid carcinoma to the kidney: a case report. *Clin Nucl Med.* 1999; 24:48–50. [PubMed: 9890493]
10. Asa SL. The role of immunohistochemical markers in the diagnosis of follicular-patterned lesions of the thyroid. *Endocr Pathol.* 2005; 16(4):295–309. [PubMed: 16627917]
11. Robboy SJ, Shaco-Levy R, Peng RY, et al. Malignant struma ovarii: an analysis of 88 cases, including 27 with extraovarian spread. *Int J Gynecol Pathol.* 2009; 28:405–22. [PubMed: 19696610]
12. Nadasdy T, Laszik Z, Blick KE, et al. Tubular atrophy in the end-stage kidney: a lectin and immunohistochemical study. *Hum Pathol.* 1994; 25:22–8. [PubMed: 7906246]

Fig. 1.

Metastatic thyroid-like follicular carcinoma of the kidney in the lung nodule biopsy specimen. A, The lung metastasis was composed of follicles of various sizes with colloid-like material. B, Follicles were lined with cuboidal to columnar cells with round nuclei. C, Immunohistochemical staining of tumor cells showed nuclear reactivity for PAX2. D, Tumor cells lacked immunoreactivity for thyroglobulin on immunohistochemical staining.

Fig. 2.

Primary thyroid-like follicular carcinoma of the kidney in the radical nephrectomy specimen. A, The tumor was tan-red and circumscribed and had extensive necrosis and fibrosis. B, The tumor was composed of follicles of various sizes containing colloid-like material. C, Colloid-like material extravasated out of the follicles. D, The tumor cells were cuboidal to columnar, with round nuclei. E, A metastasis in a lymph node also demonstrated a distinct follicular architecture with colloid-like material. F, Non-neoplastic kidney tissue showed thyroidization of tubules with atrophic epithelium and colloid-like material.