SPANDIDOS PUBLICATIONS

ONCOLOGY LETTERS 10: 449-452, 2015

Primary carcinoid tumor of the kidney with estrogen and progesterone receptor expression: A case report

CHUNHUA LIN[1,2*], JITAO WU[2*], ZHENLI GAO[2], GUIMEI QU[3], WEI WANG[3] and GUOHUA YU[3]

[1]Department of Surgery, Shandong University School of Medicine, Jinan, Shandong 250012; Departments of [2]Urological Surgery and [3]Pathology, Affiliated Yantai Yuhuangding Hospital, Medical College of Qingdao University, Yantai, Shandong 264000, P.R. China

Received July 26, 2014; Accepted April 9, 2015

DOI: 10.3892/ol.2015.3167

Abstract. Primary carcinoid tumors are uncommon neoplasms in the kidney. The current study presents a case of primary carcinoid tumor of the kidney in a 49-year-old female who suffered from painless gross hematuria for half a month. Left hydronephrosis, a horseshoe kidney and a space-occupying lesion of the left ureter were found by abdominal computed tomography scans and ultrasonic testing. Surgery was performed and an oval tumor was found under the left ureter; the tumor and left kidney were excised completely. The neoplasm was composed of solid nests of cells, trabeculae, adenoid structures and anastomosing cords in a loose and myxoid background. The tumor cells, which were consistent in volume, exhibited centrally oval nuclei with inconspicuous nucleoli, and eosinophilic finely granular cytoplasm. Upon immunohistochemical staining, the neoplastic cells were positive for AE1/AE3, vimentin, synaptophysin, chromogranin A, estrogen receptor and progesterone receptor, while being negative for epithelial membrane antigen, inhibin A, cluster of differentiation (CD)99, S-100 and CD10. Based on the histological characteristics, a diagnosis of primary carcinoid tumor of the left kidney was formed. The patient did not receive further treatment. The total follow-up period was 18 months after the surgery and repeated imaging examinations every 6 months revealed no recurrence.

Introduction

Carcinoid tumors are a group of neuroendocrine tumors that occur most frequently in the gastrointestinal tract as well as in other organs comprising argyrophil cells; ~85% these tumors occur in the digestive tract, with 10% occurring in the lung and 5% occurring in other organs such as the testis (1) and bladder (2). The clinical manifestations of carcinoid tumors may not be apparent, or limited to local symptoms. However, carcinoid syndromes often have obvious systemic symptoms, such as unexplained intermittent diarrhea, flushing, facial telangiectasia, paroxysmal asthma or psychiatric symptoms (3). The diagnosis of carcinoid tumor is dependent on biopsy, and surgical excision is the first treatment. Patients without carcinoid syndrome have a better prognosis (4).

Primary carcinoid tumor in the kidney is uncommon and the expression of the estrogen receptor (ER) and the progesterone receptor (PR) has not been reported. Due to the rarity of this tumor, its clinicopathological characteristics, prognosis and histogenesis have not been fully characterized. The current study reports an unusual case of a carcinoid tumor of the kidney with ER and PR expression in a 49-year-old female who presented with a 2-year history of hypertension. Abdominal computed tomography scans revealed a left horseshoe kidney. Clinicopathological characteristics of primary carcinoid tumors are also discussed by reviewing the literature. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Case report

Clinical data. A 49-year-old female with a history of hypertension for two years presented with a half-month history of painless gross hematuria. The patient was admitted to the Department of Urological Surgery in the Affiliated Yantai Yuhuangding Hospital (Medical College of Qingdao University, Yantai, Shandong, China). No abnormal physical signs were found during a physical examination. Abdominal computed tomography (CT) scans and ultrasonic testing revealed left hydronephrosis, a horseshoe kidney and a space-occupying lesion in the left ureter, while the right kidney and other visceral organs were normal (Fig. 1A). The hematological findings, endocrine index, erythrocyte sedimentation rate, blood biochemistry, electrolytes, blood urea nitrogen and serum creatinine levels were within the normal ranges. The surgery was performed under general anesthesia and in a right lateral decubitus position at 70˚. The left kidney, which

Correspondence to: Dr Guohua Yu or Dr Wei Wang, Department of Pathology, Affiliated Yantai Yuhuangding Hospital, Medical College of Qingdao University, 20 Yuhuangding East Road, Yantai, Shandong 264000, P.R. China
E-mail: ygh0535@hotmail.com
E-mail: yhdwangwei@163.com

*Contributed equally

Key words: kidney, carcinoid, renal tumor, estrogen receptor, progesterone receptor

Table I. Antibodies employed in the immunohistochemistry applied for the case.

Antibody	Clone	Source	Dilution
Anti-S100	4C49	Lab vision	1:150
Anti-cytokeratin	AE1/AE3	Dako	1:100
Anti-vimentin	SP20	Lab vision	1:100
Anti-Ki-67	MIB-1	Lab vision	1:100
Anti-CD99	O13	Dako	1:100
Anti-CD10	56C6	Lab vision	1:100
Anti-inhibin A	R11	Dako	1:100
Anti-EMA	E19	Dako	1:100
Anti-ER	1D5	Dako	1:100
Anti-PR	EP2	Dako	1:100
Anti-Syn	SP11	Dako	1:100
Anti-CgA	EP38	Dako	1:100

Dako, Glostrup, Denmark. Lab vision corporation, Fremont, CA, USA. CD, cluster of differentiation; EMA, epithelial membrane antigen; ER, estrogen receptor; PR, progesterone receptor; Syn, synaptophysin; CgA, chromogranin A.

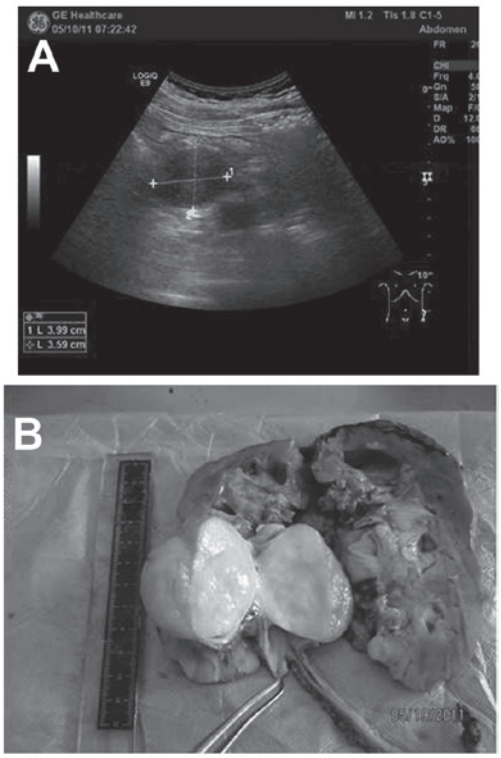

Figure 1. (A) Ultrasonic examination revealing left hydronephrosis and a space-occupying lesion in the left ureter. (B) Tumor positioned under the uterer, the with a volume of ~5x4x3.6 cm. The boundaries of the mass were clear and the section was faintly yellow.

presented with black coloration and a horseshoe appearance, was exposed and dissociated. An oval tumor, ~5x4x3.6 cm, was observed under the ureter. The boundaries of the mass were clear. The cross-section of the tumor was faint yellow, homogeneous and pliable in quality (Fig. 1B).

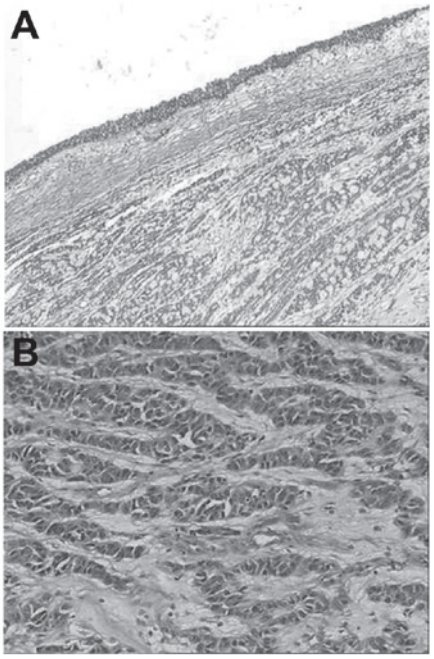

Figure 2. (A) Tumor was located under the mucosa of the pelvis and the neoplasm was composed of solid nests of cells, trabeculae, adenoid structures and anastomosing cords in a loose and myxoid background (hematoxylin and eosin staining; magnification, x100). (B) Neoplastic cells were similar in size and exhibited centrally placed oval nuclei with eosinophilic finely granular cytoplasm, and a low mitotic rate (hematoxylin and eosin staining; magnification, x200).

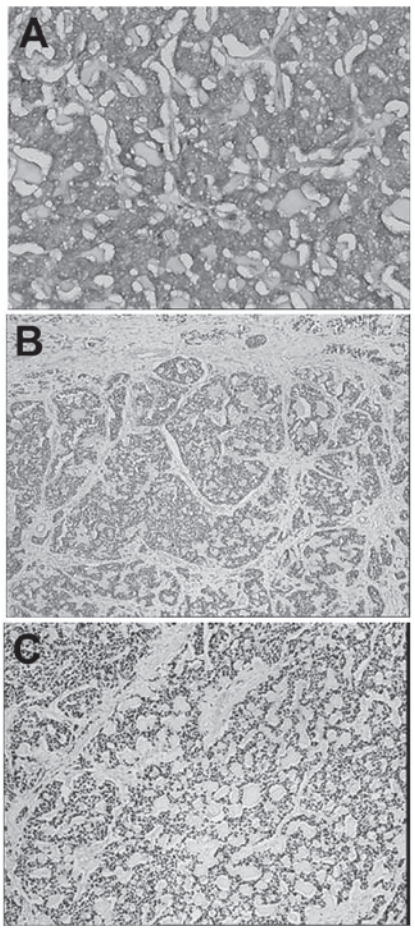

Figure 3. Immunostaining of the tumor. The tumor cells were positive for (A) synaptophysin (magnification, x200), (B) estrogen receptor (magnification, x100) and (C) progesterone receptor (magnification, x100).

Pathological findings. Microscopically, the tumor was located under the mucosa of the pelvis and showed aggressive growth. The neoplasm was composed of solid nests of cells, trabeculae, adenoid structures and anastomosing cords in a loose and myxoid background (Fig. 2A). The tumor cells, which were consistent in volume, exhibited centrally placed oval nuclei with inconspicuous nucleoli, and eosinophilic finely granular cytoplasm. The mitotic rate was <1 per 10 high-power fields (Fig. 2B).

Immunohistochemical findings. Immunohistochemical staining suggested that the neoplastic cells were positive for AE1/AE3, vimentin, synaptophysin (Syn; Fig. 3A), chromogranin A (CgA), ER (Fig. 3B) and PR (Fig. 3C), while being negative for epithelial membrane antigen, inhibin A, cluster of differentiation (CD)99, S-100 and CD10. The cells that were positive for Ki-67 were dispersive. All the primary antibodies used are listed in Table I. On the basis of histomorphology in light microscopy and the presence of immunohistochemical staining, a diagnosis of primary carcinoid tumor of the left kidney was made. The patient did not receive further treatment. The total follow-up period was 18 months after the surgery. Repeated CT scans and abdominal ultrasonography every 6 months revealed no recurrence or residual lesion.

Discussion

Carcinoid tumors of the kidney are rare. The pathogenesis of renal carcinoid tumors remains under debate (5-9). Certain previous studies have attributed the genesis of this tumor to congenital renal abnormalities, while other studies have suggested that the tumor cells are derived from multipotential primitive stem cells, which are induced to neuroendocrine differentiation (10-12). Notably, in the present case, the ER and PR sex hormone receptors were strongly expressed in the tumor cells. ER and PR expression has previously been detected not only in hormone target organs, such as the breast, ovaries and endometrium, but also in the digestive tract and pancreas (13,14). However, the expression of ER and PR in carcinoid tumors of the kidney has not been reported. The present results may not be of use in inferring the pathogenesis of the disease, as no relative literature has been found by review, however, we speculate that the ER and PR may be a potential therapeutic target in patients with this condition (13). Further study is required to investigate this association in the future.

Clinically, Hansel *et al* reported that 50% of 21 carcinoid tumor patients studied were younger than 50-years-old, and that the tumor showed no tendencies in gender and location. Bloody urine and pain in the lower back proved to be the most common clinical manifestations. Horseshoe kidneys was frequently present, while no other characteristics were known to distinguish renal cell carcinoma on imaging. Endocrine syndrome was not found in the blood examination (15). The current study reports the case of a 49-year-old female who presented with painless and gross hematuria. A horseshoe kidney on imaging was a contributory factor for the diagnosis.

Pathological examination remains the gold standard of diagnosis for renal carcinoid tumors (15,16). Under the microscope, the classic histological characteristics of renal carcinoid tumors are a band or ribbon-like pattern accompanied by solid nests of cells and adenoid structures within a loose stroma. Rosette structures are characteristic of these lesions, however, this was not found in the present case. Tumor cells are similar in size, with a granular eosinophilic cytoplasm. Round to oval nuclei are uniform, with rare mitotic events. Used together with histological features, neuroendocrine immunostaining would aid in distinguishing carcinoid tumors from other diagnoses, such as small cell carcinoma, pheochromocytoma and primitive neuroectodermal tumor. With regard to the present case, a diagnosis of renal carcinoid tumor may have been regarded as presumptive based on the observation of typical morphological characteristics by light microscopy, as this is subject to validation by positive immunohistochemical staining of cytokeratin, vimentin and endocrine markers (CgA, Syn or CD56 protein).

No standard therapy focusing on renal carcinoid tumors has yet been proposed and surgical resection is currently the only treatment (17). Hormonotherapy may be a novel method aimed at patients with positive ER and PR expression. Necrosis, metastasis, an age of >50 years, a tumor diameter >4 cm and more karyokinesis are presumed to potentially indicate an ominous prognosis. However, no clear prognosis factors are generally accepted and further case accumulation is required (18,19).

In conclusion, the current study presents the clinical manifestations and pathological features of a case of renal carcinoid tumor expressing ER and PR. The expression of ER and PR in carcinoid tumors of the kidney is unusual, and these molecules may be a potential therapeutic targets in such patients.

Acknowledgements

This study was supported by the Project of Administration of Traditional Chinese Medicine of Shandong Province (grant no. 2009222).

References

1. Han X, Yu L, Yang S and Zheng J: Primary neuroendocrine tumor of the testis: A study of clinicopathological features. Int J Clin Exp Pathol 7: 1771-1776, 2014.
2. Kaplan AL, Margolis DJ, Said J and Chin AI: Primary carcinoid tumor of urinary bladder discovered on pelvic magnetic resonance imaging. Urology 80: e55-57, 2012.
3. Pavel M, Hörsch D, Caplin M, *et al*: Telotristat etiprate for carcinoid syndrome: A single-arm, multicenter trial. J Clin Endocrinol Metab 100: 1511-1519, 2015.
4. Chi Y, Du F, Zhao H, Wang JW and Cai JQ: Characteristics and long-term prognosis of patients with rectal neuroendocrine tumors. World J Gastroenterol 20: 16252-16257, 2014.
5. Roy S, Hooda S, Huang GJ, Pantanowitz L and Parwani AV: A novel case of concurrent renal tumors: chromophobe renal cell carcinoma and carcinoid tumor of the kidney with brief review of renal neuroendocrine tumors. Int J Surg Pathol 20: 531-535, 2012.
6. Kato Y, Nakamura K, Yamada Y, *et al*: A rare case of metastatic renal carcinoid. BMC Urol 10: 22, 2010.
7. Litwinowicz R, Szpor J, Januś G, *et al*: Primary carcinoid tumour in horseshoe kidney. Pol J Pathol 62: 72-74, 2011.
8. Eble JN, Sauter G, Epstein JI and Sesterhenn IA (eds): Renal carcinoid tumour. In: World Health Organization Classification of Tumors. Pathology and Genetics of Tumors of the Urinary System and Male Genital Organs. 3rd edition. IARC Press, Lyon, France, pp81, 2004.
9. Raslan WF, Ro JY, Ordonez NG, *et al*: Primary carcinoid of the kidney. Immunohistochemical and ultrastructural studies of five patients. Cancer 72: 2660-2666, 1993.
10. Takeshima Y, Inai K and Yoneda K: Primary carcinoid tumor of the kidney with special reference to its histogenesis. Pathol Int 46: 894-900, 1996.

11. Lodding P, Hugosson J and Hansson G: Primary carcinoid tumour with ossification masquerading as calyx stone in a horseshoe kidney. Scand J Urol Nephrol 31: 575-578, 1997.
12. Kuroda N, Tanaka A, Ohe C, *et al*. Review of renal carcinoid tumor with focus on clinical and pathobiological aspects. Histol Histopathol 28: 15-21, 2013.
13. Liang JJ, Alrawi S, Fuller GN and Tan D: Carcinoid tumors arising in tailgut cysts may be associated with estrogen receptor status: case report and review of the literature. Int J Clin Exp Pathol 1: 539-543, 2008.
14. Viale G, Doglioni C, Gambacorta M, Zamboni G, Coggi G and Bordi C: Progesterone receptor immunoreactivity in pancreatic endocrine tumors. An immunocytochemical study of 156 neuroendocrine tumors of the pancreas, gastrointestinal and respiratory tracts, and skin. Cancer 70: 2268-2277, 1992.
15. Hansel DE, Epstein JI, Berbescu E, Fine SW, Young RH and Cheville JC: Renal carcinoid tumor: A clinicopathologic study of 21 cases. Am J Surg Pathol 31: 1539-1544, 2007.
16. Canacci AM and MacLennan GT: Carcinoid tumor of the kidney. J Urol 180: 2193, 2008.
17. Kawajiri H, Onoda N, Ohira M, *et al*: Carcinoid tumor of the kidney presenting as a large abdominal mass: Report of a case. Surg Today 34: 86-89, 2004.
18. McCaffrey JA, Reuter VV, Herr HW, Macapinlac HA, Russo P and Motzer RJ: Carcinoid tumor of the kidney. The use of somatostatin receptor scintigraphy in diagnosis and management. Urol Oncol 5: 108-111, 2000.
19. Romero FR, Rais-Bahrami S, Permpongkosol S, Fine SW, Kohanim S and Jarrett TW: Primary carcinoid tumors of the kidney. J Urol 176: 2359-2366, 2006.