

Primary Renal Carcinoid Tumor With Multiple Metastases

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Primary renal carcinoid tumors are extremely rare lesions of the kidney, with fewer than 60 cases reported previously. Here, we present the case of a 46-year-old man who had primary renal carcinoid tumor with multiple liver, para-aortic lymph node and bony metastases when he was diagnosed initially. In consideration of life quality, we performed cytoreductive surgery only. In the following year, the patient did not have any severe cancer-related morbidity. [*J Chin Med Assoc* 2010;73(8):435–437]

Key Words: carcinoid tumor, kidney, metastasis

Introduction

Carcinoid tumors occur most commonly in the gastrointestinal tract and respiratory tract. Their occurrence in other locations is less common. Primary renal carcinoid tumors are extremely rare lesions of the kidney, with fewer than 60 cases reported previously.¹ Due to the small number of reported cases, the behavior of renal carcinoid tumors is not well defined, and hence it is difficult to predict their prognoses.

Carcinoid tumors are believed to originate from enterochromafin or amine precursor uptake and decarboxylation cells with malignant potential. It has been hypothesized that renal carcinoid tumors originate from scattered neuroendocrine cells derived from acquired or congenital abnormalities, including: (1) metaplasia of the pyelocaliceal urothelium induced by chronic inflammation; (2) metastasis from an undiscovered primary tumor; (3) a misplaced or entrapped neural crest during embryogenesis; (4) activation of gene sequences in multipotent primitive stem cells; or (5) concurrent congenital renal abnormalities.¹

Herein, we report a case of primary left renal carcinoid tumor with para-aortic lymphadenopathy, synchronous metastases of bilateral liver lobes and bony metastases based on radiological studies.

Case Report

A 46-year-old man presented with left flank dull ache initially. On physical examination, there was a palpable left flank mass and no gross hematuria was noted. The patient's general blood routine, urine routine and renal function examination were within normal ranges. However, sonography showed a left renal mass with hypoechoic lesions in the liver. The subsequent abdominal computed tomography (CT) scan showed a left renal mass, 2 liver masses, para-aortic lymphadenopathy and thoracolumbar spinal lesions (Figure 1A). The left renal mass was heterogeneous and multilobulated, with areas of calcification in the periphery (Figure 1B), and the largest was about 6.5 cm in size. The liver masses were multiple hypovascular masses over bilateral lobes. In addition, mixed osteoblastic and osteolytic lesions over the T12, L1 and L3 vertebral bodies were noted, hence bony metastasis was considered. Tumor markers α -fetoprotein, carcinoembryonic antigen, CA153, CA19-9 and squamous cell carcinoma antigen were within normal limits. There was no leukocytosis and no impaired liver or renal function preoperatively. The initial differential diagnoses included renal cell carcinoma, lymphoma and squamous cell carcinoma. However, in consideration of rare renal cancer,



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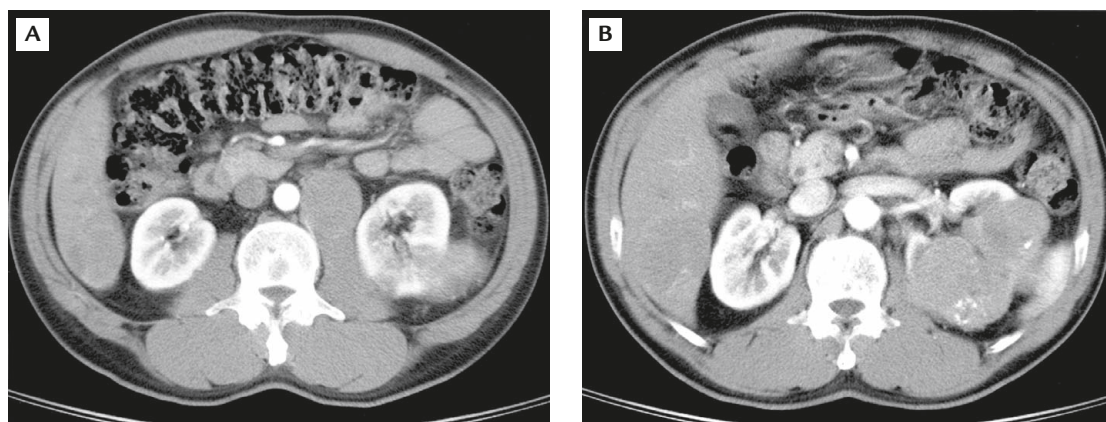


Figure 1. (A) Abdominal computed tomography (CT) shows a left renal mass with para-aortic lymphadenopathy. (B) Abdominal CT shows that the left renal mass is heterogeneous and multilobulated, with areas of calcification in the periphery.

CT-guided percutaneous biopsy of the left renal mass was performed, which the pathologist reported to be only a neoplasm with low malignant potential. We later performed tumor resection with para-aortic lymph node dissection, but we did not excise the liver lesions due to extensive involvement.

The final pathology report indicated a carcinoid tumor of the left kidney with metastatic para-aortic lymph node. Advanced immunohistochemistry revealed that the lesion was positive for neuron-specific enolase (Figure 2) and CD56, but negative for chromogranin and synaptophysin. These features are consistent with a neuroendocrine tumor.

Postoperatively, the patient presented with no specific carcinoid syndrome after almost 1 year of follow-up (Figure 3). Chemotherapy regimens seemed to not show remarkable tumor regression rates,² so we did not apply adjuvant chemotherapy postoperatively. Advanced transarterial embolization for hepatic metastases was arranged 1 year later due to the patient's personal reasons.

Discussion

The biochemical features of a typical carcinoid tumor, usually the midgut type, include the enzyme dopa decarboxylase, which converts 5-hydroxytryptophan into serotonin, which in turn develops into clinical carcinoid syndrome, including flushing, diarrhea, and bronchospasm.² However, only a few patients, even among those with gastrointestinal tract carcinoid tumor, have been reported to present with these classic symptoms, making the preoperative diagnosis of this disease difficult. Primary renal carcinoid tumor seldom has these biochemical manifestations and is indolent in nature. Patients who have a renal carcinoid tumor

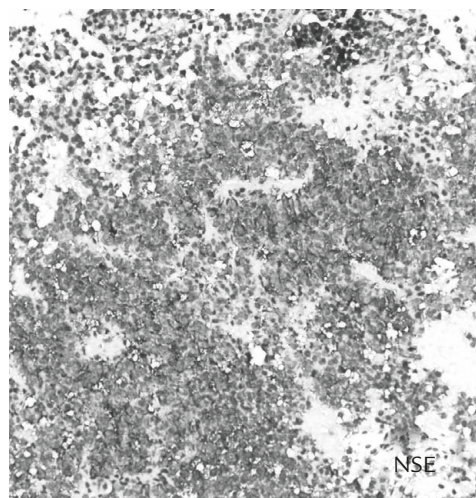


Figure 2. The tumors are composed of monomorphous cells arranged in trabecular tubulocystic and sheet-like patterns with positive staining for neuron-specific enolase.

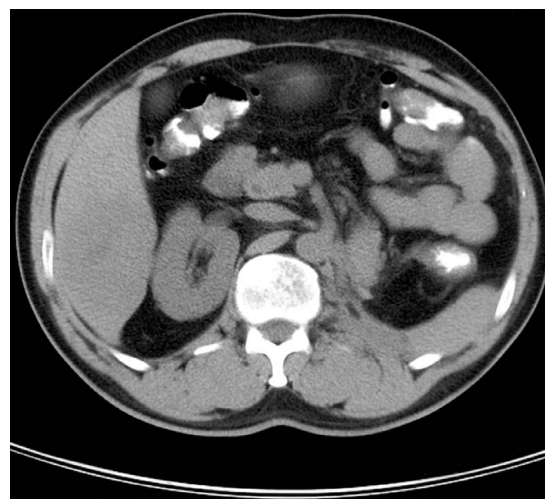


Figure 3. Abdominal computed tomography shows the follow-up image about 1 year postoperatively.

usually have a huge tumor burden of about 8.4 cm when diagnosed.¹ Urinary 5-hydroxyindoleacetic acid level measured in a 24-hour urine sample test is the most common work-up for carcinoid tumors. However, it lacks sensitivity and specificity in the diagnosis of carcinoid syndrome because it may also be elevated in other conditions such as tropical sprue, celiac disease, Whipple's disease and small bowel obstruction.² To date, no biochemical test has been developed to determine whether a known, endocrinologically silent renal mass is a carcinoid tumor. In our case, the patient did not have classic carcinoid syndrome, and that made it difficult to find a clinical link with neuroendocrine tumor.

In addition, the 3 most common renal carcinoid metastatic sites are the peri-aortic or perihilar lymph nodes, liver, and bones in sequence. As Romero and colleagues reported, good prognostic factors are age younger than 40 years, tumor size < 4 cm, and mitotic rate < 1/10 per high-powered field.¹ In other previous reports,^{3,4} the correlation of renal carcinoid tumor and horseshoe kidney was discussed. It was concluded that the relative risk of renal carcinoid tumor developing into a horseshoe kidney is markedly greater than that for Wilms' tumor or transitional cell carcinoma, yielding a calculated relative risk of 62.³⁻⁵

With regard to imaging modalities, renal carcinoid tumors have a tendency to present with minimal or poor enhancement on contrast-enhanced CT, corresponding to hypovascular or avascular lesions on renal angiography. Though octreotide scintigraphy was introduced as a sensitive imaging modality for the diagnosis and staging of carcinoid tumors, it may also play a major role in the detection of residual tumor or metastases.⁶

Radiologically, abdominal CT in our patient showed that the renal carcinoid tumor was multilobulated and hypovascular, with calcification of the periphery. In addition, the enlarged para-aortic lymph node and multiple low-signal-intensity lesions of the liver made us suspect an unusual renal tumor. Thus, CT-guided percutaneous biopsy was performed to rule out the possibility of other types of rare renal tumors. However, the pathologist only reported the lesion to be a neoplasm with low malignant potential. In such cases, it is difficult for the clinician to determine the next step.

Surgically, unlike Gedaly and colleagues, who performed extensive radical resection of the tumor including hepatectomy,⁷ we performed radical nephrectomy of the renal tumor with lymphadenectomy but left the liver lesions for further treatment. During the

operation, the pathologist reported that a frozen section of the tumor was a carcinoid. However, definitive diagnosis depended on immunohistochemistry stain with neuron-specific enolase, chromogranin, synaptophysin, glucagons, vasoactive intestinal peptide, serotonin, and somatostatin.

Recently, long-acting somatostatin analogs have been shown to be effective in controlling carcinoid syndrome. Previously, the use of indium-labeled octreotide or ¹³¹I-metaiodobenzylguanidine in receptor-targeted radionuclide therapy was reported to be beneficial symptomatically.² In addition, high-dose octreotide has also been reported to reduce symptoms and biochemical markers as well as tumor load.

The role of chemotherapy, such as streptozotocin-doxorubicin, streptozotocin plus 5-fluorouracil or dacarbazine, is limited due to poor response rate and toxicity. Even though a 50% biochemical response has been reported with a regimen of interferon combined with 5-fluorouracil, it is not recommended due to poor tolerance.²

In conclusion, further study is needed to determine the best treatment modality for rare renal tumors. Early radical debulking surgery of the tumor may improve cancer-free survival, but it could also lead to severe perioperative morbidity. Less radical surgery with adjuvant therapeutic planning may be a better choice.

References

1. Romero FR, Rais-Bahrami S, Permpongkosol S, Fine SW, Kohanim S, Jarrett TW. Primary carcinoid tumors of the kidney. *J Urol* 2006;176:2359-66.
2. Pasiaka JL, McKinnon JG, Kinnear S, Yelle CA, Numerow L, Paterson A, Rorstad O, et al. Carcinoid syndrome symposium on treatment modalities for gastrointestinal carcinoid tumours: symposium summary. *Can J Surg* 2001;44:25-32.
3. Hohenfellner M, Schultz-Lampel D, Lampel A, Steinbach F, Cramer BM, Thüroff JW. Tumor in the horseshoe kidney: clinical implications and review of embryogenesis. *J Urol* 1992;147:1098-102.
4. van den Berg E, Gouw AS, Oosterhuis JW, Störkel S, Dijkhuizen T, Mensink HJ, de Jong B. Carcinoid in a horseshoe kidney. Morphology, immunohistochemistry, and cytogenetics. *Cancer Genet Cytogenet* 1995;84:95-8.
5. Krishnan B, Truong LD, Saleh G, Sirbasku DM, Slawin KM. Horseshoe kidney is associated with an increased relative risk of primary renal carcinoid tumor. *J Urol* 1997;157:2059-66.
6. McCaffrey JA, Reuter VV, Herr HW, Macapinlac HA, Russo P, Motzer RJ. Carcinoid tumor of the kidney. The use of somatostatin receptor scintigraphy in diagnosis and management. *Urol Oncol* 2000;5:108-11.
7. Gedaly R, Jeon H, Johnston TD, McHugh PP, Rowland RG, Ranjan D. Surgical treatment of a rare primary renal carcinoid tumor with liver metastasis. *World J Surg Oncol* 2008;6:41.