TRANSITIONAL CELL CARCINOMA OF THE RENAL PELVIS WITH EXTENSION INTO THE INFERIOR VENA CAVA: A REPORT OF TWO CASES

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Of all primary malignant renal tumors, 10% to 15% originate from the renal pelvis, and 90% to 92% of these tumors are transitional cell carcinomas. Nonetheless, renal pelvis transitional cell carcinoma extending into the inferior vena cava is very rare. We report one confirmed case and one highly suspicious case of renal pelvis transitional cell carcinoma with a tumor thrombus in the inferior vena cava. Both of our patients died within 6 months of initial diagnosis, indicating the poor prognosis and advanced stage of transitional cell carcinoma with an inferior vena cava thrombus. Transitional cell carcinoma should be considered in patients with obstruction of the renal vein and the inferior vena cava.

Key Words: transitional cell carcinoma, renal pelvis, inferior vena cava

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Of all primary malignant renal tumors, 10% to 15% originate from the renal pelvis, and 90% to 92% of these tumors are transitional cell carcinomas. The incidence of transitional cell carcinoma of the urothelium in the area endemic for “blackfoot disease” in southern Taiwan is noted to be significantly higher than anywhere else in the world [1]. Among all the tumors of the kidney, the percentage of renal pelvis transitional cell carcinoma is also unusually high (40%) in southern Taiwan, which is different from the majority of reports from elsewhere in the world. Renal pelvis transitional cell carcinoma extending into the inferior vena cava (IVC) is very uncommon. Most IVC thromboses occur with renal cell carcinoma, but the incidence is very low, reportedly only 5% to 7.4% [2,3]. We report one confirmed case and one highly suspicious case of renal pelvis transitional cell carcinoma with a tumor thrombus in the IVC and review the pertinent literature.

CASE PRESENTATIONS

Case 1
A 50-year-old woman complained of right flank pain and gross hematuria for about 1 month. Physical examination revealed a large, solid mass in the right side of the abdomen and bilateral, lower-leg, pitting edema, and lower abdominal venous engorgement. Her laboratory evaluation was remarkable for anemia, leukocytosis, and renal function impairment (white blood cell count, WBC: 60,570/μL, hemoglobin, Hb: 7.1 g/dL, blood urea nitrogen, BUN: 85 mg/dL, creatinine, Cr: 3.3 mg/dL). Urinalysis showed microscopic hematuria and proteinuria. A urine culture
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was sterile and urine cytology showed no malignant cells.

A chest X-ray was normal. Right retrograde pyelography revealed multiple renal pelvis filling defects and hydronephrosis. Cystoscopy showed no evidence of a tumor in the bladder. Abdominal magnetic resonance imaging (MRI) showed severe right hydronephrosis and a right renal pelvis, soft tissue mass with diffuse parenchymal infiltration and extension into the IVC (Figure 1A). Abdominal computerized tomography (CT) also showed the same finding.

As the cytology of the urine sample was negative, the preoperative diagnosis was renal cell carcinoma with IVC extension. At surgery, a thoracoabdominal approach was used, and a large, right, renal mass was found. Due to reactive fibrosis around the renal pedicle and severe adhesion of the tumor mass to the vena cava wall, isolation of the right renal pedicle was difficult. Right radical nephrectomy was performed, and the tumor thrombus in the IVC was incompletely removed. Tumor pathology revealed high-grade transitional cell carcinoma with extensive necrotic cancer cells (Figure 1B). The patient died from respiratory failure 3 weeks after surgery.

Case 2
A 72-year-old woman suffered from chills, fever and right flank tenderness for about 3 weeks before visiting our emergency room. Laboratory evaluation revealed leukocytosis, renal function impairment, and anemia (WBC: 16,350/μL, BUN: 38.0 mg/dL, Cr: 3.5 mg/dL, Hb: 9.8 mg/dL). Urinalysis showed pyuria and microscopic hematuria. Urine cytology revealed clusters of atypical urothelial cells with hyperchromatic nuclei, high nucleus/cytoplasm ratio, and coarse chromatin, consistent with transitional cell carcinoma.

A series of radiologic evaluations were performed. Abdominal CT showed a right renal, lower-pole soft mass with abscess formation, an IVC thrombus, and para-aortic lymph node enlargement. Right retrograde pyelography showed total obstruction of the upper ureter with an intraluminal filling defect. Selective right renal arteriography demonstrated a slightly hypervascular mass with poor margins at the lower pole of the right kidney, with contrast medium drainage into the subcapsular and periureter veins (Figure 2A). Inferior venacavography demonstrated total occlusion of the IVC with a thrombosis in the right renal vein extending into the IVC (Figure 2B). A plain chest X-ray was normal. The patient refused surgical intervention or systemic chemotherapy and died 5 months after the initial diagnosis of cancer.

DISCUSSION
Malignant tumors of the kidneys account for 2% to 3% of all neoplasms in humans. About 85% of these are renal cell carcinomas, whereas 10% to 15% arise from the urothelium. Of these, 90% to 92% are transitional cell carcinomas, with the remainder being squamous cell carcinomas and, rarely, adenocarcinomas [1]. A small percentage of malignant renal tumors are lymphomas and metastatic tumors.

Extension of renal cell carcinomas into the vena cava is uncommon, with a reported incidence of 5% to

Figure 1. (A) Magnetic resonance imaging (T2-weighted) demonstrates severe right hydronephrosis and a right renal pelvis, soft tissue mass with diffuse parenchymal infiltration and extension into the inferior vena cava (arrow). (B) Histologic appearance of typical transitional cell carcinoma, with tumor thrombus in blood vessels. (Hematoxylin & eosin, x 400)
7.4% of renal cell carcinomas [2,3]. Extension of transitional cell carcinomas into the vena cava is very rare, with only 17 cases reported in the literature [4–16]. Our two cases are among the few reported cases of transitional cell carcinoma of the renal pelvis with a tumor thrombus involving the IVC.

When a patient presents with the symptoms and signs of lower extremity edema, varicocele, dilated superficial abdominal veins, albuminuria, pulmonary embolism, right atrial mass, or non-function of the involved kidney, the urologist should suspect tumor extension into the main renal vein or the IVC [17]. The majority of patients with extension of a renal tumor into the IVC have nonspecific symptoms, and the diagnosis is made radiographically.

Despite the development of radiologic examinations, correct preoperative diagnosis of transitional cell carcinoma with IVC thrombosis is very difficult. CT, MRI, or angiography can effectively detect a vena cava tumor thrombus and clarify the extent of the thrombus. However, no radiologic diagnostic imaging modality is specific enough to differentiate renal cell carcinoma from transitional cell carcinoma.

Transitional cell carcinoma of the kidney is almost invariably small at the time of diagnosis. On CT, these small lesions most commonly present as low attenuated intraluminal filling defects in the renal pelvis [18]. Other CT features of transitional cell carcinoma include tissue necrosis and calcification [19]. As the transitional cell carcinoma enlarges and infiltrates adjacent parenchymal structures, differentiation of transitional cell carcinoma from other neoplastic processes becomes much more difficult. Preservation of the reniform shape of the kidney and central location of the tumor may be of help in differentiation [10].

In the literature, most transitional cell carcinomas are hypovascular on angiography [19,20]. However, in selective arteriography obtained in nine of 19 cases, eight showed diffuse neovascularity [4,7–9,15]. The reasons for why a renal transitional cell carcinoma with an IVC thrombus is hypervascular, in contrast to the hypovascular character of most transitional cell carcinomas, remain unclear. A transitional cell carcinoma should be suspected when a renal tumor mass has venous involvement, even if the tumor is hypervascular on selective arteriography.

Some neoplastic processes involving the kidneys are characterized by diffuse infiltration and replacement of the renal parenchyma. These patterns of the neoplastic process are observed in transitional cell carcinomas, squamous cell carcinomas, and infiltrative renal cell carcinomas [21,22]. This infiltrating variety makes preoperative differentiation of renal cell carcinoma from transitional cell carcinoma very difficult. Both lesions are infiltrative and have a tendency to invade the vascular system. The renal

![Figure 2. (A) Selective right renal arteriography shows a hypervascular mass involving the lower half of the kidney. (B) Inferior venacavography via the right femoral venous approach shows complete obstruction of the inferior vena cava, with collateral vein drainage.](image)
pelvis and ureter are narrow structures, the tumor can easily infiltrate the pelvis and ureter walls and disseminate into the peripheral soft tissue. This infiltration can make some tumors inoperable.

A specific preoperative diagnosis of renal cell carcinoma or transitional cell carcinoma is important because the surgical approach is different for each. Aggressive surgical management, including radical nephrectomy and IVC tumor thrombus removal, is advocated for renal cell carcinoma with vena cava extension. Nephroureterectomy and bladder cuff excision make up the standard treatment for transitional cell carcinoma. Frozen section during surgery is recommended to differentiate renal cell carcinoma from transitional cell carcinoma. Aggressive surgery to remove the thrombus in the IVC is reported to be effective in prolonging survival in patients with renal cell carcinoma. However, its value in treating transitional cell carcinoma of the kidney is unclear because of limited data and the aggressive nature of the disease.

Sixteen of the reported 19 patients with tumor thrombi in the IVCs had right side renal pelvis tumors. Tongaonkar et al reported 47 renal cell carcinomas extending to the renal vein and IVC; 33 patients had the tumor on the right side [23]. This observation can be explained by the anatomic character of humans: the right side renal vein is closer to the IVC and is shorter than the left side renal vein.

The male to female ratio is also interesting to note. Most upper urinary tract transitional cell carcinomas have a male/female ratio of about 2 to 3. After reviewing the literature, the male to female ratio of the cases with tumor thrombi in the IVCs is about 1 (male: female = 9:10), and both of our cases were female patients. Mungan et al reported patients with bladder cancer and upper urinary tract tumors and found that the stage distribution at first presentation for both bladder cancer and upper urinary tract tumors was slightly worse in female than in male patients [24]. One hypothesis to explain the higher stage in female patients is that there may be some delay in the diagnosis of bladder cancer or upper urinary tract tumor in patients with cystitis, with or without hematuria, as the presenting symptoms. Because cystitis is more common in women, this might explain a delay in help-seeking behavior by women.

The prognosis of patients with transitional cell carcinoma accompanied by a tumor thrombus in the IVC is relatively poor compared to those with renal cell carcinoma with a vena cava tumor thrombus. Despite aggressive radical nephrectomy or nephroureterectomy, most patients died within 6 months of initial diagnosis. Systemic chemotherapy can be used as an adjuvant treatment for these patients. However, the effect of systemic chemotherapy is unclear because of the limited number of cases.

**CONCLUSION**

We presented one confirmed case and one highly suspicious case of transitional cell carcinoma of the renal pelvis with extension into the renal vein and IVC. Transitional cell carcinoma should be included in the differential diagnosis of renal tumors that cause an IVC tumor thrombus, even if the tumor is hypervascular on selective arteriography. Both of our patients died within 6 months of the initial diagnosis, indicating the poor prognosis of transitional cell carcinoma with IVC thrombus.

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