CASE REPORT

Primary Small Cell Carcinoma of the Upper Urinary Tract

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We report a case of primary extrapulmonary small cell carcinoma of the distal ureter, with a synchronous small cell carcinoma of the ipsilateral renal pelvis. These tumors, rarely reported in the urinary tract, are locally aggressive and have a poor prognosis. A 77-year-old male bedridden patient presented with fever and chills with left side-flank pain for 3 days. Following a diagnosis of ureteral urothelial carcinoma, hand-assisted laparoscopic nephroureterectomy with bladder cuff excision was carried out. Adjuvant chemotherapy was given after pathologic report of primary small cell carcinoma of the distal ureter and a synchronous small cell carcinoma of the ipsilateral renal pelvis. After 3 cycles of combination chemotherapy, the patient died 4 months postoperatively due to sepsis. [*J Chin Med Assoc* 2010;73(3):173–176]

Key Words: extrapulmonary small cell carcinoma, hand-assisted laparoscopic nephroureterectomy, urothelial carcinoma

Introduction

Small cell carcinomas (SCCs) are usually found in the lung and represent approximately 20–25% of all bronchogenic carcinomas.[1] On the other hand, extrapulmonary SCCs (EPSCCs) are rare neoplasms that are recognized as distinct clinicopathologic entities separate from lung SCC,[1] encompassing approximately 0.1–0.4% of all SCCs.[2] EPSCCs have been described in a variety of organs, including the esophagus, stomach, pancreas, gallbladder, uterine cervix, kidney, urinary bladder and prostate.[1] The clinical courses of these tumors are generally aggressive, with early dissemination and frequent recurrence. Surgical resection is not curative, with current adjuvant chemotherapy extending patient survival for a few months.[3]

SCC of the genitourinary tract has been commonly reported in the urinary bladder, with primary SCC of the upper urinary tract a rare entity. Due to its rarity, the natural history of upper urinary tract SCC is not well known. We therefore present a case and a systematic literature review regarding the clinical presentation and treatment of this rare tumor.

Case Report

A 77-year-old male bedridden patient presented to our hospital with fever and chills associated with left-side flank pain for 3 days. Physical examination showed a chronically ill-looking male with a distended urinary bladder. The patient had been a chain smoker for more than 30 years and had quit smoking 1 year ago after an episode of cerebrovascular accident. Laboratory examination revealed leukocytosis, with white blood cell count of 45,384/μL, with microscopic hematuria and pyuria on urinalysis. Renal ultrasound revealed severe left hydronephrosis; hence, percutaneous nephrostomy drainage (PCN) of the left renal pelvis was performed. Abdominal computed tomography (CT) was performed and revealed post PCN drainage of the left renal pelvis with an intravesical polypoid mass over the internal orifice of the left ureter, with severe left hydronephroureterosis, which led to the suspicion of urothelial tumor in the urinary bladder or left collecting system (Figure 1).

Cystoscopic examination showed an extruding mass over the left ureteral orifice. Biopsy was done,

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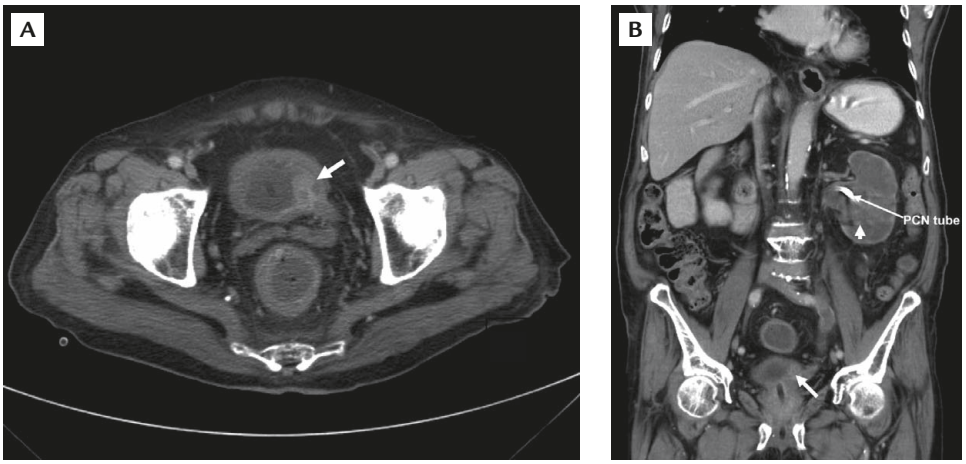

Figure 1. (A) Computed tomography of the pelvis with contrast shows an intravesical mass (arrow) over the internal orifice of the left ureteropelvic region. (B) Computed tomography reconstruction of the abdomen shows severe hydronephrosis of the left kidney (arrowhead) with post-percutaneous nephrostomy drainage (PCN); left hydroureter is also noted. The same intravesical mass (arrow) over the left internal orifice can also be seen.

and pathology revealed invasive urothelial carcinoma with neuroendocrine differentiation. Chest radiographs were reviewed, and no primary or metastatic lung lesions were noted.

Hand-assisted left laparoscopic nephroureterectomy with bladder cuff excision was carried out. Grossly, the kidney was enlarged, with multiple soft-tissue tumors in the renal pelvis measuring up to 2 cm in diameter. The ureter measured 23 cm in length and 2.5 cm in diameter, with multiple soft-tissue tumors measuring 2 cm in diameter scattered over the entire left ureter, with invasion to the left bladder cuff.

Microscopically, both tumors (Figures 2A–C) were composed of small cells, round to fusiform in shape, with scanty cytoplasm, fine granular nuclear chromatin, and absence of nucleoli. There was high mitotic activity, and the cells stained positive on chromogranin (Figure 2D). These features were compatible with SCC. The clinical stage based on CT and operative findings was compatible with the final pathologic stage of T3N0M0 (American Joint Committee on Cancer Stage III).

Abdominal CT performed 2 months postoperatively showed no tumor recurrence and no distant metastasis. Four cycles of combination chemotherapy were scheduled, consisting of etoposide 80 mg/m^2 on days 1, 2 and 3 with carboplatin 80 mg/m^2 on day 1, every 3 weeks. However, after 3 cycles of chemotherapy, the patient died 4 months postoperatively due to sepsis.

Discussion

SCC is a highly malignant and aggressive tumor that is usually found in the lung. EPSCC is a relatively rare disease that was first reported in 1930 by Duguid and Kennedy.[4] SCCs are not commonly seen in the urinary tract; frequently, they are combined with other components such as transitional cell carcinoma, adenocarcinoma, squamous cell carcinoma, and sarcomatoid squamous cell carcinoma.[5] The urinary bladder is the most common site of urinary tract SCC, with primary renal pelvis and ureteral SCC occurring extremely rarely.[6–8] In a 1998 report by Mackey et al of 180 cases of urinary tract SCC, 106 cases were located in the urinary bladder, 60 in the prostate, 8 in the kidney and 6 in the ureter.[6] With regard to the histopathogenesis of urinary tract SCC, 2 theories have been cited. One indicates that it originates from intrinsic neuroendocrine cells within the normal genitourinary tract, derived from the neural crest during embryogenesis,[9] while the other suggests that it transforms from pleuripotent epithelial reserve cells in the genitourinary tract with the ability to generate any cell type.[10] The existence of frequent combinations with transitional cell carcinoma or other histology supports the latter theory. Urinary tract SCC shares the same histologic features of lung SCC, which are small cells with round to fusiform shape, inconspicuous or absent nucleoli, scanty cytoplasm, and high mitotic activity. Tumor cells also show positivity for neuroendocrine markers such as chromogranin, synaptophysin, and neuron-specific enolase.[11,12]

The clinical features of primary urinary tract SCC are indistinguishable from those of renal clear cell carcinoma, with hematuria and flank pain being the most commonly reported symptoms. Hematuria, usually gross, is due to vascular invasion, while pain is secondary to hydronephrosis following obstruction of the ureter.[13] When such symptoms appear, the stage may already

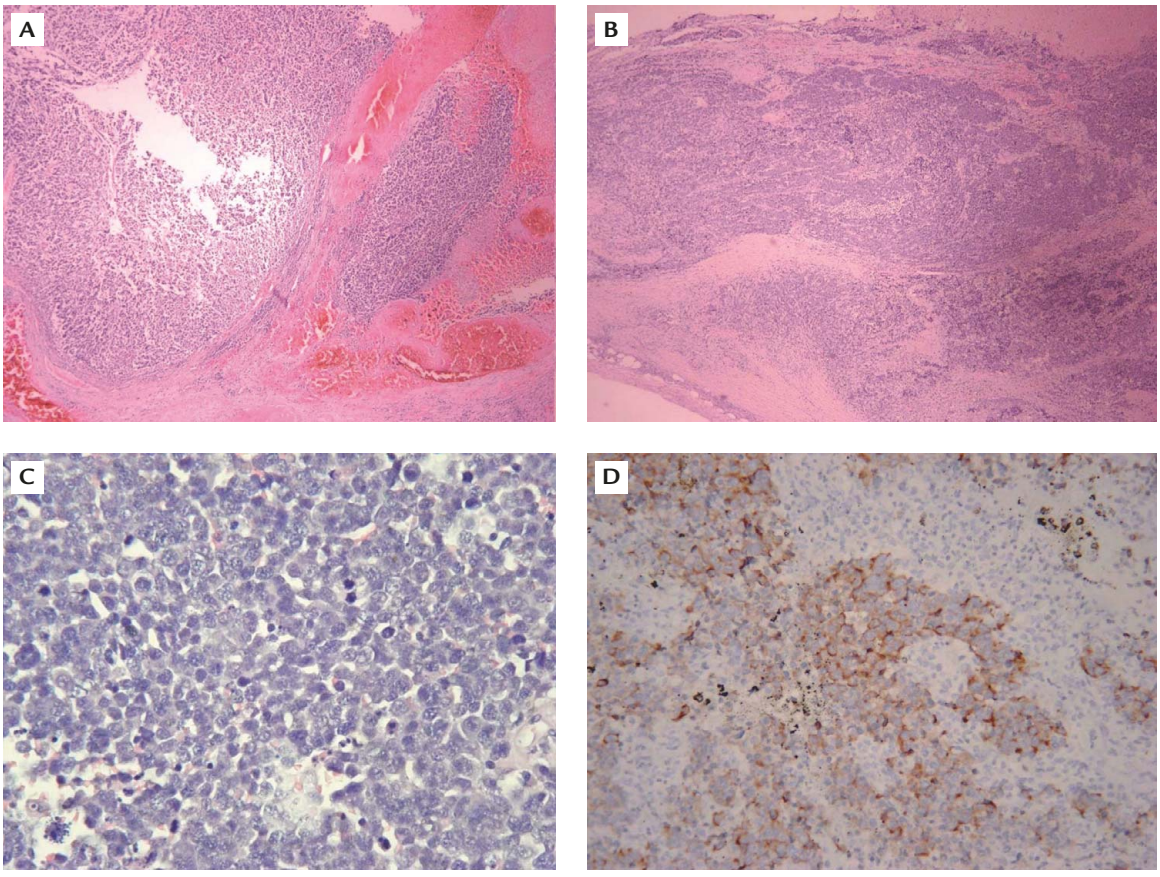

Figure 2. Light microscopy [hematoxylin & eosin (H&E), 40×] shows small cell carcinoma in: (A) renal pelvis; and (B) left distal ureter. (C) Light microscopy (H&E, 400×) shows small cells with round to fusiform shape, scanty cytoplasm with fine granular nuclear chromatin, absence of nucleoli, and with high mitotic activity. (D) Small cell carcinoma shows positivity for chromogranin (400×).

be high.[6,7] Our patient presented with fever and chills associated with left-side flank pain and severe hydronephroureterosis. Results from another study showed that excretory urography, ultrasonography, CT and magnetic resonance imaging were helpful in defining the extent and location of the tumor.[14]

The staging of urinary tract SCC is in accordance with SCC of the lung, that is, whether or not the primary tumor can be encompassed within a tolerable radiation therapy port. Thus, a tumor confined to the primary site, with or without regional lymph node involvement, is classified as limited disease, whereas spread of the disease beyond locoregional boundaries is considered extensive disease.[1] In our patient, it could not be determined whether the primary tumor originated from the ureter with extension to the renal pelvis or the other way around. However, regardless of which site the primary tumor originated from, it had already extended beyond 1 radiation port, and was therefore classified as extensive disease.

What constitutes optimal treatment of urinary tract SCC is not well established. Many clinicians advocate multimodality therapy, which includes surgery, chemotherapy and radiation.[12–15] The present recommendation of a combination of a platinum-based chemotherapeutic agent and etoposide is the most frequently used regimen because of its better response rate compared with other regimens.[15]

In conclusion, we have presented a case of primary upper urinary tract SCC. Surgical resection with adjuvant platinum-based chemotherapy was given but, unfortunately, our patient died 4 months after operation due to sepsis.

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