**Original Article**

# Rare Small Cell Carcinoma in Genitourinary Tract: Experience from E-Da Hospital

*Wei-Ting Kuo[1], I-Wei Chang[2], Kevin Lu[1], Hua-Pin Wang[1], Tsan-Jung Yu[1], Victor C. Lin[1,3]*

**Objectives:** Small cell carcinoma (SCC) of the genitourinary tract is a rare malignancy for which, to date, no treatment guideline and data of prognosis are available. The purpose of this study is to report the management and outcome at our hospital.

**Methods:** The demographics, clinical, and pathologic characteristics as well as treatment strategies and outcomes of 17 patients (men : women = 12 : 5), with pathology-proven diagnosis of small cell carcinoma of the genitourinary, between 2008 and 2014 at a single tertiary medical center were retrospectively reviewed and analyzed.

**Results:** The primary sites were as below: urinary bladder (n = 5), prostate (n = 6), and upper urinary tract (n = 6). Eight patients (47%) showed pure pathology of small cell carcinoma, while the rest exhibited mixed pathology with prostate adenocarcinoma or urothelial carcinoma. Among these 17 patients, 3 were lost to follow-up, 7 expired after adjuvant chemotherapy, and 7 had regular follow-ups with stable disease or complete regression.

**Conclusions:** Small cell carcinoma (SCC) in the genitourinary tract is an aggressive cancer, with a poor overall prognosis. Patients with genitourinary pure SCC appeared to live longer than patients with SCC mixed with other tumors in our study.

**Key words:** small cell carcinoma, genitourinary tract, chemotherapy, radical surgery, overall survival

## Introduction

Small cell carcinoma (SCC), which mostly originated from the lung, accounted for 14% of all lung cancers in the United States.[1] Only about 2.5% of all primary SCC have been reported to be found in extrapulmonary organs, including the genitourinary system.[2] Genitourinary SCC was usually an aggressive disease with rapid clinical progression. Because of its rare occurrence in the genitourinary tract, only few retrospective studies and clinical trials with small sample size were published. Neither standard treatment nor assessment of prognosis as to genito-

From the [1]Department of Urology, and [2]Department of Pathology, E-Da Hospital, and [3]School of Medicine for International Students, I-Shou University, Kaohsiung, Taiwan.
Received: November 3, 2015 Accepted: May 6, 2016
Address reprint request and correspondence to: Victor C. Lin, Division of Urology, Department of Surgery, E-Da Hospital, No. 1, Yida Road, Jiaosu Village, Yanchao District, Kaohsiung City 82445, Taiwan.
Tel: +886-7-6151100, Fax: +886-7-6150982, E-mail: victorlin0098@gmail.com

urinary SCC existed. Most experience was based on the algorithms of SCC of lung carcinoma. Therefore, the golden standard therapies remained controversial. We reported our clinical experience at E-Da hospital on the diagnosis and treatment of patients suffering from genitourinary SCC from 2008 to 2014 affter analysis of data on their demographic characteristics, clinical behaviors and treatment results.

## Patients and Methods

### Patient selection

We enrolled all cases of small cell carcinoma (SCC) of genitourinary tract diagnosed at our institute from pathology department, between January 2008 and December 2014. Age, gender, age at diagnosis, primary tumor site, tumor stage, histological component, site of metastasis, treatment modalities, and survival data were obtained from patients' medical records. We only included cases with pathologically confirmed diagnosis of small cell carcinoma of the genitourinary tract based on the World Health Organization classification of SCC.

### Definitions and tumor staging

Mixed type SCC was defined as a tumor containing SCC and non-SCC components. Patients were staged by using the TNM staging system, from the pathological staging of 2010 American Joint Committee on Cancer. This system was used to stage common urinary tract carcinoma. We defined limited stage as T1 and T2 primary tumor with or without regional lymph node involvement, and others were extensive stage. The overall survival rate (OS) was defined as the period from pathologic diagnosis to death or to the last follow-up after treatment.

### Statistical analysis

To investigate the overall survival rate between prostate small cell carcinoma (SCC) and bladder SCC, Kaplan-Meier curve and log-rank test are used by SPSS (Statistical Product and Service Solutions), version 20.0. Only variables with statistical significance ($p < 0.05$) were included in the final model.

## Results

Totally 17 patients with small cell carcinoma (SCC), diagnosed by pathology report of surgical specimen, were reviewed retrospectively at our hospital from 2008 to 2014. The characteristics and clinical information

*Table 1A. The characteristics of patients with genitourinary small cell carcinoma*

| Characteristics | |
|---|---|
| Patients, n | 17 |
| Gender, n (%) | |
| Men | 12 (70.5) |
| Women | 5 (29.4) |
| Age at diagnosis | |
| Median | 67 |
| Range | 60-91 |
| Primary sites, n (%) | |
| Bladder | 5 (29.4) |
| Prostate | 6 (35.3) |
| Upper urinary tract | 6 (35.3) |
| Histopathology, n (%) | |
| Pure | 5 (29.4) |
| Mixed | 12 (70.5) |
| Stage, n (%) | |
| Limited | 4 (23.5) |
| Extensive | 12 (70.5) |
| Unknown | 1 (5.8) |
| Adjuvant therapy, n (%) | |
| Chemotherapy | 8 (47) |
| Palliative R/T | 2 (11.8) |
| Surgery only | 3 (17.6) |
| Outcome, n (%) | |
| Stable disease | 7 (41.2) |
| Mortality | 7 (41.2) |
| Loss follow up | 3 (17.6) |
| Metastatic site, n | |
| Brain | 1 |
| Bone | 1 |

*Table 1B. The detailed clinical information of the patients and treatment*

| Patient | Primary site | Sex | Age | TNM | Radical surgery | Adjuvant therapy | OS | Pathology | Metastasis | Status |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Ureter | Female | 70 | T2 | Y | Chemotherapy | 66 | Mixed with UC | | |
| 2 | Bladder | Male | 64 | T3 | Y | Chemotherapy | 27 | Mixed with UC | | Dead |
| 3 | Bladder | Female | 78 | T1 | N | | 4 | | | Dead |
| 4 | Kidney | Female | 66 | T2 | Y | Chemotherapy | 36 | | | |
| 5 | Bladder | Male | 79 | M | N | | 3 | Mixed with Pca | | Dead |
| 6 | Bladder | Male | 67 | T2 | N | | Loss | | | |
| 7 | Bladder | Male | 83 | T1 | N | | 12 | Mixed with UC | | |
| 8 | Kidney and ureter | Female | 60 | T4 | Y | CCRT | Loss | | | |
| 9 | Ureter | Male | 78 | T3 | Y | Chemotherapy | 11 | Mixed with Pca and UC | | Dead |
| 10 | Kidney | Male | 89 | T3 | Y | Radiotherapy | 13 | Mixed with UC | Brain | |
| 11 | Ureter | Female | 72 | T3 | Y | Chemotherapy | 11 | | | |
| 12 | Prostate | Male | 64 | T4 | N | Radiotherapy | 30 | Mixed with Pca | Bone | Dead |
| 13 | Prostate | Male | 91 | T4 | N | | Loss | Mixed with Pca | | |
| 14 | Prostate | Male | 71 | T3b | Y | Chemotherapy | 24 | Mixed with Pca | Liver bone | Dead |
| 15 | Prostate | Male | 75 | T3b | Y | | 26 | Mixed with Pca | | |
| 16 | Prostate | Male | 78 | T3b | N | Chemotherapy | 12 | Mixed with Pca | | Dead |
| 17 | Prostate | Male | 72 | T4 | N | Hormonal | 14 | Mixed with Pca | | |

UC: Urothelial carcinoma; Pca: Prostate adenocarcinoma

*Table 2. The clinical information of small cell carcinoma in prostate and bladder*

| | Number | Extensive stage | Limited stage | Mortality |
|---|---|---|---|---|
| Prostate | 6 | 6 | 0 | 3 |
| Bladder | 5 | 3 | 2 | 3 |

were summarized in Table 1A and 1B. Male patients were predominant (men : women = 12 : 5). The mean age at diagnosis was 73.9 ± 8.7 years of age. The primary genitourinary sites of SCC were as follow: Bladder (n = 5), prostate (n = 6), and upper urinary tract (including kidney or ureter) (n = 6). Pure SCC was noted in 5 patients (29.4%), while the majority (12/17) had SCC mixed with prostate adenocarcinoma or urothelial carcinoma. Overall, only 5 patients had limited-stage disease (T1 or T2), whereas the other 12 had extensive-stage disease (T3 or T4). In terms of management, 11 patients (64.7%) received a combination of surgery and adjuvant therapy. Of these 11 patients, 8 received adjuvant chemotherapy after radical surgery, whereas 3 were treated with palliative radiotherapy for metastasis in brain, bone and liver/bone respectively. Only 2 patients underwent radical surgery without any adjuvant therapy. Five patients did not receive any adjuvant chemotherapy or radiotherapy for some reasons. Among these 17 patients, 3 were lost to follow-up for personal reasons, 7 expired after adjuvant chemotherapy and the other 7 has had regular follow-ups with stable disease or complete regression of disease. Prostate SCC seemed to be a more extensive disease than bladder SCC when we compared the prognosis of the two groups of patients (Table 2), including 100% of patients (6/6) with prostate SCC and 60% of patients (3/5) with bladder SCC who had extensive disease. The initial prostate specific antigen level (PSA) of the 6 patients with prostate SCC ranged from 1.2 to 438 ng/mL and the mean value was 90.1

ng/mL. Although the numbers of mortality were the same and the overall survival rates of the two groups were comparable (Fig. 1, $p = 0.301$), patients with pure type SCC had a better survival rate than those with mixed SCC.

## Discussion

Our study confirmed what had been reported in the literature that the genitourinary tract was one of the most common sites where extrapulmonary small cell carcinoma (SCC) developed. Most of the data came from our study revealed that genitourinary SCC was a disease that affected the elders, with mean age at diagnosis of 73.94 ± 8.7 years, and that this malignancy was more common in men.

Genitourinary SCC was an uncommon tumor and progresses aggressively with about survival rate of 25% and 8% in two year survival and in five year survival, respectively.[3] Similar to the results from previous studies, it mostly occurred in elderly men instead of women. Some studies reported that the prostate SCC was apt to be extensive stage compared to bladder SCC.[4] The patients with prostate SCC often presented with some lower urinary tract symptoms, which may delayed the diagnosis of prostate cancer. On the other hand, the patients with bladder SCC often complained hematuria or suprapubic pain. In the first visit of clinics, it was much easier for clinicians to detect the lesion and to make the diagnosis via the cystoscopy examination. In our study, all prostate SCC in our patients was an extensive stage disease, while about 40% of bladder SCC was in limited stage. In addition, there were two patients diagnosed as prostate SCC with distal metastasis (bone and liver metastasis); instead, no metastasis occurred in cases of bladder SCC. In Deorah et al.'s cohort study,[5] 47% of the prostate patients were diagnosed with distant metastasis. However, only 5% were reported in Choong et al.'s cohort study.[6] From the Kaplan-Meier curve and log-rank

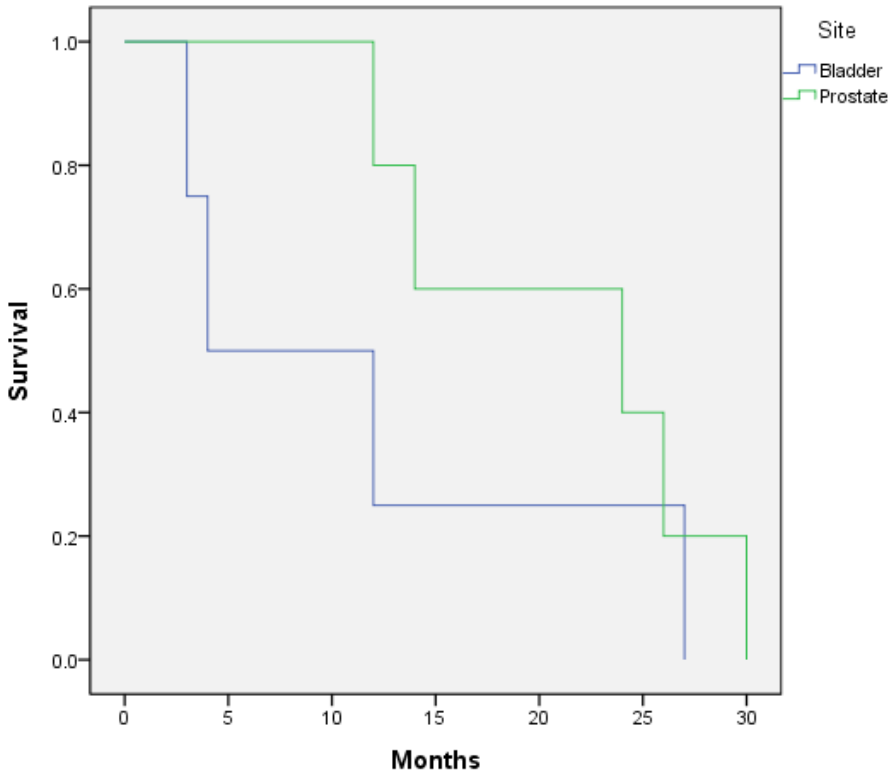


*Fig. 1 Kaplan–Meier overall survival (OS) curves and the log-rank test by the sites (Log-Rank p = 0.301)*

test, it didn't show any significant difference (Fig. 1, $p = 0.301$). This indicated that the characteristics of aggressive invasion in SCC was independent of the primary sites from which it originated. Due to the limited published articles and small case number, further research is required to validate these results. In addition, we also found that the PSA level was low in patients with pure prostate SCC, which indicated the prostate SCC might evolve into advanced disease because early diagnosis was relatively difficult when the PSA level was the only tool for diagnosis. It was said that patients post radical surgery experienced a longer overall survival compared with those who did not accept radical surgery.[4] From our study, the results did not support this demonstration, may resulting from different doctors, who may perform difficult ways in radical surgery, in charge in our hospital.

The limitation of our study is small size and retrospective of study that may lead to some bias.

In conclusion, genitourinary small cell carcinoma (SCC) is a rare but aggressive malignancy, which leads to a poor prognosis. Compared with SCC originating from the bladder, prostate SCC usually presented with advanced stages, which lead to a worse outcome because of the different presenting syndromes. In our study, patients with genitourinary pure SCC appeared to live longer than patients with SCC mixed with other tumors. Because of the limited case series on genitourinary SCC, some treatment approaches are still controversial. Therefore, prospective multicenter trials with larger cohorts are urgently needed in the future.

## References


1. Oberg K, Hellman P, Kwekkeboom D, et al: Neuroendocrine bronchial and thymic tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010;21 Suppl 5:v220-2.
2. Remick SC, Ruckdeschel JC: Extrapulmonary and pulmonary small-cell carcinoma: tumor biology, therapy, and outcome. Med Pediatr Oncol 1992; 20: 89-99.
3. Abbas F, Civantos F, Benedetto P, et al: Small cell carcinoma of the bladder and prostate. Urology 1995;46:617-30.
4. Chang K, Dai B, Kong YY, et al: Genitourinary small-cell carcinoma: 11-year treatment experience. Asian J Androl 2014;16:705-9.
5. Deorah S, Rao MB, Raman R, et al: Survival of patients with small cell carcinoma of the prostate during 1973-2003: a population-based study. BJU Int 2012;109:824-30.
6. Choong NW, Quevedo JF, Kaur JS: Small cell carcinoma of the urinary bladder. The Mayo Clinic experience. Cancer 2005;103:1172-8.