Case report

Small cell carcinoma of the prostate: Three case reports and a literature review

I-Shen Huang a,b, William J.S. Huang a,b,*, Alex T.L. Lin a,b, Kuang-Kuo Chen a,b

a Division of Urology, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC
b Department of Urology, School of Medicine, Shu-Tien Urological Science Research Center, National Yang-Ming University, Taipei, Taiwan, ROC

A R T I C L E  I N F O

Article history:
Received 25 March 2012
Received in revised form 26 April 2012
Accepted 26 September 2012
Available online 15 June 2013

Keywords:
chemotherapy
prostate
small cell carcinoma

A B S T R A C T

Small cell carcinoma (SCC) of the prostate is a high-grade malignant neoplasm with neuroendocrine differentiation and accounts for only 0.5−2% of all prostate cancers. From 2005 to 2010, there were a total of three cases of SCC at our hospital. The disease onset age was 61, 74, and 84 years, respectively. Initial presentations include urinary difficulty, bone pain, and gross hematuria. One patient had mixed tumors of both SCC and adenocarcinoma, and two had prior adenocarcinomas that recurred as SCC. The diagnosis of SCC was all made via transurethral resection. Two patients died of their diseases 7 and 15 months after diagnosis, and one survived for more than 65 months. The serum prostate specific antigen (PSA) was 1660 ng/mL, 72.8 ng/mL, and 35.7 ng/mL before definitive diagnosis. Notably, the only surviving patient was diagnosed with SCC after the transurethral resection of prostate because of the presence of lower urinary tract symptoms. The serum PSA prior to the operation was 0.11 ng/mL, and he received chemotherapy with 5 courses of cisplatin and VP-16. Palliative transurethral resection of the prostate (TURP) not only solved the obstructive symptoms of voiding but helped in removing the prostate tissue, which might have the SCC component in patients with prostate adenocarcinoma under androgen deprivation therapy.

Copyright © 2013, Taiwan Urological Association. Published by Elsevier Taiwan LLC.

1. Introduction

Small cell carcinoma (SCC) of prostate is a high-grade malignant neoplasm with neuroendocrine differentiation. It accounts for only 0.5−2% of all prostate cancer cases. Unlike patients with prostate adenocarcinoma, patients with prostate SCC usually have no elevated serum PSA. Only half of the patients presented with pure SCC at the initial diagnosis, one-quarter of the cases demonstrate a combination of adenocarcinoma and SCC, and the other 25% are presented with adenocarcinoma under hormone therapy with disease recurred as SCC.1 Herein we present three cases of prostate SCC treated in our hospital from 2005 to 2010.

2. Case reports

2.1. Case 1

A 61-year-old man had right renal stones and received extracorporeal shock wave lithotripsy (ESWL) twice at another hospital. Subsequently, he developed pain at his thoracic cage and bilateral inguinal areas and abdominal computed tomography (CT) scan revealed advanced prostate cancer with enlarged lymph nodes over the celiac axis, portocaval, aortocaval, retrocaval, paraaortic, bilateral common iliac, internal iliac, external iliac, right obturator, and bilateral inguinal regions (Fig. 1). Whole body bone scan confirmed the findings of bone metastases. Clinical stage was T4N2M1. Serum PSA levels were 1660 ng/mL. The prostate biopsy revealed a Gleason 5+5 adenocarcinoma (Fig. 2A). Androgen blockade with gosereline and flutamide were given, and his PSA dropped to the nadir 42.06 ng/mL in 2 months. However, it rose to 444 ng/mL 3 months later. Owing to an episode of hematuria, he received a cystoscopy and was treated with the palliative TURP. The pathology reported SCC (Fig. 2B–D). However, he failed to follow up and died 7 months after the diagnosis of SCC.

2.2. Case 2

A 59-year-old man was diagnosed adenocarcinoma of the prostate at another hospital with an initial PSA of 72.81 ng/mL. The tumor was Gleason 4+4, and the clinical staging was T3aN1M0. Combined androgen blockade with triptoreline and bicalutamide were used to control the disease. The PSA nadir was 0.00 ng/mL.
12 months after the commencement of medication. Owing to his persistent voiding symptoms, he received holmium laser ablation of prostate 21 months later. Pathology of the specimen disclosed SCC, which were immunohistochemically positive for cytokeratin (CKER), CD 56, chromogranin, and synaptophysin (Figs. 3 and 4A–D). The serum PSA level prior to the operation was 0.11 ng/mL. The CT images disclosed the presence of a pair of soft tissue lesions and an enlarged lymph node in the pelvic cavity adjacent to left obturator muscle (Fig. 5). Owing to the impression of disease progression, he received concurrent chemoradiation therapy (CCRT) with cisplatin and etoposide for five cycles. The clinical condition was stable after CCRT and his latest PSA was 0.40 ng/mL.

2.3. Case 3

An 84-year-old man with hypertension, type 2 diabetes mellitus, and arrhythmia came to our hospital because of acute urinary retention. The initial PSA was 35.7 ng/mL. The transurethral resection of prostate showed the findings of combined adenocarcinoma (Gleason 4+4) and SCC (Fig. 6). His clinical stage was T4N0M0 (Fig. 7). Cyproterone acetate and CCRT (with cisplatin and etoposide × 3 cycles) were given. The PSA nadir was 0.17 ng/mL at 3 months after the treatment. However, he developed bilateral lower leg weakness 1 year later. Brain CT showed evidence of tumor metastasis to brain, which was later confirmed as metastatic SCC via biopsy. Unfortunately, the disease progressed to lung metastasis and the patient died of the disease.

The demographic data and treatment results of the three patients are summarized in Table 1.

3. Discussion

The literature from western countries concluded that the prostate is the most common extrapulmonary organ to have SCC. More
than 60% of the patients with prostate SCC presented with metastatic disease, and 39.5% presented as local/regional disease. The observed survival rates 12, 24, 36, 48, and 60 months after the diagnosis of prostate SCC were 47.9%, 27.5%, 19%, 17%, and 14.3%, respectively. Data from Taiwan indicated that lung was the most common (89.2%) location of SCC. It is followed by the esophagus (1.8%), urinary bladder (1.6%), uterine cervix (1.5%), colorectum (1.4%), skin (1.0%), stomach (0.9%), head and neck (0.7%), prostate (0.3%), and small intestine (0.1%).

Abbas et al. reported 130 cases of prostate SCC, 67 (52%) were pure SCCs, and 52 (40%) were associated with adenocarcinoma. Forty-three (43%) patients were initially diagnosed as having prostate adenocarcinoma with no small cell component and later developed into prostate SCC.

Generally, the median survival time was 8 months for all SCC patients in Taiwan. For prostate SCC, the treatment is different from that of the prostate adenocarcinoma. The treatment of SCC is mainly chemotherapy. The presenting symptoms include those specific for lower urinary tract symptoms (frequency, nocturia, urinary retention, urinary obstruction) and nonspecific constitutional symptoms (poor appetite, weight loss). In our series, the three patients reported inguinal pain, urinary retention, and urinary difficulty.

The origin of prostate SCC is unclear. It has been hypothesized that prostate SCC arises from the neural crest line/amine precursor uptake decarboxylation (APUD) cell system, which is then distributed throughout the prostate and urethra. They are capable of

---

**Fig. 3.** Section shows prostate tissue infiltrated with solid aggregates of small tumor cells, which have scanty cytoplasm and a highly hyperchromatic, oval to elongated nucleus (hematoxylin and eosin stain, 400x).

**Fig. 4.** Immunohistochemical features of small cell carcinoma positive for cytokeratin (A), CD56 (B), chromogranin (C), and synaptophysin (D).

**Fig. 5.** Enlarged lymph node in the left external iliac region encompassing the left external iliac artery.
producing and releasing serotonin, chromogranin A, chromogranin B, adrenocorticotropic hormones, calcitonin, parathyroid hormone-related protein, thyroid-stimulating hormone, and somatostatin. Prostatic endocrine cells are also believed to regulate cellular growth and differentiation via autocrine, paracrine, or endocrine and neurocrine mechanisms.5 Another theory, which is based upon the finding of coexistent adenocarcinoma and SCC, postulates that SCC arises from the dedifferentiated prostatic adenocarcinoma.6 The latest and currently the most accepted theory suggests that SCC has its own stem cell origin and is not derived from dedifferentiated adenocarcinoma or from benign neuroendocrine cells of the prostatic epithelium. This hypothesis is based on the finding that the tumor cells lack typical immunohistologic characteristics of prostatic epithelial cells (PSA expression and androgen receptor positivity) and their much elevated index of MIB-1 than that of the dedifferentiated adenocarcinomas.7

The proportion of neuroendocrine differentiation in prostatic carcinoma varied from 10% to 100%, and androgen ablation therapy was considered a contributing factor in increasing the proportion of neuroendocrine differentiated malignant cells over time.8 Whether there is prognostic value in the degree of neuroendocrine differentiation is still a topic of debate.

The SCC can be divided into two types: “oat cell” type and “intermediate” cell type. The “oat cell” type is characterized by cells only slightly larger than lymphocytes with scant cytoplasm, hyperchromatic nuclei with salt, and pepper chromatin without prominent nucleoli, whereas in the “intermediate” cell type, the tumor cells have more abundant cytoplasm and visible nucleoli.1

Fig. 6. (A) Composition of SCC (right upper quadrant) and Gleason grade 4+4 adenocarcinoma. (B) SCC showed immunoreaction with chromogranin A (right), whereas the adenocarcinoma component is nonreactive with chromogranin A stain (left). (C) SCC showed immunoreaction with CD56 (upper), whereas the adenocarcinoma component is nonreactive with CD56 stain (lower). (D) SCC showed immunoreaction with synaptophysin (right), whereas the adenocarcinoma component is nonreactive with the synaptophysin stain (left). (A–D) Hematoxylin and eosin stain, 400×. SCC = small cell carcinoma.

Fig. 7. The prostate is enlarged with heterogeneous enhancement.
Yao et al.\(^9\) compared 18 SCC and 10 Gleason pattern 5b prostate adenocarcinoma cases with immunohistochemical stain. Results showed neuroendocrine markers varied in expression with chromogranin A showing strong expression (61\%) in prostate SCC only. Synaptophysin is positive in most prostate SCC (89\%) and also positive in some Gleason pattern 5b prostate adenocarcinoma (40\%). The most specific neuroendocrine markers were PSA, TTF-1 and CD56 in differentiating prostate SCC and Gleason pattern 5b prostate adenocarcinoma.

Regarding the treatment, two patients in this series received CCRT with etoposide and cisplatin. The only patient who had survived over 65 months also received further treatment with cisplatin and etoposide. He achieved complete remission 10 months after the treatment. We believe that his favorable outcome is because of the early detection of malignant neuroendocrine transformation by transurethral resection.

The combination of platinum and etoposide is the most widely used standard chemotherapeutic regimen for pulmonary SCC. The prostatic SCC was assumed to respond to this chemotherapy. Recently, favorable responses were reported using gemcitabine, docetaxel, and carboplatin.\(^10\) Primary surgery, including transurethral resection and radical prostatectomy, was the only independent factor found to predict outcome of prostatic SCC in one retrospective study.\(^11\) In the review of 241 cases with prostatic SCC, the age at diagnosis and the stage and grade of associated prostate adenocarcinoma were significant predictors.\(^2\)

Palliative TURP might not only solve the obstructive symptoms of voiding but also obtain prostate tissue for examination. Among them, there may be an SCC component in patients with prostate adenocarcinoma under androgen deprivation therapy. Prostate SCC is a distinct pathological entity, and treatment plan varies from prostate adenocarcinoma, in which prostate SCC requires further chemotherapy for disease control.

### Table 1

Clinical and demographic characteristics of the patients with prostate small cell carcinoma.

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (y)</th>
<th>Initial diagnosis</th>
<th>Emergence of SCC after diagnosis (mo)</th>
<th>Metastasis</th>
<th>Follow-up status (mo)</th>
<th>PSA (ng/mL)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>61</td>
<td>AdenoCa cT4N2M1</td>
<td>5 x 5</td>
<td>LN, Bone</td>
<td>Dead (7)</td>
<td>1660</td>
<td>Bicalutamide, goserelin, TURP</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>AdenoCa cT3aN1M0</td>
<td>4 x 4</td>
<td>LN</td>
<td>Alive (65)</td>
<td>72.8</td>
<td>Bicalutamide, decapteyl, TURP, CCRT, cisplatin, etoposide</td>
</tr>
<tr>
<td>3</td>
<td>84</td>
<td>SCC, AdenoCa cT4N0M0</td>
<td>4 x 4</td>
<td>Initial</td>
<td>Brain, lung</td>
<td>Dead (30)</td>
<td>35.7</td>
</tr>
</tbody>
</table>

CCRT = concurrent chemoradiation therapy; LN = lymph node; SCC = small cell carcinoma; TURP = transurethral resection of prostate.

---

**Conflicts of interest statement**

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

### References