



Prostatic Pure Small Cell Carcinoma v.s. Mixed-Type Small Cell Carcinoma: Analysis of Two Cases

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We analyzed 2 cases of small cell carcinoma of the prostate. One patient had pure small cell carcinoma with multiple organ metastasis, while the other had a mixed-type carcinoma. The immunohistochemical studies revealed positive reactions to chromogranin A, synaptophysin, and cytokeratin stains, and negative for PSA stain over both small cell carcinoma foci. These 2 patients were immediately treated, and partial resolution of the previous metastatic bone lesions was noted after receiving 5 courses of chemotherapy with the combination of gemcitabine, carboplatin, and irradiation therapy in case 1, while adjuvant irradiation was scheduled for case 2. (**JTUA 16:115-9, 2005**)

Key words: prostate, small cell carcinoma, neuroendocrine, immunohistochemical studies.

INTRODUCTION

Small cell carcinomas of the prostate are rare, and their clinical behavior reveals that they are highly aggressive neoplasms [1]. Some evidence has suggested that these tumors are heterogeneous and show neuroendocrine differentiation [2]. Of note, 20% of patients present with small cell carcinoma in association with a regular adenocarcinoma, 30% during the course of progression of a regular adenocarcinoma, and the remaining 50% present with pure small cell carcinoma [3,4]. It seems likely that small cell carcinoma of the prostate arises from pluripotent prostatic epithelial cells, which may have the potential for divergent differentiation into neuroendocrine and acinar tumor cells [5]. Here in, we present our experience of 2 cases of small cell carcinomas of the prostate. One of them was pure small cell carcinoma of the prostate with the common characteristics of distant metastasis upon initial diagnosis, while the other was mixed small cell car-

other was mixed small cell carcinoma and a high-grade acinar adenocarcinoma. The immunohistochemical studies, clinical presentations, and managing strategies related to these 2 different conditions are discussed.

CASE REPORT

Case 1

A 79-year-old male presented with repeated urinary retention. He suffered from hypertension, diabetes mellitus, and coronary artery disease. Mild lower urinary tract symptoms were noted without medication control. In addition, no cancer family history was apparent. A digital examination revealed an elastic, moderately enlarged prostate without abnormal nodules. The preoperative serum PSA level was 1.42 ng/ml, and cystoscopy revealed evident contact between the prostate lateral lobes. Under the impression of benign prostate hyperplasia, a transurethral prostatectomy (TUR-P) was per-

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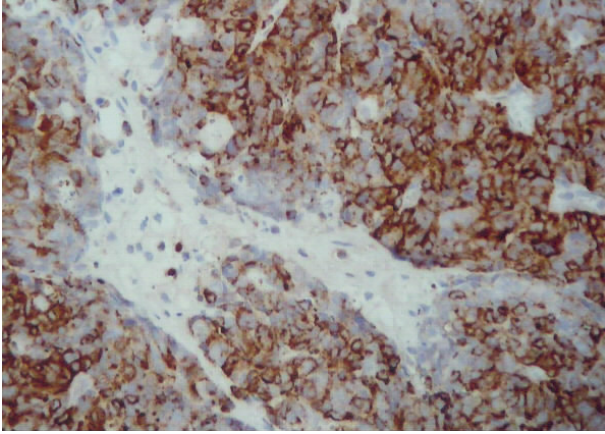


Fig. 1 Immunohistochemistry study positive for chromogranin A (400X).

formed. Specimens revealed a picture of neuroendocrine carcinoma in about 20% of the microsection area with a diffuse positive reaction to chromogranin A stain (Fig.1), a focally positive reaction to synaptophysin and cytokeratin stains, and a negative reaction to PSA stain (Fig. 2). Pure small cell carcinoma of the prostate was the diagnosis. A computed tomogram (CT) and bone scan were arranged 2 weeks after the TUR-P. The CT revealed liver, spleen, and pelvic lymph node metastatic lesions, and the bone scan showed skeletal metastasis in the ribs, T1-L5 spine, sacrum, and both sacroiliac joints. After receiving 5 courses of chemotherapy with the combination of gemcitabine and carboplatin, and palliative irradiation of 4000 cGy in 10 fractions for the bone lesions, the follow-up bone scan revealed partial resolution of the previous metastatic bone lesions, but the CT revealed that the liver, spleen, and pelvic lymph node metastatic lesions were unchanged. In the meantime, the serum PSA level had dropped to 0.06 ng/ml. He died due to sudden cardiac arrest shortly after the final course of chemotherapy with a partial response and a survival duration of 7.4 months.

Case 2

A 78-years-old male had suffered from micturition difficulty and gross hematuria for 1 month. The digital examination revealed remarkable prostate enlargement with a stony-hard consistency and a serum PSA value of 45.2 ng/ml. The cystoscopic examination revealed a severe kissing prostate with an irregular surface and intravesical invasion. The pelvic CT revealed prostate tumor invasion into the bladder and pelvic side wall with highly suspicious pelvic lymph node metastasis. A palliative TUR-P was performed, and the pathology report revealed a group of neuroendocrine carcinomas mixed with a poorly differentiated adenocarcinoma. The poorly

differentiated area of the adenocarcinoma was reactive for prostatic-specific antigen (Fig. 3), while the neuroendocrine carcinoma presented the pathological characteristics of a diffuse positive reaction to chromogranin A stain, focal positive reaction to synaptophysin and cytokeratin stains, and a negative reaction to PSA stain. Small cell carcinoma of the prostate was the diagnosis. Irradiation therapy was scheduled after the definitive diagnosis. Whole-pelvis irradiation with 5040 cGy in 28 fractions followed by a boost of 900 cGy for 5 times was given. A good response with the tumor lesion going into nearly total remission was detected on the follow-up CT scan, and the serum PSA value had decreased to 6.24 ng/ml after the irradiation therapy was completed. No hormone or chemotherapy was arranged for this patient, who was lost to follow-up 6 months later.

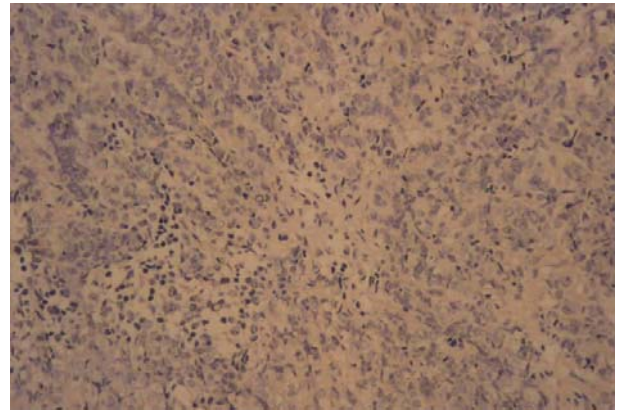


Fig. 2 Immunohistochemistry study negative for prostatic-specific antigen (400X).

DISCUSSION

We describe the clinical characteristics and pathologic findings of pure small cell carcinoma of the prostate and combined small cell and a usual acinar adenocarcinoma of the prostate. As case 1 typifies, early diagnosis of pure small cell carcinoma of the prostate is more difficult, because of a lack of concordant elevation of PSA with an acinar adenocarcinoma of the prostate.

Primary small cell carcinoma is well known in the lung, but small cell carcinoma of the prostate is a very rare condition, comprising 0.5%~2% of all prostate cancers [6]. These extrapulmonary small cell carcinomas can be distinguished from small cell lung carcinoma (SCLC) by light microscopic, ultrastructural, and immunohistochemistry examinations. Neuroendocrine differentiation of prostate cancer includes pure small cell carcinoma, carcinoid and carcinoid-like tumors and

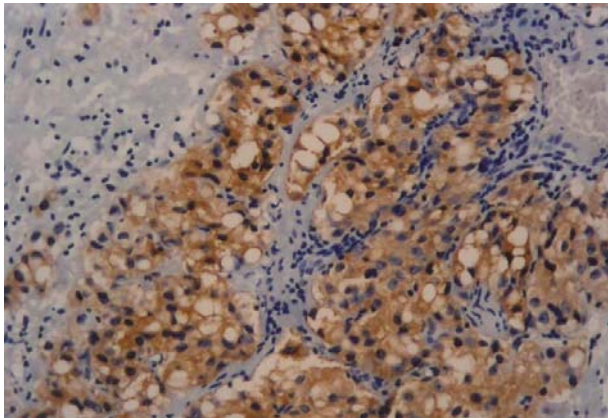


Fig. 3 Poorly differentiated adenocarcinoma of the prostate positively reactive to prostatic-specific antigen (400X).

conventional prostate adenocarcinomas with focal neuroendocrine differentiation [7]. The concordance of prostatic small cell carcinoma with an acinar adenocarcinoma also resulted from recurrence of a previous adenocarcinoma after hormone therapy [8].

Three theories of histogenesis have been proposed. First, it was suggested that prostatic small cell carcinomas arise from amine precursor uptake decarboxylation (APUD) cells of local endodermal origin [9]. Second, it was proposed that prostatic small cell carcinomas arise from dedifferentiation of prostatic adenocarcinomas, suggesting that prostatic small cell carcinoma is part of a spectrum of prostatic adenocarcinomas rather than a separate disease entity [10]. Third, due to similarities of the histologic pictures and neuroendocrine paraneoplastic syndromes with SCLC, the most-widely accepted view is that prostatic small cell carcinomas arise from totipotential stem cells of the prostate, which have the ability to differentiate into either epithelial, or neuroendocrine-type carcinomas [11,12]. Immunohistochemical studies have shown multidirectional differentiation along with epithelial, neuroendocrine, and/or mesenchymal differentiation of poorly-differentiated prostate cancers [13,14]. The diagnosis of a neuroendocrine carcinoma is mainly based on a definitive histological examination, but sometimes a confident categorization of the tumor may be difficult.

In contrast to prostatic adenocarcinomas, PSA, an unreliable tumor marker for pure prostatic small cell carcinoma, is usually normal, even when there is metastatic disease. One study suggested that the carcinoembryonic antigen is a more-reliable marker, because increases and decreases in antigen levels are found with disease progression and regression, respectively [12].

Prostatic small cell carcinoma has a propensity to

metastasize to visceral organs, including the liver, bone, lungs, central nervous system, and pericardium, and regionally to the pelvic lymph nodes, rectum, and bladder [12].

Prostatic small cell carcinoma has the same unfavorable outcome as other SCLC counterpart [15]. As in our case 1, prostatic small cell carcinoma has a highly aggressive course and a poor prognosis. Despite treatment with chemotherapy, the prognosis of prostatic small cell carcinoma is extremely poor, and the median survival is 7 months [16]. Sometimes, patients with prostatic small cell carcinoma show some paraneoplastic syndromes, such as limbic encephalitis [17], inappropriate secretion of antidiuretic hormone [18], and production of adrenocorticotrophic hormone [18].

Because of the rarity of the condition, no standard therapeutic regimen has been developed. In addition, prostatic small cell carcinoma, in contrast to adenocarcinomas, has been found to be unresponsive to hormone therapy. It is the most-aggressive variant of prostate cancer with no successful treatment to the present. By combining gemcitabine and carboplatin with irradiation therapy, we achieved a partial response to the metastatic bone lesions in case 1. Pelvic irradiation alone achieved almost complete remission in case 2. According to our experience, irradiation therapy seemed to be effective in controlling locally advanced lesions of mixed adenocarcinoma and small cell carcinomas of the prostate. Furthermore, even in patients with multiple metastatic lesions of pure small cell carcinoma of the prostate, irradiation can be palliative therapy for painful metastatic bone lesions. The combination of carboplatin and gemcitabine has emerged as a standard regimen for SCLC [19], but adjustment and modification of the regimens and dosages in small cell carcinoma of prostate are still necessary to achieve a more-effective response.

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