Small cell carcinoma of the prostate: Report of two cases

SİNAN SÖZEN¹, AYTUĞ ÜNER², TURGUT ALKİBAY³

Department of ¹Urology, Hacettepe University Medical School, Departments of ²Oncology and ³Urology, Gazi University Medical School, Ankara-Turkey

Small cell carcinoma of the prostate is a rare pathologic subtype of prostate cancer with unique clinical features. This report describes two cases of small cell carcinoma of the prostate in two clinical settings. One was seen as an initial event at the time of first diagnosis and the other was seen as a late event superimposed on the clinical history of advanced prostate cancer. [Turk J Cancer 2000;30(3):131-134]

Key words: small cell carcinoma, prostate cancer, metastasis, neuroendocrine differentiation

Neuroendocrine differentiation in prostatic carcinoma assumes one of three forms including small cell carcinoma, carcinoid-like tumors and conventional prostatic adenocarcinoma with focal neuroendocrine differentiation (1). Small cell carcinoma of the prostate is a pathologic subtype of prostate cancer with unique clinical features and accounts for approximately 1-2% of prostatic malignancies. Unlike the typical adenocarcinoma of the prostate, small cell carcinoma does not have bone tropism, nor does it express prostate specific antigen (PSA) reaching to the levels of adenocarcinoma of the prostate. In addition to differences in the distribution of metastases there are differences in the character of the bone metastases of small cell carcinomas when compared with adenocarcinomas. Adenocarcinomas of the prostate are characterized by the development of dense blastic metastases, whereas small cell carcinoma produces lytic bone metastases. The unique features permit clinicians to suspect the diagnosis of small cell carcinoma of the prostate before histologic confirmation of its presence.

This report describes two cases of small cell carcinoma of prostate occurred in two clinical settings, either as an initial event at the time of first diagnosis or as a late event superimposed on the clinical history of advanced prostate cancer.
Case 1

A 77 year old man was referred to our urology clinic with prostatic enlargement and an elevated serum PSA 70.4 ng/ml (normal: 0-4.0 ng/ml). A transrectal ultrasound guided needle biopsy was performed, and the pathological examination of the specimen showed a prostatic adenocarcinoma; Gleason score of 5+5 with perineural invasion. The patient remained asymptomatic with undetectable serum PSA under maximal androgen blockade. One year after the initiation of hormonal therapy, the patient presented with abdominal discomfort, weight loss and urinary obstruction symptoms. Imaging studies revealed multiple liver metastases. A fine-needle aspiration biopsy of the liver revealed metastases of a neuroendocrine tumor which was strongly positive for neuron specific enolase and chromogranin-A (Figure 1).

![Neuron-specific enolase immunostaining in the liver (X400)](image)

A transurethral prostatectomy (TUR-P) was performed in order to relieve the obstructive symptoms, and the pathological examination of the resected specimen showed a small cell carcinoma of the prostate. After six cycles of cisplatin+etoposide based chemotherapy, the patient gained weight and liver metastases completely disappeared. One year after the initiation of chemotherapy the patient died shortly because of cranial metastases.

Case 2
A 65 year old man with abnormal digital rectal examination (DRE) finding was biopsied and the pathological examination revealed small cell carcinoma of the prostate (Figure 2). The samples were strongly positive for neuron specific enolase and chromogranin-A. At the time of diagnosis his PSA was 1.6 ng/ml (normal: 0–4.0 ng/ml). Initially, the imaging studies including CT scan, bone scan and pulmonary radiography were all negative. He received six cycles of cisplatin+etoposide based chemotherapy. As the local tumor progression was seen six months later, 7000 cGy external beam radiotherapy was applied. One year later local tumor progression was seen and the patient died because of pulmonary embolism.

Fig 2. The infiltration of prostatic stroma with small cell tumor (X100)

Discussion

Neuroendocrine differentiation of prostatic carcinoma has been a focus of several investigations. Detailed characterization of neuroendocrine cells in primary tumors has been reported (2,3). These studies have established that adenocarcinomas of the prostate commonly contain a dispersed subpopulation of malignant cells that express a neuroendocrine phenotype. The reported incidence of focal neuroendocrine differentiation in primary tumors ranges from 10% to 100%, depending on the method of identification, markers used, method of tissue fixation and extent of tissue sampling (1,2,3). Neuroendocrine differentiated small cell carcinoma is a very rare tumor comprising 0.5%-2% of all prostatic carcinomas (4). Aprikian et al. (5) examined 16 metastatic tumors
(11 lymph nodes and 5 vertebral metastases) for the presence of neuroendocrine cells using antibodies to chromogranin-A, serotonin and neuron specific enolase. Nine of these tumors (56%) contained neuroendocrine cells. Of the three markers used, only chromogranin-A identified all 9 tumors with neuroendocrine cells. Serotonin and neuron specific enolase identified 3 and 4 cases, respectively.

Small cell carcinoma occurs in two settings, either as an initial event at the time of first diagnosis (as in our second case) or as a late event superimposed on the clinical history of advanced prostate cancer (as in our first case). The clinical picture of patients with small cell carcinoma is similar in both circumstances, although it is less striking when it occurs as a secondary neoplasm. The clinical features of small cell carcinoma may be therefore accepted as a mixture of the characteristic of adenocarcinoma of the prostate and the characteristic of small cell carcinomas (6).

The treatment of small cell carcinoma of the prostate is based on the evidence suggesting that this tumor is not hormonally sensitive. In addition, it is based on the relative chemotherapy sensitivity of neural elements of prostate carcinoma. The success of chemotherapy for the treatment of small cell carcinoma of the prostate is also not proven. It is assumed that small cell carcinoma elements are responsive to the same chemotherapy drugs that have been developed in small cell carcinomas arising in the lung. It is very clear that cisplatin+etoposide based therapy results in high response rate in the treatment of small cell carcinoma. Despite the high and frequently dramatic response rate achieved with chemotherapy, median survival was disappointingly low (7).

References