Case Report

Pure small cell carcinoma of the prostate: A rare tumor

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ABSTRACT

Pure small cell carcinoma of the prostate is a rare and aggressive neoplasm, with only few cases described in literature and poor prognosis: mean survival is 5 months. We report the case of a patient with this disease, with special attention to the evolution of neuroendocrine markers as Chromogranine A and neuron-specific enolase during the progression of the tumor, evaluating their possible role in staging and follow up.

Key words: Chromogranin A, neuroendocrine, octreoscan, prostate cancer, small cell carcinoma

INTRODUCTION

Extrapulmonary small cell carcinomas are rare neoplasms, with an incidence of 1000 cases per year in the United States.[1] These tumors develop mainly in the cervix, the esophagus, and the upper airways; pure small cell carcinoma of the prostate (SCCP) instead, meaning a tumor with no combined adenocarcinoma in the neoplastic mass, is an extremely singular finding. To our knowledge, only 20 cases of pure neuroendocrine prostatic tumors have been described in literature.[2] High aggressiveness, poor prognosis, and extensive disease on presentation are common features of this cancer. We report a case of pure SCCP with bilateral pulmonary and hepatic metastases.

CASE REPORT

A 79-year-old Caucasian male presented to the emergency department with acute urinary retention. The patient had no family history of prostate cancer. He was under treatment with alfuzosin and finasteride for lower urinary tract symptoms (LUTS) which had worsened during the last 2 months. Last urological check up performed 4 months earlier showed a PSA of 2.90 ng/ml and a PSA ratio (free PSA/total PSA) of 44%. PSA was remeasured during emergency access and had risen to 11.44 ng/ml. Digital rectal examination (DRE) was strongly suspicious for neoplasia and the patient was therefore scheduled for a trans-rectal ultrasound (TRUS) guided 12 core biopsy; a per-urethral catheter was positioned. According to a study protocol we apply to all the patients who undergo prostate biopsy in our center, Chromogranin A was measured before biopsy and its value was elevated: 318 ng/ml. TRUS showed an enlarged prostate gland (130 cc), with a hypoechogenic area in the peripheral region. During the biopsy significant rectal bleeding occurred and the procedure was stopped after obtaining eight cores.

Histological evaluation revealed the presence of pure small cell carcinoma, with no foci of adenocarcinoma on all eight cores. Immunohistochemistry confirmed the diagnosis, with CD56+, CK in paranuclear spot, Ki-67 100% and TTF-1+ [Figure 1].

The CT scan showed a tumor that measured 70 mm in width and 13 mm in length, numerous bilateral lung metastases, a VII segment hepatic lesion, and multiple lymphadenopathies in the pelvic region; the Octreoscan performed was strongly positive. Three weeks after diagnosis Chromogranin A increased to 738.60 ng/ml and neuron-specific enolase (NSE) was 99.52 ng/ml, as expected for neuroendocrine tumors. Serum electrolytes, complete blood count, and neurological evaluation showed no signs or symptoms of a paraneoplastic syndrome.

Patient was treated with chemotherapy: Cisplatin (75 mg/m^2 on day 1) and etoposide (120 mg/m^2 on days 1--3). The CT scan performed 1 month later showed no modification of the previously described metastases and an increase in size of the

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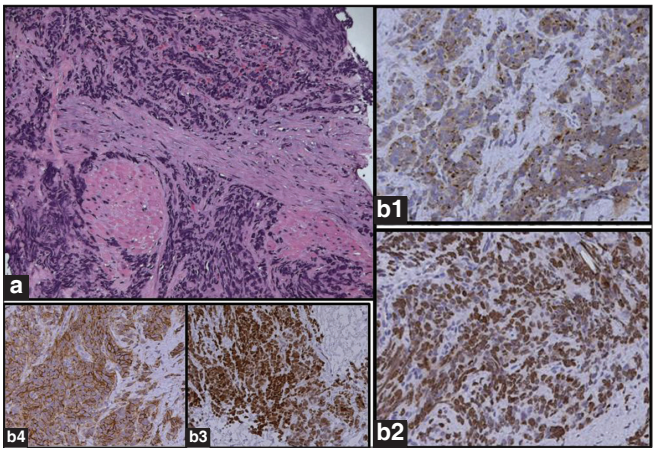

Figure 1: (a) HE stain observed at 100× showing small cell carcinoma (b) 1-4. Immunohistochemistry of the tumor shown in A observed at 200× (b1). CK in dot spot (b2). Ki67 (b3). TTF1 (b4). CD56

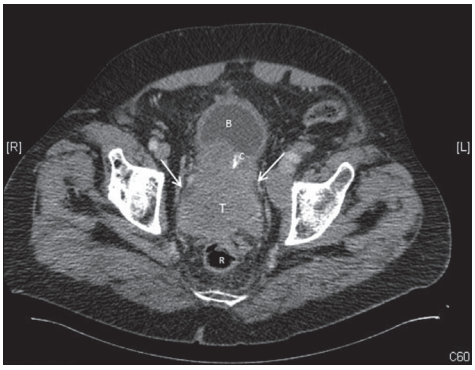

Figure 2: Pelvic CT scan with contrast. T = tumor, B = bladder, R = rectum, C = per-urethral catheter. Arrows indicate left and right ureter

primary lesion that measured 70 mm × 100 mm × 140 mm. The patient was not able to void after an attempt to remove of the per-urethral catheter, which was thus maintained during all follow-up. Even though the tumor widely invaded both ureters [Figure 2], no hydroureteronephrosis was observed and kidney function was normal (creatinine 1.30 mg/dl). Neuroendocrine marker concentrations continued to increase (Chromogranin A 2537.8 ng/ml, NSE 214.5 ng/ml) [Figure 3]. After the second chemotherapy cycle, a kidney ultrasound scan showed bilateral hydronephrosis with renal insufficiency (creatinine 4.50 mg/dl) and a nephrostomy was therefore positioned. The patient died 6 months after diagnosis due to acute respiratory failure.

DISCUSSION

Pure small cell carcinoma of the prostate (SCCP) is an extremely rare disease with different presentations. Median age of patients is 65 years and prognosis is poor, with a mean survival of 5 months:[3] nevertheless, in a few cases described in literature complete remission was achieved.[4] The finding of pure small cell carcinoma of the prostate with no foci of adenocarcinoma is rare; more frequently this tumor

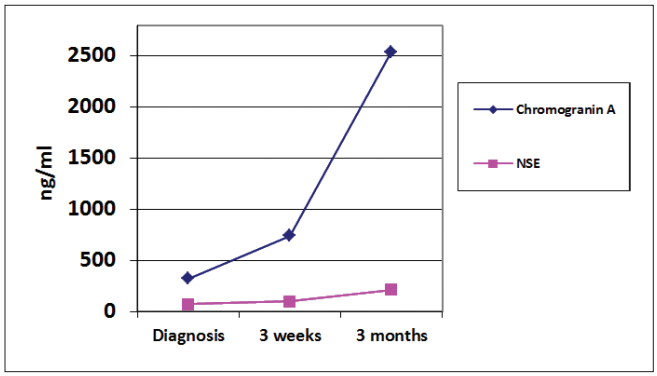

Figure 3: Evolution of neuroendocrine markers

is associated with adenocarcinoma or is the recurrence after surgery or radiotherapy is performed for an adenocarcinoma.[3] The most frequent symptoms at presentation are LUTS and acute urinary retention (72%), but in some cases pain and paraneoplastic syndromes may be the first manifestations.

Whether a heavy smoking history is a risk factor for the development of this disease remains undeterminable: even though smoking is strongly associated with pulmonary small cell carcinoma, its effects on SCCP have not been studied, and the lack of details on smoking habits of patients in other case reports did not allow us to evaluate this risk factor. Our patient was not a heavy smoker.

Neoplastic cells of SCCP do not produce PSA, but its rise is frequent in patients with this disease.[2] Our case confirms that PSA and DRE are excellent diagnostic tools and are sufficient to diagnose this type of neoplasm: PSA was increased as in other case reports[2] and DRE was strongly suggestive of malignancy. In our case PSA value could probably be related to urinary tract retention and consequent urethral catheter insertion. Even though neuroendocrine markers (Chromogranin A, NSE) were elevated, they remain of limited use in the diagnosis of SCCP, as PSA and DRE are easier to obtain and valid to diagnose this cancer.

A possible application for these markers is follow up: in our experience Chromogranin A rose in four months from 318 ng/ml to 2537 ng/ml and NSE from 99.52 ng/ml to 214 ng/ml [Figure 3], concurrently with an increase in size of the primary prostate lesions which was radiologically documented [Figure 2]. Their high concentration is linked to disease progression and their measurement may be considered to reduce the number of CT scans and add valuable information for the oncologist.

Optimal treatment for SCCP is still uncertain. Radical prostatectomy should be performed if the tumor is confined to the prostate. In pure small cell carcinomas hormone-depletion therapy should be avoided, since the androgen receptor is not expressed by the malignant neuroendocrine

cells.[4] Cisplatin and Etoposide-based chemotherapy is the standard of care;[5] in our case there was no response to treatment but no serious side effects occurred, no brain metastases developed (which are a frequent complication of extrapulmonary small cell carcinoma [6]) and the patient did not show hydronephrosis until 4 months after diagnosis. Radiation therapy may be considered for palliative care.[6]

Prognosis of SCCP is poor for its extreme aggressiveness and the frequent metastatic presentation. PSA and DRE are sufficient to suspect any type of prostate tumor as SCCP, which must nevertheless be diagnosed with a prostate biopsy. Neuroendocrine markers as Chromogranin A and NSE are important for staging, evaluating the response to treatment and the progression of the disease. Octreoscan also resulted significantly positive and may be considered for staging and follow-up.

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