A pure microcytic bladder carcinoma synchronous to prostatic adenocarcinoma

Vasileios Sakalis,1 Anastasia Gkotsi,2 Efrosyni Mylonaki,3 Aphroditi Pantzaki,4 Stavros Charalambous,1 Vasileios Rombis1
1Department of Urology, Hippokrateion General Hospital of Thessaloniki, Thessaloniki; 2Second Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Thessaloniki; 3Second Clinic of Chest Medicine, G. Papanikolauo General Hospital of Thessaloniki, Thessaloniki; 4Pathology Department, Hippokrateion General Hospital of Thessaloniki, Thessaloniki, Greece

Abstract

Small cell carcinoma (SCC) or microcytic carcinoma of the urinary bladder is a rare entity comprising approximately 0.5% of all bladder tumors. Due to its rarity, no prospective studies evaluating the most effective treatment have been published in the medical literature. Several cases of bladder SCC have been presented so far. We describe our case report and we revise the recent literature. Our patient was diagnosed with pure bladder SCC and prostatic adenocarcinoma. After the initial and complete transurethral resection of the bladder tumor (TUR-BT), he underwent a thorax and mediastinum computer tomography (CT) examination to exclude primary pulmonary small cell carcinoma and a bone scan scintigraphy for staging purposes. He received a three 14-day cycles of Cisplatin-containing chemotherapeutic schema and a single dose of Lutetinizing-Hormone Releasing hormone (LHRH) analogue injection after 14 days of bicalutamide administration. The patient is followed for 24 months without any signs of bladder SCC recurrence or biochemical or local relapse from prostatic adenocarcinoma.

Introduction

Small cell carcinoma (SCC) or microcytic carcinoma of the urinary bladder is a rare entity comprising approximately 0.5% of all bladder tumors. It belongs to the group of neuroendocrine tumors and shares many characteristics with its pulmonary counterpart in respect of aggressiveness, invasiveness and poor prognosis. Because of the rarity of the disease, no prospective studies evaluating the most effective treatment have been done. Several cases of bladder SCC have been presented so far but this is the first time that a synchronous pure microcytic bladder carcinoma and prostate adenocarcinoma case report is published, according to medical literature searching in PubMed. We describe our case report and the recent literature is revised.

Case Report

A 72-years-old man, non-smoker, presented to our emergency department due to urinary retention. He had a 2-day history of painless gross hematuria. Four years ago he had been treated for a stage T1, high-grade papillary urothelial carcinoma, with transurethral resection of the bladder tumor (TUR-BT) and he received a program of bacillus Calmette-Guerin (BCG) instillations for 12 months. Past medical history included arterial hypertension and hyperlipidemia under per Os (PO) medication and appendectomy in childhood. The physical examination revealed a tender hypogastrium on palpation and dullness on percussion. Ultrasonographically, the bladder was overdistended with more than 800 ml of fluid and a large isoechic mass was observed. A three-way catheter was inserted to evacuate the hollow organ from urine and blood clots, flushing and continuous bladder irrigation installed. Digital rectal examination (DRE) recognized a palpable hard nodular mass at the prostate’s base at the right lobe, in an otherwise normal prostate gland. Laboratory test results were within normal limits except for a hemoglobin concentration (Hb) of 8.1 g/dL and a white blood count (WBC) of 13×109/L. Renal function tests showed slight elevation creatinine and urea without electrolytic disturbances and the glomerular filtration rate (GFR) was estimated 85 ml/min/1.73 m². A three weeks before Prostatic specific antigen (PSA) examination was 1.83 ng/mL and a 6-month before measurement was 2.01 ng/mL. The patient was admitted to the Urology department for further evaluation and treatment.

On the next day, the patient underwent a multiphase helical computer tomography (CT) examination of the abdomen and pelvis with a multidetector scanner prior and after administration of PO and Intravenous (IV) contrast material. A late scanning phase was included in the study. A mass was seen on the base to the upper third of the left lateral wall while the urethra including prostatic part were free of papillary lesions except of small lesion recognized anteriorly of the bladder neck at 4 o clock position. Typical TUR-BT followed including resection of the entire visible tumor mass and multiple random bladder biopsies were obtained from the healthy looking bladder wall and prostatic urethra. Random biopsy specimens were placed in a separate tissue boxes for tumor mapping purposes.1 Due to the abnormal DRE findings, sextant transrectal ultrasonographic (TRUS) guided prostate biopsy followed the tumor resection, using a portable 8MHz probe carrying TRUS device. The surgical specimen after TUR-BT,

Kidney was seen without any clinical significance, category I according to Bosniak classification system. There was no distinct lymph node involvement neither on deep retropertioneal nor on superficial pelvic and inguinal regions as well as no involvement of parenchymal organs such as liver, spleen, pancreas and adrenals.

Subsequently, we decided to evaluate the patient in the operating theater. Under spinal anesthesia a bimanual bladder examination took place that showed a non-fixed mobile bladder. The CT findings were confirmed by rigid urethroscopy. A large based lesion was observed from the bladder neck to the middle of bladder posterior wall from the midline to the upper third of the left lateral wall while the urethra including prostatic part were free of papillary lesions except of small lesion recognized anteriorly of the bladder neck at 4 o clock position. Typical TUR-BT followed including resection of the entire visible tumor mass and multiple random bladder biopsies were obtained from the healthy looking bladder wall and prostatic urethra. Random biopsy specimens were placed in a separate tissue boxes for tumor mapping purposes.1 Due to the abnormal DRE findings, sextant transrectal ultrasonographic (TRUS) guided prostate biopsy followed the tumor resection, using a portable 8MHz probe carrying TRUS device. The surgical specimen after TUR-BT,
Case Report

Extra pulmonary SCC is a rare but well-characterized entity. It has been described in several organs including gastrointestinal, genitourinary, skin etc. The SCC of the bladder comprises approximately 0.5% of all bladder malignancies. The mean age of presentation is 66.1 years and the male to female ratio is 3.6:1. Since 1981, when Cramer et al. described the first case of bladder SCC, more than 200 cases have been reported so far. Weng et al. earlier in 1977 described the first case of prostate SCC. As their pulmonary counterpart, they share the features of aggressiveness, invasiveness, early metastasis and poor prognosis.

Several theories have been proposed to explain the histogenesis of the extra pulmonary SCC, but the theory of malignant transformation of neuroendocrine amine precursor uptake and decarboxylation (APUD) cell systems seems to prevail. Other studies suggest the malignant transformation of poorly defined submucosal or mucosal propria cells and the metaplasia of high grade transitional cell carcinoma.

The bladder SCC should be suspected when the tumor displays an aggressive behavior and advanced stage presentation. Hematuria, urinary retention, dysuria, poor stream urine, suprapubic or flank pain and rarely paraneoplastic syndromes as hypocalcemia, hypophosphatemia, Cushing syndrome and elevated cortisol are the usual presenting symptoms. The definite diagnosis is by immunohistochemistry of the resected tissue although imaging modalities (US, CT) should raise a suspicion mainly by the high volume mass. Under direct vision these tumors are usually polyoid, ulcerated and large in size from 4-10 cm, and they present on lateral walls (54%), posterior wall (20%), trigone (10%), dome (8%) and anterior wall (8%). Immunohistochemistry techniques such as chromogranin staining, neural adhesion molecule and synaptophysin are helpful since cancerous cells express markers of neuroendocrine differentiation. A metastatic disease from pulmonary systems seems to prevail. Other studies suggest the malignant transformation of poorly defined submucosal or mucosal propria cells and the metaplasia of high grade transitional cell carcinoma.

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Figure 1. A computer tomography image showing the lesion at the left lateral bladder wall after administration of contrast material.

Figure 2. The microcytic cellular pattern, typical for small cell carcinoma histological diagnosis.

Figure 3. The histological specimen shows an area which is occupied by the SCC at the left and by the typical adenocarcinoma at the right.
or extra pulmonary SCC (including prostatic SCC) should be excluded.

The treatment of bladder SCC is still a matter of concern since there are no prospective studies with big patient series. Most authors agree that a threefold therapy including surgery, chemotherapy (neoadjuvant or adjuvant) and radiotherapy should be offered, since bladder SCC is already a systemic disease at the time of diagnosis. Galanis et al., proved that a combination of chemotherapy and radiation could be as effective as surgery in patients with limited disease. Choong et al., in a 44 patient series, concluded that all patients with bladder SCC should undergo radical cystectomy except those with metastatic disease (M1), in which systemic chemotherapy is indicated. They concluded also that patients with stage III & IV should receive adjuvant platinum based chemotherapy. Siefke et al, in a larger study of 88 patients studied the neoadjuvant chemotherapy in patients with bladder SCC prior to radical cystectomy, in order to downstage the tumor. They found that patients treated with initial cystectomy median cancer survival (CSS) was 23 months, with 36% disease-free rate at 5 years, while those who received preoperative chemotherapy had CSS that couldn’t be reached and a 78% disease free rate at 5 years. Moreover, they reported that no cancer related death occur among patients with disease downstages to pT2 or less. We use a 3 14-day cycles of MVAC as proposed by Bamias et al. The therapy was well tolerated with few side effects. In case of local relapse or in development of distant metastasis we will offer a combination of chemotherapy and radiotherapy. We strongly believe that patients who present with bladder SCC of limited disease should be treated by radical surgery and adjuvant chemotherapy and those patients who present with an advanced stage of disease (M+), a combination therapy of surgery, chemotherapy and radiotherapy is the treatment of choice.

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