DOUBLE UROGENITAL CANCER: BLADDER AND PROSTATE CANCER – CASE REPORT

MANUELA ENCIU[1], MARIANA ASCHIE[2], MARIANA DEACU[3]

[1,2,3]"Ovidius" University Constanţa

Keywords: *prostate adenocarcinoma, urothelial carcinoma, bladder, poorly differentiated, immunohistochemistry*

Abstract: *According to the literature, among multiple primary urogenital tumours, the association between bladder cancer and prostate cancer is less common. We present the case of a smoker male patient, 63-year-old, who in 2007 was diagnosed with high grade malignancy poorly urothelial carcinoma. He complained, in August 2011, of incomplete chronic urinary retention, dysuria, and polachiuria and prostate specific antigen (PSA) has a value of 7 ng/dl. A transurethral prostatic resection was performed. The histopathological examination of the prostate revealed prostate tissue with poorly differentiated adenocarcinoma, Gleason Score 9=4+5. Usually, the distinction of adenocarcinoma of the prostate from urothelial carcinoma of bladder can be performed on haematoxylin-eosin (HE) staining. But in this case, because both tumours are poorly differentiated, immunohistochemical tests were mandatory by applying a panel of monoclonal antibodies. The immunonohistochemical profile proved double bladder and prostate cancer. In conclusion, immunohistochemical techniques showed two distinct types of cancer located in close proximity, especially because both were poorly differentiated. Therefore, a diagnosis of cancer in urogenital area should not exclude the existence of other concomitant malignancy, especially in patients in the sixth decade of age.*

Cuvinte cheie: *adenocarcinom de prostată, carcinom urotelial, vezică urinară, slab diferenţiat, imunohistochimie*

Rezumat: *Conform literaturii de specialitate, în cadrul neoplaziilor multiple din sfera urogenitală, asocierea dintre cancerul de vezică urinară şi cel de prostată este mai rară. Prezentăm cazul unui pacient în vârstă de 63 de ani, fumător, care în 2007 a fost diagnosticat cu carcinom urotelial cu grad înalt de malignitate (G3) de vezică urinară. În august 2011 s-a prezentat pentru disurie, polachiurie, retenţie incompletă de urină iar antigenul specific de prostată (PSA) a avut valoarea de 7ng/dl. S-a efectuat rezecţie transuretrală prostatică. Examenul histopatologic a evidenţiat un adenocarcinom de prostată slab diferenţiat, scor Gleason 9=4+5. De regulă diferenţierea dintre un adenocarcinom de prostată şi un carcinom urotelial de vezică urinară se poate realiza pe preparatele uzuale colorate Hematoxilin-Eozină. Însă, în acest caz, datorită faptului că ambele tumori sunt slab diferenţiate, s-au recomandat teste de imunohistochimie prin aplicarea unui panel de anticorpi monoclonali. Profilul imunohistochimic a evidenţiat tumoră malignă dublă de prostată şi vezică urinară. În concluzie, tehnicile de imunohistochimie au fost extrem de utile în diagnosticul a două tipuri distincte de cancer slab diferenţiate, localizate în imediată proximitate. Astfel, diagnosticarea unei tumori maligne urogenitale nu ar trebui să excludă posibilitatea existenţei unei alte tumori maligne, mai ales la bărbaţii aflaţi în decada a şasea de vârstă.*

INTRODUCTION

In a review, the reported prevalence of multiple primary malignant neoplasms varies between 0.734% and 11.7%. Increased frequency of this entity in males is also due to increased incidence of prostate cancer, but also with increasing age.(1) Koyama et al found that among multiple primary urological tumours, is more common association between prostate and kidney cancer, while the diagnosis of bladder cancer is less common.(2) Such combinations of primary prostate and bladder malignant tumours have been reported by other authors.(3,4,5)

CASE REPORT

We present the case of a smoker male patient, BT, 63-year-old, hospitalized in 2007 in the Department of Urology, Clinical Hospital of Constanta, for hematuria. Following clinical examination and laboratory investigations, a transurethral bladder resection surgery was performed.

Histopathological examination revealed fragments of bladder with poorly differentiated urothelial carcinoma (high grade malignancy) (figure no. 1.) He complained, in August 2011, of incomplete chronic urinary retention, dysuria, and polachiuria. PSA has a value of 7 ng/dl. A transurethral prostatic resection surgery under spinal anesthesia was performed.

The histopathological and immunohistochemical analysis was performed in the Clinical Service of Pathology was performed in the Clinical Service of Pathology, Emergency County Hospital, Constanta.

[1]Corresponding author: Manuela Enciu, B-dul Tomis, Nr. 145, Cod 900591, Constanţa, România, E-mail: iftimemanuela@yahoo.com, Tel: +40767 745497

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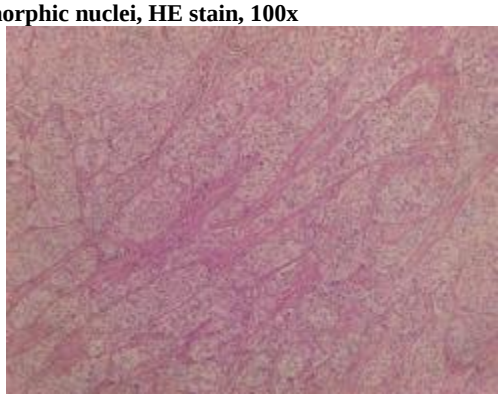
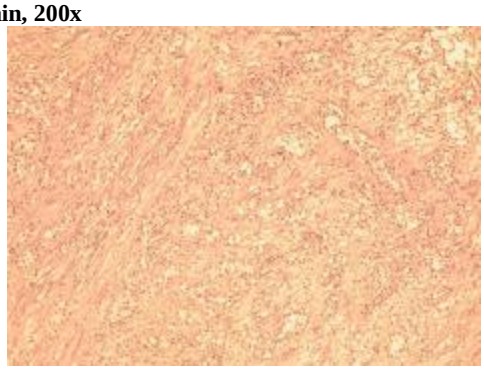
Figure no. 1. High-grade urothelial carcinoma with solid pattern, composed of cells with clear cytoplasm and pleomorphic nuclei, HE stain, 100x



Macroscopic examination revealed the presence of multiple fragments with variable diameters, which measures overall 8/5,5/1,5 cm, weighting 40 g, gray-pinkish coloured, low consistency. The specimen was fixed in 10% formalin and paraffin-embedded. The sections were stained with Hematoxylin-Eosin (HE). The histopathological examination of the prostate revealed prostate tissue with poorly differentiated adenocarcinoma, Gleason Score 9=4+5 (figure no. 2)

Figure no. 2. Poorly differentiated prostate adenocarcinoma, HE stain, 200x



Immunohistochemical tests were mandatory for differentiating on transurethral resection of the prostate between a poorly differentiated urothelial carcinoma of the bladder and a poorly differentiated prostatic adenocarcinoma.

There were applied:

- monoclonal Mouse anti-Human Prostatic Specific Antigen (PSA), Clone ER-PR 8, Isotype IgG1 Kappa (DAKO);
- monoclonal Mouse anti-Human High Molecular Weight Cytokeratin, Clone 34βE12, Isotype IgG1, Kappa (DAKO)
- monoclonal Mouse anti-Human Citokeratine 7, Clone OV-TL 12/30 (DAKO);
- monoclonal Mouse anti-Human Citokeratine 20, Clone Ks20.8 (DAKO).

The application of monoclonal antibodies on transurethral prostatic resection tissue revealed these features:

- positive reaction for PSA (figure no. 3)
- negative immunoreaction for High Molecular Weight Cytokeratin in tumor cells;
- negative immunoreaction for citokeratine 7 (CK7) and citokeratine 20 (CK20) in cytoplasm of neoplastic cells;

The application of monoclonal antibodies on transurethral bladder resection tissue revealed these features:

- positive cytoplasmic immunoreaction for High Molecular Weight Cytokeratin in tumour cells;
- positive immunoreaction for CK7 (figure no. 4) and CK20 in cytoplasm of neoplastic cells;
- negative reaction for PSA

Figure no. 3. Positive immunoreaction for PSA in prostatic epithelial cells, 100x

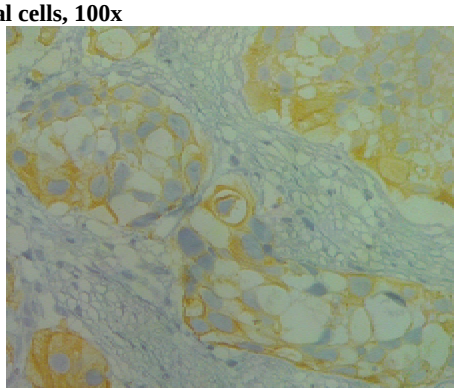
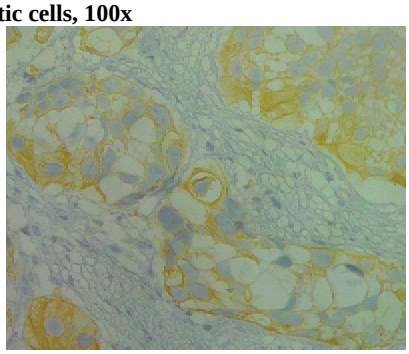


Figure no. 4. Positive immunoreaction for CK7 in cytoplasm of neoplastic cells, 100x



The immunonohistochemical stains proved the primary character of the two malignant neoplasms.

In October 2011, the patient underwent radiotherapy.

In May 2012, the patient was hospitalized for bilateral ureterohidronephrosis and severe general condition. Paraclinical explorations revealed hyperkalemia, marked nitrogen retention syndrome (12 mg/dl creatinine, 386 mg urea), severe lactic acidosis (ph of 7.1). Computed Tomography showed recurrence of prostate tumor with invasion of the bladder, seminal vesicles and ureters.

The evolution was unfavourable, with cardiopulmonary arrest and death has been declared.

DISCUSSIONS

Prostate cancer is the most prevalent cancer and the second leading cause of death in western male population. Bladder cancer is the fourth in prevalence of cancer in the same population.(6) Over 90% of prostate cancers are adenocarcinomas, most with an acinar pattern.(7)

Among bladder tumours, 90% are urothelial or transitional carcinomas (8), as in this case.

In terms of etiopathogenesis, several hypotheses have been issued. One of them refers to the fact that the genitourinary region is under the influence of the same carcinogenic stimuli. Another hypothesis refers to the fact that the first malignant tumor affects the adjacent environment, predisposing to the development of second malignancies.(9) On the other hand, the mean age of prostate cancer is 65 years and prostate cancer incidence increases exponentially with each decade of age.(10)

Most bladder cancers occur after 50 years of age. Although many factors have been incriminated in its etiopathogenesis, the only factor present in this case was

smoking. The cigarette smoke may cause changes in transitional epithelium genome and thus can initiate carcinogenesis. Bladder cancer is a disease recognized for molecular alterations.(8)

In this case it was important to establish the primary nature of both tumours and to exclude invasion of the prostate with poorly differentiated urothelial carcinoma. Differentiation of two types of malignant tumours is imperative, because therapy for these two conditions differ significantly.

Unlike adenocarcinoma of the prostate, bladder urothelial carcinoma is characterized by a pronounced nuclear pleomorphism and mitoses on haematoxylin eosin stained preparations. However, in a tumour with both prostate and bladder location, in the absence of glandular differentiation in the prostate, it is recommended immunohistochemistry.(11)

One of the markers useful in highlighting prostatic origin of poorly differentiated tumour is PSA, especially when used with High Molecular Weight Cytokeratin (HMWCK), CK7 and CK20.(10,11)

According to the medical literature, CK7 and CK20 show positive immunostaining in urothelial carcinoma invading the prostate. Unlike urothelial carcinoma, prostate adenocarcinoma show immunostaining only very rarely for CK7 and CK20.(12)

According to Lindeman and Weidner's study, there were analyzed 5 cases of poorly differentiated carcinomas of uncertain origin, which could be of prostatic or urothelial origin.

A panel of antibodies was applied, represented by prostate specific antigen (PSA), prostatic acid phosphatase (PAP), CK7, CK20 and carcino-embryonic antigen. One of the cases proved to be of the prostate origin, another was of bladder origin and three cases were positive for all markers, which showed overlapping issues. This result may be due to the common origin of the two organs of the urogenital sinus.(13,14)

However, some studies have described the positivity of these markers in prostate adenocarcinoma, and therefore are not considered specific in making the differential diagnosis.(15,16) In contrast, HMWCK is absent or rarely expressed in prostate adenocarcinoma (17) while 90% of urothelial bladder carcinomas are positive.(18,19)

CONCLUSIONS

Using immunohistochemical techniques showed two distinct types of cancer located in close proximity, especially because both were poorly differentiated. Therefore, a diagnosis of cancer in urogenital area should not exclude the existence of other concomitant malignancy, especially in patients in the sixth decade of age. In this respect, it is recommended monitoring of the patients by PSA determination.

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