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Incidentally detected prostate cancer in patients undergoing radical cystoprostatectomy

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BOGDAN BRATICEVICI[1], RAZVAN PETCA[1*], AMELIA PETRESCU[2], VIOREL JINGA[1], LUCIAN IONIȚĂ[3]
[1] *Department of Urology, "Prof. Dr. Th. Burghele" Clinical Hospital, 20, Panduri street, 050659, Bucharest, Romania*
[2]*Department of Anatomic Pathology, Prof. Dr. Th. Burghele" Clinical Hospital, 20, Panduri street, 050659, Bucharest, Romania*
[3] *Faculty of Veterinary Medicine, University of Agronomical Sciences and Veterinary Medicine, 105, Splaiul Independentei,050097, Bucharest, Romania*
**Address correspondence to: Department of Urology, "Prof. Dr. Th. Burghele" Clinical Hospital, 20, Panduri street, 050659, Bucharest, Romania;*
Tel: +40214106910; Fax: +40214111055; Email: drpetca@gmail.com

Abstract

Objectives: To review all features of incidentally discovered prostate adenocarcinoma in patients who underwent radical cystoprostatectomy for bladder urothelial carcinoma. Cystoprostatectomy specimens obtained from patients with bladder cancer provide a unique opportunity to assess the features of silent prostate adenocarcinoma (PCa).

Materials and Methods: Sixty-eight male bladder cancer patients who underwent radical cystoprostatectomy at our center between January 2010 and December 2012 were included in this study. The mean age of the patients was 63.18 years (range: 47-78 years). Prostate of all patients were embedded and sectioned at 2-mm intervals. Two uropathologist examined the prostatic tissues from radical cystoprostatectomy specimens.

Results: Incidentally prostate cancer was found in 26/68 (38.23%) of cystoprostatectomy specimens. All were acinar adenocarcinoma. Of these, 16 (61.54%) were located in the peripheral zone. 22 cases (84.61%) was stage pT_2. Gleason score was 6 or less in 16 (61.54%) patients. Negative margins were present in 96.15% of cases. All cases were pN_0 for PCa.

Conclusions: The occurrence of incidentally prostate cancer in radical cistoprostatectomy specimens in Romania is similar to Western countries. For those who are candidates for prostate-sparing surgery, it is indicate to include a routine prostate biopsy.

Keywords: bladder cancer, cystoprostatectomy, incidental, prostate cancer, adenocarcinoma

Introduction

Bladder and prostate cancer share similarities at different levels. Epidemiologically, bladder cancer is almost four times more prevalent in men and prostate cancer (PCa) is exclusively limited to this population.

Radical cystoprostatectomy (RCP) combined with bilateral pelvic lymphadenectomy remains the standard and effective treatment for muscle-invasive and refractory superficial bladder cancer. The standard technique of RCP consists of removing together the bladder, prostate, the seminal vesicles, a part of the vasa deferentia and distal ureter along with the regional lymph nodes. In cases of bladder tumors that invade the prostate and/or the prostatic urethra, urethrectomy is associated to the procedure. The procedure also consists of a urinary diversion, which can be internal or external, either of which has various complications. One

technique of urinary diversion is the orthotopic diversion, which has complications that consist of urinary incontinence and erectile dysfunction. Many authors have proposed a radical cystectomy and orthotopic neobladder with preservation of prostatic capsule and implicit sparing of the external bladder sphincter as a method to improve continence and preserve erectile function [1-3]. Preserved autonomic and sensory pelvic nerves can determine better urination and potency results. However, these techniques have raised some concerns, essentially because of two essential risks: a possible association with incidental prostate cancer and local invasion of the prostate by the urothelial cancer. These operations can be related with neither the radical elimination of tumor nor a higher risk of positive margins and worse oncological results.

Prostate cancer can be found incidentally when the prostate is removed during cystoprostatectomy for bladder cancer (incidentally detected cancer), found latently at autopsy without ever having caused symptoms during the person's lifetime, or clinically diagnosed by physical examination, laboratory tests, and/or symptoms [4]. Prostate cancer is frequently asymptomatic, or its symptoms can be confused with those of bladder neoplasms. The prevalence of latent PCa is much higher in autopsy series than that found in clinically diagnosed cases [5].

It is widely known that prostate cancer has great discrepancy between its high incidence and its comparatively low morbidity and mortality rates. For example, the lifetime probability of being diagnosed with prostate cancer is 16% and the probability of dying of prostate cancer is 3% [6].

We evaluated prostate tumors in patients with transitional bladder carcinoma who underwent radical cystoprostatectomy, to asses if preoperative information can be useful in identifying prostate adenocarcinoma.

Material and methods

Between January 2010 and December 2012, 75 consecutive male patients diagnosed with cancer of bladder underwent RCP at our hospital. The inclusion criteria comprised a serum PSA level < 4 ng/ml and normal digital rectal examination. Seven patients did not fulfill these criteria and were excluded from the study. None of the patients had a known history of PCa before surgery, and none had a history of radiotherapy or chemotherapy.

Preoperatively all patiens underwent physical and digital rectal examination, laboratory studies, chest radiographies and abdomino-pelvic either computed tomography (CT) or magnetic resonance imaging (MRI). The serum prostate-specific antigen (PSA) levels were determined routinely before RCP.

Table 1 details the patient characteristics and associated pathologic findings. The ages of the patients ranged from 47 to 78 years (mean = 63.18 years). Eight (11.76%) and five (7.35%) patients had clinical TIS and T1 disease involving the bladder, respectively, while the remaining 55 (80.88%) had muscle-invasive tumors.

Table1 Characteristics of patients with bladder cancer		
	Frequency	%
N	68	
Mean Age	63.18	
Mean PSA	2.51	
CIS (carcinoma in situ) in bladder	8	11,76
Focality		
Unifocal bladder tumor	27	39.71
Multifocal bladder tumor	41	60.29
pT (TNM system)		
T_{is}	8	11.76
T1	5	7.35
T2	15	22.06
T3	17	25
T4	23	33.82
Grading		
G1	-	-
G2	31	45.59
G3	37	54.41
Nodes		
Negative	48	70.59
Positive	20	29.41
Location		
Proximal to trigone	41	60.29
Trigone and bladder neck	27	39.7
Pattern		
Transitional cell carcinoma	64	94.12
Sarcoma	4	5.88

The product from the radical cystoprostatectomies was fixed and processed according to the usual standards for fixation and inclusion routinely employed in pathology services. After receiving the specimens, they were measured and weighed, the outer surface of the specimen was inked and they were opened totally and fixed in 10 % neutral buffered formalin for 24 hours. After fixation, the prostate including prostatic urethra was sectioned in quadrants. Sections, about 2 mm in thickness, from transitional and peripheral zones of the prostate and from apical, middle and basal regions in both lobes were included, resulting, in average, 40 blocks per case. The margin of prostatic urethra was represented separately. The blocks were sectioned in slices with 3- to 5- micrometers in thickness and the resultant histological slides were stained with hematoxylin-eosin. If adenocarcinoma was discovered, then tumor location and Gleason score was determined and involvement of the margins or seminal vesicle extension was evaluated. If there was HGPIN, it was also mentioned. Cancer location and extent were determined and mapped in each section. The presence of tumor cells at the inked margin of resection (defined as the presence of ink on neoplastic cells) was considered to present a positive surgical margin. A positive surgical margin in an area where no capsule was identified was referred to as pT2+ and was thought to indicate where the plane of dissection entered the prostatic capsule or otherwise where no capsule was present. Two genitourinary

pathologists reviewed all tumors for tumor stage (2002 AJCC TNM classification) [7], tumor grade (2005 modified Gleason scoring system) [8], and surgical margin status. All disease-containing areas were outlined in each prostatectomy specimens section. Data on the features listed in Table 2 were obtained.

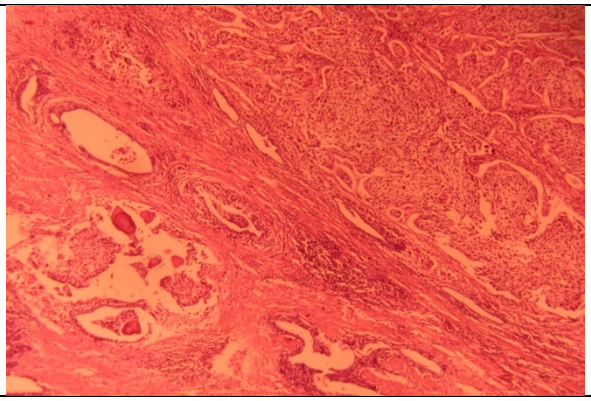

Figure 1. Cystoprostatectomy piece presenting high grade urothelial carcinoma and normal structured prostatic glands. Hematoxylin – Eosin Stain, magnification 20

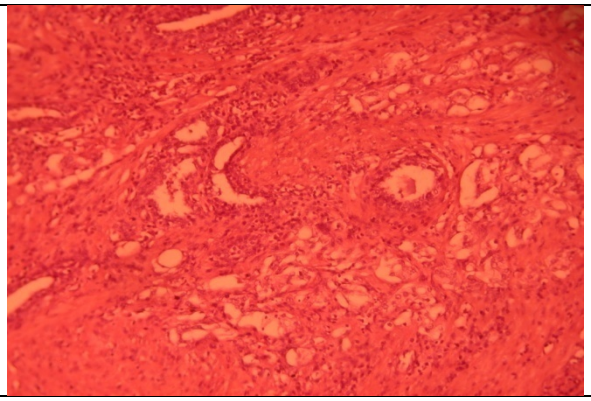

Figure 2. Normal structured prostatic glands and prostate adenocarcinoma with Gleason scor 3+4=7. Hematoxylin – Eosin Stain, magnification 20

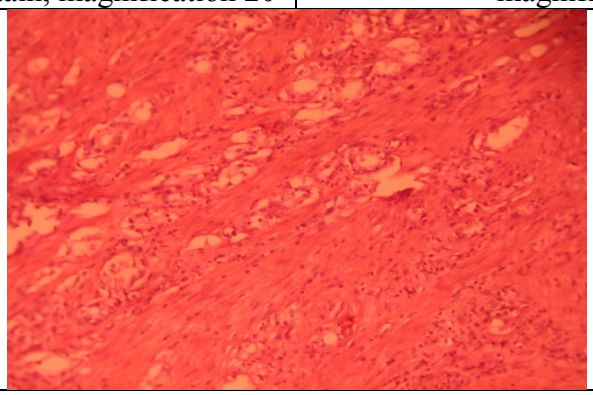

Figure 3. Prostate adenocarcinoma, detaild. Hematoxylin – Eosin, magnification 40

Results and discussions

Of 68 patients, 26 (38.23%) had the incidental finding of PCa within the radical cystoprostatectomy specimen. The ages of the patients ranged from 49 to 76 years (mean = 64.73 years). All were diagnosed as acinar adenocarcinomas, and 16 (61.54%) were located in the peripheral zone. Of incidentally detected prostate cancer, 61.54% were scored Gleason six or less. Incidental prostate cancer in our cystoprostatectomy cases was usually stage pT2 – 84.61% (22/26). Negative margins were present in 96.15% of cases. All cases were pN_0 for PCa.

Table 2 Characteristics of patients with incidentally detected prostate cancer (PCa)

	Freq.	%
N	26	
Mean Age	64.73	
Mean PSA	2.83	

Focality		
Monofocal	6	23.08
Multifocal	20	76.92
Tumor location		
Peripheral zone	16	61.54
Transition zone	2	7.69
Central zone	5	19.23
All 3 zones	3	11.54
Gleason score		
≤ 6	16	61.54
7 (3+4)	7	26.92
7 (4+3)	2	7.69
8-10	1	3.85
pT (TNM system[7])		
pT_2a	5	19.23
pT_2b	6	23.08
pT_2c	11	42.31
pT_3a	3	11.54
pT_3b	1	3.85
pT_4	-	-
Stage of bladder cancer		
pTis	2	7.69
pT1	1	3.85
pT2	7	26.92
pT3	8	30.77
pT4	8	30.77
Surgical margin status		
Negative	25	96.15
Positive	1	3.85

RCP represents the most effective treatment for muscle invasive nonmetastatic bladder cancer [9]. The frequent high coincidence of prostate and bladder cancer occurring together could be explained by a common carcinogenic pathway. In this respect, Singh et al. reported that some tumor suppressor genes such as p53 and pRb play a major role in the development of both prostate and bladder cancers [10]. Prostate cancer is diagnosed nine times more for men with bladder cancer. If not to count the mistakes of cases inclusion, prostate cancer is nineteen times more often between patients with bladder cancer than by age, sex, or race in adequate population [11].

The incidence of prostate cancer varies considerably across populations. The highest incidence of prostate cancer in the world is in Jamaica. The average age adjusted incidence of prostate cancer in Kingston, Jamaica is 304/100.000 men [12]. In spite of striking differences in the frequency of clinical carcinoma (in Asian countries being the lowest), the frequency of histological (incidentally found) carcinoma is fairly similar around the world.

Prostate cancer is unique among the potentially lethal human malignancies in the wide discrepancy between the high prevalence of histological (incidentally found) cancer and the much lower prevalence of the clinical disease. In 50 year-old men and with an expectancy of life more than 25 years, the risk for prostatic carcinoma is estimated to be 42% for histological (incidentally found) cancer, 9.5% for clinical cancer, and 2.9% for fatal cancer [13].

Incidentally found carcinoma can be studied in two ways: in autopsies and in cystoprostatectomies. Cystoprostatectomy specimens obtained from patients with bladder cancer provide a unique opportunity to assess the features of silent PCa. The frequency of incidentally discovered PCa in these specimens is extremely variable. This variability can be explained by several factors, including pathologic sampling techniques. A detailed examination of prostatic tissue specimens is of paramount importance in the detection of small cancers. In this respect, the slice thickness of the prostate and whether the prostate is totally embedded represent two important issues.

Incidentally found cancer after RCP was diagnosed for 38.23% of all examined patients in our study. It is similar to many other studies which were made inWestern Europe countries. In these studies, rate of incidentally found prostate cancer was from 23% to 51% [14, 15]. Though the discrepancies between studies could be related to the method of pathologic evaluation employed, all indicate the presence of a significantly high incidence of prostate cancer.

Stamey et al. first defined the clinically significant adenocarcinoma of PCa in RCP specimens [16]. According to these authors clinically significant prostate cancer is based on Gleason score, tumor volume and stage, lymph node status and resection margin [16]. We evaluated clinically significant PCa features as any of the following: Gleason score > 6, extracapsular extension, seminal vesicle invasion, and/or a positive surgical margin according to the criterion advocated by Epstein et al [17]. According to this definition, the ratio of clinically significant PCa in our study was 42,3% (11/26). Tumor volume was not part of the clinically significant PCa definition, as it was in other studies on the same matter, as consequence, the clinically significant PCA in our study might be underestimate.

Careful preoperative evaluation to diagnose concurrent PCa is very important. Some authors have tried to use PSA into predictive models of tumor significance. Stamey et al. reported that serum PSA had been associated with cancer volume [16]. According to our study, the median PSA level for patients with and without prostate cancer was not significantly different.

There are no many studies where influence for patients' survival of incidentally found prostate cancer after RCP was examined. Abdelhady et al. [18] found that the combination of prostate and bladder cancers has no influence on patients' survival prognosis and is related with one or another cancer stage.

Conclusions.

The percentage of incidentally detected PCa in RCP specimens in Romania is similar to the reported rates in Western countries. We therefore assumed regional differences in prostate cancer incidence rates to be related to environmental and racial factors. Also the method of pathohystological examination of the prostate varies considerably and can be main cause of these frequency differences.

We recommend digital rectal examination and PSA test as part of the bladder cancer work up in men and complete removal of the prostate as cystoprostatectomy to prevent residual prostate cancer.

More than a third of the patients undergoing RCP for urothelial cancer of the bladder had cancer involving the prostate. The majority are considered clinically insignificant. The clinical significance of these incidentally discovered cancers remains questionable because the outcome of patients with both malignancies depends on the prognosis of the bladder tumor.

The present preoperative staging criteria are not enough to accurately identify those patients that can be selected for radical cystectomy with preservation of the prostatic capsule. Lack of relevant PSA values to exclude cancer justifies routine preoperative prostate biopsy.

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