

PROSTATIC ADENOCARCINOMA IN CYSTOPROSTATECTOMY SPECIMENS REMOVED FOR BLADDER TUMORS IN BILHARZIAL PATIENTS

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Objective To determine the incidence of prostatic adenocarcinoma in bilharzial patients who previously underwent radical cystoprostatectomy for bladder tumors.

Patients and Methods From February 1997 to February 1999, 249 male patients with bladder cancer were screened for prostate cancer prior to cystectomy using DRE and total PSA assay, as well as transrectal ultrasound-guided prostatic biopsies. Then the cystoprostatectomy specimens were serially sectioned (every 3 mm) and histologically examined.

Results Prostatic adenocarcinoma was detected by ultrasound-guided prostatic needle biopsies in 2 cases, while in 18 it

was discovered incidentally after cystoprostatectomy (total 20 patients = 8%). Gleason score was 6 in 16 patients, 7 in 3 patients and 8 in the remaining patient. Perineural lymphatic permeation was observed in 4 cases and extracapsular extension in one.

Conclusion Compared to previous reports on non-bilharzial patients, the incidence of prostate cancer in the cystoprostatectomy specimens of bilharzial patients was low, and the tumors were clinically insignificant in most of the cases.

Keywords incidental cancer, prostate cancer bladder cancer, bilharzial

INTRODUCTION

The combination of bladder and prostatic carcinomas has been reported to be the second most common combination after skin and colon cancers¹. Prostate cancer is frequently asymptomatic, or its symptoms can be confused with those of bladder neoplasms. Moreover, there is much disparity between the clinical incidence of prostatic adenocarcinoma and the prevalence of histologically diagnosed disease in autopsy studies. The incidence of the clinical disease in white men in the USA was reported to be 75.3 per 100 000 men², while on histologic diagnosis in autopsy studies the prevalence was noted to be 30% in the 7th decade, 40% in the 8th decade and 50% in the 9th decade of life³.

A coincidence of bladder and prostatic carcinomas has previously been reported in cases with transitional cell carcinoma of the bladder in the United States and European countries⁴⁻⁶. In Egypt, where bilharziasis is endemic, bladder cancer is the most common solid tumor in adult men⁷. Furthermore, a causal relationship

between urinary bilharziasis and bladder cancer has been reported⁸. A relationship between cancer of the prostate and bilharziasis has not been established, as yet, possibly due to the rarity of prostatic involvement by bilharziasis.

We conducted this study to detect the coincidence of carcinomas of the bladder and the prostate in bilharzial patients who had been subjected to radical cystoprostatectomy.

PATIENTS AND METHODS

Between February 1997 and February 1999, 249 patients with a mean age of 53.5 ± 8.03 years underwent radical cystoprostatectomy for bladder cancer.

Prior to cystectomy, the patients were screened for prostatic adenocarcinoma by serum PSA assay considering PSA <4 ng/ml a normal level (IMx total PSA Assay / Abbott Laboratories) and digital rectal examination (DRE). Ultrasound-guided sextant prostatic biopsies were obtained from patients with PSA

Table 1: Age Distribution in Decades

Age (Decades)	No.	%
4 th decade	15	6.0%
5 th decade	59	23.7%
6 th decade	116	46.6%
7 th decade	56	22.5%
8 th decade	3	1.2%

Table 2: Type of Bladder Tumors

Bladder Pathology	No.	%
Transitional Cell Carcinoma (TCC)	149	59.8%
Squamous Cell Carcinoma (SCC)	81	32.5%
Adenocarcinoma	13	5.2%
Mixed tumor (SCC + TCC)	3	1.2%
Undifferentiated carcinoma	3	1.2%

levels ≥ 4 ng/ml and/or a DRE suspicious for prostatic malignancy. The biopsies were obtained bilaterally from the apex, middle and base of the gland via an 18-gauge needle from a spring-loaded gun⁹. Then radical cystoprostatectomy and pelvic lymphadenectomy were carried out.

Specimens of the prostate gland included in the cystoprostatectomy specimens were fixed in 10% formalin for 24 hours and serially blocked in transverse planes at 3mm intervals. The blocks were sectioned at 5 μ m, the slides were stained with hematoxylin and eosin and examined histologically. When prostatic adenocarcinoma was discovered, the histopathologic characters of the tumor such as site, Gleason score, extracapsular extension and lymph node metastases were recorded.

Patients with histologically diagnosed prostate cancer were followed up by assessment of serum PSA level and DRE every 6 months. Chest, abdominal and pelvic CT studies were carried out to diagnose any chemical or radiological evidence of recurrence of either bladder or prostate cancer.

RESULTS

Mean patients' age was 53.3 years \pm 8.03 SD. The age distribution in decades is illustrated in Table 1. The types of bladder tumors are summarized in Table 2. Bilharzial ova were histologically detected in 85.4% of the bladder specimens (220 specimens).

On preoperative screening, DRE was suspicious for prostate cancer in 3 cases (2 of them had PSA levels $<$ 4 ng/ml). Total serum PSA was more than 4ng/ml in 22 patients. Therefore, ultrasound guided prostatic biopsies were obtained from 24 patients leading to the diagnosis of prostatic adenocarcinoma in two patients.

Histologic examination of the prostate gland after cystectomy revealed microscopic foci of prostatic adenocarcinoma in another 18 patients and high-grade prostatic intraepithelial neoplasia (PIN) in 24 patients (9.6%). Invasion of the prostate by transitional cell carcinoma of the bladder was detected in 15 patients (6%).

As a result of the preoperative screening and post-cystectomy histologic examination of the prostate, 20 out of 249 patients (8%) had prostatic adenocarcinoma associated with bladder tumors. The mean age of the affected patients was 58.45 \pm 7.45 years. A total serum PSA $>$ 4 was found in 9 cases while DRE was suspicious in another 2 patients.

The Gleason score was \leq 6 in 16 patients (80%), 7 in three patients and 8 in one case. Perineural lymphatic permeation was detected in 4 cases, while extracapsular extension with a positive safety margin was observed in one case. Prostate cancer within the apical tissue was detected in 6 cases, in the mid-zone of the prostate in 6 and in the base in 8 cases. Prostate cancer associated with transitional cell carcinoma of the bladder was found in 18 patients, squamous cell carcinoma in one and adenocarcinoma in another case.

PIN was of high grade in 24 patients. Twelve of them were not associated with prostatic adenocarcinoma. The resected regional lymph nodes showed metastatic deposits from the bladder tumors in 56 patients (22.5%). Histopathologic examination of the prostate in 24 clinically suspicious cases showed prostatic adenocarcinoma in 3, PIN in 6 and BPH in 14 specimens.

Further treatment included radiation therapy for one patient who had a positive safety margin.

Follow up ranged from 3.6 to 52 months (median 26.2 months). No biochemical evidence of prostate cancer recurrence was found in any patient. Among 14 living patients, 10 are free of any tumors, 4 have local recurrence of bladder tumors and 6 patients died from metastatic bladder tumor.

DISCUSSION

The incidence of bladder carcinoma associated with prostatic carcinoma has been estimated by various authors to range from 27-45%⁴⁻⁶, while in the present study it was only 8%. This lower incidence may be explained by the younger age of our patients which is related to the fact that bladder tumors develop two decades earlier in bilharzial patients than in non-bilharzial patients¹⁰. In our study, 76.3% of the patients were younger than 60 years compared to 15% of the patients in a study carried out by Pritchett⁵. Also, the mean age of 53.3 years in our study was lower than the mean age of 64.3 years reported by Abbas et al.⁶. Similarly, the low incidence of PIN in our patients (9.6%) compared to the group of patients studied by Abbas et al. (47.4%) may be due to the same cause (age related). The association of prostate cancer with transitional cell carcinoma (TCC) in most of the cases may also be related to the age of the patients; patients with TCC of the bladder are usually older than those with SCC⁸, and prostate cancer is a disease of the older age group.

Nearly all patients with prostatic adenocarcinoma presented with symptoms related to the bladder tumor such as haematuria, cystitis syndrome and suprapubic pain. Only one patient presented with obstructive lower urinary tract symptoms. The same was observed by Abbas et al. Prostate cancer is usually asymptomatic or its symptoms may be masked by bladder symptoms. Furthermore, patients with chronic bilharzial infestation, like in our study, have recurrent or persistent cystitis syndrome.

Pre-cystectomy screening for prostate cancer carried out for 249 patients detected only 2 cancer cases because the other 18 cases had only microscopic foci of the tumor. Such small volume tumors are difficult to be

detected by sextant ultrasound-guided prostatic biopsies.

In our study, the tumor volumes could not be estimated, because prostate cancer was detected in microscopic foci of the gland after cystoprostatectomy. Incidentally diagnosed prostatic adenocarcinoma had favourable histopathologic characteristics such as low Gleason score (≥ 6) in 80% of the cases and only microscopic foci of the tumors in 90% of cases. Therefore, based on Stamey's proposal of clinically insignificant prostate cancer¹¹, no further treatment was applied in 18 cases diagnosed after cystectomy.

Invasion of the prostate by transitional cell carcinoma of the bladder was detected in 6% of cases which is comparable to the findings of Schellhammer et al. (5%) and Wood et al. (6%)^{12,13}.

Incidentally diagnosed prostate cancer was located within the prostatic apex in 6 patients (30%). Therefore, preservation of the prostatic apical tissue is not advised during cystoprostatectomy to ensure complete removal of any prostatic tissue. Abbas et al. had the same observation in their study⁶.

We conclude that, in comparison to previous reports on non-bilharzial patients, the incidence of prostate cancer in the cystoprostatectomy specimens of our bilharzial patients was low and the tumors were clinically insignificant in most of the cases.

REFERENCES

1. Merscheimer WL, Ringel A, Eisenberg H. Some characteristics of multiple cancer. *Ann NY Acad Sci* 1964, 114:896.
2. Devesa SS, Silverman DT, Young JL. Cancer incidence and mortality trends among whites in the United States 1947 - 87. *J Natl Cancer Inst* 1987, 79:701.
3. Scardino PT. Early detection of prostate cancer. *Urol Clin N Amer* 1989, 16:635.
4. Winfield HN, Reddy PK, Lang PH. Coexisting adenocarcinoma of the prostate in patients undergoing cystoprostatectomy for bladder cancer. *Urology* 1987, 30:100.
5. Pritchett TR, Moreno J, Warner NE et al. Unsuspected prostatic adenocarcinoma in patients who have undergone radical cystoprostatectomy for transitional cell carcinoma of the bladder. *J Urol* 1988, 139:1214.

6. Abbas F, Hochberg D, Civantos F, Soloway M. Incidental prostatic adenocarcinoma in patients undergoing radical cystoprostatectomy for bladder cancer. *Eur Urol* 1996, 30:322.
7. El-Bolkainy MN, Mokhtar NM, Ghoneim MA, Hussein MH. The impact of schistosomiasis on the pathology of bladder carcinoma. *Cancer* 1981, 48:2643.
8. Abdel-Tawab GA. Studies on the aetiology of bilharzial carcinoma of the urinary bladder. *Int J Cancer* 1966, 1:377.
9. Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. *J Urol* 1989, 142:71.
10. Ghoneim MA, El-Mekresh MM, El-Baz MA, El-Attar IA, Ashamalla A. Radical cystectomy for carcinoma of the bladder: critical evaluation of the results in 1026 cases. *J Urol* 1997, 158:393.
11. Stamey TA, Freiha FS, McNeal JE, Redwine EA, Whitmore AS, Schmid HP. Localized prostate cancer: Relationship of tumor volume to clinical significance for treatment of prostate cancer. *Cancer* 1993, 71:933.
12. Schellhammer PF, Bean MA, Whitmore WF Jr. Prostatic involvement by transitional cell carcinoma: Pathogenesis, pattern and prognosis. *J Urol* 1977, 118L399.
13. Wood DP Jr., Montie JE, Medendorp SV, Levin HS. Transitional cell carcinoma of the prostate in cystoprostatectomy specimens removed for bladder cancer. *J Urol* 1989, 141:346.

RESUME

Adénocarcinome Prostatique dans les Pièces de Cysto-Prostatectomie pour Tumeurs de Vessie Bilharzienne

Objectif Déterminer l'incidence de l'adénocarcinome prostatique chez des patients bilharziens qui ont subi une cysto-prostatectomie radicale pour tumeur de vessie. **Patients et Méthodes** De Février 1997 à Février 1999, 249 patients de sexe masculin ont bénéficié d'un dépistage de cancer prostatique avant une cystectomie. Le dépistage a consisté en un toucher rectal, un dosage du taux de PSA total et des biopsies prostatiques guidées par échographie trans-rectale. Puis des coupes sériées tous les 3 mm ont été pratiquées sur les pièces de cysto-prostatectomie suivies d'un examen histologique. **Résultats** Un adénocarcinome prostatique a été détecté chez deux patients avec les biopsies écho-guidées, tandis que 18 cas ont été retrouvés fortuitement sur les pièces de cysto-prostatectomie (total 20 patients = 8%). Le score de Gleason était de 6 chez 16 patients, 7 chez 3 patients et 8 chez 1 patient. Une perméation lymphatique péri-nerveuse a été observée chez 4 patients et une extension capsulaire chez un patient. **Conclusion** Comparée aux études antérieures portant sur des patients non bilharziens, l'incidence du cancer de la prostate dans les pièces de cysto-prostatectomie chez les patients bilharziens est très faible. De plus, les tumeurs sont cliniquement insignifiantes dans la plupart des cas.

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