REVIEW ARTICLE

Prostatic involvement by urothelial carcinoma in patients with bladder cancer and their implications in the clinical practice

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KEYWORDS
Urothelial carcinoma; Prostate; Prostatic urothelial carcinoma; Bladder cancer; Cystectomy

Abstract

Objectives: Urothelial carcinoma (UC) is a multifocal disease that may develop in any location of the urinary tract, including the prostate. We analyze the types of prostate diseases due to UC, their diagnosis, risk factors and the clinical implications of this entity.

Material and methods: Analysis of original, review articles and publications related to prostate involvement due to UC. The study included works published in the period of 1985–2011, most of which were obtained from the search in PubMed.

Results: Prostate involvement due to UC has been observed frequently in both non-muscle infiltrating bladder cancer (NMIBC) series and prolonged follow-up (39%) as in radical cystectomy series (15–48%). Prostatic involvement may occur in the mucosa and ducts (superficial involvement) or prostate stroma (infiltrating involvement), a fact that has prognostic and therapeutic implications. Stromal involvement may have both a bladder and intraurethral origin. Carcinoma in situ (CIS), multifocality, bladder neck/trigone cancer, and previous history of tumor recurrence are the factors that have been more consistently associated to prostate involvement due to UC. The incidence of prostatic involvement by UC in patients with NMIBC increases over time when risk factors exist. In these cases, a prostatic urethral biopsy should be performed during the follow-up. Conservative treatment with transurethral resection and BCG is possible in case of superficial involvement of the prostatic urethra, assuming its risk of progression. Patients subject to cystectomy and with prostate involvement due to UC have a greater risk of urethral recurrence. The elevated incidence of prostatic adenocarcinoma and prostatic involvement by UC in cystectomy sections makes it necessary to be very selective when indicating prostate-sparing cystectomy. Chemotherapy may be an option in an attempt to improve survival of patients with prostatic stromal involvement.

Conclusions: Prostatic involvement by UC is not uncommon and it has important implications in the management of patients with NMIBC and in those who have an indication for or have undergone radical cystectomy.

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PALABRAS CLAVE
Carcinoma urotelial; Próstata; Carcinoma urotelial prostático; Cáncer de vejiga; Cistectomía

Afectación prostática por carcinoma urotelial en pacientes con tumor vesical y sus implicaciones en la práctica clínica

Resumen
Objetivos: El carcinoma urotelial (CU) es una enfermedad multifocal que puede desarrollarse en cualquier parte de la vía urinaria incluyendo la próstata. Analizamos los tipos de afectación de la próstata por CU, su diagnóstico, factores de riesgo y las implicaciones clínicas de esta entidad.

Material y métodos: Análisis de artículos originales, de revisión y publicaciones relacionadas con la afectación por CU de la próstata. Trabajos publicados en el periodo 1985-2011 y obtenidos mayoritariamente la búsqueda en PubMed.

Resultados: La afectación prostática por CU se ha observado con frecuencia tanto en series de tumor vesical no músculo-infiltrante (TVNMI) y seguimiento prolongado (39%), como en series de cistectomía radical (15-48%). La afectación prostática puede producirse a nivel de mucosa y ductos (afectación superficial) o estroma prostático (afectación infiltrante), hecho que tiene implicaciones pronósticas y terapéuticas. La afectación estromal puede tener a su vez un origen vesical o intrauretral. Cir, multifocalidad, tumor en cuello vesical/trigono, e historia previa de recidiva tumoral, son los factores que se han asociado con mayor consistencia a la afectación por CU de la próstata. La incidencia de afectación prostática por CU en pacientes con TVNMI se incrementa con el tiempo si existen factores de riesgo. En estos casos es aconsejable la realización de biopsias de uretra prostática durante su seguimiento. Es posible el tratamiento conservador con resección transuretral y BCG en caso de afectación superficial de uretra prostática, asumiendo su riesgo de progresión. Los pacientes sometidos a cistectomía y con afectación por CU de la próstata tienen mayor riesgo de presentar recidiva uretral. La elevada incidencia de adenocarcinoma prostático y de afectación prostática por CU en piezas de cistectomía obliga a ser muy selectivo al indicar cistectomía con preservación de próstata. La quimioterapia puede ser una opción en un intento de mejorar la supervivencia de pacientes con afectación prostática estromal.

Conclusiones: La afectación prostática por CU no es infrecuente y tiene importantes implicaciones en el manejo de los pacientes con TVNMI, así como en los que tienen indicación o han sido sometidos a cistectomía radical.

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Introduction

Urothelial carcinoma (UC) is a multifocal disease that can develop in any part of the urinary tract including the prostate.1 In patients with bladder tumor CU prostatic involvement has been observed frequently both in series of non-muscle infiltrating bladder cancer (NMIBC) and prolonged follow-up (39%).2,3 as in series of radical cystectomy (15-48%).4-7

Prostatic involvement may occur at the level of the mucosa, ducts, or prostatic stroma, a fact that has prognostic and therapeutic implications.2-7 In this review, an overview of the histological characteristics of the prostate is carried out to better understand the different forms of prostatic involvement by UC and its implications. The difficulties to make its correct endoscopic diagnosis and the major risk factors associated with the presence of UC at the prostatic level are also analyzed.

Subsequently, the implications that the involvement by prostate UC has in clinical practice are assessed. In NMIBC patients, the risk of progression increases and mandates a strict follow-up when opting for conservative treatment.2,3 In patients requiring or undergoing cystectomy, the risk of urethral recurrence (UR)6,9 increases, making the use of prostate-sparing techniques10 inadvisable, and in the case of stromal involvement, its poor prognosis involves assessing the use of systemic chemotherapy.11 Finally, we analyzed the primary prostate UC, a rare entity that in order to establish its proper diagnosis, must rule out concomitant bladder pathology.12

Histological characteristics of the prostate

The knowledge of the histological structure of the prostate is essential for the understanding of the different possibilities of involvement of this organ by UC (Fig. 1). The prostate consists of 20–40 glands embedded in fibromuscular stroma. The surface epithelium of the secretory part (acini) and excretory part (ducts) of the glandular tissue is identical, except in the ductal portion immediate to the prostatic urethra, in which a minimum lined transitional epithelium (urothelium) is recognized. In the prostatic urethra, the majority of prostatic ducts will lead to both sides of the veru montanum. The glandular epithelium consists of a double row of cells, secretory and basal. The secretory cells are cylindrical, with abundant cytoplasm, with the core in basal position, resting on the basal cell layer. The basal ones have scant cytoplasm, they are considered to act as precursors for the other epithelial cells, and they are located on the basal membrane. The
prostatic stroma is contiguous with the epithelium and it is made up of fibroblasts and smooth muscle.

At the level of prostatic urethra, the prostate (with its glandular and stromal component) is lined by non-keratinizing polystratified type (mucosa) transitional epithelium (urothelium) and by a thin connective-muscular tissue (submucosa).\textsuperscript{13}

**Types of prostatic involvement by urothelial carcinoma and its prognostic implications**

The first descriptions on UC affecting the prostate predate 1960.\textsuperscript{14,15} In the late ’70s, there were already works with entity on the different forms of involvement of the prostate by UC,\textsuperscript{16} but it was in 1996 when two key works appeared highlighting its prognostic significance. At that time, the TNM classification of the bladder tumor considered pT4 for all the bladder tumors with prostatic involvement. Pagano et al.\textsuperscript{4} and Ersing et al.\textsuperscript{5} were the first to describe different ways and types of prostatic involvement by UC. In their works, they suggested changes in the TNM, since not all the patients with prostatic involvement by CU had the same evolution and, therefore, they should not be grouped all as pT4 tumors. Later works have confirmed their results.\textsuperscript{6,7}

There is prostatic involvement by CU radical cystectomy series in 15–48%. This variability can be explained by differences in the design of the studies, patient populations, methodology, and, above all, by the extension of the anatomicopathological study of the cystectomy specimen.\textsuperscript{4,7,15–19}

However, there is currently insufficient evidence to indicate that the prostatic involvement by UC may be originated at the level of the prostatic urethra (intraurethral involvement) or produced by a direct invasion from the bladder, going through all its layers (extravesical involvement) (Fig. 2).

In studies examining pieces of cystectomy, the intraurethral involvement is seen more frequently (76–86%) than the extravesical one (14–24%) (Table 1). The intraurethral involvement may be limited to the mucosa and prostatic ducts or extend into the stroma. The 5-year survival of the patients with mucosal or prostatic duct involvement is in 49–71\%, and the prognosis will be determined by the stage of the bladder tumor. Although some have observed a better evolution in patients with mucosal involvement than with duct involvement, most authors group them and consider both as forms of surface prostatic involvement.\textsuperscript{4,7,17–19}

**Figure 1** Microscopic anatomy of the prostate glands (A, A1)—a: acini; Bc: basal cells; Sc: secreting cells; d: prostatic ducts; S: stroma; arrow: basement membrane. Histological structure of the prostatic urethra (B)—S: stroma; arrow: basement membrane; Ct: subepithelial connective tissue (submucosa); U: urothelium.

**Figure 2** Extravesical (E) and intraurethral (I) involvement of the prostate by urothelial carcinoma.
Table 1  Types of involvement of the prostate by urothelial carcinoma.

<table>
<thead>
<tr>
<th>Origin (%)</th>
<th>Types of involvement [TNM 2010]</th>
<th>Prognostic division</th>
<th>Survival 5 years (reference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraurethral (76–86%)</td>
<td>Mucosa/submucosa pTis, pTa, pT1 [up]</td>
<td>54–83%</td>
<td>Surface involvement</td>
</tr>
<tr>
<td>Extravesical (14–24%)</td>
<td>Stroma [pT2]</td>
<td>17–46%</td>
<td>Infiltrating involvement</td>
</tr>
<tr>
<td></td>
<td>Stroma [pT4]</td>
<td>14–24%</td>
<td></td>
</tr>
</tbody>
</table>

p: NS (statistically not significant difference); pT2 ≈ pT4: series of patients with intraurethral and extravesical stromal involvement and similar survival.

In the patients with extravesical involvement, as we said, the prostatic stromal invasion occurs from the bladder.

The prostatic stromal invasion both intraurethrally and extravesically is clearly associated with a worse prognosis than the tumor extension to mucosa and ducts, and it is therefore considered as an infiltrating-type prostatic involvement. Pagano et al. [4] observed a 40 and 7% 5-year survival in patients with stromal intraurethral and extravesical involvement, respectively. To Ersing et al. [3], the prognosis of patients with intraurethral stromal involvement worsened as the stage of the bladder tumor increased. So, only the survival of patients with intraurethral stromal involvement and non-organ-confined (pT3) bladder disease was equated to that of patients with extravesical stromal involvement, those with the worst prognosis (25% 5-year survival). In other words, the 5-year survival of the bladder pT1 and pT2 with intraurethral stromal involvement was higher than that of patients with extravesional stromal involvement.

Herr et al. [2] in 186 patients with NMIBC treated with BCG and followed for 15 years found prostatic stromal involvement in 27 cases. The 15-year survival was 75 and 9% in the 16 patients with intraurethral stromal involvement and in the 11 patients with extravesical involvement, respectively. The work by Herr is the one that probably shows a greater difference in survival between the 2 forms of prostatic stromal involvement. It should be noted that the bladder stage of 11 out of the 16 cases with intraurethral stromal involvement was non-muscle-invasive.

Although the extravesical stromal involvement appears to be associated with a worse prognosis (7–22% 5-year survival), there are series in which survival is not statistically different from that of patients with intraurethral stromal involvement. [4–7, 19] All these findings have led to the fact that the 2010 bladder TNM considers only stromal prostatic invasion produced directly from the bladder stage T4. Thus, intraurethral prostatic infiltration is excluded from the T4 stage (from prostatic urethra). [20]

It is assumed, therefore, that in patients with bladder tumor and intraurethral prostatic involvement, we need to use, on the one hand, the bladder TNM and, on the other hand, the prostate urothelial carcinoma TNM (included in the urethral TNM) (Table 2); and the bladder stage and the prostatic urethral stage must be shown.

Table 2  Staging of patients with bladder cancer and prostatic involvement according to the TNM 2010.

<table>
<thead>
<tr>
<th>Bladder</th>
<th>Urethra (prostate urothelial carcinoma)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T4a</td>
<td>Tumor invading: prostatic stroma, uterus, and vagina</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invading abdominal or pelvic wall</td>
</tr>
<tr>
<td>Tis pu</td>
<td>Carcinoma in situ. Involvement of prostatic urethra</td>
</tr>
<tr>
<td>Tis pd</td>
<td>Carcinoma in situ. Prostatic duct involvement</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invading the subepithelial connective tissue</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invading the prostatic stroma, corpus spongiosum, periurethral muscle</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invading the corpus cavernosum beyond the prostatic capsule, bladder neck</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor invading other adjacent organs (bladder)</td>
</tr>
</tbody>
</table>

The subepithelial invasion from the prostatic urethra is not a T4 stage.

\[ a \] T4a involves prostatic stromal invasion from the bladder.
Endoscopic diagnosis of prostatic involvement by urothelial carcinoma

Cystoscopy has 83% sensitivity and 95% specificity when evaluating suspicious gross lesions at the level of the prostatic urethra.\textsuperscript{21} We know there can exist involvement of the prostatic urethra by UC without visible gross lesions.\textsuperscript{21,22} Mungan et al.\textsuperscript{21} found that of 21 initial NMIBCs with mucosal involvement of the prostatic urethra, 12 had gross lesions and in 9 the diagnosis was microscopic. This involvement macroscopically not visible of prostatic urethra becomes even more evident in patients with multiple, relapsed tumors, with carcinoma in situ (CIS), which have been treated with BCG and with prolonged follow-up.\textsuperscript{2} Huguet et al.\textsuperscript{22}, in a series of cystectomies of patients with NMIBC who failed with the BCG, objectified UC affecting prostate in cystectomy specimen in 9 (19.1%) out of 47 cases with prior cystoscopy and no gross lesions at that level.\textsuperscript{22}

Similarly, in the transurethral resection (TUR) of gross lesions in prostatic urethra, there is the possibility of under-staging. Analyzing the pre-cystectomy TURs of the same series, 2 out of 6 cases with Ta–T1 tumor in the TUR and 3 out of 6 with prostatic duct involvement had stromal involvement in cystectomy specimen.\textsuperscript{22}

Works in which the involvement of the prostate by pre-cystectomy UC is assessed have shown that the best way to identify the tumor at that level is performing lateromontanal biopsies (from neck to verumontanum, area where the prostatic ducts flow).\textsuperscript{24,25} Donat et al.\textsuperscript{25}, by performing lateromontanal biopsies, detected prostatic involvement by UC in 80 out of 99 patients (81%), but the specificity (77%), the sensitivity (53%), and the positive predictive value for the diagnosis of stromal involvement were poor, similar to other results.\textsuperscript{24}

Therefore, in case you want to detect prostatic involvement by UC, or if there is gross tumor at that level, it is advisable to make the TUR of the lesion, including lateromontanal biopsies; assuming that it will not always be possible to detect the stromal involvement.

Risk factors for prostatic involvement by urothelial carcinoma

CIS, multifocality, tumor in the bladder neck/trigone and previous history of tumor recurrence are the factors that have been associated with greater consistency to the involvement of the prostate by UC.\textsuperscript{11,17,18,21} Nixon et al.\textsuperscript{21}, in 192 patients undergoing cystectomy, observed prostatic involvement by UC in 31 and 34% of those with CIS and multifocal tumor, respectively. Both factors were associated with an increased risk of prostatic involvement by UC.

Patel et al.\textsuperscript{17} observed involvement of the prostate by UC in 121 out of 308 patients (39%) undergoing radical cystectomy. The multivariate study showed that the presence of CIS and trigonal tumor was an independent risk factor for the involvement of the prostate by UC. Recently, Mazzucchelli et al.\textsuperscript{18} devised a mathematical formula to estimate the risk of involvement of the prostate by UC or prostatic adenocarcinoma. The statistical analysis discriminated and selected the best variables to predict the risk of prostatic involvement by UC: tumor of trigonal location, multifocality, and history of previous recurrence. The intravesical treatment failure and involvement of distal ureter have also been associated with prostatic involvement by UC.\textsuperscript{11}

Prostatic involvement by urothelial carcinoma in patients with non-muscle-invasive bladder cancer and its implications in clinical practice

Incidence and evolution

There are few data regarding the involvement of the prostate by UC in initial NMIBCs. Mungan et al.\textsuperscript{23}, in 340 initial NMIBCs treated with TUR and after performing multiple bladder biopsies including prostatic urethra, observed mucosal involvement of the prostatic urethra in 21 (6.2%), 4 of them presenting CIS (1.2%). Millán-Rodríguez et al.\textsuperscript{26}, in 1529 initial NMIBCs, also with multiple biopsies, observed CIS in prostatic urethra in 2.7% of the cases. Although the prostatic involvement by UC in initial tumors does not seem frequent, its incidence increases with the follow-up, and especially if there are risk factors associated with its occurrence: CIS, multifocality, tumor in the bladder neck/trigone, and previous history of tumor recurrence.

In multifocal, recurrent, and treated with BCG NMIBCs, the prostatic involvement by UC at 5 and 15 years of follow-up is observed in 10–15% and 20–40% of the cases, respectively.\textsuperscript{1,13} This high percentage of prostatic involvement by UC in patients with NMIBC who have received BCG is due to the fact that this group of patients usually present most of the risk factors associated with the presence of UC in the prostate mentioned above.

Herr et al.\textsuperscript{1} observed prostatic involvement by UC in 72 (39%) out of 186 NMIBC patients treated with BCG and followed for 15 years. In 45 patients (62%), the prostatic involvement was superficial (mucosa/ducts) and its 15-year survival was 82%, which means a high survival, like in series of cystectomies with prostate surface involvement (49–71% 5-year survival) (Table 1).

In 27 patients (38%), the prostatic involvement was stromal and their 15-year survival was 48%, slightly higher than cystectomy series with similar characteristics.

The authors considered that these latter patients had suffered a silent progression through the prostate that significantly influenced their survival. They did not carry out any lateromontanal biopsies or any other action systematically for detection of the prostatic involvement by UC.

Huguet et al.\textsuperscript{22,27} obtained similar results by analyzing 66 cystectomies performed in NMIBC who failed BCG treatment. In 17 cases (27%), the pathological stage of the specimen was ≥pT2. 10 out of the 15 men in this group (66%) had prostatic stromal involvement by tumor, unidentified in the pre-cystectomy TUR which included, at least, one prostatic urethra cold forceps biopsy. It was also considered that these patients had had a subclinical progression of their disease through the prostate.\textsuperscript{22,27}

Therefore, as it is observed in cystectomy series, the prognosis of the patients with NMIBC and prostate involvement is good, but if the prostatic involvement is stromal, the prognosis worsens considerably. This silent or subclinical stromal involvement should be considered. Her et al.
observed it in 27 (15%) out of 186 patients treated with BCG and prolonged follow-up.2

Treatment

The treatment of the patients with NMIBC and involvement of the prostate by UC is controversial. Numerous series have reported good response to the conservative treatment with TUR and BCG in patients with surface involvement (mucosa and ducts),11 the performance of a prostate TUR not being essential to facilitate its action.28

The scarce impact on the survival of the prostatic surface involvement by UC in patients with NMIBC undergoing cystectomy would also support a conservative action. What is clear is that the conservative treatment should not be applied to patients with stromal involvement. But the conservative treatment of patients with prostatic surface involvement has some problems and involves taking risks: (a) the involvement of the prostate by UC in many cases is not macroscopically visible and for its detection it requires taking biopsies; (b) the prostatic urethral lateromontal biopsy is a good method for detecting surface involvement, but insufficient to demonstrate the prostatic stromal involvement; (c) in the TUR of gross lesions, understaging is possible; and (d) in patients with prostatic surface involvement, the simple invasion of the basement membrane will involve stromal involvement, which, as we know, is associated with an adverse prognosis.

The TUR and BCG treatment of patients with NMIBC and CIS or Ta–T1 tumor in prostatic urethra (mucosal involvement) has objectified complete responses at prostatic surface level in 70–100% of the cases, but which decrease to 47–72% when considering the complete response at the bladder level as well.11,29–32 In series including only patients with CIS in prostatic urethra, the responses at the prostatic level are equally high, but globally (for the bladder and prostatic disease) they are around 40%, with a 25% chance of disease progression.28 Therefore, if you opt for a conservative treatment with TUR and BCG of a NMIBC with mucosal involvement of prostatic urethra (CIS, Ta, T1), a biopsy TUR will be necessary at that level after the end of the treatment.

Considering the particularity of the prostatic involvement by UC, a prostatic TUR prior to the BCG would also be a valid option, as suggested by the EAU 2011 guidelines, especially in patients with CIS in the prostatic urethra.33

In highly selected cases and with strict control by means of biopsies, the conservative treatment with TUR and BCG of patients with prostatic duct involvement has also been described. In the largest series, Palou et al. observed in 12 years, 24 patients with NMIBC and prostatic duct involvement. In 11, treatment with initial TUR and BCG was chosen, bladder preservation being possible in 8 (70%). Only one patient died from tumor.34

The high risk of stromal involvement that the patients with ductus involvement have makes other authors consider that radical cystectomy is the best initial option.3 There seems to be a consensus on the need to consider the treatment with radical cystectomy in patients with prostatic surface involvement and who fail conservative treatment.11

Conclusions

The incidence of prostatic involvement by UC in patients with NMIBC increases in time in patients with multifocal, relapsed tumors located in the neck and associated with CIS. In these cases, the performance of biopsies of the prostatic urethra during follow-up is advisable. Conservative treatment with TUR and BCG is possible in patients with prostatic urethral surface involvement assuming that they are patients at risk of progression and in whom strict control is necessary. The post-BCG persistence or tumor recurrence in prostatic urethra is probably an indication of radical cystectomy.

Prostatic involvement by urothelial carcinoma in patients with indication or undergoing radical cystectomy and its implications in clinical practice

Urethral recurrence risk

The attitude with the urethra before, during, and after the cystectomy has always been controversial. This issue is of paramount importance with the development of the orthotopic bladder substitutions (OBS). By extending their use, the urologist is required to make a balance between the functional benefit of the OBS and the risk of presenting UR. The overall incidence of UR in contemporary cystectomy series is between 4 and 6%.8,9,35

The most consistent risk factor associated with the occurrence of UR is the involvement of the prostate by UC, and particularly prostatic stromal involvement.8,36 Some authors have reported an increased risk of UR in patients with surface prostatic involvement, probably related to an increased survival compared to patients with stromal involvement.9 Other factors associated with multifocality, as the previous history of NMIBC, the presence of NMIBC in the cystectomy specimen, diffuse CIS, multiple tumor, and upper urinary tract tumor, have often been observed in patients with UR.37 The orthotopic urinary diversions have been associated with a lower risk of UR by a hypothetical protective effect of the passage of urine and substances originated in the intestinal mucosa.36

Therefore, in patients who are candidates for OBS, the performance of pre-cystectomy biopsies of the prostatic urethra is advisable. This is the approach followed for years, and in which the presence of tumor in prostatic urethra would contraindicate the orthotopic reconstruction. Recently, many authors suggest that what will determine whether performing an OBS or a urethrectomy is the intraoperative biopsy of the urethral margin (IBUM). In the case of negative IBUM, OBS could be performed, even in patients with prostatic urethral tumor in the endoscopic biopsy, and in the case of IBUM with tumor, a urethrectomy should be performed.8,9,38

The use of the IBUM is conceptually appealing. It implies an increase in patients candidate for OBS without apparent increased risk of UR. But really, despite being widely accepted, there are few results and experience with its systematic use.39
Prostatic involvement by urothelial carcinoma in patients with bladder cancer

Possibility of prostatic sparing

In recent years, some authors have defended the prostatic sparing cystectomy with the intent to improve the postoperative sexual and urinary function. In selected cases, the removal of only the adenoma or the preservation of the prostatic apex would decrease the chance of injury to the neurovascular bundles and sphincter system. With this technique, percentages of power, daytime and nighttime continence have been reported in 80–100%, 80–100%, and 30–100%, respectively.40–42 By contrast, the partial resection of the prostate would involve the possibility that there was hidden UC or adenocarcinoma, and, thus, poorer oncological results. To avoid this, a suspicious DRE or elevated PSA would be an indication of pre-cystectomy transrectal biopsy. The multifocal CIS and the macroscopic involvement by UC of the neck or prostatic urethra would contraindicate the entry procedure, biopsy taking of the prostatic urethra being mandatory in the prospective candidates.43

The critics of this technique argue that, from the oncological point of view, the incidence of prostatic involvement by UC in cystectomy specimens is high (15–48%), the endoscopic biopsy will not always detect the presence of tumor at that level, and that the incidence of incidental prostatic adenocarcinoma is also high (23–47%). For them, these factors lead to oncological outcomes being inferior to radical cystectomy series in the same subgroup of patients. From a functional point of view, they indicate that with a refined technique, the results of the conventional radical cystectomy may resemble the prostatic sparing techniques.10,44 Therefore, at present, the prostatic sparing cannot be considered a standard technique. In addition, there are authors who strongly advise against it.10

Use of adjuvant or neoadjuvant chemotherapy

We know that the patients with prostatic stromal involvement are at high risk of dying from a tumor. In the cases where the diagnosis was made pre-cystectomy, extension study will have to be performed including abdominal axial tomography because of the high risk of lymph node involvement (40–50%). The peak incidence of positive lymph nodes will be in the patients with extravesical stromal involvement.11

Neoadjuvant chemotherapy might have some benefit in the survival of these patients. In the case of not using it and having the diagnosis of postoperative stromal involvement, adjuvant chemotherapy is an option. Although there are no clear data to justify its use, it is often used in clinical practice.11

Conclusions

The patients with involvement of the prostate by UC have increased risk of UC. The pre cystectomy prostatic urethra biopsies or IBUM will be useful to select the candidates for OBS. The high incidence of prostatic adenocarcinoma and the involvement of the prostate by UC in cystectomy specimens require the clinicians to be very selective when indicating cystectomy with prostatic sparing techniques.

Chemotherapy may be an option in an attempt to improve the survival of patients with prostatic stromal involvement.

Primary urothelial carcinoma of the prostate

The primary prostate UC is a rare entity, with poor prognosis, and accounting for 0.4–2% of the prostatic tumors.45,46 Conceptually, it originates in the transitional epithelium (urothelium) overlying the prostate at the level of the prostatic urethra. The primary prostate UC can be pure or with squamous or adenocarcinoma differentiation.47 The experience on the attitude with these tumors is limited to isolated cases or very short series. The appearance of obstructive clinic, hematuria, or incidental finding after a prostatic TUR are the usual forms of presentation. Although it is possible to diagnose early-stage tumor (involvement of the mucosa, submucosa, or ductus), stromal involvement is usually the norm. It is important to know that in order to establish the diagnosis of primary prostate UC, there must not exist prior history of bladder UC and it is necessary to rule out its presence with multiple biopsies. The frequent involvement of the bladder neck in patients with primary UC sometimes makes it difficult to identify where the tumor originated.46

We recommend a study of thoracic and abdominal extension. Radical cystectomy with or without neoadjuvant chemotherapy is probably the treatment of choice, although there have been some cases reported treated only with radical prostatectomy.12,45–47

Conflict of interest

The author declares that he has no conflict of interest.

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