



Management of Intradiverticular Urothelial Carcinoma of Bladder

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ABSTRACT

The intradiverticular bladder carcinoma (IDUCB) is a rare and poorly known entity. To analyze diagnostic and therapeutic features of urothelial carcinoma within the bladder diverticulum. Twenty eight men with an average age of 65 years were included. The main reason for consultation was hematuria. The intradiverticular tumor was suspected by radiological assessment in 11 patients. All these patients underwent an endoscopic resection of the tumor. The histological study concluded to a pTa stage in 10 patients, pT1 stage in 11 patients and invasive tumors in 7 patients. A complementary endovesical BCG-therapy and cystoprostatectomy were performed in patients depending on the stage, grade, recurrence and multifocality. With an average follow-up of 31 months, seven recurrences were found in the group of superficial tumors, including 5 cases of progression to invasive stage and 2 cases of nodes invasion. Intradiverticular bladder tumors are rare and more common in elderly. They are distinguished from conventional bladder tumors by a triple specificity: pathological specificity with high frequency of >T3a tumor, diagnostic specificity with a risk of under-staging of the extent and tumor multifocality, therapeutic specificity linked to a worse prognosis than conventional tumors which encourages a strict limitation of the indication of conservative treatment.

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Introduction

Intra-diverticular transitional cell carcinoma of bladder is a rare and heterogeneous entity. Its incidence varies from 0.8 to 10.8% [1]. Classically, it is most often invasive tumor with a poor prognosis due to the diverticulum nature and the structure of its wall. This location causes serious diagnostic and therapeutic problems. Through a series of 28 cases, we study the characteristics of this entity and propose the diagnostic and treatment.

Materiel and methods

Between September 2005 and April 2014, 28 patients were operated for IDUCB. All patients were male with an average age of 65 years (51-78 years).

Eighteen patients were smoking large (> 30 PA). Nine patients had an extradiverticular superficial tumor history treated by endoscopic resection and intravesical BCG therapy. The treatment of IDUCB consisted of endoscopic resection (ER) under spinal anesthesia with a semi-filled bladder to reduce the risk of perforation.

Our BCG therapy protocol consisted of a weekly intravesical instillation of 81 mg for 6 weeks (1st session after 4 weeks of endoscopic resection) and followed by three more sessions after verifying the absence of tumor recurrence in cystoscopy. Patients were followed later by quarterly cystoscopy. The Chi2 test was used to compare qualitative data. A difference is statistically significant with a p value less than 0.05.

Results

Twenty-two tumors (78%) were diagnosed at the time of hematuria. 30% of patients are bearers of superficial tumors and nontumoral diverticulum. IDUCB was discovered during endoscopic controls. Obstructive urinary symptoms were observed in 10 patients (35%).

Echography, performed in 16 patients, confirmed the diagnosis of IDUCB and show specific images of intradiverticular tissue process in 10 cases (Figure 1).



Figure 1. Ultrasound image of a IDUCB

The uroscan was realized for 12 patients and showed a IDUCB. All patients had an intradiverticular bladder tumor in cystoscopy. Concomitant extradiverticular tumors were found in 9 cases (Figure 2).

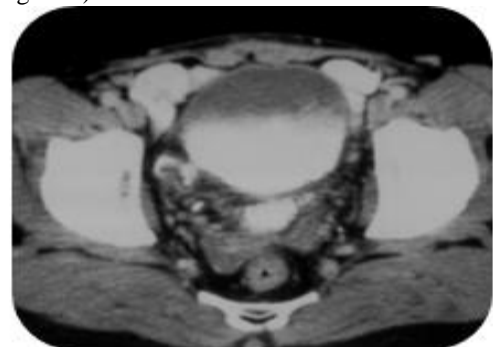


Figure 2. Scannographic image illustrating a IDUCB of the lateral wall of the bladder

The endoscopic appearance of IDUCB was papillary with fine fringes and a wide base in the majority of cases (n = 26).

Fifteen patients (53%) had a complete RE tumor followed by intravesical BCG therapy. 10 cases were pTa stage and 5 Pt1 stage (Table 1).

Table 1. Histological results of IDUCB

	GI	GII	GIII	TOTAL
Ta	7	2	1	10
T1	2	3	6	11
>T1	0	1	6	7
TOTAL	9	6	13	28

In the initially pTa group, 8 patients (28%) had a superficial intradiverticular tumor recurrence treated again by RE and BCG therapy. It failed in 4 cases, which necessitated radical treatment (Table2).

Table 2. Evolution of pTa / pT1 IDUCB after complete RE and BCG therapy

Number of patients	pTa =10	pT1= 11
No recurrence	4	2
Intra-diverticular recurrence		
- progression-free	0	0
- With progression	3	2
Extra diverticular recurrence		
- progression-free	2	0
- With progression	1	1

In the group of initial Pt1, 3 of the 5 patients who received BCG therapy, developed recurrence with stage progression treated by radical cystectomy. The two remaining have evolved without recurrence with a 32-month decline. Six patients had large tumors can not be resected and with high grade, which indicated immediately radical treatment (Table2).

In the group of initially pT3a (histology + scanner), all patients underwent radical cystoprostatectomy with extended lymph node dissection. Adjuvant chemotherapy was performed in 5 patients for the presence of malignant lymphadenopathy. Four cases developed lung and bone metastases within 10 months following the intervention and are now stabilized by chemotherapy. Two other cases died of pulmonary embolism without local or systemic recurrence.

Discussion

The incidence of IDUCB is between 0.8% and 13.5%, most often in men between 60 and 70 years [2]. The large majority of tumors thrives in acquired diverticulum (developed upstream of a sub-bladder obstacle), while they are rare in congenital diverticulum [3,4,5].

Besides the classic etiological factors of bladder tumors, the risk of occurrence of a tumor in a bladder diverticulum is increased by urinary stasis and chronic inflammation, responsible for a chronic irritation of the mucosa; the cause of dysplasia and malignant transformation. Some authors found squamous metaplasia of the mucosa in 80% of diverticulum [3,5,6].

By definition, diverticular mucosa does not rest on the bladder muscle, but it is directly in contact with the perivesical fat. Therefore, the IDUCB can not be classified T2 (tumor invading muscle) but will progress directly to the T \geq 3 stage. This characteristic explained the estimated frequency to 60% of T3 stage tumors [7,8]. Many authors have proposed to consider all IDUCB as readily invasive tumors [9,2,3,10,11].

The histological diagnosis was sometimes made difficult by two factors

- A peridiverticular fibrosis
- The hypertrophic muscularis mucosae which can be confused with the bladder muscle

The clinical symptoms was not specific [12,7,13]. Hematuria was most frequently reported (49-87% of cases).

Conventional bladder ultrasound performance has been described as lower in the diagnosis [14,15].

The development of ultrasound contrast-injection or three-dimensional reconstructions open up prospects.

Pelvic CT scan with contrast injection and late acquisition cliches have allowed variable diagnostic performance [16]. It also allows the assessment of the node and metastatic extension that is a supplementary interest in the IDUCB context often infiltrative.

Fibroscope has demonstrated its superiority over the rigid cystoscope for diagnosis [17,18,19]. It allowed the diagnosis of 60% of IDUCB. Its contribution is important in the exploration of diverticula, especially in case of a narrow collet.

Endoscopic resection of IDUCB had the same targets as any bladder tumor: the complete resection of the tumor without bladder perforation.

The particularities of the diverticulum resection were related to the limited viewing angle by the rigidity of the material and the narrowness of the diverticular collet. Some authors have proposed to conduct a preliminary incision of the collet order to facilitate resection. [20]

The interest of the fluorescence of hexyl-aminolevulinate diagnosis in the specific context of IDUCB has not been the subject of any specific study. However, the diagnostic performance of endoscopy for the detection of in situ carcinoma and multifocal tumors have been improved by this technique.

The treatment of IDUCB still controversial between the partisans of immediately aggressive treatment associating radical surgery with systemic chemotherapy, and those who propose a conservative treatment with the combination of the RE and intravesical chemotherapy.

Endoscopic resection could theoretically be sufficient to treat a CUID provided that it is complete and the tumor does not exceed the basement membrane.

Instillation bladder studies were low level of evidence and do not evaluate toxic risk increased by the frequent residual post void in the diverticulum [20].

Partial cystectomy that is akin to an expanded diverticulectomy, requires removing the diverticulum through in safe area, away from the tumor. It has been correlated with poor oncological results related to a pT \geq 3a tumor rate of 60% and 33% of positive margins. Disease-free survival was 50% [7,8]. In these conditions we have not adopted this attitude in our patients.

If IDUCB pT \geq 1, high grade, multifocal or associated to in situ carcinoma, cystectomy with pelvic lymph node dissection is the standard treatment.

More recent studies have shown an improvement in these results: while Micic et al. reported a specific survival of 50% at 2.2 years in 1983 [13], Golinajin et al. and Tamas et al. reported respectively in 2003 and 2009, a rate of 66% at 4.2 years and 75% at 2.7 years. [7]

Conclusion

The IDUCB are rare and prevalent in elderly patients. In a diverticulum, there are superficial tumors (pTa and pT1 stages) and perivesical fat invasive tumors. The complete endoscopic resection without bladder perforation associated with intravesical immunotherapy should be reserved for low-grade superficial tumors, unifocal and without in situ carcinoma. In the other cases, cystectomy is the reference treatment.

Conflict of Interest

The authors declare no conflict of interest.

Authors Contribution

All authors mentioned have contributed to the development of this manuscript. All authors also declare to have read and approved the final manuscript.

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