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Value of Bladder Biopsy after Bladder Instillation of BCG, in Case of Bladder Cancer Not Infiltrating the High-Risk Muscle?

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Introduction

In almost 80%, bladder tumors are those that do not infiltrate the detrusor muscle, only the epithelium or the chorion is invaded. Its management is currently well codified with the development of new diagnostic techniques for early management. Immunotherapy, particularly the BCG vaccine, is one of the most used means in NIMBC therapy and the indications for which are well known [1-2]. Urinary cytology is, along with cystoscopy, one of the benchmark examinations for the detection and monitoring of NIMBC, especially of high grade [3]. This surveillance for NIMBC is essential because the risk of recurrence is high with a risk of progression of 10-20% and a mortality of 3% of cancer deaths, then an increasing incidence of about 1% per year. Few data exist in the literature mentioning the place of post-BCG bladder biopsies up to date. So should you do it? As a result, we carried out this study to assess the place of post-BCG bladder biopsies.

Patients and Methods

We conducted a retrospective study in the urology department of CHU Bichat-Claude-Bernard from January 2016 to December 2019 at (i.e. 4 years) in patients followed for high risk muscle bladder tumor that did not infiltrate BCG post-instillation biopsies. We included all patients with non-infiltrating bladder tumors and we did bladder biopsies after the induction phase of BCG instillation, who then had urine cytology. Our variables were clinical, paraclinical, therapeutic as well as prognostic. Clavien Dindo's classification had been used for possible post-operative complications.

The categorical and continuous data were compared respectively to the chi-square and Student t tests. Sensitivity, specificity, positive predictive value, negative predictive value, positive and negative likelihood ratios and diagnostic accuracy were calculated for cystoscopy and cytology separately and in combination. One and more variable logistic regression models assessed the factors associated with the occurrence of a positive biopsy. The analyzes were carried out with SPSS (v24) and R, version 2.10.1.

Results

A total of 62 patients were included, including 47 men (76%) and 15 women (24%). The median age was 71 years (IQR 13). Urothelial carcinoma was the only histological type noted before biopsy with a predominance of pT1 (Figure 1) and a concomitant Cis was detected in 32 patients (52%). After BCG, a total of 342 bladder biopsy were taken with a median of 5 (IQR 2) per case. The biopsy was positive in 13 patients (21%). The median number of positive biopsy was 2 (IQR

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1) and the total number of positive biopsy was 27 (8%).

The biopsy was positive at the initial tumor site in 8 patients (61.5%). the only histologic type noted after the biopsy was urothelial carcinoma and the high pTa stage was predominant after biopsy (Table 1). No complications of Clavien III to V have been reported. Out of 62 patients who underwent systematic transurethral biopsy, only 3 (5%) presented complications from grade I to II. Two patients (3%) had prolonged hematuria requiring bladder irrigation, one patient (2%) presented with acute urinary retention requiring the placement of a bladder catheter. No perforation of the bladder was recorded. We found a significant association of positive biopsy with positive urinary cytology (p <0.001) and the presence of erythematous lesions (p <0.02) or visible tumors (p <0.001) at cystoscopy. The pre-BCG stage T (p = 0.32), the presence of CIS (p = 0.71), the multifocal tumor (p = 0.41) and the size (p = 0.52) were not associated with a positive biopsy occurrence.

Cystoscopy appeared normal in 39 patients (63%), showed only erythema in 11 (18%) and tumor in 12 (19%). The biopsy was positive (p <0.001) with normal cystoscopy, erythema and tumor respectively in 2 (5%), 2 (18%) and 9 (75%). The predictive value of a positive urine cytology for a positive biopsy was 80%. The association of negative urine cytology and normal cystoscopy was associated with the occurrence of negative biopsy in 97% of cases.

Table1: Distribution of patients according to post-biopsy histology

	n	%
pTa	5	62,5
pT1	2	25
Cis	1	12,5
Total	8	100

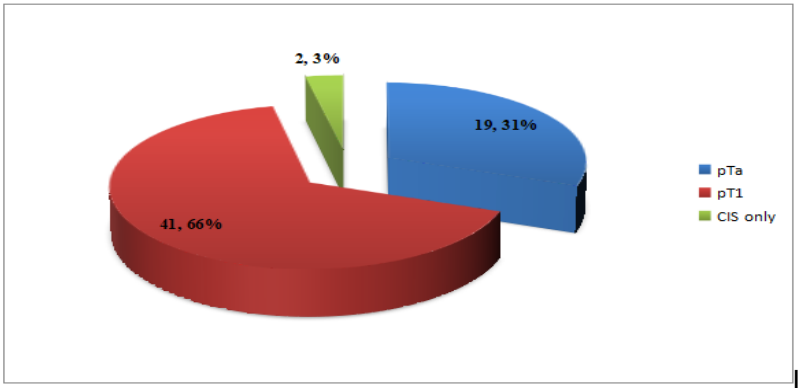

Figure 1: Distribution of patients according to histological type.

Discussion

One of the most important features of urothelial cancer is the formation of tumors in multiple foci throughout the urinary tract, synchronously and / or metachronically. In fact, intravesical recurrence after TURBT has been reported in 30 to 80% of patients with NMIBC, which could be explained in part by the presence of malignant lesions of normal appearance at the time of endoscopy [4]. To detect such concomitant urothelial cancers during NMIBC endoscopy, random biopsies targeting normal-looking urothelial mucosa were performed. However, there have been few large series studies assessing the importance of random bladder biopsies, and they have presented conflicting conclusions [5-6]. In this context, several authors have suggested that in the presence of negative cystoscopy and cytology, biopsies are not guaranteed [7-8]. Dalbagni et al. were the first to suggest that routine biopsies were not warranted in normal office cystoscopy or cystoscopy with signs of erythema in the presence of normal bladder cytology [9]. Limitations of this study included a lack of description of the biopsies and the fact that the cytology of the isolated upper tract was not evaluated.

In contrast, our study showed that pre-BCG stage pathologies and the presence of Tis were not associated with the positive results of the biopsy. Only cystoscopy and urinary cytology which have been identified as significant variables. However, the positivity of urinary cytology should be interpreted with caution, since several cytological changes induced by BCG are easily detectable in the first 3 months after the last instillation, including enlarged hyperchromatic nuclei with prominent nucleoli, anisokaryosis, and increased granulocytes [10-11]. These cellular changes can be interpreted as positive.

We have objectified a correlation between the presence of erythema of the bladder mucosa / tumor lesions (seen on cystoscopy) to the positivity of biopsies, which is noted by several authors in the literature [12-13]. We have a rate of 5% of complications in our series and lower than those found by other authors [14]. To our knowledge, perioperative complications of transurethral biopsy have not yet been analyzed according to the modified Clavian classification.

It has been recognized that performing bladder biopsies is associated with certain risks, including bleeding, perforation, infection and spread of cancer [15]; therefore, it is necessary to develop new strategies to avoid this procedure. One strategy is to accumulate a much larger number of patients with NMIBC undergoing random biopsies of the bladder prospectively and to identify predictive parameters with acceptable sensitivity as well as specificity in each group classified according to the risk tables of the EORTC [16]. Another approach is to introduce new diagnostic methods for concomitant urothelial cancer, such as fluorescence cystoscopy [17]. However, the substantial costs of.

Conclusion

In summary, routine transurethral bladder biopsies are not required after induction therapy for BCG. However, a personalized approach is recommended based on cystoscopy and cytology. the pace and the means of surveillance (cytology, fibroscopy, uro-CT) of NMIBC must be adapted to the risk of recurrence and progression defined according to the tables of the EORTC.

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