

## Inconclusive Urinary Bladder Biopsy; Facts and Lessons

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### ABSTRACT:

#### BACKGROUND:

To review the pathologic analysis of urinary bladder biopsies and study the frequency and causes of inconclusive biopsies among Iraqi patients.

#### METHODS:

This is a retrospective study in which 933 patients underwent 1047 urinary bladder biopsy procedures during endoscopic evaluation, or transurethral resection of a known bladder cancer in Surgical Specialties Hospital, Baghdad, Iraq between June 2000 and June 2007. Pathologic records of patients were reviewed.

#### RESULTS:

In 933 patients aged 2-100 years with a mean age of  $56.87 \pm 14.3$  years who underwent 1047 urinary bladder biopsy procedures, pathologic review showed bladder cancer in 655 (62.56%) biopsies, no overt malignancy in 340 (32.47%) biopsies, no pathological diagnosis could be made in 43 (4.11%) biopsies, and normal biopsy in 9 (0.86%) biopsies. In 238 bladder cancer biopsies, pathologic analysis of muscle invasion was not carried out due to their lack of muscular tissue.

#### CONCLUSION:

Urinary bladder biopsy is one of the most common biopsies in urology practice. Every effort is made to prevent technical defects of taking and processing such biopsies, to optimize pathologic analysis and surgical management.

**KEYWORDS:** Bladder biopsy, Cystoscopy

### INTRODUCTION:

Bladder cancer is the second most common cancer of the urinary tract after prostate cancer, the fourth most common malignancy in men, and the seventh most common in women<sup>(1)</sup>. Cystoscopy is the most efficient method presently available to detect primary or recurrent transitional cell carcinoma (TCC) of the bladder but it is both costly and invasive and causes discomfort to the patient<sup>(2)</sup>. The ideal method for resection of a bladder tumor is to resect first the bulk of the tumor and then the deep portion along with some underlying bladder muscle, sending each specimen separately for histologic examination. This approach usually enables complete removal of the tumor and provides valuable diagnostic information about the grade and depth of infiltration of the tumor. Small tumors may be resected using the cold cup biopsy forceps<sup>(3)</sup>. The accurate diagnosis, staging, and grading of bladder neoplasms depend heavily on the pathologic interpretation of biopsies and transurethral resection (TUR) specimens. The pathologic material examined from the bladder may be limited by the size, depth, or location of the tumor, or by the surgeon's ability and experience<sup>(4)</sup>. Cauterization has to be avoided as much as possible to prevent tissue destruction. Necrotic and

cauterized tissue hampers correct staging and grading<sup>(5)</sup>.

Denuding cystitis is often encountered in tissue biopsies of bladder mucosa performed by either cold-cup forceps or wire loop electrocautery to evaluate hematuria or to rule out recurrent urothelial carcinoma. Lack of urothelium in these biopsies is often a frustrating experience, leading to a nonspecific interpretation<sup>(6)</sup>.

In this study pathologic analysis of urinary bladder biopsies and evaluation of the frequency and causes of inconclusive biopsies among Iraqi patients was carried out.

#### METHODS:

In this retrospective study 933 patients underwent 1047 urinary bladder biopsy procedures from bladder tumors or suspicious lesions discovered incidentally during endoscopic evaluation of urinary bladder wall for other benign conditions in Surgical Specialties Hospital, Baghdad, Iraq between June 2000 and June 2007. Some patients had repeated urinary bladder biopsies and/or transurethral resection of a known bladder cancer giving a total of 1047 urinary bladder biopsy procedures. Different surgeons in the center performed the endoscopic procedures under general or spinal anesthesia using a rigid cystoscope.

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All samples were taken from formalin – fixed, paraffin – embedded archival specimens.

Representative 5 µm H and E – stained sections were reviewed by different pathologists in the center. The histological grade was determined according to the 1973 World Health Organization grading system<sup>(7)</sup> and tumor stage according to the tumor, node, metastases (TNM) system<sup>(8)</sup>. The choice of endoscopic bladder biopsy or transurethral resection for every patient in this study followed the ethical guidelines that ensured the optimum outcome. Pathologic records of patients were reviewed.

Inconclusive bladder biopsy was defined as that biopsy, which could not be interpreted by the pathologist due to an inadequate tissue content or poor preservation during its transfer to pathology department, or biopsy of bladder cancer lacking muscular tissue for pathologic staging.

Statistical analysis: Data were analyzed using mean ± standard deviation (SD), frequency and percentage. The software used in this paper was the Microsoft office Excel 2003.

### RESULTS:

In this study 933 patients aged 2-100 years with a mean age of 56.87±14.3 years underwent 1047 urinary bladder biopsy procedures were evaluated. There were 667 (71.49 %) males and 266 (28.51%) females.

Out of the total 1047 urinary bladder biopsies, 655 (62.56%) biopsies showed bladder cancer while 340 (32.47%) biopsies did not show overt malignancy but one or more of the following lesions; cystitis, schistosomiasis, urothelial benign lesions such as cystitis cystica, cystitis glandularis, ..etc and dysplasia. Pathologic diagnosis was not made in

43 (4.11%) biopsies and 9 (0.86%) biopsies were normal. Table (1) illustrates the criteria of different urinary bladder biopsies.

Pathologic staging of bladder cancer based on the urinary bladder biopsy could not be achieved in 238 out of 655 bladder cancer biopsies due to lack of muscle in the biopsy. Table (2) demonstrates pathologic staging of bladder cancer biopsies.

Out of 1047 urinary bladder biopsies in this study, the inconclusive biopsies were 281 (26.8%) biopsies including 43 biopsies with no pathologic diagnosis due to inadequate tissue (33 biopsies) and poor preservation with autolysis (10 biopsies), and 238 bladder cancer biopsies with no muscular tissue to assess muscle invasion as part of pathologic staging. The causes of inconclusive bladder biopsies are shown in Table (3).

### DISCUSSION:

Carcinoma of the bladder is the third most common tumor in Iraq<sup>(9)</sup>. Therefore, endoscopic bladder biopsies of suspected lesions and transurethral resection of many proved cancers are common procedures in the urology departments of major hospitals in our country. Histopathologic analysis of urinary bladder biopsy remains the standard with which other methods of assessment of the depth of infiltration of urothelial carcinoma such as computerized tomography (CT) scan and transurethral intravesical echotomography (TIE) are compared<sup>(10)</sup>. Seventy percent of patients with a diagnosis of bladder cancer present with non-muscle invasive lesions that are now categorized as either of low or high malignant potential, though previously all were treated as superficial bladder cancer from Ta to T1 and had frequently included carcinoma in situ (CIS)<sup>(11)</sup>. On the other hand one third of patients with transitional cell carcinoma (TCC) of the urinary bladder will be diagnosed as having muscle – invasive or metastatic tumor<sup>(12)</sup>. Radical cystectomy with urinary diversion remains the gold standard for the treatment of invasive bladder tumors. It has been suggested that delaying radical cystectomy in organ confined disease is associated with poorer survival<sup>(13)</sup>.

In this study pathologic review of 1047 biopsies showed that bladder cancer contributed to 655 (62.56%) biopsies of the total number. The combined number of CIS (13), Ta (6) and T1 (193) was 212 (32.36% of bladder cancer biopsies). This figure could not accurately reflect the true pathologic frequency of non – muscle invasive bladder cancer among Iraqi patients because unfortunately there were about one third (238) of bladder cancer biopsies which lacked muscular tissue. Consequently these biopsies were considered inconclusive regarding staging. Pathologic diagnosis was not made in 43 (4.11%) biopsies due to inadequate tissue for pathologic analysis in 33 biopsies and poor preservation with autolysis in 10 biopsies.

Inconclusive biopsies due to failure of pathologic cancer staging, inadequate tissue content, or autolysed biopsies dictate a repetition of the biopsy with associated delay regarding the surgical decision. In addition there is an increased morbidity due to hospitalization and anesthesia requirement and ultimately an increase in the overall cost of such procedures. Although technical defects of lacking muscular tissue during endoscopic bladder cancer biopsies or taking tiny pieces inadequate for pathologic analysis may occur during routine surgical work, all the junior

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urologists and residents must be aware of such mishaps and every effort is made to avoid them. Similarly it is the responsibility of the surgeon to supervise the proper preservation and transfer of the biopsy/biopsies to the pathology department and educate the medical staff to ensure proper management of such procedure.

In 340 (32.47%) biopsies no overt malignancy was detected but many of them showed urothelial metaplasia, dysplasia or both and depending on the site and number of biopsies taken some of these biopsies could be taken from patients with an underlying bladder carcinoma. Estimation of the frequency of each benign and/or pre - malignant lesions such as severe dysplasia among biopsies is beyond the scope of this study.

In this study pathologic records were reviewed in the pathology department of Surgical Specialties Hospital which includes efficient pathologists and paramedical staff. However the method of recording pathologic data depends upon an old manual writing in copybooks and every time the patient had a biopsy, a different serial number would be given to him/her. This makes any research involving large series of patients a difficult task. Besides such valuable archive is highly susceptible to loss with time. It is strongly recommended to use a computer system as in many

other international pathology centers, to keep this surgical pathology archive and facilitate further research as the patient would have a single serial number whenever there is a need for a future biopsy. It is also recommended that future pathology reports will document data, provided by the urologist peroperatively, such as the site from which the biopsy was taken, number of tumors seen, gross appearance of tumor (papillary or sessile) and whether the biopsy had been taken by cold – cup forceps or by TUR in addition to the pathologic findings regarding the cancer cell type, grade and stage and any other relevant information. To my knowledge this is the first study in the urology department of Surgical Specialties Hospital that reported the pathologic review of urinary bladder biopsies and the frequency and causes of inconclusive biopsies among Iraqi patients with a period extending over 7 years. Further prospective studies are needed to follow up the recurrence and progression of bladder cancer among Iraqi patients.

### CONCLUSION:

Urinary bladder biopsy is one of the most common biopsies in urology practice. Every effort is made to prevent technical defects of taking and processing such biopsies, to optimize pathologic analysis and surgical management.

**Table 1 :Criteria of urinary bladder biopsy(n= 1047)**

Urinary bladder biopsy	N (%)
Normal	9 (0.86%)
No overt malignancy *	340 (32.47%)
Bladder cancer	655 (62.56%)
No pathologic diagnosis	43 (4.11%)
* Inflammatory cystitis, schistosomiasis, urothelial benign lesions, and dysplasia.	

**Table 2 :Urinary bladder cancer pathologic staging(n= 655)**

Pathologic stage	N (%)
CIS *	13 (1.98%)
Ta	6 (0.9%)
T1	193 (29.47%)
T2	205 (31.3%)
No pathologic staging	238 (36.34%)
* CIS: carcinoma in situ	

**Table 3 : Causes of inconclusive bladder biopsy**

Inconclusive bladder biopsy	n = 281
No pathologic staging of bladder cancer	238
No pathologic diagnosis	
i- Inadequate biopsy for pathologic diagnosis	33
ii- Autolysed specimens	10

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