

A Study on Histopathological Spectrum of Lesions in Urinary Bladder Specimens

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ABSTRACT

Introduction: Urinary bladder lesions constitute an important source of clinical signs and symptoms. Both non-neoplastic and neoplastic lesions are quite common. Neoplastic lesions are responsible for significant morbidity and mortality throughout the world. Urinary bladder cancer is 2nd most common cancer after prostate cancer in genitourinary system. Histopathological analysis of cystoscopic bladder biopsy and Transurethral resection of the bladder tumor (TURBT) material are the mainstay for cancer diagnosis.

Objective: To describe the histopathological spectrum of urinary bladder lesions in TURBT and cystoscopic biopsies.

Methodology: All urinary bladder specimens were included in the study. The specimens were grossly examined and entire tissue was processed in all cases as per standard protocol. Multiple sections of 3-5 micron thickness were obtained and stained with H&E, followed by histopathological examination to classify them into non – neoplastic & neoplastic lesions on light microscopy.

Results: Total 48 cases were studied, out of which 20 were cystoscopic bladder biopsies and 28 were TURBT specimens. Non-neoplastic lesions was predominantly comprised of chronic non-specific cystitis. Among the neoplastic lesions, urothelial carcinoma is the predominant type and was most commonly seen in age group of 51-80 years constituting 92.85%. These neoplastic lesions were more common among males (71.43%) with M:F ratio of 2.5:1. Invasive urothelial carcinoma was the predominant type followed by various noninvasive urothelial lesions.

Conclusion: Urinary bladder lesions are heterogenous and awareness regarding the various histological features of these lesions, their neoplastic potential, risk of recurrence and possible pitfalls can help pathologists for accurate diagnosis.

Keywords: Urothelial Neoplasm, Invasive Urothelial Carcinoma, Cystoscopic Bladder Biopsy, Transurethral Resection of the bladder Tumor.

Introduction

Urinary bladder lesions constitute an important source of clinical signs and symptoms, these are more disabling than lethal. ^[1] Both non-neoplastic and neoplastic lesions are quite common. The non-neoplastic lesions include cystitis, malakoplakia, urachal lesions and tuberculosis. ^[2] Cystitis constitutes an important source of clinical signs and symptoms. Neoplastic lesions are responsible for significant morbidity and mortality throughout the world. ^[3]

Both benign and malignant tumors occur, the latter being more common. Majority of urinary tract tumors are epithelial in origin. ^[4] Urothelial carcinoma is the most common tumor of the bladder, representing 90% of the malignancies with this origin. ^[3] Urothelial carcinomas are also seen at other sites such as renal pelvis, ureters, urethra in the decreasing order of frequency only next to urinary bladder. ^[5]

Urinary bladder cancer is the 9th most common cancer worldwide and second most common malignancy of

genitourinary tract after prostate cancer. Bladder neoplasms accounts for 6% and 2% of the cancer incidence in the men and women respectively. Most cases present over the age of 50 years. ^[3] As per Indian cancer registrar data, it is the 9th most common cancer accounting for 3.9% of all cancers. ^[2]

Bladder cancer, with rare exceptions, is not familial. ^[1] The association between some of the etiological agent in evolution of bladder cancer is well established. They can be either genetic abnormality or external risk factors like cigarette smoking, occupational carcinogens from chemical industry, schistosoma hematobium infection in endemic areas, use of artificial sweeteners, patients on long term use of cyclophosphamide and analgesics and patients receiving radiation therapy for uterine cancers. ^[1,6,7]

Genetic factors such as null GSTM-1(Glutathione-S transferase) and slow NAT-2(N- acetyl transferase) polymorphism increases the risk of bladder cancer. The first degree relatives are at increased risk of developing urothelial cancers by two times than the normal population.

Mutations involving TP53, RB, PTEN pathways are most commonly associated with invasive carcinoma and the combined mutations of all the three pathways follows a much worse prognosis.^[8]

Cystoscopy is the primary diagnostic tool for patients who are suspected of having bladder tumors, which is useful in localizing bladder tumors and biopsies of the suspected lesions.^[9]

Transurethral resection of the bladder tumor (TURBT) is a therapeutic procedure that allows assessment of the degree of differentiation, depth of tumor invasion, parameters useful for elaboration of diagnosis and prognosis.^[3]

Thus the present study was conducted to describe the histopathological spectrum of urinary bladder lesions in TURBT and cystoscopic biopsies.

Materials and Methods

This was a prospective study was carried out in the histopathology laboratory of Department of Pathology in collaboration with Department of Urology, BLDEU's Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura, Karnataka, India from 1st November 2015 to 30th June 2017. It includes 48 cases of cystoscopic biopsies and TURBT specimens which were received in the histopathological department of Pathology. The present study was approved by institutional ethical committee.

Methods of Collection of Data: This is a prospective study of lesions of Urinary bladder and includes 48 specimens (Cystoscopic bladder biopsies and TURBT specimens) from patients received for histopathological examination, in the Department of Pathology. The specimen were received in 10% formalin. The tissue was grossly examined first and findings were noted. The entire tissue was processed in all the cases.

The specimens were fixed in 10% formalin and processed as per standard procedure. Multiple sections of 3-5 microns thickness were obtained from the paraffin block and stained with hematoxylin and eosin. Histopathological examination of cystoscopic bladder biopsies and TURBT specimens was carried out and the lesions were classified into various lesions on light microscopy.

Result

A total of 48 urinary bladder specimens were studied which included both cystoscopic bladder biopsy and TURBT which were performed among wide age range of 2-80 years for varied etiologies.

There were 20 cases of non-neoplastic lesions (41.67%) and 28 cases of neoplastic lesions (58.33%) among all urinary bladder lesions (Table 1). Out of 48 patients, 29 were males (60.42%) and 19 were females (39.58%) with a male to female (M:F) ratio of 1.5:1

Among non-neoplastic lesions, the chronic nonspecific cystitis was the predominant type constituting up to 60% of all non-neoplastic lesions. Other types of cystitis studied were one case each of granulomatous, acute on chronic, polypoidal, eosinophilic and follicular cystitis (Figure 1). The variants of normal histology included in the study were one case each of cystitis cystica, cystitis glandularis along with one case of fibroepithelial polyp which was present in a 2 year boy (Table 2).

Among the neoplastic lesions, there was clustering of cases in the age group of 51 to 80 years together constituting 92.85% with nil cases observed in younger age group and there was male predominance constituting of 71.43% of all cases with a M:F ratio of 2.5:1 (Table 1).

Out of all neoplastic lesions of various histomorphological categories, invasive urothelial carcinoma (IUC) was more common which included 7 cases of superficially invasive bladder cancer (invasion up to lamina propria) and 10 cases of muscle invasive bladder cancer (invasion into muscularis propria). There were various histological differentiation seen among IUC which included squamous, glandular, clear cell and sarcomatoid variant constituting 5.88% each (Figure 3).

Apart from IUC, various non-invasive lesions were studied which included 4 cases (14.29%) of papillary urothelial neoplasm of low malignant potential, 5 cases (17.86%) of non-invasive urothelial carcinoma- low grade and 2 cases (7.14%) of non-invasive urothelial carcinoma- high grade (Table 3 & Figure 2).

Table 1: Showing age wise and gender wise distribution of both non neoplastic and neoplastic lesions

Age group (years)	Non-neoplastic lesions		Total number of cases & Percentage (%)	Neoplastic lesions		Total number of cases & Percentage (%)
	Males	Females		Males	Females	
<20	2	1	3(15)	0	0	0
21-30	0	0	0	0	0	0

Age group (years)	Non-neoplastic lesions		Total number of cases & Percentage (%)	Neoplastic lesions		Total number of cases & Percentage (%)
	Males	Females		Males	Females	
31-40	1	3	4(20)	0	0	0
41-50	1	2	3(15)	1	1	2(7.14)
51-60	1	2	3(15)	6	2	8(28.57)
61-70	2	3	5(25)	7	3	10(35.71)
71-80	2	0	2(10)	6	2	8(28.57)
Total	9	11	20(100)	20	8	28(100)

Table 2: Histopathological spectrum of various non-neoplastic lesions in urinary bladder.

Type of lesion	Number of cases (N)	Percentage (%)
Cystitis	N=17	85
Chronic nonspecific cystitis	12	
Acute on chronic cystitis	1	
Granulomatous cystitis	1	
Polypoidal cystitis	1	
Follicular cystitis	1	
Eosinophilic cystitis	1	
Variants of normal histology	N=2	10
Cystitis cystica	1	
Cystitis glandularis	1	
Fibroepithelial polyp	1	5
Total	20	100

Table 3: Histopathological spectrum of various neoplastic lesions in urinary bladder.

Type of lesion	Number of cases	Percentage (%)
Papillary urothelial neoplasm of low malignant potential	4	14.29
Non-invasive papillary urothelial carcinoma, low grade	5	17.86
Non-invasive papillary urothelial carcinoma, high grade	2	7.14
Invasive urothelial carcinoma	17	60.71
Total	28	100

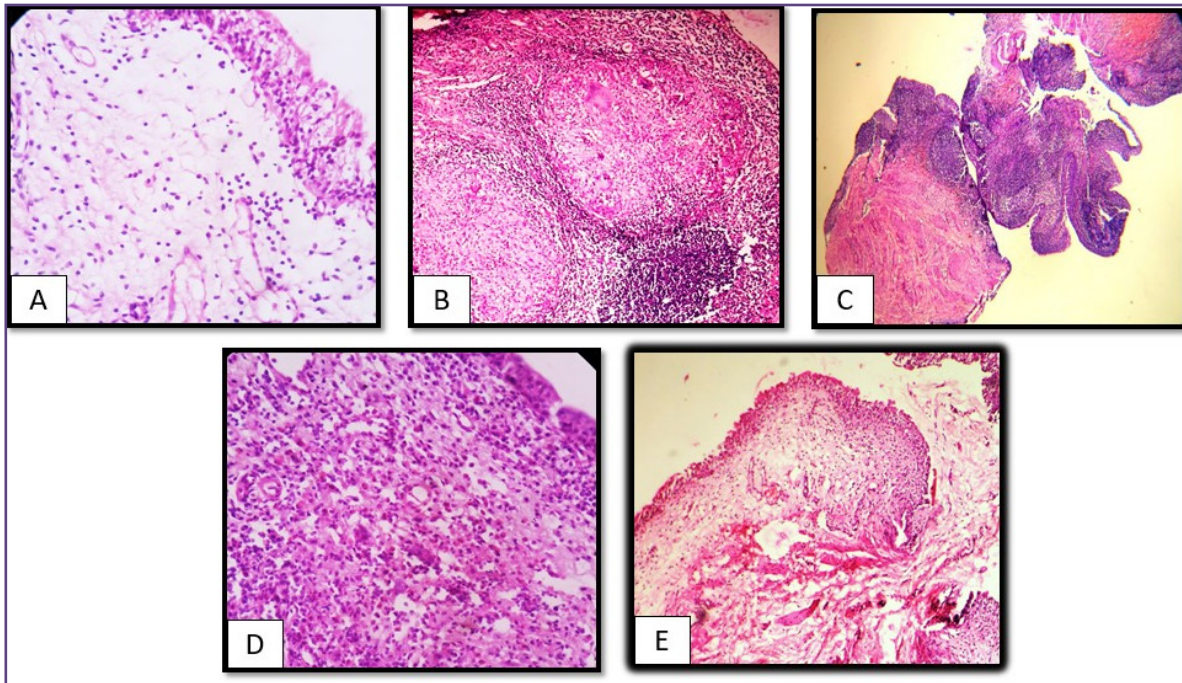


Fig. 1: Various forms of cystitis. A) Chronic non specific cystitis, B) Granulomatous cystitis, C) Follicular cystitis, D) Eosinophilic cystitis and E) Polypoidal cystitis.

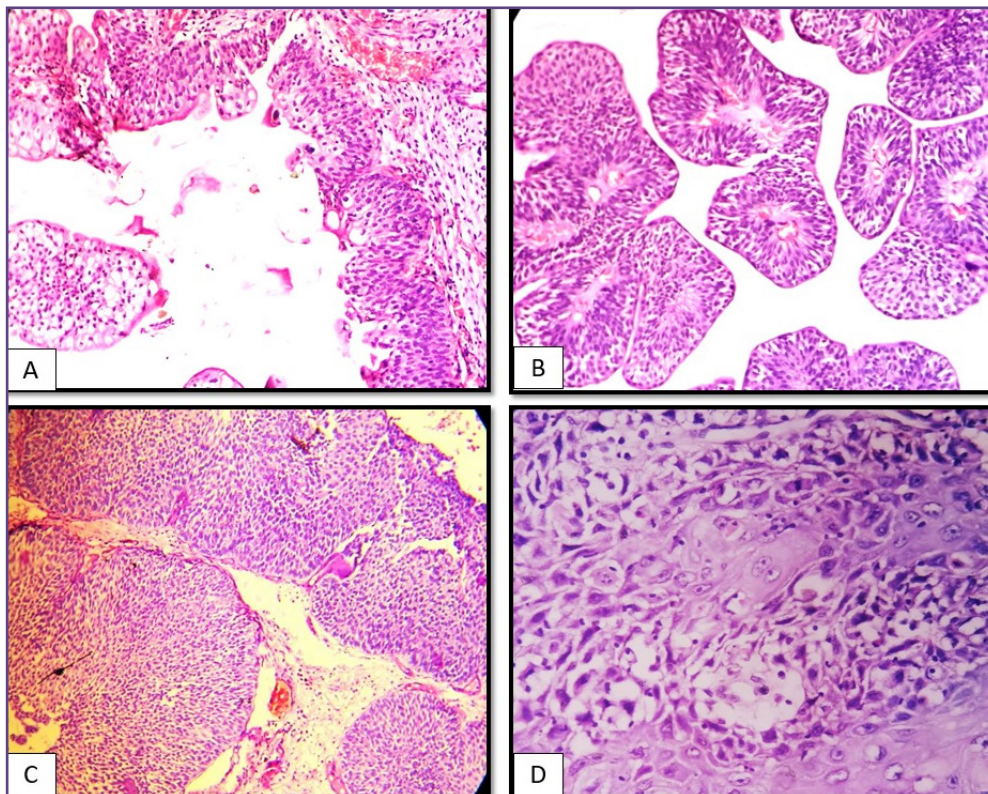


Fig. 2: Various neoplastic lesions- urinary bladder. A) Papillary urothelial neoplasm of low malignant potential [H&E, 100x], B) Non-invasive papillary urothelial carcinoma, low grade [H&E, 100x], C) Non-invasive papillary urothelial carcinoma, high grade [H&E, 100x,400x], D) IUC-squamous differentiation [H&E, 400x].

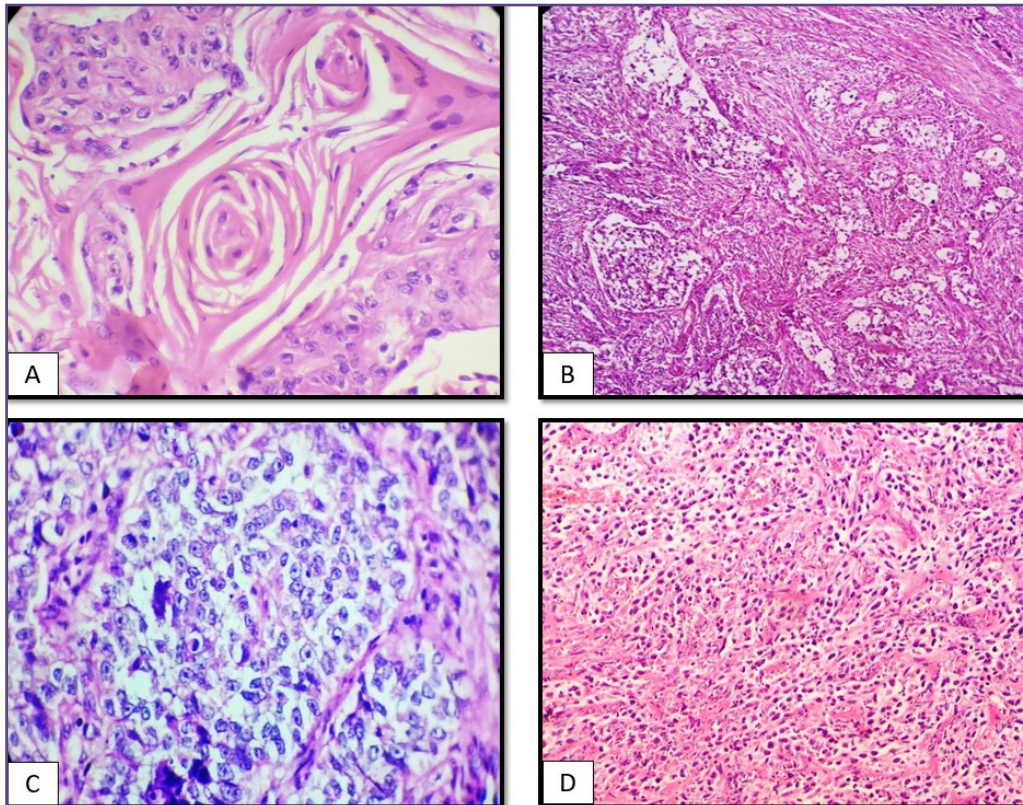


Fig. 3: Various forms IUC with differentiation, A) IUC with squamous differentiation – keratin pearl formation [H&E, 400x], B) IUC- glandular differentiation [H&E, 100x], C) IUC- Clear cell variant [H&E, 400x], D) IUC-Sarcomatoid variant [H&E, 400x].

Discussion

Both neoplastic and non-neoplastic lesions of urinary bladder collectively accounts for notably high amount of morbidity and mortality.^[4] Cystoscopy, which is a gold standard, primary diagnostic tool and TURBT being the most commonly practiced therapeutic and diagnostic procedure allows urologists to completely visualize bladder mucosa followed by sampling of the tissue for the histopathological examination.^[4,10]

There were clustering of cases between 51-60 years (22.92%), 61-70 years (31.25%) and 71-80 years (20.83%) of age groups, having 11, 15 and 10 cases respectively in the present study. This finding was in concordance with study series by various authors like Grandhi B *et al*¹¹ having 66.7% of cases, Shruti HP *et al*⁴ having 64% of cases in the age group of 51-80 years.

The male to female ratio from various studies highlights the association bladder neoplasms and increased male susceptibility. Present study also had male preponderance with a M:F ratio of 2.5:1. However, there is wide range of M:F ratio observed between various studies ranging from least being observed is 2.29:1 in study by Shah PY *et al*¹² to highest observed in study by Srikoustubah *et al*¹³

having M:F ratio of 5.25:1. Smoking had a predominant role in development of Bladder cancer in males along with other factors like occupational carcinogens. However, this increased incidence among females in the present study could be explained by use of smokeless tobacco in the forms like gutka, paan, khaini or surti. These contain many procarcinogenic agents like tobacco, betel nuts, saccharin, sugar coated fennel and heavy metals like silver.^[14]

Out of 20 non-neoplastic lesions in the present study, 12 cases were chronic non-specific cystitis and 5 cases of other forms of cystitis were diagnosed like granulomatous, polypoidal, acute on chronic form, follicular and eosinophilic cystitis. These results were similar to study done by Srikoustubah *et al*¹³ and Shruti HP *et al*⁴ with chronic non-specific cystitis as predominant type studied. Apart from this few variants of normal histology like cystitis cystica and cystitis glandularis along with a case of fibroepithelial polyp was also included.

Among the neoplastic lesions which were studied, urothelial neoplasm was the predominant type with a significant proportion of lesions seen in males. It included 4 cases of papillary urothelial neoplasm of low malignant potential, 5 were low-grade non-invasive urothelial carcinoma, 2 were

high grade non-invasive urothelial carcinoma and 17 were invasive urothelial carcinoma.

Out of all urothelial neoplasms in the present study, 11(39.29%) were non-invasive papillary carcinoma, 7(25%) were showing invasion in to lamina propria (superficially invasive bladder carcinoma) and 10(35.71%) cases showing invasion in to muscularis propria (muscle invasive bladder carcinoma). Other authors like Laishram *et al*¹⁵ showed 53.85% of non-invasive papillary carcinoma, 15.38% of superficially invasive bladder carcinoma and 30.77% of muscle invasive bladder carcinoma in their study.

In our study, invasive urothelial carcinoma without any differentiation was the predominant type (76.48%) which was similar to studies done by Shruti HP *et al*¹ having 86.67% and Goyal VK *et al*² having 92.13%. Apart from this, IUC with squamous and glandular differentiation and IUC having clear cell and Sarcomatoid variant were also included in the present study.

However, the risk of recurrence and disease progression does not solely depend on growth pattern and histologic grade of tumor. It also depends on various other factors such as size, multifocality, time of recurrence, prior intravesical therapy. Much of the controversies regarding grading will be solved by use of ancillary techniques like immunohistochemistry (IHC) or Molecular assay.^[16]

Conclusion

Urinary bladder lesions are most frequently encountered by surgical pathologists and are heterogenous. Both benign and malignant lesions are well documented but latter being more common. Many of these are more common in elderly people with male predilection and are often associated with smoking. However, there is increasing incidence in the female population in the recent years which might be due to increased exposure to environmental and occupational carcinogens along with exposure to smokeless tobacco.

Identifying the extent of invasion by microscopic examination constitutes an important aspect in urothelial carcinomas. Invasion of muscularis mucosa and muscularis propria has to be differentiated carefully as the prognostic and therapeutic aspects are entirely different in both of them. In cases of dilemma IHC is most helpful. Awareness regarding the various histological features of these lesions, their neoplastic potential, risk of recurrence and possible pitfalls helps for accurate diagnosis.

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