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Original Research Article

Spectrum of Lesions in Urinary Bladder Biopsies - A Histopathological Study

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ABSTRACT

Urinary bladder lesions both non-neoplastic and neoplastic are common. These diseases are more disabling than lethal. Bladder tumor is the seventh most common tumor worldwide. Although progress has been made in the field of non-invasive imaging, histopathological analysis of biopsy material is the mainstay for cancer diagnosis and treatment.

Objectives: To study the histopathological features of various lesions in the urinary bladder biopsies and to categorize the neoplastic lesions according to WHO/ISUP 2004 classification.

Results: Histologically 76 cystoscopic biopsies were studied. 75 cases were satisfactory and 1 was inadequate for evaluation. Non neoplastic lesions accounted for 24 cases (32%), Neoplastic lesions accounted for 51 cases (67.9%). Among the non-neoplastc lesions there were 19 cases (79.17%) of chronic non specific cystitis, 3 cases (12.5%) of acute or chronic cystitis, and 1 case each of Tubercular cystitis and polypoidal cystitis. Among the neoplastic lesions there were 2 cases of inverted papilloma, 47 cases of urothelial neoplasms and one case each of squamous cell carcinoma and sarcomatoid carcinoma.

Conclusion: Urinary bladder biopsy is one of the most common biopsies in urology practice and a wide variety of interesting lesions are seen. Knowledge of the histological characteristics of these lesions, their preneoplastic potential and the possible pitfalls can help the pathologist in accurate diagnosis of the lesions.

Key Words: Cystoscopic biopsies, Cystitis, Urothelial neoplasms

INTRODUCTION

Diseases of the urinary bladder both non-neoplastic and neoplastic are quite common. The non-neoplastic lesions especially cystitis constitute an important source of symptoms and signs. These diseases are more disabling than lethal. Neoplastic lesions are responsible for significant morbidity and mortality. Bladder tumor is the seventh most common tumor worldwide. Urothelial carcinoma is the commonest type accounting for 90% of all primary tumors of the bladder. [1] As per Indian Cancer Registry data in men, it is the 9th most common cancer accounting for 3.9% of all cancers. [2] The incidence rates of urinary bladder cancer per 100,000 males in Bangalore are 3.3, 5.8 in Delhi and 4.8 in Mumbai. [3]

According to SEER STAT FACT SHEETS: URINARY BLADDER [4]

Estimated new cases in 2014 : 74,690
% of all new cancer cases : 4.5%
Estimated death in 2014 : 15, 580
% of all cancer deaths : 2.7%
5 years survival rate : 77.4

Urinary bladder cancer is a complex and heterogeneous disease with a broad spectrum of histologic findings and potentially lethal behavior. Despite advances in surgical techniques, as well as intravesical and systemic therapies, upto 30% of patients with non-muscle invasive urothelial carcinoma and 50% of patients with muscle invasive carcinoma experiences disease progression, recurrence and eventual death. [5]

Although progress has been made in the realm of non-invasive imaging and scientists continue to identify and characterize potential markers or surrogate end points for bladder tumor, physical examination, cystoscopic evaluation and histopathologic analysis of biopsy material are the mainstays of contemporary bladder cancer diagnosis and treatment. [6]

Aims and Objectives

1. To assess various types of urinary bladder lesions with regard to frequency, age and sex distribution.
2. To describe the Histopathological features of various lesions in the urinary bladder biopsies.
3. To categorize the neoplastic lesions according to W.H.O (2004)/ISUP classification.

MATERIALS AND METHODS

The present study was conducted in the Central laboratory, Department of Pathology, Kempegowda institute of Medical Sciences, Bangalore, during the period August 2009 to August 2014. Seventy six cystoscopic biopsies from patients attending KIMS Hospital were studied.

Clinical details, cystoscopy findings were obtained and maintained according to the proforma. Apparent pathology was noted during the cystoscopic procedure and biopsies taken from the representative areas. For the retrospective cases all relevant details were obtained from hospital records.

Inclusion Criteria: All cystoscopic biopsies taken from the urinary bladder, received in Central Laboratory KIMS, Bangalore were considered for the study.

Exclusion Criteria: Inadequate 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 the pathology department, or biopsy of bladder cancer lacking muscular tissue for pathologic staging. [7]

All cystoscopic biopsies were immediately fixed in 10 % formalin for 24 hours. It was then routinely processed and embedded with the mucosal surface uppermost. Five microns thick serial sections were prepared and stained with Hematoxylin and Eosin.

Detailed study was performed under the light microscope. Adequacy of the biopsy was assessed and attempt was made to correlate the histopathological diagnosis with the cystoscopic diagnosis obtained.

RESULTS

76 urinary bladder biopsies were studied. Among 76 cases 51 were neoplastic, 24 non- neoplastic and one was classified as biopsy specimen inadequate or unsatisfactory for evaluation. study urinary bladder biopsies was performed on patients of all age groups, ranging from 26-89 years. There was clustering of cases between 41-80 years with maximum cases seen in 51-70 years of age together having 39 cases (52%) (Table.1). The least number of cases were

seen in the extremes of age groups. In the present study there were 54 male patients (72%) and remaining 21 patients were females (28%)(Table.2). Hematuria was the most frequent complaint that the patients presented with followed by Dysuria, increased frequency of micturition, urgency and pain abdomen (Table.3). Among the non-neoplastic lesions 19 were chronic non specific cystitis, 3 were Acute or chronic cystitis, 1 granulomatous cystitis of tubercular etiology and 1 was polypoidal cystitis (Table.4).

Table 1: Age Distribution Of All Cases

Age in years	Non- Neoplastic		Neoplastic	
	No of cases	%	No of cases	%
21-30	4	16.67	1	1.9
31-40	4	16.67	2	3.9
41-50	7	29.17	5	9.8
51-60	6	25	15	29.4
61-70	4	16.67	14	27.4
71-80	0	0	9	17.6
81-90	0	0	4	7.8
Total	24	100	51	100

Table 2: Sex Distribution Of All Cases

Sex	Non- neoplastic		Neoplastic	
	No of cases	%	No of cases	%
Male	14	58.4	40	67.7
Female	10	41.6	11	18.6

Table 3: Distribution Of Clinical Features Of All Cases

Complaints	Non- Neoplastic No of cases	Neoplastic No of cases
Hematuria	1	43
Frequency	17	5
Urgency	16	5
Dysuria	20	5
Pain abdomen	6	5

Table 4: Distribution Of Non- Neoplastic Lesions

Diagnosis	No of cases	%
CNSC	19	79.1
ACC	3	12.5
TB	1	4.1
PC	1	4.1
Total	24	100

Among the neoplastic lesions most of the cases were in the 5th and 6th decade of life with as many as 29 cases (56.8%) together and more than half the patients were smokers. There was strong association of smoking as risk factor in bladder neoplasms.

In our study out of 51 cases , 2 were inverted papillomas, 3 were Papillary urothelial neoplasms of low malignant potential,17 were Low grade papillary urothelial neoplasms.14 were high grade papillary urothelial neoplasms,13 were Invasive urothelial neoplasms and one case each of Squamous cell carcinoma and Sarcomatoid carcinoma (Table.5).

On follow up during the study period 7 out of 17 Low grade urothelial cases (41.1%) came back with recurrence. In high grade urothelial tumors the recurrence rate was 21.4%. Overall recurrence rate among the urothelial neoplasms was 23.9% (Table.6).

Table 5: Distribution Of Neoplastic Lesions

Diagnosis	No of cases	%
Papilloma	2	3.9
PUNLMP	3	5.8
LGPUN	17	33.3
HGPUN	14	27.4
IUN	13	25.4
SCC	1	1.9
SC	1	1.9
Total	51	100

Table 6: Distribution Of Recurrent Cases In Urothelial Neoplasms

Lesion	No of cases	No of Recurrenences	%
PUNLMP	3	0	0
LGPUN	17	7	41.1
HGPUN	14	3	21.4
IUN	12	1	8.33
Total	46	11	23.9

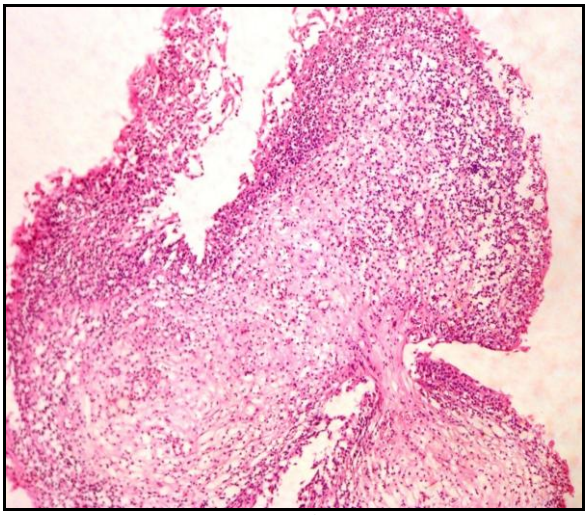

Figure 1. Chronic Non Specific Cystitis (H& E 100 X)

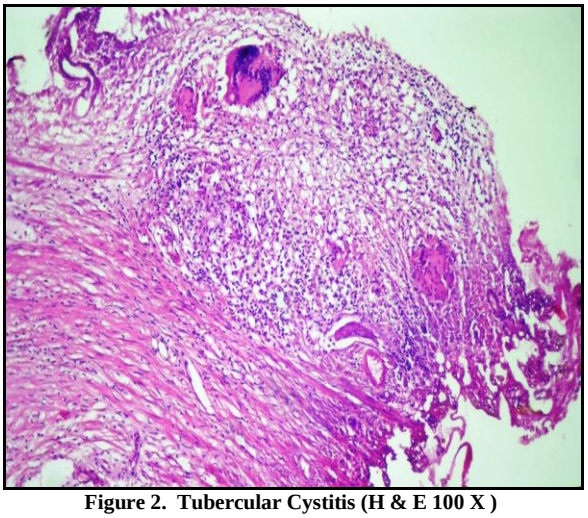

Figure 2. Tubercular Cystitis (H & E 100 X)

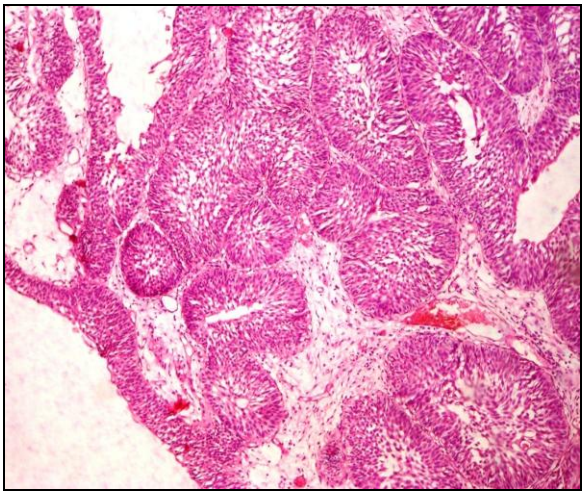

Figure 3. Inverted Papilloma (H & E 100 X)

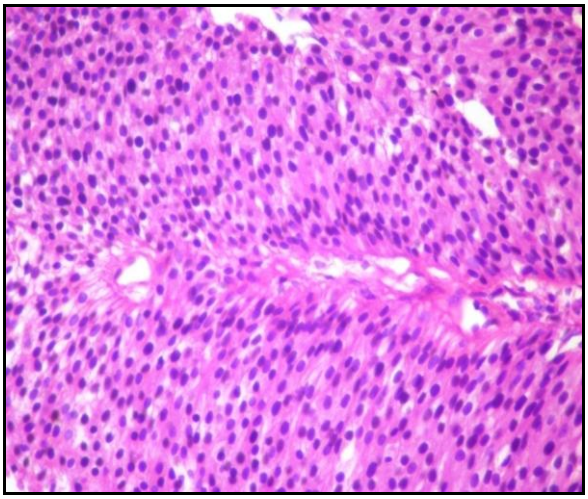

Figure 4. PUNLMP - Cells Maintain Polarity (H & E 400x)

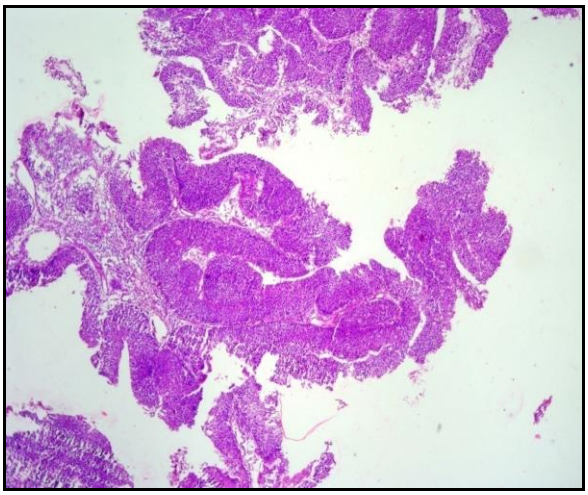

Figure 5. LGPUN With Papillary Architecture (H & E 50 X)

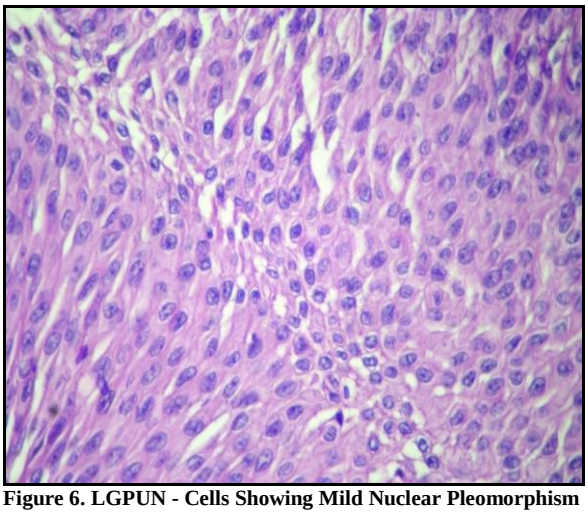

Figure 6. LGPUN - Cells Showing Mild Nuclear Pleomorphism And Inconspicuous Nucleoli (H & E 400x)

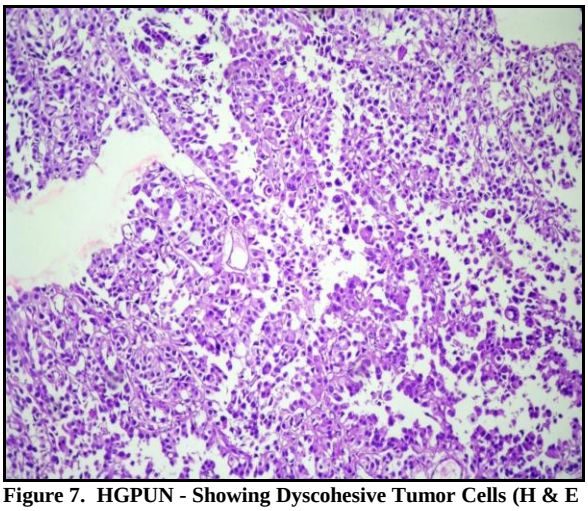

Figure 7. HGPUN - Showing Dyscohesive Tumor Cells (H & E 100x)

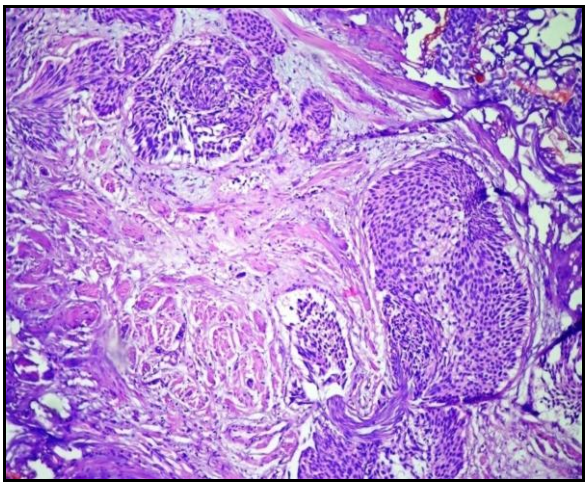

Figure 8. IUN With Invasion In To Muscularis Propia (H & E 100 X)

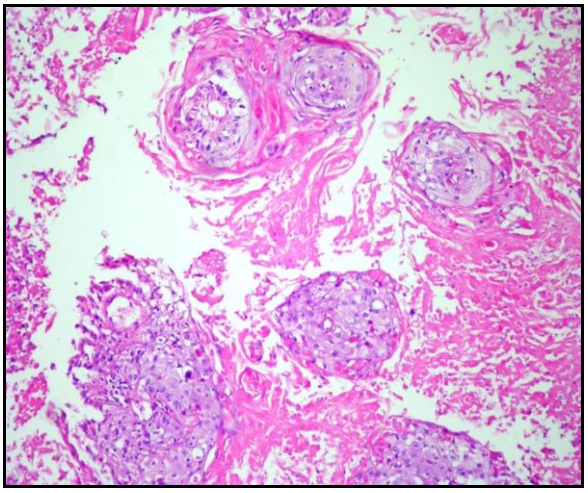

Figure 9. SCC With Attempted Pearl Formation (H & E 100 X)

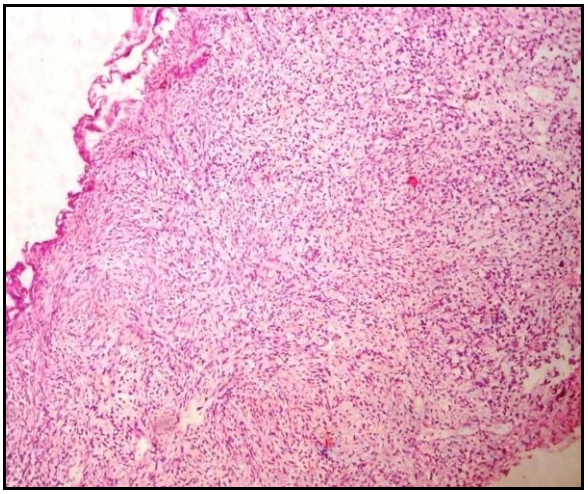

Figure 10. Sarcomatoid Carcinoma (H & E 100 X)

DISCUSSION

Urinary bladder lesions, non-neoplastic and neoplastic are collectively responsible for significant morbidity and mortality throughout the world. Cystoscopy is the primary diagnostic tool for the patients, who are suspected of having bladder tumors, which allows a direct visualization of the bladder mucosa and biopsies of the suspected lesions. Bozzoni in 1805 described the first cystoscope consisting of a metal tube which on the extravesicle end applied a spark plug through which the vesicle field was illuminated and limited at the other end of the tube. The first bladder biopsy forceps were independently described by Young and Manon in 1929 by which it was possible to extract portions of tumor tissue. [8]

Despite the general reliability and popularity of cystoscopy this technique has some distinct limitations. The possibility of occult neoplastic change in flat urothelium and the risk of not identifying tumors located in sanctuary sites support the widespread use of cytological analysis on voided urine or bladder biopsy specimens. [6]

With approximately 260,000 new cases per year worldwide tumors of the urinary system contributes significantly to the overall human cancer burden. Progress in the early detection and treatment of bladder cancer has improved the prognosis with five year survival rate of 60-80%. [9]

In our study Chronic non specific cystitis was characterized by transitional cell epithelium, subepithelially there were predominantly lymphocytic infiltrate, at places forming lymphoid aggregates admixed with few plasma cells. Few cases showed reactive atypia of the transitional epithelium. (Fig:1).

Acute or chronic cystitis was characterized by transitional cell epithelium showing subepithelial mixed inflammatory

infiltrate comprising of neutrophils, eosinophils, lymphocytes and plasma cells.

TB cystitis showed well formed granulomas comprising of epithelioid cells, Langhan's giant cells and rimmed by lymphocytes was diagnosed as tubercular cystitis with the help of urine culture being positive. (Fig:2). Polypoidal cystitis showed polypoidal structure covered by transitional epithelium focally and showed extensive squamous metaplasia. Lamina propria showed edema with chronic inflammatory infiltrate.

Similar results were also seen in study conducted by Issam Salman AL-Azzawi in 64 patients with a persistent symptom complex of supra pubis pain, dysuria, frequency and urgency for 12 months and above. Histopathological examination revealed variable lesions as chronic inflammatory cell infiltration, Brunns nests, cystitis cystic, metaplasia, Bilharzial reaction and ova and in situ carcinoma. [10] Cystitis may be classified according to cause, duration and histological appearances. Causes are numerous and include bacterial, viral, fungal and protozoan agents but most result from coliform bacteria, especially E. coli. [11]

Among the neoplastic lesions Inverted papilloma of urinary bladder is an uncommon urothelial neoplasm of which makes up to <1% of all urothelial neoplasms. [12]

The two cases of inverted papillomas showed anastamosing islands and trabeculae of urothelium originating from the overlying mucosa and growing downwards in to the stroma. The surface epithelium was flat. Individual cells were bland looking. (Fig:3).

In the present study urothelial neoplasms made up to 49 cases (95%) and one case each of squamous cell carcinoma and sarcomatoid carcinoma. Mahesh Kumar et al, [1] Syed Mehmood Hasan et al [13] and Matalka I et al [14] also showed that urothelial neoplasms were the most common tumors of the urinary bladder.

About 70 % of all carcinomas of the urinary bladder are either non- invasive (pTa) or only minimally invasive (pT1) at the time of presentation. [15] Correct histologic grading and tumor staging is crucial for proper and optimal patient management. The corner stone of bladder cancer diagnosis, treatment and staging is a high quality transurethral resection of the bladder tumor (TURBT). [16] After transurethral resection of the tumor up to 60-70 % of patients develop recurrent disease, most frequently with in the first year after the presentation. [17]

In our study Papillary urothelial neoplasm of low malignant potential were characterized by delicate papillae with mild increase in the thickness of the urothelium and superficial umbrella cells were preserved. There was no loss of polarity and mild nuclear enlargement was noted. (Fig:4).

Low grade papillary urothelial neoplasms, featured papillary architecture with increase in thickness of the urothelium, mild loss of polarity. Individual cells were cohesive with mild anisonucleosis, some showing inconspicuous nucleoli. Mitotic figures were restricted to the basal layers.(Fig:5,6)

High grade urothelial neoplasms, showed papillary pattern that showed branching and fusion. Individual cells were dyscohesive with loss of polarity, increased N: C ratio, pleomorphic hyperchromatic to vesicular nuclei with prominent nucleoli. Mitotic figures were seen even in the uppermost layers of the urothelium. Focal areas of necrosis were noted. (Fig:7).

Invasive urothelial neoplasms, showed either low grade or high grade of features with invasion. There were 7 cases showing lamina propria invasion and 6 cases showing muscularis propria invasion.

Invasion was in the form of groups and nests of cells in lamina propria and muscularis propria. These invasive lesions were also showing bizarre forms with many atypical mitotic figures. Areas of necrosis and hemorrhage were seen. (Fig:8).

Pure squamous cell carcinoma of the bladder is an uncommon cause of bladder cancer in the developed world accounting for 2.7% of bladder cancers in recent series. [18]

However it is the most common cause of bladder cancer in areas where Schistosomiasis is endemic; where it accounts for up to 5.9% of bladder cancers.

Squamous cell carcinoma of bladder is much less frequent worldwide; it constitutes about 1.3% of bladder tumors in males and 3.4% in females. The main etiological factors being tobacco smoking, Schistosomiasis and chronic inflammation. [19]

In our study one case of moderately differentiated squamous cell carcinoma was seen in a 66 year old male patient and presented as a posterior wall growth. This lesion was characterized by sheets, groups and nests of cells having abundant eosinophilic cytoplasm with hyperchromatic to vesicular nuclei. Individual cell keratinisation and attempted pearl formation was seen, with invasion in the muscularis propria. (Fig: 9).

Sarcomatoid carcinoma of the urinary bladder is an unusual malignancy composed of both carcinomatous and sarcomatous components. It is an aggressive tumor that presents at an advanced stage and confers a much poorer prognosis than conventional urothelial carcinoma. The proper nomenclature and histogenesis of these tumors have been subjects of debate for some time. There is an emerging consensus that sarcomatoid carcinoma is the most appropriate term for these neoplasms. The recent World Health Organization classification has applied this term to all tumors showing morphologic and/or immunologic evidence of both malignant epithelial and mesenchymal differentiation. [20]

In our study one case of Sarcomatoid carcinoma was diagnosed. It was characterized by high grade transitional cell carcinoma containing variably sized areas composed of atypical spindle cells arranged in the form of fascicles. At places these spindle cells were seen lying in a loose myxoid stroma. (Fig:10)

CONCLUSION

Urinary bladder biopsy is one of the most common biopsies in urology practice. In our study bladder tumors were the commonest lesions seen in cystoscopic biopsies and TCC was the predominant tumor type. Hematuria was a common symptom in our series and the clinicians showed a keen awareness to the dangers of this symptom and investigated these patients further, which led to discovery of the urothelial tumors. In our study Smoking and bladder cancer showed strong associations and hence we stress the significance of public health education and awareness amongst patients and health care professionals. An important feature of TCC is its propensity for multiple recurrences. Identification of these patients has an important impact on prognosis as well as on therapeutic approach. A wide variety of interesting lesions is seen in urinary bladder and is more commonly encountered by the general surgical pathologist. Knowledge of the histological characteristics of these lesions, their preneoplastic potential and the possible pitfalls can help the pathologist serve the patient better.

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