Research Article

Histopathological overview of cystoscopic bladder biopsies- A retrospective analysis

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Abstract

Background: Wide spectrums of nonneoplastic and neoplastic lesions are observed in urinary bladder. Correlation between clinical findings and histopathological features is essential in arriving at a correct diagnosis. This study is undertaken to analyse the pattern of lesions in cystoscopic bladder biopsies. **Methods:** This retrospective study consists of 70 cases of cystoscopic bladder biopsies carried out in the department of pathology. Clinical details of the patients were retrieved from the file. Specimens were processed routinely and stained with hematoxylin and eosin. **Results:** Three specimens out of 70 biopsies were inadequate for reporting. Of the remaining 67 cases, 38 were (56.7%) neoplastic and 29 (43.3%) were nonneoplastic lesions. The majority of the cases were seen in the age group of 41-50 yrs (29.9%) with a male predominance (73.1%). Urothelial tumours (94.7%) were the predominant lesions observed under neoplastic category, of which invasive papillary urothelial carcinoma (80.6%) was the most common subtype. Among nonneoplastic lesions, chronic nonspecific cystitis (51.7%) was the commonest lesion noted **Conclusion:** There are wide ranges of lesions exist in the bladder. Urothelial tumours were the predominant lesions seen in cystoscopic biopsies followed by cystitis. Accurate diagnosis and early intervention is the key for better treatment outcome.

Keywords: Cystoscopy, Urothelial tumour, chronic nonspecific cystitis, Invasive papillary urothelial carcinoma, neoplastic

Introduction

Wide Spectrums of nonneoplastic and neoplastic lesions are common in urinary bladder, ranging from inflammatory conditions, infections, tumour like lesions, benign and malignant tumours. Bladder tumours are the second most common tumours of genitourinary tract. Developed countries show higher prevalence than developing countries [1]. The incidence of bladder tumours in men and women is 6% and 2% respectively [2]. About 90% of the tumours are urothelial cancers.

These tumours rank 5th in the world and causes significant morbidity & mortality [3]. In view of increasing trend in the occurrence of both neoplastic and nonneoplastic lesions of bladder, our study aims at evaluating the histomorphological features of cystoscopic biopsies. Cystoscopy helps in direct visualization of bladder and obtaining biopsies from suspicious areas. However, correlation is needed between urologic, radiologic findings and histo-pathological features to arrive at an accurate diagnosis.

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Objectives

1. To study the histomorphological spectrum of non neoplastic and neoplastic lesions of bladder in cystoscopic biopsies.
2. To find out the incidence of various lesions of the bladder.

Materials & Methods

This was a retrospective study conducted in the department of pathology. Cystoscopic biopsies of 70 cases were included in the study. Detailed clinical history and cystoscopic findings were retrieved from the patient record. All the specimens received were

fixed in 10% buffered neutral formalin for a period of 24 hrs. Entire tissue was submitted for processing. Paraffin embedded sections of 5µ size were cut and stained with Hematoxylin & Eosin. Light microscopy was used for diagnosis. The malignant lesions were classified according to WHO/ISUP(2004) classification. Results were tabulated according to age & sex.

Data source: Our study includes all the cystoscopic biopsies performed in the patients who visited surgery/urology department with urinary symptoms.

Inclusion Criteria- All the cystoscopic biopsies received in the department of pathology were included in the study.

Exclusion criteria-Unfixed autolysed specimens and biopsies which were inadequate for reporting were excluded from the study.

Statistical analysis-Microsoft office 2007 was used to generate tables. It is a descriptive study and the results are presented as mean and percentage.

Results

The majority of the cases were observed in the age group of 41-50 yrs (29.9%) followed by 51-60 yrs (22.4%). The age of the patients ranged from 9 yrs to 83 yrs in which 73.1% were males and 26.9% were females (Table 2). The common clinical presentation was hematuria followed by dysuria, frequency and suprapubic pain.

Of the 29 non neoplastic lesions, 15(51.7%) were chronic nonspecific cystitis, 5(17.2%) were follicular cystitis and 3(10.3%) were granulomatous cystitis of tubercular etiology. Other lesions like eosinophilic cystitis, hemorrhagic cystitis and vonbrunn's nest were observed in 2 (6.9%), 1(3.5%) and 3(10.3%) cases respectively. (Table 4) (Fig. 2a,b)

Table-1: Distribution of cases.

Type of lesion	Number of cases	Percentage
Non neoplastic	29	43.3%
Neoplastic	38	56.7%
Total	**67**	**100%**

Table-2: Age & Sex wise distribution of cases.

Age (in years)	Number of cases (n=67)		Percentage
	Males	Females	
0 -10	1	0	1.5%
11-20	1	0	1.5%
21-30	1	1	2.9%
31-40	6	3	13.4%
41-50	12	8	29.9%
51-60	13	2	22.4%
61-70	9	3	17.9%
71-80	5	1	9%
81-90	1	0	1.5%

Neoplastic lesions were commonly seen from fourth to sixth decades of life. However the peak age of presentation was between 41-50 years. They were predominantly observed in male patients 81.6% (n=31). Urothelial tumours formed the largest group of the neoplastic category. They constituted 94.7% (36 cases) of all neoplastic lesions. The remaining 2 cases (5.3%) were secondary adenocarcinomas. Among all urothelial tumours, invasive papillary urothelial carcinoma was the most common subtype accounting for 29 cases (80.6%) with low grade comprising 8 cases and high grade 21 cases. Four of the high grade tumours showed squamous differentiation and one was clear cell variant of invasive urothelial carcinoma. Out of 5 (13.9%) noninvasive papillary urothelial carcinomas, 4 were low grade lesions and one was high grade lesion. Papillary urothelial neoplasm of low malignant potential was observed in 2 (5.6%) cases. (Table 3) (Fig 1a,b,c,d)

Table-3: Frequency of neoplastic lesions

Type of lesion	No of cases(n=38)	Percentage
PUNLUMP	3	7.9%
Non invasive papillary urothelial carcinoma	11	28.9%
Invasive urothelial carcinoma	18	47.4%
Invasive urothelial carcinoma with squamous differentiation	4	10.5%
Adenocarcinoma -metastatic	2	5.3%

Table-4: Frequency of nonneoplastic lesions

Type of lesion	No. of cases (N=29)	Percentage
Chronic nonspecific cystitis	15	51.7%
Follicular cystitis	5	17.2%
Eosinophilic cystitis	2	6.9%
Granulomatous cystitis	3	10.3%
Hemorrhagic cystitis	1	3.5%
Von brunn's nest	3	10.3%

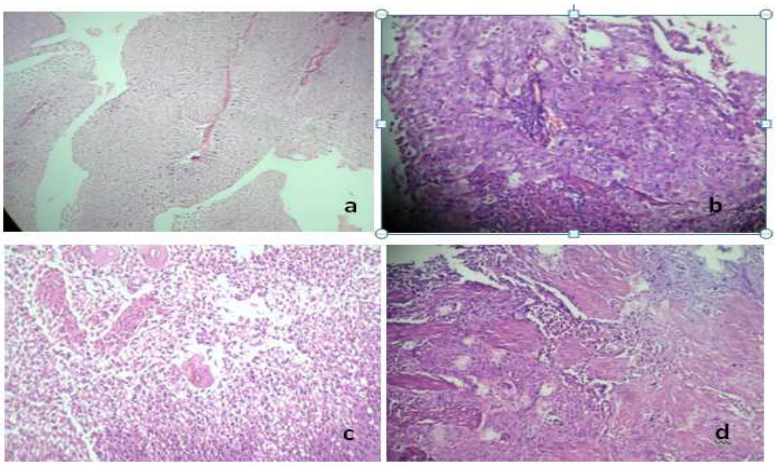

Fig.-1: Photomicrograph of neoplastic lesions of bladder: a) Non invasive high grade urothelial carcinoma b) Infiltrating papillary urothelial carcinoma-high grade c) Clear cell variant of urothelial carcinoma d) Detrusor muscle invasion in infiltrating urothelial carcinoma

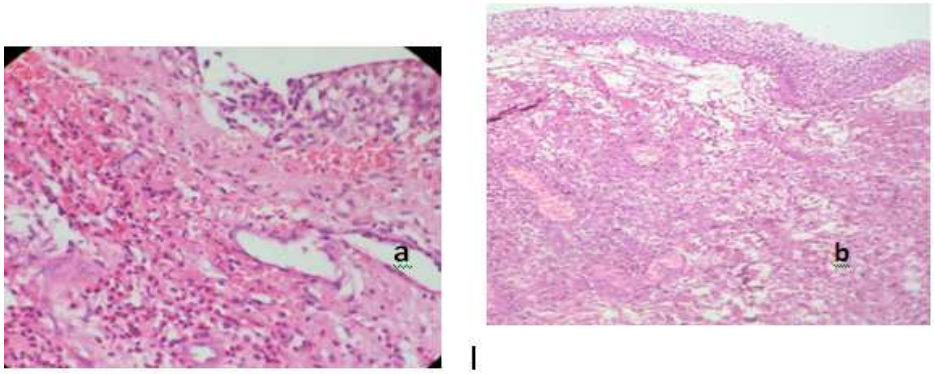

Fig.-2: Photomicrograph of non neoplastic lesions of bladder: a) Eosinophilic cystitis showing prominent infiltrate of eosinophils and edema in lamina propria. b) Mononuclear cell infiltrate with edema in the lamina propria in chronic nonspecific cystitis.

Discussion

Bladder cancer is the most common urological malignancies and a major cause of morbidity and mortality. It is the fourth most common malignancy in men and eighth common in women in the western countries [4]. According to Indian cancer registry data in men, it is the ninth most common cancer [5]. It is more commonly seen in males with a male to female ratio of 8.9:1[6]. 90% of the bladder tumours are urothelial carcinoma. The median age of presentation is 69 years in men and 71years in women, though it can occur in any age group including children. It is very uncommon below 30 yrs and when occurs they have an excellent prognosis because they are mostly low grade tumours with early stage [7, 8].

The strongest environmental risk factor is smoking, followed by exposure to aromatic amines, hydrocarbons and schistosoma hematobium. Growing evidence suggest that genetic factors also play a significant role [9,10]. Bladder tumours classically present with painless hematuria. In our study 92% of the patients presented with hematuria. The common neoplastic lesion observed in our study was urothelial tumour (94.7%). Among all the urothelial neoplasms invasive papillary urothelial tumour (80.6%) was the most common subtype followed by non invasive papillary urothelial neoplasm (13.9%) and PUNLUMP (5.6%). This is comparable with other studies [11,12,13].

Detrusor muscle was not seen in 27.6% of the biopsies of invasive tumours. In the remaining cases muscle invasion was identified in 42.9%. Other authors observed 26%, 25%, 35.8% and 42.1% of muscle invasion respectively in their studies [1,5,14,15]. The incidence of squamous differentiation in urothelial carcinoma ranges from 11% to 60% of the cases. The prognostic significance of squamous differentiation is controversial. Some studies have found unfavourable response to chemotherapy and radiotherapy [16,17]. In the present study squamous differentiation was seen in 13.8% of cases of invasive tumours.

The clear cell variant of urothelial carcinoma is defined by the presence of either focal or extensive clear cell change with glycogen rich cytoplasm. It is important to differentiate from clear cell adenocarcinoma of bladder and metastatic renal & prostatic carcinomas. It is more commonly observed in poorly differentiated urothelial carcinoma [18]. Clear cell variant was observed in one of the high grade urothelial tumours in our study. Primary adenocarcinoma of bladder is uncommon and accounts for 0.5% -2% of all bladder tumours. It is more common in males and more frequent in 6^{th} and 7^{th} decades of life. Morphologically it shows varying growth patterns including enteric, mucinous, signet ring cell, clear cell and mixed type. Metastatic adenocarcinoma is commoner than primary tumours [19,20,21]. In this study, we reported 2 cases of secondary adenocarcinoma in elderly males. Both the patients were known case of carcinoma prostate underwent surgery 5 and 7 years back respectively.

The most common non neoplastic lesion in our study was chronic nonspecific cystitis comprising 51.7% of cases with the age range of 19-75 yrs. This is in accordance with other studies [11,13,22]. Microscopy revealed chronic inflammatory infiltrate associated with edema and congestion in lamina propria. Some of the cases showed partial ulceration of the overlying urothelium.

In the present study granulomatous cystitis was found in 10.3% of all non neoplastic lesions with a male predominance. Various infections and iatrogenic conditions can lead to granulomatous cystitis. However TB remains the most frequent cause in developing countries like India. It is frequently secondary to renal tuberculosis. Men are more commonly affected than women with a mean age of 40.7 years. The lesions are most commonly found near ureteric orifices [23,24,25].

Eosinophilic cystitis is an uncommon entity of bladder, reported in all ages and both sexes equally. Though the exact etiology is unclear it has been associated with allergy, asthma and autoimmune conditions. Microscopy shows dense transmural infiltrate of eosinophils with variable stromal edema often associated with intramural fibrosis [26, 27, 28, 29]. In current study eosinophilic cystitis was observed in 6.9% of all cases.

There were 3 cases (10.3% of all nonneoplastic lesions) of von brunn nest seen in our study. It is characterised by the presence of solid nests of urothelium in lamina propria with no continuity to the overlying mucosa. Florid von brunn nest resembles nested variant of urothelial carcinoma which may be a diagnostic concern [30, 31].

Conclusion

Cystoscopic biopsies play an important role in early diagnosis of bladder tumours. Malignant tumours were the most common bladder lesions followed by inflammatory conditions. Urothelial tumours are the most common malignant lesions and observed mainly in middle aged males. Chronic nonspecific cystitis is the commonest nonneoplastic lesion encountered in routine practice. Accurate diagnosis and early intervention is the key for better treatment outcome.

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