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Original article

Histopathological Spectrum of Non-neoplastic and Neoplastic Lesions of Urinary Bladder

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ABSTRACT

Introduction: Urinary bladder is a site of various non-neoplastic and neoplastic lesions, both of which can present with hematuria. Cystoscopy allows for direct visualization of the bladder mucosa and also obtaining tissue for histopathologic evaluation. The most common non-neoplastic and neoplastic lesion of the urinary bladder is non-specific cystitis and urothelial carcinoma respectively.

Materials and methods: This study is a 4-year retrospective study conducted in the Department of Pathology at Patan Hospital, Nepal. All cases from the urinary bladder i.e., both cystoscopic and cystectomy samples were included in the study. Hematoxylin and eosin-stained slides were re-evaluated whenever required.

Results: A total of 145 cases were included which consisted of 17 cystectomy specimens and 128 cystoscopic biopsies. There was a male predominance. The non-neoplastic and neoplastic cases consisted of 32% and 68% respectively. Chronic non-specific cystitis and high-grade infiltrating urothelial carcinoma were the most common non-neoplastic and neoplastic lesions respectively. 56.1% of cystoscopic biopsies had the presence of detrusor muscle with 21.7% showing its invasion.

Conclusions: Urinary bladder lesions have a wide spectrum ranging from non-neoplastic to neoplastic conditions. The presence of detrusor muscle in a cystoscopic biopsy, and its evaluation for invasion helps in diagnosis and further planning of patient management.

Keywords: Cystectomy; Cystoscopy; Urinary bladder; Carcinoma;

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INTRODUCTION

The urinary bladder is the site of various non-neoplastic and neoplastic pathologies which can cause alarming signs and symptoms. The most common sign of bladder lesion is hematuria which is seen in both benign and malignant conditions. Cystoscopy is the principal diagnostic tool in investigating bladder lesions. It provides direct visualization of the bladder mucosa and allows for the collection of biopsy for histopathologic evaluation.[1] Cystitis is a common non-neoplastic lesion and urothelial carcinoma is the most common malignancy in the bladder.[2,3] The incidence of bladder tumors is higher in males than females and more common in urban areas than in rural locations. The WHO/ ISUP classification of urinary bladder tumor, 2016 has laid down the classification of invasive and non-invasive bladder tumors.[4]At least 75 – 80 % of newly diagnosed bladder tumors are superficial, non-invasive papillary urothelial carcinoma, and at least 50 – 75% of these tumors recur over time.[5]

This study aimed to determine the demographics and spectrum of the various non-neoplastic and neoplastic urinary bladder lesions and the histological characteristics of these lesions in patients presenting to Patan Hospital.

MATERIALS AND METHODS

This is a 4-year retrospective study carried out in the Department of Pathology at Patan Hospital and includes data from 1st January 2017 to 31st December 2020, retrieved from the departmental records. All cases from the urinary bladder i.e., both cystoscopy and cystectomy samples were included in the study. Hematoxylin and eosin-stained slides were re-evaluated whenever required. The neoplastic lesions were classified according to the 2016 WHO classification of tumors of the urinary bladder.

The variables including age, gender, non-neoplastic and neoplastic lesions were summarized in frequency, mean, median, and range whichever applicable. The presence or absence of detrusor muscle in cystoscopic biopsies was evaluated. All the data were filled into a predesigned proforma and compiled in Microsoft Excel. The data were analyzed using SPSS version 21.0.

RESULTS

A total of 145 cases were included in the study which consisted of 17 cystectomy specimens and 128 cystoscopic biopsies. There was a male predominance with 97 (67%) males and 48 (33%) females with a male: female ratio of 2:1. The majority of the cases were neoplastic (99 cases, 68%) and 46 cases (32%) were non-neoplastic. High-grade infiltrating urothelial carcinoma was the most common neoplastic lesion and chronic non-specific cystitis was the most common non-neoplastic lesion (Table 1). The age of the patients ranged from 21- 86 years with a mean age of 62 years. The mean age for non-neoplastic and neoplastic lesions was 57 years and 64 years respectively.

Table 1: Histological types of non-neoplastic and neoplastic lesions

	Diagnosis	Number (%)
Non-neoplastic lesions	Chronic non-specific cystitis	31 (21.4%)
	Cystitis cystica	6 (4.1%)
	Tuberculosis	3 (2.0%)
	Granulomatous inflammation (fig. 1)	2 (1.4%)
	Brunn nest	1 (0.7%)
	Chemotherapy-induced changes	1 (0.7%)
	Hemorrhagic cystitis	1 (0.7%)
	Urothelial hyperplasia	1 (0.7%)
	Total	**46**
Neoplastic lesions	Infiltrating urothelial carcinoma, high grade	37 (25.5%)
	PUNLMP (fig. 2)	9 (6.2%)
	Non-invasive papillary urothelial carcinoma, low grade (fig. 3)	21 (14.5%)
	Infiltrating urothelial carcinoma, low grade	14 (9.7%)
	Non-invasive papillary urothelial carcinoma, high grade (fig. 4)	7 (4.8%)
	Neuroendocrine tumors	3 (2.0%)
	Squamous cell carcinoma	2 (1.4%)
	Urothelial dysplasia	2 (1.4%)
	Inverted urothelial papilloma	2 (1.4%)
	Urothelial papilloma	2 (1.4%)
	Total	**99**

*PUNLMP: Papillary urothelial neoplasm of low malignant potential

All 46 non-neoplastic lesions were diagnosed on cystoscopic biopsy. Of the 99 neoplastic lesions, 82 cases were diagnosed on cystoscopic biopsy and 17 were on cystectomy specimens. 46 cases (56.1%) out of the 82 neoplastic cases diagnosed on cystoscopic biopsy had muscularis propria included in the biopsy with 10 cases showing its invasion. Most cases with an invasion of the muscularis propria were high-grade infiltrating urothelial carcinoma (8, 80%) and 2 cases of neuroendocrine tumor (20%). The neuroendocrine tumor consisted of 1 case each of small cell neuroendocrine carcinoma (fig. 5) and large cell neuroendocrine carcinoma.

Out of the 17 cystectomy specimens, most cases had high-grade infiltrating urothelial carcinoma (12 cases, 70 %), low grade infiltrating urothelial carcinoma and squamous cell carcinoma (fig.6) was seen in 2 cases (12%) each, and the neuroendocrine tumor was noted in 1 case (6%). The majority of the cystectomy cases(9 cases, 53%) were in stage pT2a, 3 cases (18%) each in pT3a and pT4a stages, and 1 case each (6%) in pT1 and pT2b stages.

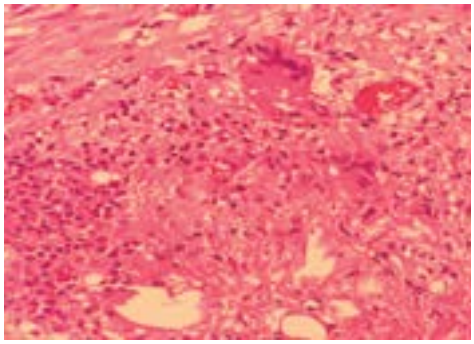

Figure 1: Granulomatous cystitis in a patient with history of intravesical BCG instillation (H and E stain, 400X)

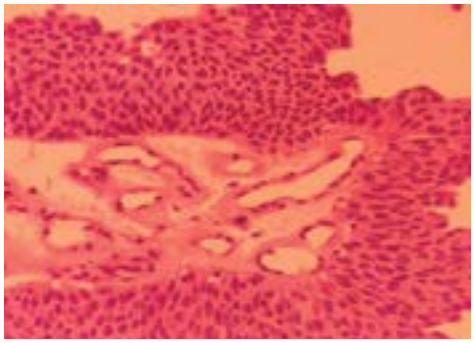

Figure 2: Papillary urothelial neoplasm of low malignant potential (H and E stain, 400X)

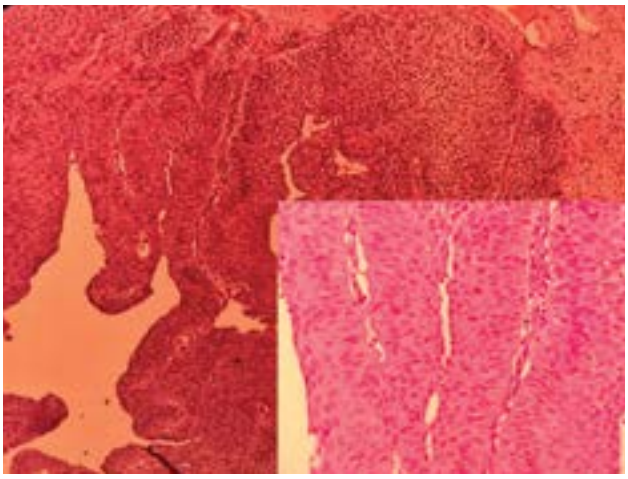

Figure 3: Non- invasive papillary urothelial carcinoma, low grade (H and E stain, 100X, inset: 400X)

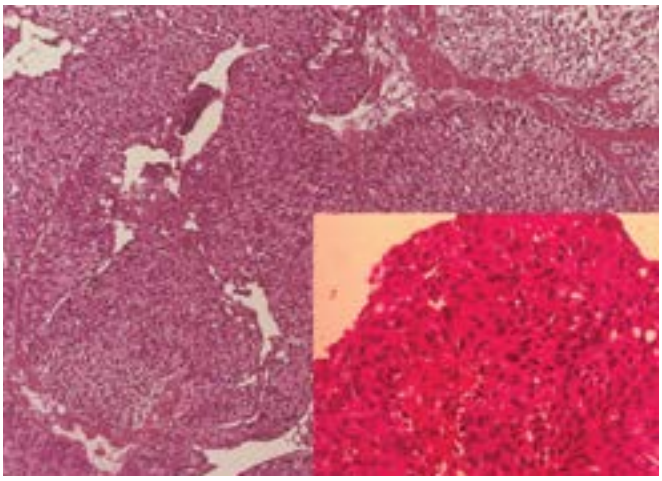

Figure 4: Non- invasive papillary urothelial carcinoma, high grade (H and E stain, 100X, inset: 400X)

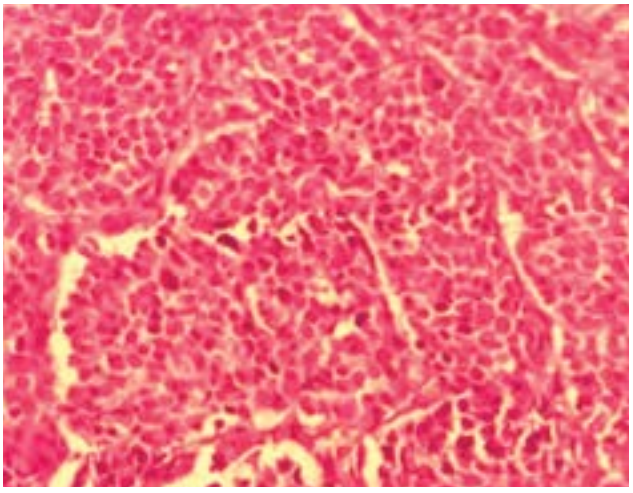

Figure 5: Small cell neuroendocrine carcinoma of urinary bladder (H and E stain, 400X)

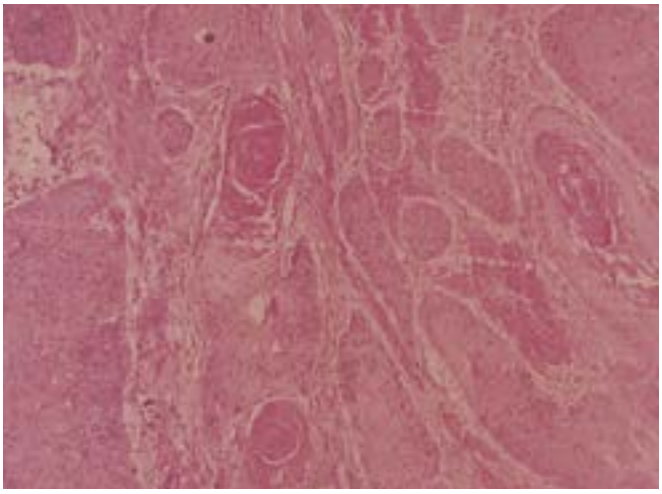

Figure 6: Pure squamous cell carcinoma of urinary bladder (H and E stain, 100X)

DISCUSSION

Cystoscopy assists not only in diagnosis but the additional information obtained from a cystoscopic biopsy can also help in the planning of further treatment for the patient.[6]

In the present study, males were predominant over females with a male to female ratio of 2:1, and the mean age of patients with non-neoplastic lesions was 57 years as compared to the mean age of patients with a neoplastic lesion which was 64 years, which is comparable to other studies.[3,6] Most of the cases in this study consisted of neoplastic lesions (68%). This is was a similar finding in the studies by Srikousthubha et al[1] and Pudasaini et al[6].

The most common non-neoplastic lesion was chronic non-specific cystitis, which is similar to other studies.[1,3,6] Non- specific cystitis can present clinically with hematuria, which can warrant a need for cystoscopy and biopsy. Tuberculosis was noted in 3 cases (2%), which showed necrosis and granuloma with ulceration of the lining epithelium. This is similar to the findings by Srikousthubha et al[1] from Sri Lanka. Urogenital tuberculosis is noted in 2-20% of pulmonary tuberculosis patients. South Asia still has a high prevalence of pulmonary tuberculosis, hence leading to tuberculosis in the urinary bladder in some cases. In the present study, granulomatous inflammation was noted in 2 cases and both the cases had intravesical BCG immunotherapy. Intravesical instillation of BCG activates MHC class II linked cascade of local immune reaction and is characterized microscopically by small loosely textured granuloma in the superficial lamina propria and denudation of the lining epithelium.[7]

The most common neoplastic lesion was infiltrating urothelial carcinoma followed by non-invasive papillary urothelial carcinoma. This is similar to the findings of other studies from Nepal.[2,3,6,8] Studies from India and China also show invasive urothelial carcinoma to be the most common neoplastic lesion of the urinary bladder.[9,10]However, Srikousthubha et al[1] found 87.5% of neoplastic cases to be non-invasive urothelial carcinoma. Urinary bladder cancer is the 10th most common cancer in the world and the 6th most common cancer in males.[11]It is the 5th most expensive cancer in terms of medical care in the United States.[12] The need for lifelong monitoring and treatment along with the long-term survival of patients could be one of the contributing factors.

The frequency of high-grade invasive urothelial carcinoma was more than low grade, which is similar to the findings by Baidya et al.[3] High-grade lesions are more aggressive and thus are more susceptible to invasion.[4] This could also explain the finding of most of the muscle-invasive urothelial carcinomas to be high grade in the present study. Hashmi et al[13] also found that high-grade urothelial carcinoma was associated with deep muscle invasion, higher rates of recurrence, and poor patient survival.

In the present study, detrusor muscle was included in 56.1% of cystoscopy specimens and absent in 43.9%. Pudasaini et al[6] found no detrusor muscle in 33.3% of cystoscopy specimens. Muscle invasive bladder cancers have increased rates of microscopic spread to lymph nodes reducing the chances of cure. Treatment options considered in these cases are also more invasive and include radical cystectomy, chemotherapy, and radical radiotherapy.[14] Therefore, in a cystoscopic biopsy, the presence of detrusor muscle for evaluation of tumor invasion is of utmost importance.

In cystectomy specimens, most of the cases (53%) were in stage pT2a. A study by Cheng et al[15] found most cystectomy specimens had stage pT3 followed by pT2 and pT1. The recent WHO classification of tumors of the urinary bladder warrants the sub-classification of T2 into T2a and T2b i.e., invasion of the inner half and the outer half of the detrusor muscle respectively.[4] Studies have found T2a to be associated with less lymph node metastasis and better survival rates as compared to T2b.[16,17]

In the present study, other than invasive urothelial carcinoma, the invasion of muscularis propria was noted in neuroendocrine carcinoma (1 case each of small cell carcinoma and large cell neuroendocrine carcinoma). Neuroendocrine carcinoma of the urinary bladder is diagnosed at an advanced stage and has an unfavorable prognosis.[13] Squamous cell carcinoma was noted in 2 cases (1.4%), which were in stage pT3a and pT4a respectively. Squamous cell carcinoma of the urinary bladder is noted in patients with Schistosoma infection, spinal injury, and those with long-term use of an indwelling catheter. Studies have shown worse prognosis and rapid disease course when compared to urothelial carcinoma.[18,19]

In the present study, non-invasive papillary urothelial carcinoma constituted 19.3% of all cases, with 21 low grade and 7 high-grade cases. Pudasaini et al[6] had a comparable finding with higher number of low-grade cases. PUNLMP consisted of 9 cases (6.2%), which is similar to other studies.[1,3,6] 2016 WHO classification of tumors of the urinary bladder reconfirms the use of PUNLMP as a separate entity in Ta tumors.[4] Contrary to this, Hentschel et al[20] do not recommend the continued use of PUNLMP. In the present study, there were 2 cases (1.4%) each of urothelial papilloma and inverted papilloma. Thapa et al[8] included 5 cases (8.9%) of papilloma, whereas Pudasaini et al[6] and Srikousthubha et al[1] did not find any such cases. McKenney et al[21] state that urothelial papillomas are histologically and probably biologically distinctive tumors and merit distinction from other high-risk papillary neoplasms of the urinary bladder.

CONCLUSIONS

Non-neoplastic and neoplastic lesions of the urinary bladder have a wide spectrum with the majority of the cases being neoplastic. High-grade urothelial carcinoma and non- urothelial carcinoma have a poor prognosis. The assessment of invasion of the detrusor muscle plays a valuable role in determining the prognosis and management of patients with urinary bladder carcinoma.

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