

## Cystoscopic bladder biopsies: A histopathological study

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### ABSTRACT

Urothelial carcinoma is the most common tumor of the bladder and is a major cause of morbidity and mortality. Cystitis constitutes an important source of clinical signs and symptoms. In this study 31 cystoscopic biopsies subjected for histopathological examination were taken. The study was conducted in the department of Pathology of Nepal Medical College Teaching Hospital over a period of two years (October 2012 to September 2014). The mean age of the patient undergoing cystoscopic biopsy was 61.3 years, most of the patients being elderly male. 51.6% cases were clinically malignant. The most common histopathological diagnoses were cystitis (29%) and non invasive papillary urothelial carcinoma, low grade (29%). 58% are neoplastic lesions. 51.6% of the case was malignant lesions on histopathology. Among the malignant lesion of urinary bladder 93.7% were urothelial tumor and 6.3% were glandular neoplasm (adenocarcinoma, signet ring cell). There was no detrusor muscle in 33.3% cases of urothelial tumor to assess the muscle invasion. 26.7% cases of urothelial tumor shows muscle invasion. Histopathological study of cystoscopic biopsy helps in early detection of tumor and its management.

**Keywords:** Urinary bladder, biopsy, cystoscopy, urothelial tumor

### INTRODUCTION

Neoplastic urinary bladder lesions are responsible for significant morbidity and mortality throughout the world.<sup>1</sup> Urothelial carcinoma is the most common tumor of the bladder, representing 90% of malignancies with this origin.<sup>2,3</sup> Urinary bladder cancer is the sixth most common cancer worldwide and the second most common malignancy of the genitourinary tract after prostate cancer.<sup>4</sup> Bladder neoplasms account for 6% and 2% of the cancer incidence in men and women respectively. Most cases present in patients over the age of 50 years.<sup>5,6</sup>

The prevalence of these tumors is higher in developed countries as compared to developing countries. The most common sign is gross and microscopic hematuria and is seen in more than 75% of the patients. Men are affected more often than women and about 80% of patients are between the age of 50 and 80 years.<sup>6</sup> Cystoscopy is the primary diagnostic tool for patients of bladder tumors.<sup>1</sup> Bladder transurethral resection of the tumor is a therapeutic procedure that ensures the material necessary for histopathological diagnosis because it allows assessment of the degree of differentiation, depth of tumor invasion, parameters useful in elaboration of diagnosis and prognosis assessment.<sup>2</sup>

The present study aimed to study the histopathological features of various lesions of the urinary bladder through cystoscopic biopsy over a period of two years in a teaching hospital.

### MATERIALS AND METHODS

This is a study conducted in the department of Pathology of Nepal Medical College Teaching Hospital over a period of two years (October 2012 to September 2014). All patients who visited urology Out Patient Department (OPD) and subjected to cystoscopic biopsy were included in this study. The cystoscopic biopsies taken by Urologist were sent to the Department of Pathology for processing. Biopsies were fixed in 10% formalin for 24 hours before the tissue is processed for paraffin blocking. Five micron sections were cut and the prepared slides were stained with Hematoxylin and Eosin (H & E) stain. The histopathological features were studied and relevant findings were noted. Patient's history, clinical diagnosis and any significant preoperative or operative findings were also obtained from the patient's record file and histopathological forms. The World Health Organization (WHO) classification of the urinary tract was used to grade the tumors into infiltrating urothelial carcinoma, non invasive urothelial neoplasia (low grade and high grade) and glandular neoplasm.

### RESULTS

A total of 31 cystoscopic biopsies were taken in a study period. Out of these cases 80.6% were male and 19.4% were female with a male to female ratio of 4.2:1. Malignancy was more commonly seen in male patients (87.5%). The age ranges from 23 years to 80 years with mean age of 61.3 years. Out of 31 cases, 18 cases (58%)

were above 60 years and 26 cases (83.9%) were above 50 years. 83.9% patients came with urinary complaints like difficulty and burning micturition, other 58% came with hematuria. Table-1 shows the clinical diagnosis and table-2 shows the histopathological diagnosis.

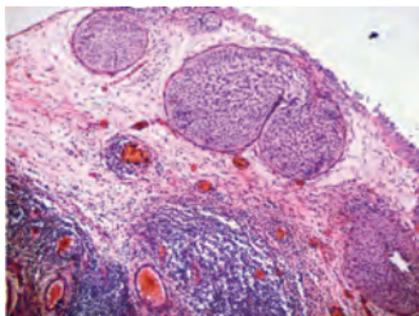
**Table - 1:** Clinical diagnosis

| Clinical diagnosis    | No. of cases | Percentage  |
|-----------------------|--------------|-------------|
| Urinary bladder mass  | 4            | 12.9%       |
| ? Carcinoma bladder   | 16           | 51.6%       |
| Urinary bladder polyp | 1            | 3.2%        |
| Papillary tumor       | 3            | 9.7%        |
| Cyst                  | 2            | 6.5%        |
| Cystitis              | 5            | 16.1%       |
| <b>Total</b>          | <b>31</b>    | <b>100%</b> |

**Table-2:** Histopathological diagnosis

| Histopathological diagnosis                                | No. of cases | Percentage  |
|--|--------------|-------------|
| Infiltrating urothelial carcinoma                          | 4            | 12.9%       |
| Non invasive Papillary urothelial carcinoma, low grade     | 9            | 29%         |
| Non invasive Papillary urothelial carcinoma, high grade    | 2            | 6.5%        |
| Glandular neoplasm, Adenocarcinoma, signet ring cell       | 1            | 3.2%        |
| Urothelial dysplasia (Low grade intraurothelial neoplasia) | 2            | 6.5%        |
| Cystitis   | 9            | 29%         |
| Necrosis and inflammation                                  | 4            | 12.9%       |
| <b>Total</b>   | <b>31</b>    | <b>100%</b> |

Clinically 51.6% cases were diagnosed as malignant lesion. In 12.9% cases mass was seen but it was not diagnosed as either malignant or benign lesion. Necrosis and inflammation was seen in histopathology in 12.9% cases. However one case showed the urothelial lining epithelium with hyperplasia but no dysplasia or malignancy. Cystitis (29%) was the most common non malignant lesion including follicular and polypoid type. Brunn's nests were seen in 44.4% cases of cystitis (Fig 1). Urothelial tumor (93.7%) was the commonest type of malignant lesion in the urinary bladder and 6.3% were glandular neoplasm (adenocarcinoma, signet ring cell) (Fig 2). There was no detrusor muscle in 33.3% cases of urothelial tumor to assess the muscle invasion. Muscle invasion was seen 26.7% cases of urothelial tumor. Vascular invasion was seen in one case of infiltrating urothelial carcinoma.



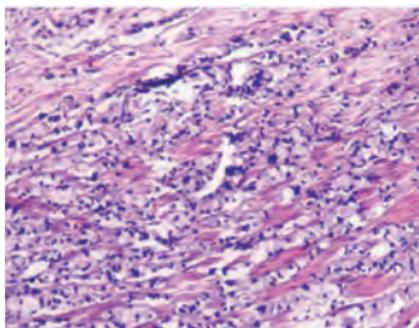
**Fig 1:** Cystitis with Brunn's nests (100X, H and E Stain)

## DISCUSSION

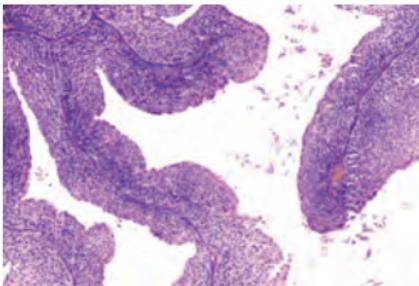
Cystoscopy is the primary diagnostic tool in the diagnosis of urinary bladder carcinoma. The histopathological study of the cystoscopic biopsy not only gives the diagnosis but also provides the additional information to the urologist that can have impact on the treatment.

In the present study 80.6% were male and 19.4% were female with a male to female ratio of 4.2:1. Similar finding was seen in several studies of cystoscopic biopsy.<sup>4,7</sup> Bladder carcinoma is more common in elderly males. The sex incidence of bladder tumor in our study was 87.5% male and 12.5% female. 58% patients were above 60 years and 83.9% were above 50 years. This is similar to that reported in the existing literature.<sup>2,5,8</sup>

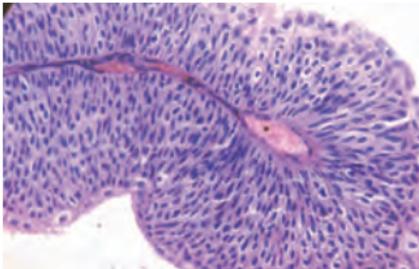
Hematuria is the most common symptom that will bring the patient to the hospital. In our study, 58% patients came with hematuria. More than 75% of patients of urinary bladder tumor had presented with hematuria in other studies.<sup>8-11</sup>



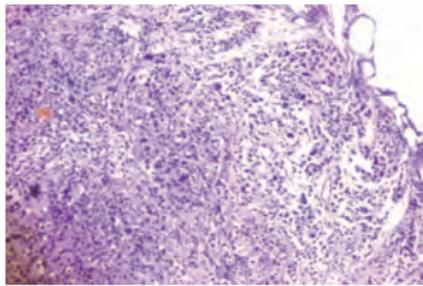
**Fig 2:** Adenocarcinoma, Signet ring cells splitting the muscle fibres (400X, H and E Stain)



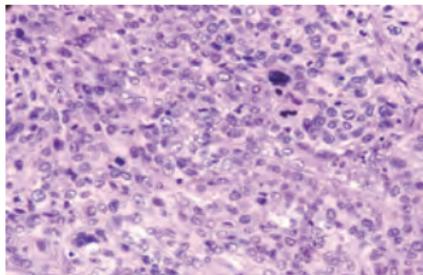
**Fig 3:** Non invasive papillary urothelial carcinoma, low grade (100X , H and E Stain)



**Fig 4:** Non invasive papillary urothelial carcinoma, low grade (400X, H and E Stain)



**Fig 5:** Infiltrating urothelial carcinoma (100X, H and E Stain)



**Fig 6:** Infiltrating urothelial carcinoma with highly pleomorphic cells increased atypical mitosis (100X , H and E Stain)

Cystitis (29%) was the most common lesion among the non neoplastic lesion. There were cases of follicular cystitis and polypoid cystitis. One study done in India showed 35% of cystitis and another study done in Kathmandu valley showed 44% of cystitis.<sup>7,12</sup> Brun's nests are reactive proliferative changes within the urothelium and are common in biopsy of inflammatory lesions and in bladder carcinoma. In our study, 44.4% cases of cystitis and 11.8% cases of urothelial neoplasm showed brun's nest. Srikousthuba et al<sup>1</sup> had shown the association of brun's nest with cystitis in his study.

Urothelial tumor (93.7%) was the commonest type of malignant lesion. Among the urothelial neoplasm, the most common histopathological diagnosis was non invasive papillary urothelial carcinoma, low grade (29%) (Fig 3& Fig 4) followed by infiltrating urothelial carcinoma (12.9%) (Fig 5 & Fig 6) and non invasive papillary urothelial carcinoma, high grade (6.5%). This correlates well with other studies.<sup>1,5,6,7,10</sup> The only case of adenocarcinoma, signet ring cell was seen in 80 years old male patient. Primary signet ring cell carcinoma of the urinary bladder is a rare histologic variant of adenocarcinoma with poor prognosis. It accounts for 2% of all malignant urinary bladder tumors.<sup>13</sup> Studies had also shown that adenocarcinoma is a rare variant of urinary bladder carcinoma.<sup>5,9</sup>

There were 6.5% cases of dysplasia (low grade intraurothelial neoplasia) in our study. Ranadive et al<sup>11</sup> also showed the similar finding in his study. Dysplasia has appreciable cytological and architectural changes felt to be preneoplastic but which fall short of carcinoma in situ.<sup>14</sup>

In contrast to the studies done in South East Asian countries and Western countries, Nigeria has squamous cell carcinoma as the most common type of urinary bladder carcinoma. This is because of high frequency of association of squamous cell carcinoma with schistosomiasis.<sup>15</sup> However this pattern has been changing in Egypt in the last few years. There is decline in squamous cell carcinoma and increase in urothelial carcinoma.<sup>16</sup>

In 33.3% cases, there was no detrusor muscle in the biopsy specimens of urothelial tumor. Hence, the invasion was assessed only in 66.7% cases. Laishram et al<sup>5</sup> could also assess only 83% cases for invasion and out of that 42.1% cases showed muscle invasion.<sup>5</sup> Our study showed 26.7% cases of invasive urothelial carcinoma. Other studies showed 35.8%, 27.2% and 26% of muscle

invasion in urothelial carcinoma respectively.<sup>6,17,18</sup>

This study documents a high frequency of urothelial tumor, mostly non invasive papillary urothelial neoplasm, low grade with a male preponderance in the age group above 60 years. Invasion to the muscle layer correlates with high grade tumor. Hence, inclusion of detrusor muscle in the cystoscopic biopsy is very important.

#### REFERENCES

1. Srikoushubha, Suresh, Raghuvver C.V, Hingle S. Profile of Lesions in Cystoscopic Bladder Biopsies -A Histopathological Study. *J Clin Diagn Res* 2013; 7: 1609-12.
2. Stepan A, Simionescu C, Margaritescu C, Ciurea R. Histopathological study of the urothelial bladder carcinomas. *Current health Science Journal* 2013; 39:147-150.
3. Stepan A, Florescu A, Mitrut A, Margaritescu C, Simionescu C. Histological variants of urothelial bladder carcinoma. *Current health Sciences Journal* 2010; 36:139-42.
4. Al- Samawi AS, Aulqi SM. Urinary bladder cancer in Yemen. *Oman Med J* 2013; 28: 337-40.
5. Laishram RS, Kipgen P, Laishram S, Khurajam S, Sharma DC. Urothelial tumors of the urinary bladder in Manipur: a histopathological perspective. *Asia Pacific Journal of Cancer Prevention*. 2012; 13: 2477-9.
6. Viadya S, Lakhey M, KC S, Hirachand S. Urothelial tumors of the urinary bladder: a histopathological study of cystoscopic biopsies. *J Nepal Med Assoc* 2013; 52: 475-8.
7. Kumar UM, Yelkar BR. Spectrum of lesions in cystoscopic bladder biopsies- a histopathological study. *Al Ameen J Med Sci* 2012; 5: 132- 6.
8. Islam AHMT, Mostafa SN, Rahman M, Nahar Z. Role of ultrasound in the evaluation of urinary bladder neoplasm with histopathological correlation. *Journal of Teachers Association TAJ* 2008; 21:155-9.
9. Murphy DM, Zincke H, Furlow WL. Management of high grade transitional cell cancer of the upper urinary tract. *J Urol* 1981; 125: 25-9.
10. Ahmed Z, Muzaffer S, Khan M *et al*. Transitional cell carcinomas of the urinary bladder: a histopathological study. *J Pak Med Assoc* 2002; 52: 396-9.
11. Ranadive NU, Deodhar KP, Bapat SD. Usefulness of urinary bladder biopsies- study of 98 cases. *J Postgrad Med* 1983; 29:10-4.
12. Rauniyar SK, Agrawal A, Shah A. A study of cystoscopic biopsies in Kathmandu valley. *J Nepal Med Assoc* 2001; 40: 181- 5.
13. Kapur P, Lotan Y, King E *et al*. Primary Adenocarcinoma of the urinary bladder. *Am J Clin Pathol* 2011; 135: 822-30.
14. Pindiga UH, Bama ML, Abdullahi M. Carcinoma of the urinary bladder in Maiduguri, Nigeria: a retrospective histopathological study of 100 cases. *Highland Medical Research Journal* 2004; 2:41-44.
15. Felix AS, Soliman AS, Khaled H *et al*. The changing patterns of bladder cancer in Egypt over the past 26 years. *Cancer Causes & Control* 2008;19: 421-9.
16. Eble JN, Sauter G, Epstein JI, Sesterhenn IA, *editors*. World Health Organization of tumors- tumors of the urinary system and male genital organs. *IARC Press, Lyon*, 2004.
17. Biswas RR, Mangal S, Guha D, Basu K, Karmakar D. An epidemiological study of cases of urothelial carcinoma of urinary bladder in a tertiary care centre. *Journal of Krishna Institute of Medical Sciences* 2013; 2: 82-8.
18. Gupta P, Jain M, Kapoor R, Muruganandham K, Srivastava A, Mandhani A. Impact of age and gender on the clinicopathological characteristics of bladder cancer. *Indian J Urol* 2009; 25: 207-10.