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A histopathologic study of urinary bladder tumors at tertiary care center in Mid-Western region of Nepal

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ABSTRACT

Background: Urinary bladder cancer is an important cause of morbidity and mortality due to urological conditions. It is tenth most common cancer overall in both sexes. It is seventh most common cancer overall and second most common cancer of genitourinary tract in males. Ninety five percent of bladder tumors are epithelial and the rest are mesenchymal, of which majority are primary urothelial tumors. Urothelial tumors are classified into infiltrating urothelial carcinoma with its variants and non-invasive urothelial neoplasias. Tumor stage is the strongest prognostic parameter. **Aims and Objectives:** The current study was designed with an aim to elucidate the histologic pattern of bladder tumors and observe whether any association between histologic grade and muscle invasion exists. **Materials and Methods:** This descriptive study was carried out on 84 cases of urinary bladder tumors received in Department of Pathology, College of Medical Sciences and Teaching Hospital during a time period of 5 years from January 2012 to December 2016. **Results:** The mean ± SD of age of presentation was 63 ± 13 years with a male female ratio 3.2:1. Ninety-five percent cases were primary epithelial tumors and 93% cases were of urothelial origin. Low grade papillary urothelial carcinoma was the most common urothelial tumor (40.5%) followed by high grade papillary urothelial carcinoma (34.5%). Some rare types like primary adenocarcinoma and small cell carcinoma were also seen in this study (1.2% each). Muscle invasion was significantly higher in high grade (66%) as compared to low grade papillary urothelial carcinoma (3%). Muscle tissue was absent in 8 (9.5%) cases. **Conclusion:** There is relationship of histologic grade with aggressiveness of tumor. Most of the high grade tumors are muscle invasive at presentation. Submission of muscle tissue is important for optimal patient management.

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Key words: Urinary bladder; bladder tumor; urothelial tumor

INTRODUCTION

Lesions of urinary bladder are responsible for significant morbidity and mortality throughout the world.[1] Bladder cancer is the tenth most common cancer overall in both sexes with 430,000 new cases diagnosed in the year 2012 worldwide. It is seventh most common cancer overall and second most common cancer of genitourinary tract in males.[2] In Nepal, it is fourth most common cancer in males.[3] It is three times more common in males than females worldwide with 80% cases occurring in between 50 to 80 years age group.[4] Prevalence of bladder tumors is six times higher in developed as compared to developing countriesand is higher in urban areas than rural areas.[4,5]

The most common presenting problem of bladder cancer is painless hematuria.[4,6] Other symptoms may be dysuria, urgency, frequency, palpable pelvic mass or weight loss and bone pain in advanced disease. Various imaging modalities like ultrasonography, intravenous urography, computed tomography and magnetic resonance imaging can be used for detection and staging.[5] Diagnosis can be confirmed by cystoscopic examination.[1,5] However, cystoscopic examination has a limited role in staging process for which transurethral

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resection (TURB) of visible tumor down to the base is required which can accurately assess depth of tumor invasion.[7,8]

Ninety-five percent of bladder tumors are epithelial and the rest are mesenchymal. Urothelial tumors account for approximately 90% cases of primary urinary bladder tumors. These range from benign, innocuous lesions that do not recur to aggressive tumors that can be fatal.[4, 9, 10] The ISUP/WHO (2004) classify urothelial tumors into infiltrating urothelial carcinoma with its variants and non-invasive urothelial neoplasias. The latter is further subclassified into urothelial carcinoma in situ, papillary urothelial carcinoma, high grade and low grade, papillary urothelial neoplasm of low malignant potential (PUNLMP), urothelial papilloma and inverted urothelial papilloma.[5]

There are several clinical and morphological prognostic factors for bladder tumors like patient age, topography of the lesion, multifocality, tumor size, growth pattern, concurrent dysplasia/carcinoma in situ, histologic type, grade and tumor stage.[4, 5,11] Strongest of these is tumor stage for prognosis and treatment.[5, 10-13]

This study was aimed to elucidate the histomorphological profile of bladder tumors in this region of Nepal and correlate its histological grade with muscle invasion.

MATERIALS AND METHODS

This Hospital record based cross-sectional study (historical)was carried out in Department of Pathology, College of Medical Sciences and Teaching Hospital. Ethical approval from the Institutional Review Committee was obtained. Eighty-four consecutive cystoscopic biopsies, TURBT specimens and radical cystectomies received in the Histopathology section of Department of Pathology of College of Medical Sciences and Teaching Hospital during a time period of 5 years from January 2012 to December 2016 diagnosed with bladder tumor were included in the study. Suboptimal biopsies with crushing artefacts were excluded from the study. All the cases of urinary bladder tumors received in the study period were reviewed.WHO(2004)/ISUP classification was used to classify bladder tumors.[5] Data was analyzed with SPSS 16. Presence of muscle tissue was noted in the cystoscopic biopsies and TURBT specimens. Association between muscle invasion and histologic grade was tested using Chi-square test. Level of significance was considered as 5%.

RESULTS

Total 84 cases of urinary bladder tumors were received in the study period. Age of the patients ranged from 22 to 87 years with maximum cases 25 (30%) in more than 70 years age group. The mean ± SD of age was 63±13 years. There were 64 (76%) males and 20 (24%) females with male to female ratio 3.2:1.

Histopathological diagnoses made were urothelial dysplasia in 1 (1.2%), urothelial papilloma (Figure 1) in 4 (4.8%), inverted urothelial papilloma (Figure 2) in 1(1.2%), PUNLMP (Figure 3, 4) in 9 (10.7%), low grade urothelial carcinoma (Figure 5, 6) in 34 (40.5%), high grade urothelial carcinoma (Figure 7, 8) in 29 (34.5%), adenocarcinoma (Figure 9) in 1 (1.2%), small cell carcinoma (Figure 10) in 1 (1.2%) and secondaries from other sites in 4 (4.8%) cases (Table 1).

Out of 34 cases of low grade urothelial carcinoma, 18 (53%) were non-invasive, 12 (35%) showed lamina propria

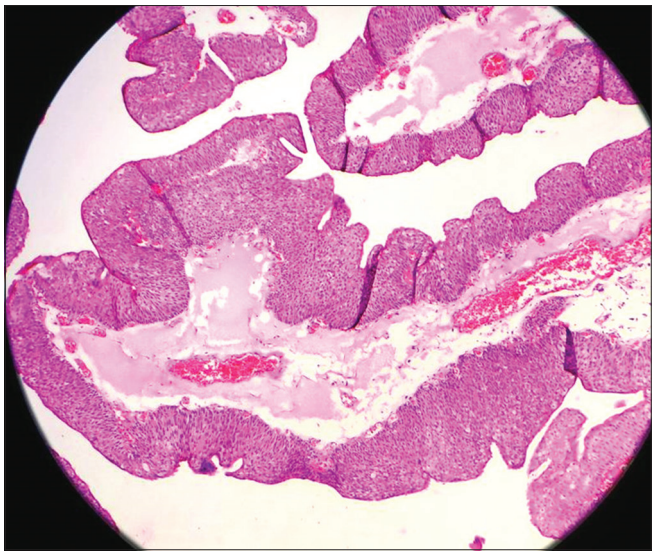

Figure 1: Urothelial papilloma (H and E X100)

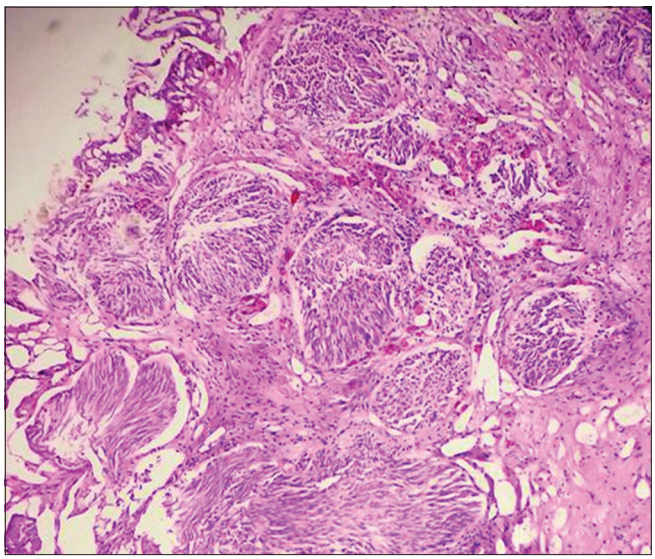

Figure 2: Inverted urothelial papilloma (H and E X100)

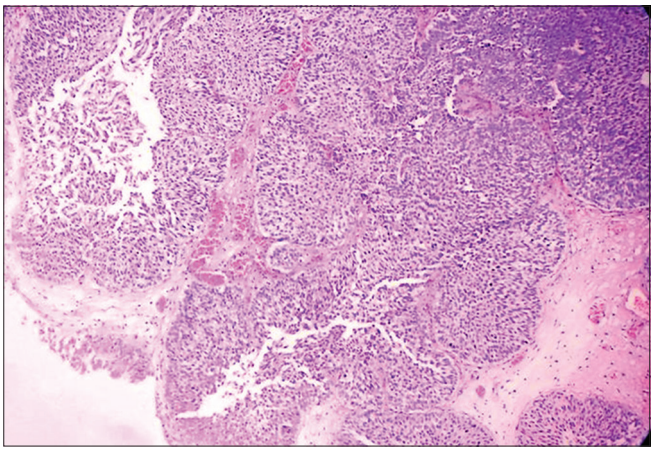

Figure 3: PUNLMP (H and E X100)

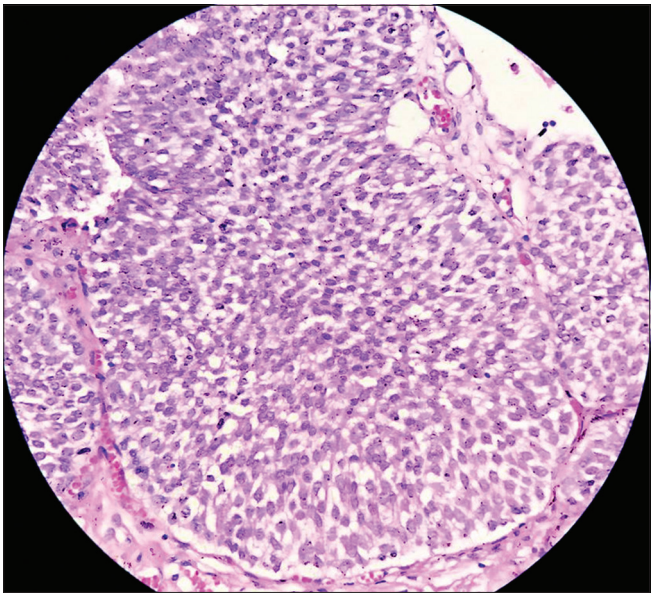

Figure 4: PUNLMP (H and E X400)

invasion, 1 (3%) showed muscle invasion and muscle tissue was not seen in 3 (9%) cases. Out of 29 cases of high grade urothelial carcinoma, 19 (66%) showed muscle invasion (Figure 11), 5 (17%) showed lamina propria invasion and 5 (17%) cases had no muscle tissue (Table 2). There was statistically significant association between muscle invasion and histologic grade ($\chi^2 = 33.71$, d.f = 1, p-value < 0.001).

DISCUSSION

Urinary bladder neoplasms are a heterogeneous group with different subtypes having varied behavior and outcomes.[9, 14] More than 95% tumors are epithelial, out of which majority are of urothelial origin and very few are other histological types.[5]

In this study on 84 cases of urinary bladder tumors, mean age of presentation was 63 years (range 22 to 87 years) which is comparable to other studies.[9, 10, 15] Five (6%) cases of

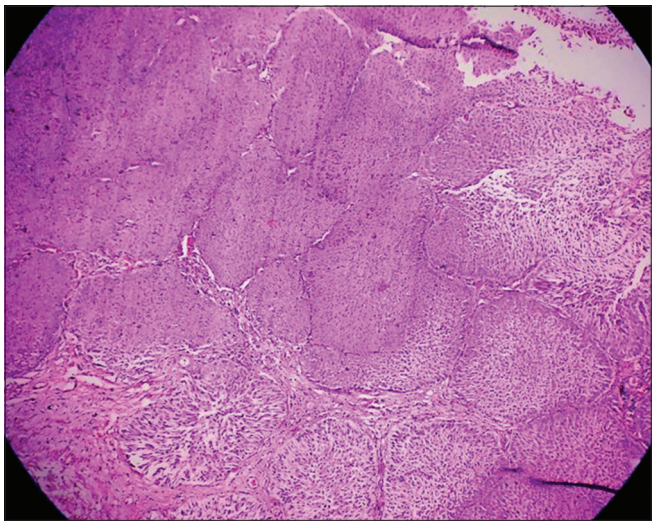

Figure 5: Low grade urothelial carcinoma (H and E X100)

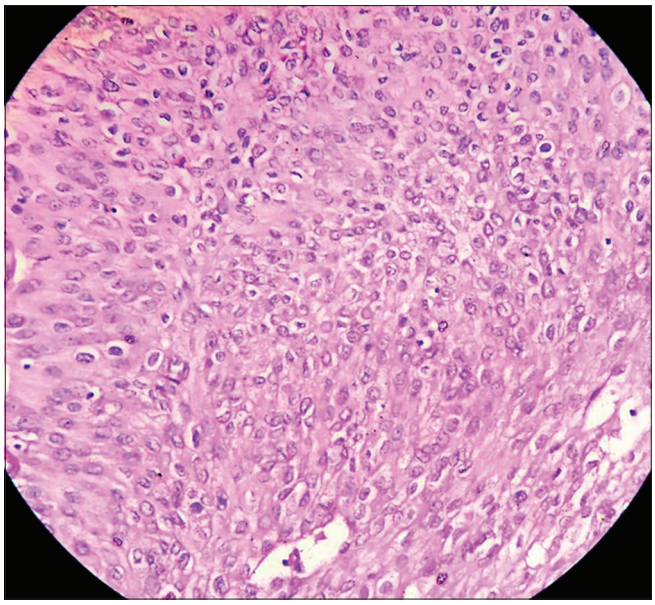

Figure 6: Low grade urothelial carcinoma (H and E X400)

bladder tumors were seen in patients younger than 40 years out of which 3 were high grade urothelial carcinoma, 1 was primary adenocarcinoma and 1 was urothelial papilloma. Various literatures state that bladder tumors present at low grade and low stage in younger individuals.[16-18] However, this was not supported by this study where high grade urothelial carcinoma was more common in younger individuals. Larger sample size is required for conclusive results. Males are more commonly affected.[9, 10, 15, 16] This was supported by the present study where male female ratio was 3.2:1. Higher incidence in males may be due to differences in smoking habits and occupational exposure.[4, 16]

Primary epithelial tumors were more common in this study (95.2%). Secondaries from other sites like cervix (in 3 cases) and colon (in 1 case) were seen in 4 (4.8%) cases.

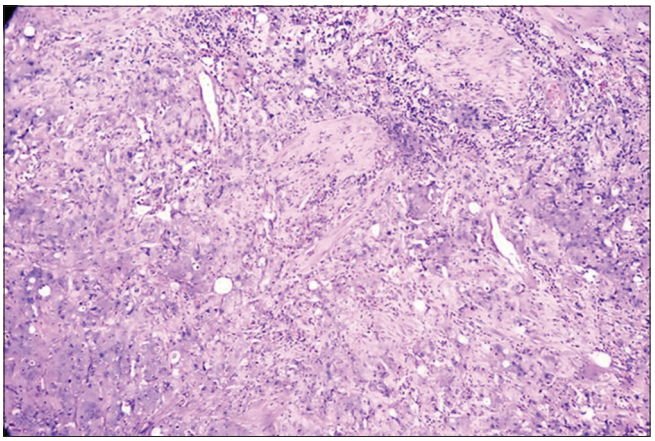

Figure 7: High grade urothelial carcinoma (H and E X100)

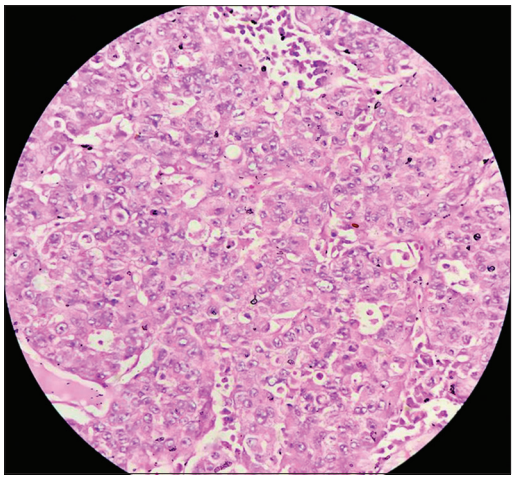

Figure 8: High grade urothelial carcinoma (H and E X400)

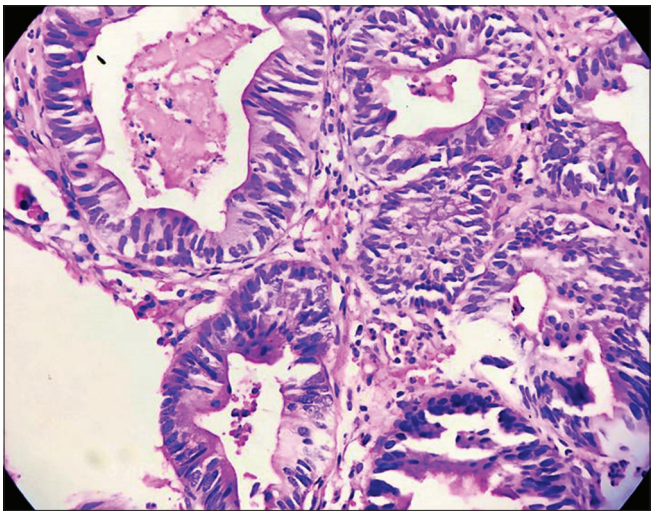

Figure 9: Primary adenocarcinoma of urinary bladder (H and E X400)

Ninety-three percent tumors were of urothelial origin. This finding was similar to other studies.[9, 10, 15] Low grade papillary urothelial carcinoma was the most common urothelial tumor (40.5%) in this study which is similar to

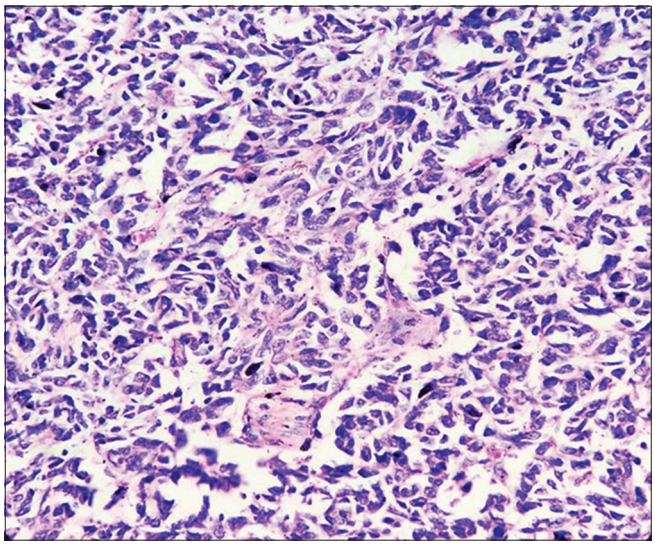

Figure 10: Primary small cell carcinoma of urinary bladder (H and E X400)

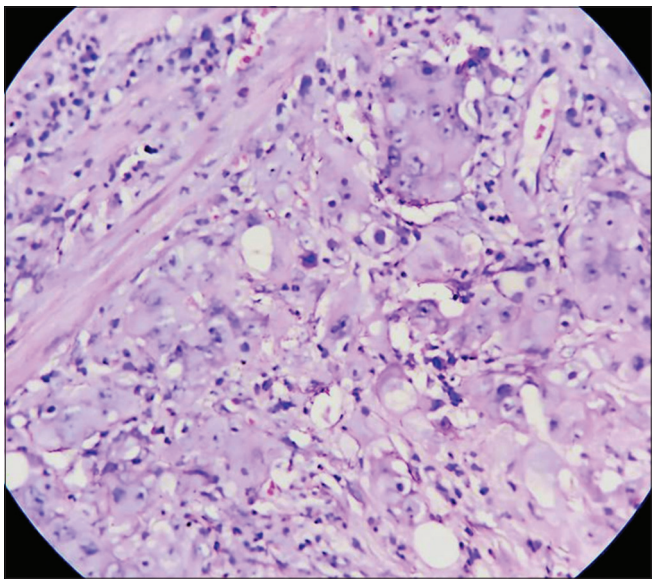

Figure 11: Muscle invasion in high grade urothelial carcinoma (H and E X400)

findings of Laishram et al. (2012)[10] and Pudasaini et al. (2014).[15] However, high grade papillary urothelial carcinoma was more common in study done by Vaidya et al. (2013).[9] Small cell carcinoma is a rare and aggressive malignancy in urinary bladder and its incidence varies between 0.35 to 1.8% in various studies.[15, 19, 20] Small cell carcinoma was seen in 1 (1.2%) case in this study in a 66 years old male. One case (1.2%) was primary adenocarcinoma in a 34 years old male patient. Primary adenocarcinoma is a rare malignancy occurring in urinary bladder with secondary extension from colorectal adenocarcinoma being more common.[9, 15, 21, 22]

Most important prognostic parameters are histologic grade and stage of tumor.[9, 23] Detection of muscle invasion is

Table 1: Histopathological diagnoses in various age groups

S.N	Histopathological diagnosis	Age group (years)					Total
		<40	41 – 50	51 – 60	61 – 70	>70	
1.	Urothelial papilloma	1	1	0	2	0	4
2.	Inverted urothelial papilloma	0	0	1	0	0	1
3.	PUNLMP	0	1	0	3	5	9
4.	Low grade urothelial carcinoma	0	4	10	9	11	34
5.	High grade urothelial carcinoma	3	5	6	7	8	29
6.	Adenocarcinoma	1	0	0	0	0	1
7.	Small cell carcinoma	0	0	0	1	0	1
8.	Urothelial dysplasia	0	0	0	0	1	1
9.	Secondaries from other sites	0	2	1	1	0	4
Total		5	13	18	23	25	84

Table 2: Level of invasion in histopathological diagnoses

S.N	Histopathological diagnosis	Level of invasion				Total
		Muscularispropria	Lamina propria	Non-invasive	No muscle tissue	
1.	Urothelial papilloma	0	0	4	0	4
2.	Inverted urothelial papilloma	0	0	1	0	1
3.	PUNLMP	0	0	9	0	9
4.	Low grade urothelial carcinoma	1	12	18	3	34
5.	High grade urothelial carcinoma	19	5	0	5	29
6.	Adenocarcinoma	1	0	0	0	1
7.	Small cell carcinoma	1	0	0	0	1
8.	Urothelial dysplasia	0	0	1	0	1
9.	Secondaries from other sites	4	0	0	0	4
Total		26	17	33	8	84

of paramount importance because of its influence on therapy and prognosis.[24] Muscle invasion was significantly seen more in cases of high grade urothelial carcinoma as compared to low grade urothelial carcinoma (66% versus 3%). This finding is also seen in various other studies in literature supporting correlation of histologic grade with aggressiveness of tumor.[9, 10, 15] Muscle tissue was absent in 8 (9.5%) cases. This emphasizes the need of submission of muscle tissue for optimal patient management.

CONCLUSION

Bladder tumors are important urological conditions. Primary epithelial malignancies are more common. Urothelial tumors are the most common bladder tumors. Though rare, other primary epithelial malignancies can also present in urinary bladder. More than 50% of high grade urothelial carcinomas were found to be muscle invasive at presentation suggesting correlation of histologic grade with aggressiveness.

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Authors Contribution:
BG - Concept and design of the study, manuscript preparation, statistically analyzed and interpreted,critical revision of the manuscript; **TSR -** Concept and design of the study, critical revision of manuscript and review of the study; **RS -** reviewed the literature, helped in preparing first draft of manuscript, collected data; **SJ -** collected data, statistically analyzed and interpreted, helped in preparing first draft of manuscript.

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