

Histopathological Spectrum of Urinary Bladder Tumors: One Year Study in a Tertiary Health Care Centre

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ABSTRACT

Introduction: This study was conducted to describe the Histopathological spectrum of various urinary bladder tumors and to classify them according to W.H.O(2004)/ISUP classification of urinary bladder tumors.

Methods: This was a cross-sectional, observational study carried out between June 1, 2019 to May 31, 2020 for a period of one year in the Department of Pathology and Urology, Indira Gandhi Medical College, Shimla. One hundred and ninety seven patients (TURBT and radical cystectomy) with primary epithelial urinary bladder cancer were included in the study. However, Patients with inflammatory and metastatic lesions of urinary bladder and post chemoradiotherapy were excluded from the study.

Results: The age of patients ranged from 36 to 89 years with mean age of 62 years. Male preponderance was observed with male to female ratio of 6.9:1. Most common histological type found in our study was urothelial carcinoma (98%) followed by other types such as Squamous cell carcinoma (1%), Small cell carcinoma (0.5%) and Adenocarcinoma (0.5%). In urothelial tumors (193), majority, 126(65.3%) cases, were high grade urothelial carcinoma followed by 67(34.7%) cases of low grade urothelial carcinoma.

Conclusion: High grade urothelial carcinomas were mostly associated with muscularis propria invasion.

Keywords: Urinary Bladder Tumors, Histopathological Spectrum, High grade urothelial carcinomas

INTRODUCTION

Bladder cancer has become quite prevalent today with approximately 5,50,000 new cases reported worldwide in 2018 and are responsible for significant morbidity and mortality throughout the world. It is the 6th most commonly occurring cancer in men and ranks 17th in women¹. In India, the incidence of urinary bladder cancer has been reported as 3.67% among males and 0.83% in females with overall incidence being 2.25%².

Majority of bladder tumors are epithelial in origin. Most common are urothelial/transitional neoplasms comprising approximately 90% of all primary tumors followed by squamous cell carcinoma (5%) and primary adenocarcinoma (2%). Small cell carcinoma and sarcomas are encountered much less frequently³.

Most cases of urothelial carcinoma present in patients between 50 -80 years of age group with male to female ratio of 3 to 4:1³. Cigarette smoking, occupational carcinogens from chemical industry, Schistosoma hematobium infection in endemic areas, use of artificial sweeteners

are known risk factors⁴. Most common presenting symptom is painless hematuria. Others symptoms may be dysuria, urgency, frequency, palpable pelvic mass, weight loss etc⁵.

Cystoscopy is the primary diagnostic modality for patients with suspected bladder tumors used for localization and performing biopsy of suspected lesions. Trans urethral removal of bladder tumor (TURBT) is a therapeutic procedure that allows assessment of degree of differentiation and depth of tumor invasion which are important parameters for diagnosis and prognosis. Tumor size, stage, grade and multifocality are important factors predictive of tumor progression⁴

Low grade urothelial tumors usually arise from simple hyperplasia or minimal dysplasia of normal urothelium. They are characterized by loss of heterozygosity (LOH) of chromosome 9 and activating mutation of fibroblast growth factor receptor 3 (FGFR3), telomerase reverse transcriptase (TERT) and phosphatidylinositol 4,5 bisphosphate 3-kinase catalytic subunit alpha isoform (PIK3CA). Low grade NMIBC can progress to MIBC as a result of gaining cyclin-dependent kinase inhibitor 2A (CDKN2A) loss⁶⁻⁹.

MIBC arise from flat dysplasia or carcinoma in situ (CIS) and have TP53 mutations and LOH of chromosome 9. They can further acquire metastatic potential by gaining retinoblastoma (RB) mutations and phosphatase and tensin homolog (PTEN) gene loss along with other alterations⁶⁻⁹.

Thus, the present study described the histopathological spectrum of urinary bladder tumors and classified them according to W.H.O(2004)/ISUP¹⁰ classification of urinary bladder tumors.

METHODS

This was a cross-sectional, observational study carried out between June 1, 2019 to May 31, 2020 for a period of one year in the Department of Pathology and Urology, Indira Gandhi Medical College, Shimla. Patient consent and ethical clearance from institutional ethical committee was taken. One hundred and ninety seven patients (TURBT and radical cystectomy) with primary epithelial urinary bladder cancer were included in the study. Patients with inflammatory and metastatic lesions of urinary bladder and post chemoradiotherapy were excluded from the study. Clinical presentation of these patients was noted. All samples were fixed in 10% neutral buffered formalin and followed by standard processing and staining. Diagnosis was made as per WHO/ISUP classification (2004)¹⁰. Urothelial tumors were graded into low grade and high grade categories and their invasion into lamina propria and muscularis propria was assessed according to WHO/ISUP (2004) classification.

RESULTS

One hundred ninety seven specimens including both TURBT (191) and cystectomy (6) were received in the Department of Pathology. The age of patients ranged from 36 to 89 years with mean age of 62 years. Male preponderance was observed in this study with male to female ratio of 6.9:1.

Most common histological type found was urothelial carcinoma (98%) followed by other types such as squamous cell carcinoma (1%), small cell carcinoma (0.5%) and adenocarcinoma (0.5%). Among urothelial tumors (193), majority, 126 (65.3%) cases, were high-grade urothelial carcinoma followed by 67(34.7%) cases of low-grade urothelial carcinoma. Among HGUC, 99 cases had papillary configuration and 27 were non-papillary invasive carcinomas and its variants.(Table 1).

Table 1. Histopathological spectrum of urinary bladder tumors according to WHO 2004 classification

S. No.	Histological type of tumor	No. of cases	Percentage
1.	Urothelial carcinoma-high grade	126	64%
1.1	Papillary	99	
1.2	Non - papillary invasive	27	
	Invasive urothelial	16	
	Squamous differentiation	4	
	Glandular differentiation	2	
	Sarcomatoid	1	
	Clear cell	2	
	Plasmacytoid	2	
2.	Urothelial carcinoma-low grade	67	34%
3.	Squamous cell carcinoma	2	1%
4.	Small cell carcinoma	1	0.5%
5.	Adenocarcinoma	1	0.5%
	Total	197	100%

Out of 67 cases of low grade urothelial carcinoma (LGUC), in 11 cases no muscle tissue was included in the specimen. Hence, invasion was assessed in 56 cases. Forty-six (82.1%) cases were non-invasive while in 10 (17.9%) cases invasion was limited up to lamina propria. None was muscle invasive (Table 2). Out of 11 cases (muscle tissue not included), 10 (90.9%) cases were non-invasive while in 1 (9.1%) case there was lamina propria invasion (Table3).

Out of 126 cases of high-grade urothelial carcinoma (HGUC), in 4 cases no muscle tissue was included in the specimen. Hence, invasion was assessed in 122 cases. Majority, 95 (77.9%) cases, showed both lamina propria and muscle invasion. Invasion was limited up to lamina propria in 24(19.7%) cases while 3(2.4%) cases were non-invasive (Table 2). In all 4 cases (muscle tissue not included), lamina propria invasion was present (Table 3).

Table 2. Invasion in different histological grades of urothelial tumors

Grade of tumor	Non-invasive	Invasive		Total cases
		Invasion up to lamina propria	Invasion into lamina propria and muscle	
LGUC	46(82.1%)	10(17.9%)	-	56
HGUC	3(2.4%)	24(19.7%)	95(77.9%)	122

Table 3. Invasion assessment of specimens in which muscle tissue was not included

Grade of tumor	Non-invasive	Lamina propria invasion	Total cases
LGUC	10(90.9%)	1(9.1%)	11
HGUC	None	4(100%)	4

DISCUSSION

The urinary bladder is a hollow organ for storing urine until micturition. It is lined by a specialized transitional epithelium known as urothelium which has the ability to flatten under pressure so as to accommodate large volume of urine. It is constantly exposed to potentially mutagenic environmental agents which are filtered into urine by the kidneys. The wall of the urinary bladder has smooth muscle called detrusor.

Hence, majority of the bladder cancer cases are urothelial cancers comprising more than 90 percent of cases^{3,5,11,12}. Squamous cell carcinoma varies from 1.2 per cent to 33.3 per cent. Glandular neoplasms account for 1 per cent to 3.9 per cent. Other rare variants

noted in different studies were sarcoma (2.5%), pheochromocytoma (1.26%), small cell carcinoma (1.2%), hemangioma (0.6%), plasmacytoma (0.6%)^{3,5,11}. In our study, urothelial tumors were diagnosed in 193 (98%) cases followed by other types such as Squamous cell carcinoma (1%), Small cell carcinoma (0.5%) and Adenocarcinoma (0.5%). These findings are comparable with the observations made by other authors.

Among urothelial tumors commonest were low grade papillary urothelial neoplasms followed by high grade papillary urothelial tumors, papilloma and papillary urothelial neoplasm of low grade potential (PUNLMP) in decreasing order of frequency in most of the studies^{3,13}. In the present study, among

urothelial tumors (193), majority, 126(65.3%) cases, were high grade urothelial carcinoma followed by 67(34.7%) cases of low grade urothelial carcinoma. Papilloma and PUNLMP were not seen.

However in some studies cases of high grade urothelial carcinoma outnumbered cases with low grade morphology. In 2011 a decade long retrospective study which included 26 biopsies, there were 53.9 % LGPUN followed by HGPUN (34.6%), papilloma (7.7%) and PUNLMP (3.9%)¹⁴.

Low grade papillary urothelial carcinoma are mostly noninvasive or limited upto lamina propria. High grade papillary urothelial carcinoma shows much higher frequency of muscle invasion as compared to low grade papillary urothelial carcinoma. None of the cases of papilloma or PUNLMP show invasion^{3,5}.

In a retrospective study done in 2016 about 85% of high grade urothelial carcinomas showed muscle invasion while 15% show lamina propria invasion¹⁵. Among low grade urothelial carcinomas, 75% were non invasive while lamina propria and muscle invasion each was seen in 12.5% cases. In another retrospective study done in 2017; 57.3% of high grade urothelial carcinoma showed muscle invasion and 40.5% cases showed lamina propria invasion; while 2.2 per cent cases were non-invasive³. Low grade urothelial carcinomas showed muscle invasion in 1.9% cases in this study. None of the low grade urothelial carcinoma was muscle invasive in our study.

CONCLUSION

Urinary bladder cancer is a major health problem in elderly population and contributes towards significant morbidity and mortality in India. Majority of the urinary bladder tumors were urothelial carcinomas. Inclusion of muscle layer in the cystoscopic biopsy samples will help in the accurate diagnosis.

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