Research Article

Histological Spectrums in Transurethral Resection of Bladder Tissue

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Abstract

Background: Urinary bladder carcinoma is more common in elderly males than females. Urothelial (Transitional cell) carcinoma is the most common histological subtype.

Objective: The purpose of present study was to describe the different histological features observed in transurethral resection of bladder tissue and to determine the association of tumor grade with stage and also of the age with grade and stage of tumor.

Methods: An analytical Cross sectional study, conducted in the Department of Pathology Fatima Jinnah Medical University Lahore, Pakistan from August 2019 – April 2021. Total 80 specimens of transurethral resection of bladder tissue (TURBT) were included. All the specimens were fixed in 10% formalin and stained with Hemotoxylin Eosin stain and studied under the light microscope. urinary bladder malignancies were classified, staged and graded according to the WHO/ISUP guidelines.

Results: Total n=80 cases were included in the study. Mean age of the male patients was 59 ± 1.13 years and 50 ± 1.1 years in females. N=76(95%) were malignant and only 4 (5%) were benign cases. Out of 76(95%) malignant cases, 48 (63.1%) were high grade urothelial carcinoma and 28 (36.8%) were low grade carcinoma. N=33 (43.4%) were invading the lamina propria (T1) and 43 (56.5%) were invading the detrusor muscle (T2).Low grade tumors showed lamina propria invasion (T1) in 18 (64.2%) cases and muscular invasion (T2) was seen in only 10(35.7%) cases. N=33(68.7%) of high grade tumor were invading the deep muscle (T2) and 15 (31.2%) were limited to lamina propria(T1). Tumor with high grade morphology were diagnosed at advanced stage and was observed more frequent in elderly patients. Statistically significant association of tumor histological grade with stage and also of patient's age with tumor grade and stage was observed ($p<0.05$).

Conclusion: The study concluded that urinary bladder carcinoma is more common in males than females. Urothelial carcinoma is the most common type of bladder neoplasm. Patients presented with urothelial carcinoma in older age group and with high grade morphology were diagnosed at advanced stage (invading the detrusor muscle). Statistically there is significant association of tumor histological grade with stage and also of patient's age with the tumor grade and stage.

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Key words: Papillary urothelial carcinoma, Transurethral resection of bladder, Detrusor muscle

Introduction:

Urinary bladder lesions either malignant or non-malignant both are responsible for morbidity and mortality[1]. Carcinoma of urinary bladder is a disease of old age, observed more in males than in females but the disease progression is significantly higher among females. It is the 12th most common cause of death worldwide[2].

In general, the prevalence of urinary bladder carcinoma is 6 times higher in the developed countries in comparison with under developed countries[2,3,4]. The age standardized incidence rate (ASIR) is 11.9 in North America (5.1 in women, 19.7 in men), 11.3 (4.3 in women, 20.2 in men) in Europe and 3.6 (1.5 in women, 6 in men) is observed in Asia. The incidence of bladder carcinoma is high in North America. In developing countries like Pakistan, urinary bladder cancer is ranked

at 8th among other malignancies and the incidence of bladder carcinoma in men is 4.9 and in women is 1.7 (world) per 100,000. According to the data available, it is being predicted that the incidence of urinary bladder carcinoma will start rising in developing countries as well in the coming years[2,5,6].

Development of bladder malignancies is associated with many environmental, occupational and genetic factors. Most common histological type of bladder carcinoma is urothelial carcinoma followed by squamous cell carcinoma. Squamous cell carcinoma of the bladder is caused by schistosomiasis and its prevalence and incidence is high in Middle East and African regions[5]. Urothelial carcinoma has different morphological patterns ranges from papillary to flat non-invasive papi-llary carcinoma to invasive flat carcinoma. Urothelial carcinoma is graded based upon the cytological and architectural atypia[3,7].

For correct diagnosis of urinary bladder lesions, cystoscopy, urine cytology and bladder biopsy are of great importance. Tumors diagnosed timely and those that are superficial in situ or invasion to the lamina propria can be treated successfully. Invasion of the detrusor muscle has poor prognosis[8,9].

The present study was based on the histopathological features of various lesions of bladder in transurethrial resection of bladder tissue (TURBT) and association of the tumor grade with stage and also of age with the tumor histological grade and stage.

Method:

This was an analytical cross sectional study conducted in the Department of Pathology Fatima Jinnah Medical University Lahore, Pakistan from August 2019 – April 2021. A sample size of 80 was calculated by using Cochran formula by taking margin of error (e) 0.05, an estimated proportion of population (p) 0.5, population of 90, and Z score from the Z table at 95% confidence interval which was 1.96 by using following formula.[9]

$$n = \frac{n_0}{1 + \frac{(n_0 - 1)}{N}}$$

Non-probability convenient sampling method was adopted for sample collection. Total 80 specimens of transurethral resection of bladder tissue (TURBT) were included in our study. Autolysed specimens, inadequate biopsies and post treatment specimens were excluded from our study. All the specimens were fixed in standard 10% formalin. Tissue were submitted entirely for histological study and were processed as per routine and paraffin sections were cut and stained with Hemotoxylin Eosin stain and studied under the light microscope with two consultant pathologists independently. In case of any bias in findings, further deeper sections of the tumor were taken and observed by third consultant pathologist independently. All the urinary bladder malignancies were classified, staged and graded according to the WHO/International society of Urological Pathology (WHO/ISUP) guidelines as low grade and high grade tumors[6]. The grading of the tumor was based upon the cellular and architectural atypia. Low grade urothelial carcinoma shows minimal to moderate architectural complexity (fused, branching papillae at places with increased epithelial thickness) and cytological atypia (mild to moderate pleomorphism, prominent nucleoli, mitosis at any level) whereas high grade shows marked architectural (complex papillae, discohesive cells) and cytological atypia (marked pleomorphism, brisk atypical mitosis). Stage was based upon the extent of tumor invasion i.e., either limited to lamina propria (T1) or invading the detrusors muscle (T2)[6].

Collected data were entered and analyzed in SPPS 21 for statistical analysis. Mean and standard deviation were used for all quantitative variables which include age of the patient. Frequencies and percentages were used for all the qualitative variables (gender, stage and grade of tumor). Chi-square test was applied in order to determine the relationship of tumor grade with stage of the tumor and also of age with tumor grade and stage. Value of p <0.05 was considered as statistically significant.

Results:

Total of 80 specimens of transurethral resection of bladder tissue (TURBT) full filling the inclusion and exclusion criteria were included in present study. Out of total 80 cases, 68 (85%) were male and 12 (15%) were female patients. Mean age of the male patient was 59 ± 1.13 and of female was 50 ± 1.1 years. In males, bladder carcinoma is seen between 32-80 years of age

and from 40-57 years in females. Peak age range of the occurrence of urothelial carcinoma among male patients was 55-60 years and among female patients was 45-55 years.

Both benign and malignant lesions were recorded in totally submitted tissues. Out of total 80 cases, n=76(95%) lesions were malignant (papillary urothelial carcinoma) and only 4(5%) were benign. Out of 4 benign lesions, n=2 (50%) were inverted papillomas and n=2 (50%) were inflammatory lesions (Figure 1).
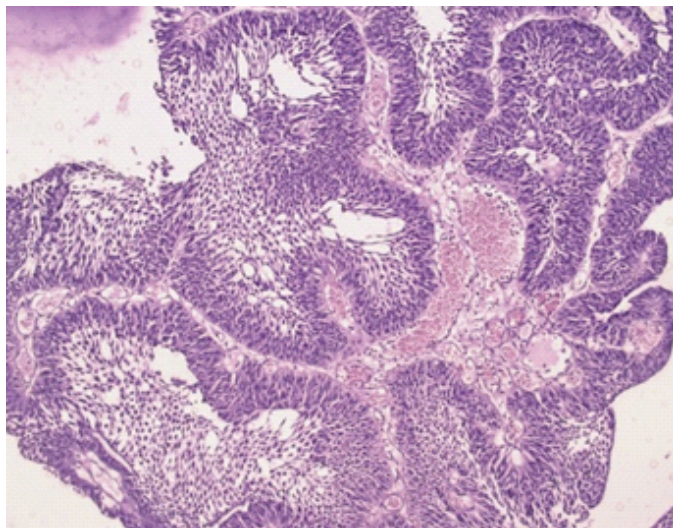

Figure 1: *Inverted papilloma, note the inward growth of benign surface epithelium.*

Out of 76 (95%) urothelial carcinoma cases, 48 (63.1%) were diagnosed as high grade papillary urothelial carcinoma (Figure 3) and 28 (36.8%) low grade papillary urothelial carcinoma (Figure 2, Table 1)
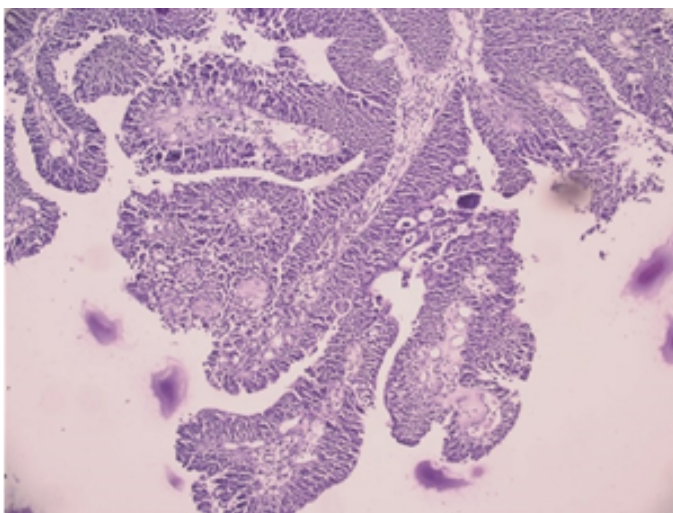

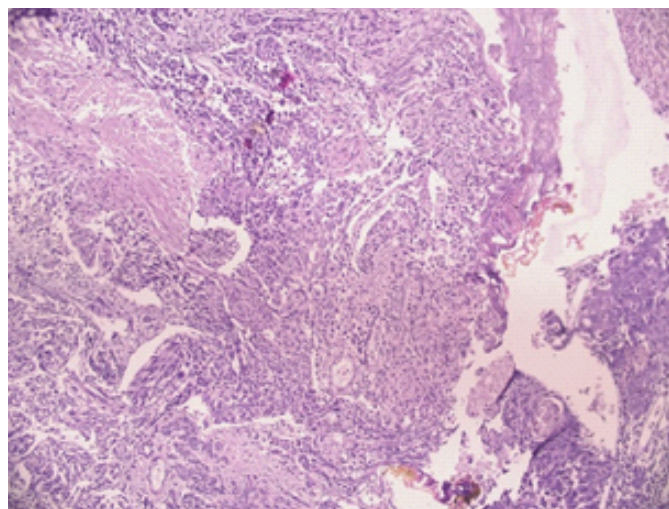**Figure 2:** *Low grade papillary urothelial carcinoma*

Figure 3: *High grade papillary urothelial carcinoma*

Out of 76 cases of urothelial carcinoma, 33 (43.4%) were invading the underlying lamina propria (T1) and 43 (56.5%) were invading the deep muscle (T2).

Depth of the invasion was also brought in consideration with the grade of the tumor. Low grade tumors showed lamina propria invasion (T1) in 18 (64.2%) cases and muscular invasion (T2) was seen in only 10 (35.7%) cases. High grade tumors showed more cases at advanced stage, 33 (68.7%) were invading the deep muscle (T2) and only 15 (31.2%) were limited to lamina propria (T1).Table1
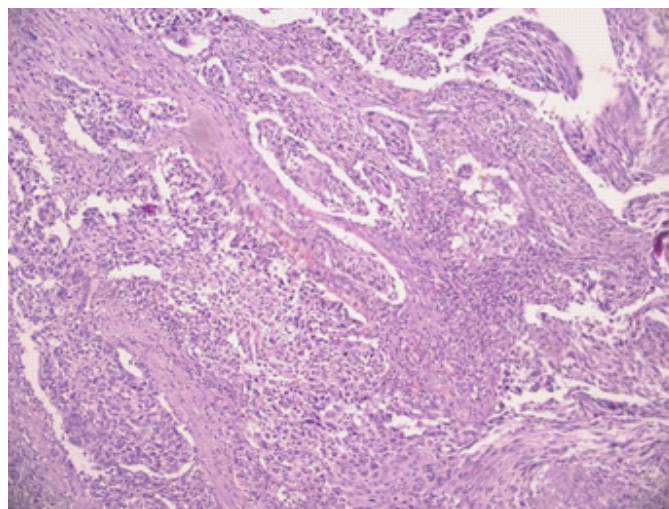

Figure 4: *High grade tumor invading the detrusor muscle*

Cross tabulation between tumor grade and stage of the tumor was done using Chi-square test to determine their relationship, which turned out statistically significant (p = 0.000). Table 1.

Table 1: Comparison of Tumor Grade with Stage (n=76)

Tumor Grade	Tumor stage			
	T1	**T2**	**Total**	**P value**
Low grade	18 (64.3%)	10 (35.7%)	28 (100%)	
High Grade	15 (31.3%)	33 (68.8%)	48 (100%)	0.000
Total	33 (43.4%)	43 (56.7%)	76 (100%)	

In present study frequent number of cases were diagnosed with high grade morphology and at advanced stage. Out of 76(95%) cases of urothelial carcinoma n=2(2.6%) showed extensive squamous cell differentiation in tumors with high grade morphology and at advanced stage (T2). Tumors with high grade morphology and at advanced stage were more frequent in elderly patients. Chi-square test was applied to determine the relationship of patient's age with tumor grade and stage. Statistically significant relationship of patient's age with histological grade and stage of the tumor was observed (p< 0.05). Table 2.

Table 2: Comparison of patient's Age with Tumor Grade and stage (n=76)

Age	Tumor Grade		Tumor stage		P value
	Low Grade	**High Grade**	**T1**	**T2**	
30-40	2 66.6%	1 33.3%	2 66.6%	1 33.3%	
41-50	3 30%	7 70%	5 50%	5 50%	
51-60	7 25.9%	20 74%	15 55.5%	12 44.4%	
61-70	10 37%	17 62.9%	7 25.9%	20 74%	P <0.05
71-80	6 66.6%	3 33.3%	4 44.4%	5 55.5%	
Total	28 36.8%	48 63.1%	33 43.4%	43 56.5%	
	N=76 (100.0%)				

Discussion:

Urinary bladder carcinoma is the 8th most common malignancy in elderly males. Its incidence is more in developed countries and increasing gradually in developing countries because of increase smoking[10].

In present study urinary bladder carcinoma was seen more in males (42; 84%) with mean age 59 years as compare to females (8; 16%). Rukhsana et al, Akhter et al and mahdi et al reported that the bladder carcinoma is 3-4 times more common in elderly males than females and the reason of this excess in males is not explained fully[9,10,11].

In this study, the neoplastic lesions were more common (46; 92%) than benign lesions (4; 8%) which correlates with Rantam KP et al[9]. Histological grading and staging of the tumor was done according to WHO/International society of Urological Pathology (WHO/ ISUP) guidelines. All the cases were diagnosed with papillary urothelial carcinoma and high grade was observed more frequent (31; 67%) than low grade papillary urothelial carcinoma (15 ;32%) which correlate with other similar studies of Akhter et al and Rantam KP et al and Kim TJ et al[9,10,12]. They also concluded papillary urothelial carcinoma most common type of malignancy than other histological types. Histological types that includes squamous cell carcinoma and sarcomatoid lesions are very rare. The studies of Mainali N et al and Thapa R et al concluded low grade urothelial carcinoma the most common lesion with the peak age range of 61-70 years which contradict our results[13,15].

Staging of tumor is the most common prognostic factor. Urothelial carcinoma invading deep muscle is the most important marker of prognosis and treatment. Out of 46 cases of bladder carcinoma, 28 (60.8%) were invading the deep muscle (T2) and 18 (39.1%) were invading the superficial lamina propria. Tumors invading the deep muscle were more frequent in elderly patients. According to the studies of Khalid Hussain et al and Sherestha EP high urothelial carcinoma was observed more in elderly patients and at advanced stage1,[15].

In present study comparison of depth of invasion was also observed with the tumor grade. Low grade tumor showed lamina propria invasion in 9(60%) cases and deep muscle involvement in only 6(40%) cases. In tumor with high grade morphology 22 (70%) were invading the deep muscle (T2) and only 9 (29%) were limited to lamina propria (T1). The study done by Shrestha EP

and Akhtar ZM et al concluded detrusor muscle invasion in 16% of cases of low grade urothelial carinoma and 76.92% cases of high grade tumors which correlate well with our study[1,12].

Recurrence of the tumor is proven to be more common in patients with squamous differentiation. N=2 (8.4%) cases with high grade morphology showed extensive squamous differentiation in present study. The study of Gang Liconcluded squamous differentiation less common in general but more in high grade urothelial carcinoma. These findings are similar to our present study results. Different studies have shown an association of high grade morphology with tumor stage and also the association of patient's age with the tumor grade and stage which are similar to our study results[16,17,18]. One of the local study's results conducted by RP Samo et al based on association of urothelial carcinoma with age and gender are in contrast to our study results[4].

In our country Pakistan an awareness campaign about the risk factors and most common symptoms of bladder carcinoma is needed, so that early diagnosis can be made. The lack of knowledge causes significant delay in patient's presentation at hospital. Timely diagnosis of the lesion can prevent aggressive outcome and high stage of the tumor.

Our study includes limited number of cases collected from single center. Therefore, the authors suggest a study based on maximum number of cases and includes date from other hospitals as well to ascertain more depth knowledge about bladder lesions and to confirm our study results.

Conclusion:

The study concluded that urinary bladder carcinoma is more common in males than females. Urothelial carcinoma is the most common type of bladder neoplasm. Patients presented with urothelial carcinoma in older age group and with high grade morphology were diagnosed at advanced stage (invading the detrusor muscle). Statistically there is significant association of tumor histological grade with stage and also of patient's age with the tumor grade and stage.

Ethical Approval: Given

Conflict of Interest: The authors declare no conflict of interest.

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