

Retrospective Analysis of Urinary Bladder Tumours- A Study from Central India

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Abstract: Urinary bladder cancer accounts for approximately 7% cancers and 3% of cancer mortality in west, while in India it is the ninth most common cancer. Malignancy of the urinary bladder contributes significantly to the morbidity and thus adding to the burden on the health care system and society. There are very limited studies on urinary bladder tumours, especially from central India. The main objectives of the study was to analyze the histomorphological pattern of urinary bladder tumours especially urothelial tumors of the urinary bladder and their relation with age, sex and correlation of tumor grade with muscle invasion and necrosis. We reviewed all bladder tumour cases reported in the Department of Pathology, BMHRC, Bhopal, M.P., India over a period of 13 years from Jan 2002 to Dec 2014. Total 165 cases of urinary bladder tumours were analyzed. The male to female ratio was 6.5:1 and the average age was 63 years (range: 17 to 90 years). 90% patients presented with painless hematuria. 153 cases (92.7%) were of urothelial carcinomas, 1.2% were squamous cell carcinoma and 6.1% were the other variants including sarcomas, metastatic adenocarcinoma etc. In the Urothelial carcinomas, high grade was observed in 60.7%, whereas low grade was in 33.9% cases. 146 cases (95.4%) were with papillary configuration and 1.4% was carcinoma in situ. Muscle invasion and Necrosis were more common in high grade tumours. Urothelial carcinoma is the predominant urinary bladder cancer, with significant male predominance in central India population. Younger age had low grade urothelial carcinoma. Muscle invasion is noted more in high grade tumours.

Keywords: Bladder, cancer, carcinoma, high grade, low, muscle invasion, transitional cell, urothelial, urinary.

INTRODUCTION

Urinary bladder cancer is the 7th most common cancer worldwide [1]. Cancer of the urinary bladder accounts for about 3.2% of all cancers worldwide. Urinary bladder cancer accounts for approximately 7% cancers and 3% of cancer mortality in west [2]. As per Indian cancer registry data in men, it is the ninth most common cancer accounting for 3.9% of all cancers [3]. About 95% are of epithelial origin, the remaining being mesenchymal tumors. Urothelial (Transitional cell) neoplasms comprise approximately 90% of all primary tumor of this organ [2]. Cases of squamous cell carcinoma (5%)[3], primary adenocarcinoma (2%) [3], small cell carcinoma and sarcomas are encountered much less frequently. Bladder tumors are more common in industrial areas and their incidence increased with

exposure to cigarette and arylamines. Most cases of urothelial carcinoma of bladder present in patients over the age of 50 yrs, but they can also appear in young adults and children, the latter tend to be low grade, indolent neoplasm [3]. Carcinoma of the bladder affects men more than women at a ratio of 3 to 4:1 [4].

In 85% cases, most common presenting symptom is painless hematuria [5]. Urine cytology may be performed; however, diagnosis usually requires cystoscopy and biopsy. These two had been the gold standards in the diagnosis of bladder cancers and in the follow up period. Transurethral resection of the bladder tumour (TURBT) is the initial step in the management of non-muscle invasive tumours. This procedure

removes all the visible lesions and also provides specimen for histopathology evaluation.

Malignancy of the urinary bladder contributes significantly to the morbidity and thus adding to the burden on the health care system and society. There are limited studies on urinary bladder tumours from India and a few studies from central India. The main aims of this study are to analyze the histomorphological patterns of urinary bladder tumours especially urothelial neoplasms in relation with age and sex and to analyse the relation between stage and grade of urothelial tumors.

MATERIALS AND METHODS

Study Design

This is a retrospective study which is carried out in the Department of Pathology, Bhopal Memorial Hospital and Research Centre (BMHRC), Bhopal, Madhya Pradesh, India. BMHRC is one of the major referral hospitals in and around Bhopal. The study was approved by the Institutional ethics committee. All the consecutive cases of urinary bladder tumours (TURBT biopsies and cystectomy specimens) that were received in the department between January 2002 and December 2014 were included for analysis. The TURBT specimens consist of both superficial biopsy and deep biopsy including muscularis propria to assess the depth of invasion by tumour. In case of small biopsies the entire tissue was processed and the radical cystectomy specimens were processed according to ISUP guidelines.

From the medical record section, the patient's files were retrieved to record the age, sex, presenting complaints and cystoscopic findings including size and location of tumour. The gross and microscopic features of the specimens were recorded from signed out reports. Histopathology slides [Hematoxylin and Eosin (H&E) stained slides and immunohistochemistry (IHC)] of all the cases were reviewed. Wherever required the faded slides were restained. We recorded histological type, grade, muscle invasion, necrosis and other associated histological findings of all the tumours. The pathologic grading of the urothelial neoplasms was done in accordance with the 1998 ISUP/2004 WHO classification¹. The tumours may be of flat or papillary type or a combination of both. They can be non-invasive or invasive. The non-invasive papillary urothelial neoplasms were divided into four categories designated as papilloma, papillary urothelial neoplasm of low malignant potential (PUNLUMP), low grade urothelial carcinoma and high grade urothelial carcinoma. Invasive tumours may be of low or high grade and they can either invade lamina propria or muscularis propria or beyond.

RESULTS

In this study 165 cases of bladder tumours were reviewed including 147 TURBT specimens and 18 radical cystectomy specimens. In the present series, 90% patients had history of gross or microscopic hematuria. In 51 cases, cystoscopic findings were available in records and revealed chiefly involvement of right posterolateral wall by the tumour (31 cases). Other locations were base, trigone, anterior and posterior walls of the bladder. The urinary bladder tumours were found in between 17-90 years of age, with an average age of 63 years. The commonest age group involved was 61-70 years (34.6%) followed by 51-60 years (23%). The distribution of bladder tumours was more in males (86.7%) as compared to females (13.3%) with male to female ratio of 6.5:1 (Table 1).

Among 165 cases of urinary bladder tumour, urothelial tumours were found in 153 cases (92.7%), while the rest were non-urothelial in origin (7.3%) (Table 2). In the non-urothelial malignancies, sarcoma accounted 2.5% followed by metastatic adenocarcinoma (1.8%), squamous cell carcinoma (1.2%), hemangioma (0.6%), amyloidosis (0.6%) and plasmacytoma (0.6%).

Among the 153 cases of urothelial bladder tumours, there were 146 cases (95.4%) of tumours with papillary configuration while 3.2% cases were non-papillary invasive type and 1.4% were carcinoma-in-situ (Figure-1). The age wise distribution of urothelial tumours is shown in (Table 3). High grade urothelial carcinoma was the commonest tumour (60.7%), while the low grade urothelial carcinoma accounted 33.9%, PUNLMP 3.3%, Papilloma 0.7% and carcinoma-in-situ 1.4%. High grade tumours accounted 61.6% in males and 55% in females while low grade tumours accounted 34.5% in males and 30% in females. PUNLMP was diagnosed in 15% females and in 1.5% males. High grade as well as low grade urothelial carcinomas was found more in the 51-70 years of age group while the PUNLMP was found more in patients younger than 50 years of age. The youngest patient (17 years) had PUNLMP.

In the total 153 urothelial tumours, 146 were papillary urothelial carcinomas. Out of these 146 cases, 57.3% cases of high grade papillary urothelial carcinomas had muscle invasion and 40.5% cases revealed invasion into the lamina while 2.2% were non-invasive (Table 4). Most of the low grade urothelial carcinomas (67.3%) were limited to lamina and only 1.9% cases revealed muscle invasion. None of the Papilloma and PUNLMP was invasive. Necrosis was found in 48.3% cases of high grade urothelial carcinoma and only in 1.9% cases of low grade urothelial carcinoma.

Additional pathologic findings were more commonly seen in high grade papillary tumours. Squamous metaplasia was the most common additional pathologic finding (11.1%). In addition giant cell

change/ nuclear pleomorphism was noted in 6.5% cases, adenomatous change, clear cell change, spindling and myxoid change were also found in less than 3% cases.(Figure-2).

Table-1: Age and sex distribution of bladder tumours

Age Group (in years)	Male (%)	Female (%)	Total
Less than 30	02(1.2%)	01(0.6%)	03 (1.8%)
31-40	05(3%)	01(0.6%)	06(3.6%)
41-50	15(9.1%)	02(1.2%)	17(10.3%)
51-60	31(18.8%)	07(4.3%)	38(23%)
61-70	52(31.5%)	05(3%)	57(34.6%)
71-80	28(17%)	05(3%)	33(20%)
81-90	10(6.1%)	01(0.6%)	11(6.7%)
Total (%)	143(86.7%)	22(13.3%)	165

Table-2: Different types of urinary bladder tumours

Type of tumour	Number / % of total
Papilloma	01(0.6%)
PUNLMP	01(0.6%)
Low grade Urothelial carcinoma	52(31.5%)
High grade Urothelial carcinoma	93(56.4%)
Ca-In situ	02(1.2%)
Squamous cell carcinoma	02(1.2%)
Sarcomas	04(2.5%)
Metastatic adenocarcinoma	03(1.8%)
Hemangioma	01(0.6%)
Plasmacytoma	01(0.6%)
Amyloidosis	01(0.6%)

Table-3: Age-wise distribution of Urothelial tumours according to WHO/ISUP classification

Age (years)	Papilloma No/%	PUNLMP No/%	Low grade Urothelial Carcinoma No/%	Carcinoma-In-Situ No/%	High grade Urothelial carcinoma No/%
17-50	-	03(1.9)	09(5.9)	01(0.7)	08(5.2)
51-70	-	01(0.7)	31(20.2)	-	58(37.9)
71-90	01(0.7%)	01(0.7)	12(7.8)	01(0.7)	27(17.6)
Total no of cases (153)	01(0.7%)	5(3.3)	52(33.9)	02(1.4)	93(60.7)

Table-4: Lamina and Muscle Invasion in different Grades of Papillary Urothelial tumours

	Lamina No / %	Muscle No / %	No invasion No / %
High grade (89)	36 (40.5%)	51 (57.3%)	02 (2.2%)
Low grade (52)	35 (67.3%)	01 (1.9%)	16 (30.8%)
PUNLMP (05)	-	-	-
Total no. of Tumours (146)	71 (49%)	52 (35.6%)	18 (12.3%)

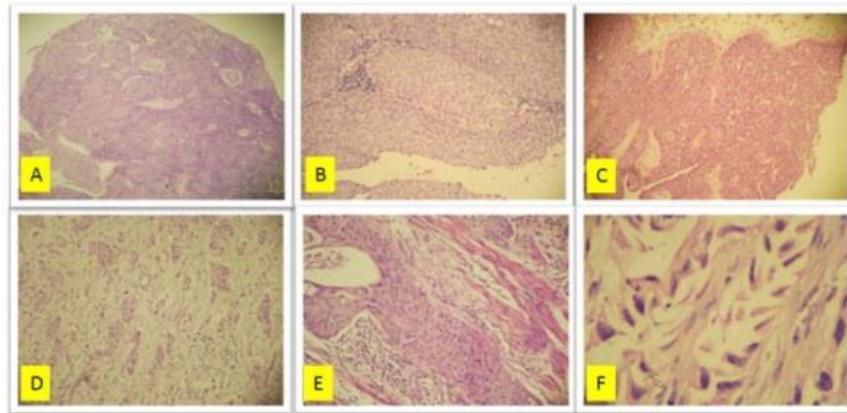


Fig-1:(H&E stained photomicrographs of types of Urothelial tumors): A- Inverted papilloma (x5), B- Low grade urothelial carcinoma (x10), C- High grade urothelial carcinoma (HGUC) (x10), D- HGUC with myxoid areas(x10), E- HGUC with muscle invasion(x20), F- Sarcomatoid urothelial carcinoma (x40).

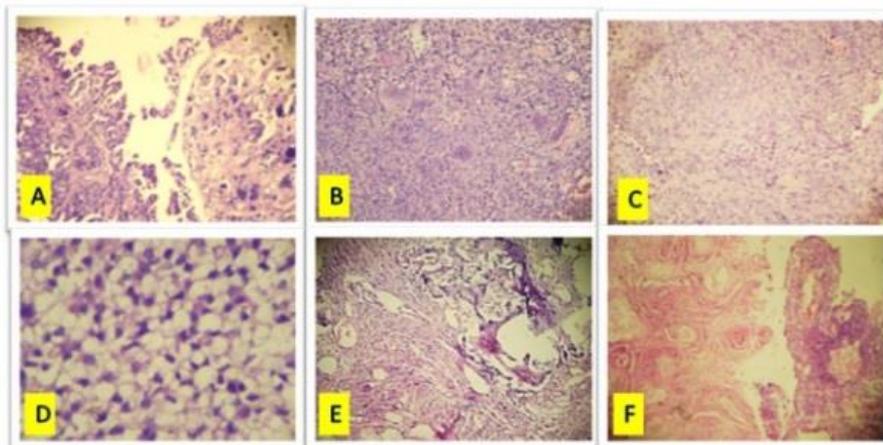


Fig-2: (H&E stained photomicrographs of morphological variants in high grade urothelial carcinoma): A- Nuclear pleomorphism with bizarre forms(x20), B-multinucleated giant cells(x20), C-Spindling of tumour cells(x20), D- Clear cell change(x40), E-Osteoid formation(x10), F- Squamous differentiation with keratin pearls (x10).

DISCUSSION

Urinary bladder tumours are heterogeneous group of tumours with different subtypes and behavioural patterns. Despite significant improvement in the methods of diagnosis and treatment, they produce high toll in morbidity. Population based studies in different cities and states of India have placed bladder cancer in top ten malignancies [6-9].

Bladder cancer presents with painless hematuria in 80-85% cases. However, in reality, almost all patients presented with hematuria. In the present series, 90% patients had history of gross or microscopic hematuria. This high incidence is may be due to lack of routine screening facility. In 51cases cystoscopic findings were available in records and this revealed chiefly involvement of right posterolateral wall by the tumour.

Most common age group at the time of presentation was 61 to 70 years (34.6%) and younger

patients present more frequently with low grade tumours than the elderly patients. Similar findings were noted in other studies[10,11]. These may be because the genetic alterations are frequently seen in older persons.

Male to female ratio in this study was 6.5:1 which is similar to the study of Johansson *et al.* (3:1 to 4:1)[5] and Biswas *et al.*(6.2:1) [12]and different from other studies, i.e. Rajesh singh *et al.* (1.5:1)[10] and Selhi *et al.* (4.7:1)[13]. The higher incidence of urothelial tumors in male is probably related to difference in smoking habits and occupational exposure as well as due to anatomic differences, urination habits or hormonal factors[14] and in India, females tend to present less to the hospital because of social reasons.

In this study, urothelial carcinoma was the most common tumour of urinary bladder (92.7%) which is similar to the reports of western literature[15]. Variability is noted in the incidence of squamous cell carcinoma (SCC) of the bladder. SCC accounts for 1%

of bladder cancers in England, 3 to 7% in the united states[5].In our study SCC accounted for 1.2%.

M.Sathya *et al.*[16] reported 62.85% cases of high grade and 25% low grade urothelial carcinoma. Higher incidence of high grade urothelial carcinoma was also reported in other study[17]. Similar findings were also observed in our study, whereas contrast results were noted in some studies with higher incidence of low grade carcinoma[10,18].

In our series, high grade urothelial carcinomas showed muscle invasion in 51 cases (57%) and lamina propria invasion in 36 cases (40.5%) while low grade tumours were mostly restricted to lamina (67.3%). Similar finding was observed by others[10,16,18]. Low grade tumors can be invasive but significantly lower than high grade papillary carcinoma[19].This indicates that as the grade increases the chances of muscle invasion are more[20] and the inclusion of the muscle in the biopsy specimen may prevent under staging in many patients. Necrosis was found more in high grade carcinomas.

In this study, urothelial carcinomas showed morphological variation in focal areas and this is more commonly seen with high grade tumours. The common variants include squamous metaplasia, giant cell reaction, clear cell change, etc. There were 12 cases (7.3%) of non-urothelial malignancies including sarcomas (2.5%) followed by metastatic adenocarcinoma (1.8%), squamous cell carcinoma (1.2%), hemangioma (0.6%), amyloidosis (0.6%) and plasmacytoma(0.6%). Lamina and muscle invasion was seen in most of these tumours.

Our hospital is a major multispecialty tertiary care institute in Central India. Although our data is not a representative of exact incidence but it does shows prevalence of bladder tumours in this region.

CONCLUSION

To conclude, urothelial carcinoma is the most common urinary bladder tumour with male preponderance and commonly occurred in sixth decade. Older patient presents more with high grade tumours while low grade tumours are comparatively common in younger population. There is a definite correlation between advancing tumor grade and muscle invasion. Inclusion of smooth muscle in the biopsy specimens needs to be emphasized. Awareness is needed among the public, as they tend to ignore hematuria, resulting in advanced stage of tumour.

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