RESEARCH COMMUNICATION

Urothelial Tumors of the Urinary Bladder in Manipur: A Histopathological Perspective

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Abstract

Objective: To study the histomorphological pattern of urothelial tumors of the urinary bladder in Manipur and to evaluate whether any correlation exists between tumor grade and muscle invasion. Methods: A 10 year retrospective study of all consecutive cases diagnosed in the Department of Pathology RIMS – Imphal, between 1st January 2001 to 31st December 2010. Results: The study included 26 cases of transitional cell tumors of urinary bladder. The male to female ratio was 1.5: 1 and the ages ranged from 38 years to 73 years (medians of 60 and 64 years, respectively). Of the total, 14 (53.9%) cases were low grade, 9 (34.6%) were high grade, 2 (7.7%) were papillomas and 1 (3.9%) was a papillary urothelial neoplasm of low malignant potential (PUNLMP). Pathological staging showed that 14 (53.9%) of the cases were stage PTa, four (15.4%) PT1, and eight (30.9%) PT2. Some 18.2% of low grade tumors and 75% of high grade tumors were invasive to the detrusor muscle layer. Conclusion: Bladder cancer is an uncommon disease, transitional tumors being the only histological type observed. It was more common in males than females, with peak incidence in seventh decade. Most of the tumors were non- invasive (PTa) and invasion to the detrusor muscle layer was seen in more than half of the high grade tumors. There is a definite correlation between advancing tumor grade and muscle invasion.

Keywords: Bladder cancer - urothelial tumors - urinary bladder

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Introduction

Urothelial carcinoma comprises about 90% of all primary tumors of the urinary bladder (Robbani & Cordon-Cardo, 2000). More common in industrial areas and their incidence is increased with exposure to cigarette smoke and arylamines. Most cases present in patients over the age of 50 years (Nelson et al., 2009). As per Indian cancer registry data in men, it is the ninth most common cancer accounting for 3.9% of all cancer (Kurkure, 2001). Men are effected more often than women (3-4:1) (Reutor VE, 2004). According to WHO (2004)/ISUP, Urothelial tumors may be of flat or papillary on the basis of the pattern of growth of the intraepithelial lesion, which may lead to invasive Urothelial carcinoma. Papillary tumors recognised in this classification are, Urothelial Papilloma , Urothelial neoplasm of low malignant potential, Papillary urothelial carcinoma , low grade and Papillary urothelial carcinoma, high grade. The higher incidence of urothelial tumors in male than in female is probably related to difference in smoking habits and occupational exposure (Gupta et al., 2009). Low grade tumors can be invasive but significantly lower than high grade papillary carcinoma (Grignon, 2009). Patholgical stage is the most important determinant of prognosis and treatment (Cheng et al., 2009).

The aim of the present study was to see the histomorphological pattern of urothelial tumors of the urinary bladder with regards to age and sex, and to determine the stage and grade of Urothelial tumors, the presence of muscle invasion, and to see its correlation with the tumor grade.

Materials and Methods

This retrospective study was carried out in histopathology section, department of pathology, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, India. RIMS is one of the major referral hospital in north eastern India. All consecutive cases of urothelial carcinoma of urinary bladder received in the section of histopathology, RIMS during the 10 years study period between 1st January 2001 and 31st December 2010 were included in the study. Ethical approval from the institutional committee was obtained. All the histopathology slides of Urothelial tumors of urinary bladder received during the study period were reviewed. Those faded slides were restained with Hematoxylin and Eosin (H&E) stain. The New WHO (2004)/ ISUP classification were used for pathologic grading. Data were recorded as Ta- for Papillary; urothelial confined carcinoma, T1- for lamina invasive carcinoma and T2-

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for muscles invasive carcinoma (Gupta et al., 2009). For the purposed of statistical analysis, grade 1 tumors were classified as papillary urothelial neoplasm of low malignant potential (PUNLMP), grade 2 tumors - low grade and grade 3 as high grade. The biopsy specimens in which there was no evidence of detrusor muscle was recorded separately. The presence of tumors infiltrating the muscle was noted.

Results

A total of 26 cases of urothelial tumours of the bladder were reported during the study period. Age ranged from 38 to 73 years. Male to female ratio was 1.5:1. Median age in males was 60 years and 64 years in females. The commonest age group was seen in the 61-70 years (38.5%) followed by 51-60years (30.8%).80% (16out of 22) patients were 50 years or older at the time of presentation.

Among the 26 cases, low grade papillary urothelial carcinoma was found to be the commonest with 14 cases (53.85%) followed by high grade urothelial carcinoma with nine cases (34.61%). Urothelial papilloma comprised of two cases (7.69%) and there was one case (3.85%) of PUNLMP.

Pathological staging of the cases studied showed that maximum cases i.e 14 cases (53.85%) were in stage PTa (Papillary urothelial confined carcinoma) followed by stage PT2 (muscle invasive carcinoma) with eight cases(30.77%). Four cases (15.38%) were in stage PT1 (lamina propria invasive carcinoma).

Urothelial carcinoma comprised 23 cases. None of the papilloma and PUNLMP was invasive. In 17 % (04 cases out of 23), no muscle was present in the biopsies specimens. Invasion could only be assessed only in 19(83 %) cases. 18% are of low grade and 75 % of high grade tumors were invasive beyond muscle layer.(Table 4) The muscle invasiveness and the grade of the tumour is found to be significant (p: 0.002).

Table 1. Age and Sex Distribution of Urothelial Tumors

Age group	Males	%	Females	%	Total	%
≤ 40	1	3.8	0		1	3.8
41-50	4	15.4	2	7.7	6	23.1
51-60	5	19.2	3	11.5	8	30.8
61-70	4	15.4	6	23.1	10	38.5
≥71	1	3.8	0		1	3.8
Total	15	57.7	11	42.3	26	100

Table 2. Stage of the Urothelial Tumors

Stage	Total	%
PTa	14	53.85
PT1	4	15.38
PT2	8	30.77
Total	26	100

Table 3. Grade Distribution of Cases by Stage

Grade	Stage			Total No (%)
	PTa	PT1	PT2	
PAPILLOMA	2	0	0	2 (7.69)
PUNLMP	1	0	0	1 (3.85)
LOW GRADE	8	4	2	14 (53.85)
HIGH GRADE	3	0	6	9 (34.61)
TOTAL	14	4	8	26 (100)

Table 4. Grade and Muscle Invasion

Grade	Muscle invasion	Muscle not invaded	Total
Low grade	2 (18.18)	9 (81.81)	11
High grade	6 (75)	2 (25)	8
TOTAL	8	11	19

Discussion

Bladder cancer ranks 8th in Manipur accounting for 3.2% of all cancer in males as per population based Cancer registry, RIMS (PBCR, 2009). Urothelial tumors were the only histological type seen in our study which was also reported (Rafique et al., 2006; Al-Bazzaz, 2009). Bladder cancer is rare in people younger than 50 years of age even though it can occur at any age. Incidence of bladder cancer increases with age with median age at diagnosis of around 70 years (Lynch & Cohen, 1995). The median age was 60 years old in our study, similar to a study in India (Gupta et al., 2009).

In our study 73.07% patients were older than 50 years of age at the time of presentation similar to other study which showed that 80.6 % presents older than 50 years (Al-Bazzaz, 2009). Younger patients frequently present with lower grade and lower stage tumors than their elder counter parts (Wan, 1989). This is in contrast to the common belief that behaviour of cancer is more aggressive in younger age groups. More research should be carried out to know the reasons for this. It has also been reported that Urothelial neoplasms in children and young adults appear to be biologically distinct and lack genetic instabiliy in most cases (Wild et al., 2007).

Male to female ratio in our study was 1.5: 1 which was lower than finding in USA, (3:1 to 4:1) (Nelson et al., 2009). The male-female ratio in different parts of the world is varied. It was less than three in India, Thailand and US black (Yavari Pet al., 2009). Possible reason could be that females also consume tobacco even though smoking is more common among males. Commonest age group at the time of presentation was 61-70 years 38.5% (10/26) which was also reported (Waihenya et al., 2004).

Analysis of stage of presentation in our study revealed that early stage (PTa, PT1) tumors comprised 73.07% (19/26) of the cases which is similar to findings by Matalka et al, 2008 (71.8%). 17 Eight cases (36.36%) had muscle invasion (PT2), similar to study by Ahmed etal (37.6%) (Ahmed et al., 2002). There were no patients with carcinoma in situ, also reported (Al-Bazzaz, 2009).

Histological grading of the tumors was done according to WHO (2004)/ISUP grading of urothelial neoplasms (Epstein, 1999). In our study, papillary urothelial carcinoma, low grade was 14 cases (53.85%) were more common than high grade with nine cases (34.61%). Similar finding by Ahmed et al 18 was also reported where 44% were low grade and 29.5% were high grade (Ahmed et al., 2002).

Pathologic grade and muscle invasion are the most valuable prognostic predictors of survival. This is

supported by Blaveri et al, who evaluated the association between genomic instability and muscle invasive tumours and found that worse outcome is associated with muscle invasive tumours (Blaveri et al., 2005). Out of the 23 cases of urothelial carcinoma, muscle invasion could be assessed in 19 cases (83%). Six cases (75%) of papillary urothelial carcinoma, high grade, showed detrusor muscle layer invasion while only two cases (18.18%) of low grade carcinoma showed muscle invasion. Not including muscle layer in the biopsy specimens may leads to under staging of tumors in many patients. The importance of including smooth muscle in the biopsy specimen needs to be emphasized. Other authors also reported a high percentage of muscle invasions in higher grade tumours (Ahmed et al., 2002; Hussain et al., 2009).

In conclusion, bladder cancer is a very rare disease, Urothelial tumors was the only histological type observed. It was more common in males than females, with peak incidence in the seventh decade.Most of the tumors were non-invasive and invasion to the muscle layer was seen in more than half of the high grade tumors. There is a definite correlation between advancing tumor grade and muscle invasion.

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