Histopathological Pattern, Classification and Staging of Papillary Neoplasms of Urinary Bladder

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Abstract

Background: To study the histopathological pattern of papillary tumours of the urinary bladder with regards to age and sex and to classify the tumours according to WHO/ISUP Consensus Classification of Urothelial (Transitional Cell) Neoplasms of the Urinary Bladder, the presence of muscle invasion, and to assess its relation with the tumor grade, in patients presenting to a tertiary care hospital of Pakistan.

Methods: It was a case series study conducted in the Department of Pathology Benazir Butto Hospital. All the consecutive 47 cases of papillary urothelial neoplasms of the urinary bladder presented during a period of two years (2014-2016) were studied in terms of muscle invasion and grade and classified according to 2004 WHO/ISUP classification of the urothelial neoplasms of urinary bladder. SPSS version 22 was used for data entry and analysis and descriptive statistics were calculated.

Results: Among 47 cases of urothelial tumors of urinary bladder, male to female ratio was 8.4:1. The ages ranged from 27-90 years with the median age of 61 years in males and 55 years in females. Low grade papillary urothelial carcinoma was the commonest (74.5%) followed by High grade papillary urothelial carcinoma (23.4%). Only one case of papillary urothelial neoplasm of low malignant potential was recorded while no case of urothelial papilloma was reported. Muscularis propria was invaded in 15 cases (31.9%) majority of which were high grade.

Conclusion: Urothelial carcinoma of urinary bladder is one of the leading malignancies and more common in males. Low grade papillary urothelial carcinoma is the commonest type observed in our set up.

Key words: Urinary bladder, Neoplasms, Urothelial carcinoma, Papillary carcinoma.

Introduction

Urinary bladder carcinomas are the heterogeneous group of neoplasms which show wide morphological variability1. Carcinoma of bladder is the 7th most common cancer seen worldwide, with higher incidence in the USA and Europe compared with Asian countries 2. An estimated 429,800 new cases of bladder cancer and 165,100 deaths occurred in 2012 worldwide3. Urinary bladder carcinoma is considerably more common in males than females (male: female ratio is seen 3.5:1) worldwide 4. It is considered as the 13th most common cause of cancer related deaths worldwide5. As far as the occurrence is concerned with respect to Pakistan, according to AFIP (Armed Forces Institute of Pathology) data urothelial carcinoma of bladder constitutes 93.4% of all bladder cancers6. In approximately 75-85% bladder cancer patients, the disease is confined to the mucosa and has a prolonged clinical course with multiple recurrences after local resection without tumor progression7.

The World Health Organization (WHO) system classifies papillary urothelial neoplasms into four types; papilloma, papillary urothelial neoplasm of low malignant potential (PUNLMP), low grade carcinoma and high grade carcinoma, with detailed structural and cytological criteria8. Papillomas are benign tumors, grossly papillary, and usually pedunculated, with few layers of completely uniform transitional cells. The papillary neoplasms of low malignant potential are grossly papillary, may be pedunculated or sessile, have much thicker layers compared to papillomas and cells show cytologic atypia. They still have an overall orderly appearance histologically as shown in figure 1a and 1b. Most high grade papillary urothelial carcinomas are grossly sessile and cauliflower-like. Microscopically, cellular atypia and pleomorphism are marked and may obscure the transitional cell nature of the tumor as seen in figure 2. Mitotic figures are frequent and often atypical and are seen at all levels of the urothelium9.

In early bladder cancer, also called superficial bladder cancer or non-muscle invasive bladder cancer, the cancer cells are only in the bladder’s inner lining and have not grown through the inner lining and into the deeper muscle layer of the bladder. While in invasive bladder cancer the cancer has spread into or through the muscle layer of the bladder.
A study of 342 cases conducted in United States showed that according to WHO criteria, 25.7% of tumors were papillary urothelial neoplasms of low malignant potential (PUNLMP), 34.3% low-grade papillary carcinomas, 22.6% high-grade papillary carcinomas, 1% non-papillary urothelial carcinomas and 5.5% carcinoma in situ. In a 4 year study conducted in Karachi 13.7% tumors were PUNLMP while low grade and high grade urothelial carcinomas were in 46.6% and 39.7% cases.

**Patients and Methods**

This case series study was conducted in the Department of Pathology of Benazir Bhutto Hospital (BBH), a tertiary care facility in Rawalpindi. All the consecutive cases of papillary urothelial neoplasms of the urinary bladder presented during a period of two years (2014-2016) were studied. Standard tissue sections were made from the specimen obtained by transurethral resection (TUR) of bladder tumor and stained by hematoxylin and eosin. All cases of papillary neoplasm were included whereas all poorly fixed specimens were excluded. The slides were studied and classified according to 2004 WHO/ISUP classification of the urothelial neoplasms of urinary bladder that is papilloma, papillary urothelial neoplasm of low malignant potential, low grade papillary urothelial carcinoma, high grade papillary urothelial carcinoma. The data was analyzed using SPSS 21. Descriptive statistics like frequencies and percentages were calculated. Cross tabulations were also constructed for variables of gender and age groups according to type of tumor and muscle invasion.

**Results**

A total of 47 cases of urothelial tumors of urinary bladder were reported in the Pathology department of BBH during the study period of two years. Out of these, 42 patients (89.4%) were male while 5 (10.6%) were female. The male to female ratio was 8.4: 1. The ages ranged from 27 -90 years with the median age of 61 years in males and 55 years in females. Majority of patients were between ages 61-70 years (44.8%) as displayed in figure 3.

The tumors were classified according to 2004 WHO/ISUP classification system. Low grade papillary urothelial carcinoma was the commonest finding with 35 cases (74.5%) followed by High grade papillary urothelial carcinoma with 11 cases (23.4%). Only one case of papillary urothelial neoplasm of low malignant potential was recorded while no case of urothelial
papilloma was reported. The distribution of these tumors according to age and gender (Table 1). Out of 47 cases muscularis propria was invaded in 15 cases (31.9%) as shown in figure 4 all of which were males. Among these, 8 cases were low grade papillary urothelial carcinoma while 7 were high grade carcinoma. In females all the 5 cases reported were low grade papillary urothelial carcinoma without muscle invasion while in males 30 cases (71.4%) were low grade papillary urothelial carcinoma, 11 cases (26.19%) were high grade papillary urothelial carcinoma and only 1 case (2.38%) of papillary urothelial neoplasm of low malignant potential was reported. With advancing age, an increase in the percentage of muscle invasive tumors was seen with 60.0% of the muscle invasive tumors in 7th and 8th decades of life while 38.1% cases in the 6th decade, 25.0% cases in 5th decade and 11.1% cases were aged less than 50 years.

Discussion

Over the years, the staging of TCC has been evolving due to better understanding of tumor biology and potential for progression. Noninvasive techniques of imaging have a definite role and are likely to undergo further refinements to achieve accuracy, however clinical and pathological staging has been popular amongst clinicians and pathologists. In 1973, Dr. F. K. Mostofi proposed a three-tiered system (World Health Organization [WHO] Grades 1, 2, and 3) to grade urothelial (transitional cell) carcinoma of the urinary bladder on the basis of anaplasia seen⁹. Recognizing that high levels of inter- and intra-observer variability of histologic grading exists, the definition and histologic criteria for grading (LMP, low grade, and high grade) were further refined in 1998.
WHO/ ISUP classification as papillary urothelial neoplasm of low malignant potential, low grade urothelial carcinoma, and high grade urothelial carcinoma. In 1999 low and high-grade categories of the 1998 WHO/ISUP classification were split into three groups (grades 1, 2 and 3). Finally in 2004 meeting of WHO it was agreed to essentially reproduce the 1998 WHO/ISUP classification as the 2004 WHO recommended classification scheme. A comparison between 1973 and 2004 WHO grading system is as follows.

Bladder cancer is the second most common genitourinary malignancy with urothelial carcinomas comprising 90% of all primary bladder carcinomas. In our study the ratio of male to female patients was 8.4:1. Similar studies show such a high incidence of urothelial tumors in males. The increased frequency of bladder cancer in men versus women is explained by smoking habits of men and estrogen-progesterone hormonal influence in the female reproductive life and reduced exposure of women to occupational hazards. Similarly, studies have shown that parous women have a lower risk of bladder cancer than nulliparous women. Our study showed the highest incidence of bladder cancer at age between 61-70 years similar to other studies.

According to our study the most common lesion was low grade papillary urothelial carcinoma (74.5%) followed by high grade papillary urothelial carcinoma (23.4%). Similar results were found in other studies. Majority of the tumors were noninvasive and invasion was seen in only 31.9% cases similar to other studies.

In our study, 63.6% patients of high grade papillary urothelial carcinoma showed muscle invasion where as only 26.7% patients of low grade TCC showed muscle invasion. A study by Alan R. Schned showed similar results with 64.9% of high grade TCC with muscle invasion. Similarly an Indian study showed 75% of high grade tumors invasive to the detrusor muscle layer. Our study showed a significant relation between advancing age and the incidence of muscle invasion similar to an Indian research that showed muscle-invasive tumors were more common in the group of patients who were older than 60 years. Our study included only one patient of papillary urothelial neoplasm of low malignant potential which had no invasion of muscularis layer. Other researches have also shown low incidence of PUNLMP. However in some studies there is a relatively higher incidence of PUNLMP i.e., 25.7%. No case of urothelial papilloma presented in our study.

Grading and muscle invasion are important predictors for overall survival and recurrence. Early detection and avoidance of risk factors like smoking etc. can help decrease the mortality and morbidity due to this potentially life threatening carcinoma.

**References**

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