

CLINICOPATHOLOGICAL SPECTRUM OF UROTHELIAL CARCINOMA OF THE URINARY BLADDER – A STUDY OF 541 CASES AT AFIP PAKISTAN

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ABSTRACT

Objective: To analyze the clinicopathological spectrum of urothelial carcinoma of urinary bladder.

Study Design: Descriptive case series.

Place and Duration of Study: Armed Forces Institute of Pathology (AFIP), from 1st January 2012 to 31st October 2013.

Patients and methods: All cases of urothelial carcinoma were retrieved from AFIP tumour registry. Age, gender, histological type, grade and variant of tumour was noted. The data was analyzed by using computer software program SPSS version 19. Descriptive statistics and frequencies were calculated for age, gender, histological type, grade and variants.

Results: A total of 541 cases of urothelial carcinoma were included in the study. The age at presentation ranged from 22 to 94 years with median age of 63.56 ± 12 years. A number (61%) of the cases were from 6th to 8th decade of life. The gender distribution showed 92.8% of patients (n=502) were males and 7.2 % (n=39) were females with male to female ratio of 12.9: 1. The most common histological type was papillary urothelial carcinoma; present in 493 cases (91.1%) followed by nonpapillary urothelial carcinoma; 48 cases (8.9%). Among papillary urothelial carcinomas, 302 cases (61.3%) were high grade and 191 cases (38.7%) were low grade. Among nonpapillary urothelial carcinomas, all were high grade and variant histology was observed in all cases. The variants included squamoid differentiation which was present in 27 cases (56.3%), nested variant in 8 cases (16.7%). The sarcomatoid, undifferentiated and clear cell variants in 3 cases (6.3%) each, micropapillary variant in 2 cases (4.2%), lymphoepithelial-like and plasmacytoid variant in 1 case (2.1%) each.

Conclusion: Urothelial carcinoma is more common in males. Most of the tumours are papillary urothelial carcinomas. Most of them are high grade and pure urothelial carcinomas. A number of histologic variants are also recognized. Among them, squamoid differentiation is the most common variant histology.

Keywords: Papillary Urothelial ca, histological variants, Urothelial carcinoma.

INTRODUCTION

Carcinoma of the urinary bladder ranks ninth in worldwide cancer incidence. It is the fourth most common malignancy in men and the eighth most common malignancy in women in the United States¹. Among the South Asian countries, Pakistan has the highest incidence of bladder cancer². According to AFIP tumour registry data, bladder carcinoma is the second most common malignancy after breast carcinoma, accounting for 7.4% of all tumours in both genders³. Urothelial carcinoma (UC) accounts for 90% of the bladder tumors⁴. It is known for its divergent differentiation and a spectrum of morphologic variants has been

recognized. The importance of recognizing these variant histologies lies in the diagnostic and prognostic implications associated with them⁵.

UC is either of papillary/non invasive or non papillary/infiltrating type depending upon the presence or absence of papillae with well-defined fibrovascular cores. The grade of tumour is based on the architectural features and cytologic atypia of lining urothelium. Histologically, the neoplastic cells of urothelial carcinoma invade the bladder wall as nests, cords, trabeculae, small clusters or single cells having pleomorphic nuclei with grooves and abundant cytoplasm. There is frequent lymphovascular invasion⁶. UC with squamoid differentiation which is composed of squamoid cells with intracellular keratin, intercellular bridges or keratin pearls is the most common histological variant⁷. It is associated with high grade tumours, and is less chemo-

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radiosensitive. Nested variant appears as nests which have a bland cytology in the superficial part while more atypia in the deeper portions and mimics von Brunn nests⁹. Sarcomatoid variant is grossly gray white, solid, exophytic and polypoid. It histologically resembles mesenchymal tumours most commonly malignant fibrous histiocytoma or undifferentiated sarcoma with or without heterologous foci¹⁰. The clear cell variant is composed of cells with clear, glycogen-rich cytoplasm and needs to be differentiated from metastatic clear cell carcinomas¹¹. The micropapillary variant comprises of delicate, filiform papillary processes that do not contain distinct fibrovascular cores and have a glomeruloid appearance¹². The plasmacytoid variant is composed of single malignant cells having eccentric nuclei and abundant eosinophilic cytoplasm. It has to be differentiated from plasma cell tumour and squamous cell carcinoma of the bladder¹³. Lymphoepithelial like carcinoma reveals proliferating, single, malignant, round or oval epithelial cells with eccentric nuclei. It has to be differentiated from other poorly differentiated tumors or inflammatory infiltrate¹⁴. Studies have shown that all variants are associated with aggressive clinical course except lymphoepithelial-like carcinoma which has a slightly better outcome⁸.

This study was conducted to analyze the clinico pathological aspect of urothelial carcinoma; including the histologic variants and their relative frequencies.

MATERIAL AND METHODS

This retrospective descriptive case series was carried out at Armed Forces Institute of Pathology, from 1st January 2012 to 31st October 2013. All cases of urothelial carcinoma were retrieved from AFIP tumour registry and included in the study irrespective of the age and gender of the patient. Cases with recurrent tumours were excluded from the study. Age, gender, pathologic stage, histological type, grade and variant histology of tumour were noted. A total of 541 cases were included in the study by non-probability consecutive sampling data collection procedure. The data was

analyzed by using computer software program SPSS version 19. Descriptive statistics and frequencies were calculated for age, gender, histological type, grade and variants.

RESULTS

The tumour registry record from 1st January 2012 to 31st October 2013 showed that a total of 541 of UC were diagnosed at AFIP, Rawalpindi during this period. The clinicopathologic characteristics of urothelial carcinoma are summarized in Table.

Table-: Clinicopathological characteristics of 541 patients of urothelial carcinoma.

Characteristics	Number of cases	Percentage
Age		
<50 years	59	10.9%
>50 years	482	89.1%
Gender		
Male	502	92.8%
Female	39	7.2%
Histologic type		
Papillary	493	91.1
Non papillary	48	8.9%
Histologic grade		
Low	191	35.3%
High	350	64.7%
Stage		
pT1	350	64.7%
pT2	191	35.3%

All the diagnosed cases presented between the age of 22-94 years with a mean age of 63.56 ± 12.0 years. The maximum prevalence was seen in the seventh decade. Majority (61%) percent of the cases (n=420) were noted from 6th to 8th decade of life. The median age of low grade UC was 61.06 ± 12.98 years and that of high grade was 64.96 ± 11.31 years.

The gender distribution showed 92.8% of patients (n=502) were males and 7.2 % (n=39) were females with male to female ratio of 12.9: 1. Histological type, grade and stage are given in Table.

All of the low grade tumours were papillary urothelial carcinomas. Among the high grade tumours, 302 cases (86.3%) were papillary and 48 cases (13.7%) were

nonpapillary urothelial carcinomas. Among the stage I urothelial carcinomas, 164 cases (46.9%) were high grade and 186 cases (53.1%). Among stage II tumours, 186 cases were high grade 97.4% while 5 cases (2.6%) were low grade.

The histological variants included 27 cases (56.3%) of squamoid differentiation, 8 cases (16.7%) of nested variant, 3 cases (6.3%) each of sarcomatoid, undifferentiated and clear cell variants, 2 cases (4.2%) of micropapillary type along with 1 case (2.1%) each of plasmacytoid and lymphoepithelial type. Out of the total 350 high grade tumours, 13.7% (48 cases) exhibited variant histology. However, all low grade tumours were pure UC.

DISCUSSION

UC accounts for the majority of the epithelial neoplasms which arise in the urinary bladder⁶. WHO has documented a number of histological variants which pose a diagnostic challenge and affect the prognosis as well⁷. Our study shows that the mean age at time of diagnosis in our population is 63.56 ± 12.0 years. The mean age reported by Zhang et al¹⁵ was 61.67 ± 12.97 years, by Laishram et al¹⁶ 60 years and Rafique et al¹⁷ 55 years, is in concordance with the mean age of the current study. The male to female ratio in our study of 12.9:1 is considerably higher as compared to Zhang et al (5:1), Laishram et al (1.5:1) and Rafique et al (3.6:1)¹⁵⁻¹⁷.

In our study 64.7% of urothelial carcinomas were Stage II tumours, while Stage I tumours were more prevalent in studies conducted by Laishram et al, Zhang et al and Ahmed et al^{15,16,18}. In study carried out by Zhang et al¹⁵ 69.9% and 30.4% cases had papillary and nonpapillary growth pattern while 91.1% and 8.9% cases in our study were papillary and non papillary UC respectively. Analysis of histologic grade shows that Zhang et al¹⁵ reported 50.1% cases were high grade. Our study also showed that high grade UC was more prevalent and was seen in 64.7% of the cases. These results are in contrast to study by Laishram et al,¹⁶ in which 53.85% tumours were low grade and in study by Ahmed et al¹⁸, 44% were low grade.

In our study variant histology was identified in 8.9% of all urothelial tumours, in comparison to studies carried out by Shah et al, Wasco et al and Stefan et al which showed a frequency of 19.5%, 25% and 68.8% respectively^{19,5,7}. All of the high grade infiltrating urothelial carcinomas in our study exhibited variant histology, whereas WHO data shows that histological variants in high-grade urothelial carcinomas account for 40% of the cases²⁰. Alternatively, all tumours with variant histology were high grade which is in concordance with the results of Wasco et al⁴. The most common variant in our study was squamoid followed by nested, sarcomatoid, undifferentiated, clear cell, micropapillary, lymphoepithelial and plasmacytoid. This is in concordance with the WHO data where the variants in order of prevalence are squamous, glandular, sarcomatoid and micropapillary⁷. In the study by Stefan et al, 43.4% (n=113) of the tumours exhibited squamoid differentiation, clear cell in 13.8% (n=36), glandular in 4.5% (n=11), micropapillary in 1.9% (n=5), giant cell in 1.6% (n=4), papilloma-like in 0.8% (n=2) and plasmacytoid variant in 0.4% (n=11)⁷. In a study carried out by Shah et al, squamous morphology (32%) was also the most common variant histology followed by glandular (13%), micropapillary (12%), nested (8%), sarcomatoid (6%), lymphoepithelial (3%) and plasmacytoid (1%) type¹⁹. These results are quite similar to our study but we did not encounter cases with glandular, papilloma-like or giant cell differentiation.

CONCLUSION

Urothelial carcinoma is more common in males. High grade and pure urothelial carcinomas are more common, however a number of morphologic variants are also encountered. Squamous differentiation is the most common variant histology. The variant histology should be documented because of their resemblance to various benign and malignant lesions, association with poor prognosis and preservation of the variant morphology in metastatic foci.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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