Original Article

Various Histomorphologic Patterns of Urothelial Carcinoma in TURBT Specimen

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Abstract

Objective: To evaluate the various morphologic patterns of urothelial carcinoma in transurethral resection specimen of urinary bladder.

Method: One hundred ninty three biopsies of transurethral resection of bladder from different age groups without exception of sex and race were included in this study from year 2013-2019 in Services Hospital Lahore.

Result: Eighty-eight cases from 193 biopsies from services hospital Lahore in 2013 to 2019 were reported as high-grade urothelial carcinoma. While 52out of 193 cases were diagnosed as nested variant of urothelial carcinoma.03 cases neuroendocrine differentiation of urothelial carcinoma is identified and 21 cases having squamous and 12 cases with sarcomatoid differentiation of urothelial carcinoma is reported.

Conclusion: Urothelial carcinoma has many histological variants each having different prognosis and clinical implications. So accurate subtyping of the tumor is important for patient's better management.

Key Words: Urothelial carcinoma, sarcomatoid, divergent differentiation

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Introduction

Definition of histological variants is idiosyncratically dissimilar histomorphologic phenotypes of a particular neoplasm.[1]

Urothelial carcinomas are one of those tumors which demonstrate the numerous histological variants. Some of these variants have good prognosis and some are clinically aggressive. Almost 90% of bladder carcinomas are originate from the urothelium. While little proportion 7% of urothelial carcinomas represent as primary squamous cell carcinoma and another 2% represent as primary adenocarcinoma of the bladder.[1] As per literature out of 90% urothelial carcinomas 33% display some constituent of the deviating differentiation. This deviating differentiation includes squamous, glandular, small cell, rhabdoid differentiation and even rarely trophoblastic and Mullerian features. According to 2016 WHO categorization, urothelial carcinoma is reported with its ten histological variants so far. It includes nested, microcytic, micro papillary, lymphoepithelioma like, plasmacytoid, sarcomatoid, giant cell, poorly differentiated, lipid rich and clear cell.[8]

Some of the histomorphologic patterns of urothelial carcinoma are associated with poor prognosis more clinical aggressive as well as poor response to therapy. Presence of various histology within the same tumor lesion can affect the diagnosis, management and prognosis of the patient. Therefore, it is critically significant to diagnose precisely the various morphological patterns of urothelial carcinoma. To notify the majority of these histomorphologic patterns co-exist with the conventional urothelial carcinoma and do not usually arise in pure form is necessary. Here we discuss some of the histomorphologic patterns of urothelial carcinoma are commonly found in our biopsies.

Nested/Solid histomorphologic pattern of urothelial

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carcinoma is low grade and rare variant, it has deceivingly bland appearance of tumor cells with mild cytological atypia and mild pleomorphic and occasional prominent nucleoli arranged in small and large nests.[5] However this innocent morphology has a definitive malignant behavior and can be presented as locally advanced or metastatic disease in a patient due to delay in diagnosis therefore 3 nested variant of urothelial carcinoma is at an advanced stage at the time of clinical presentation.[18] Diagnosis is not confirmed until muscle invasion is present. Nested/Solid pattern of urothelial carcinoma has good prognosis but the optimal treatment has not yet been resolute because of a rare histomorphologic pattern. Further research is required to define the effective approach.[18]

Next is the sarcomatoid pattern of urothelial carcinoma. It is high grade, display both epithelial and sarcomatoid morphology.[2, 17] Malignant spindle cells leiomyosarcoma-like or another nonspecific heterologous component such as osteosarcoma or chondrosarcoma demonstrate in the sarcomatoid component of this tumor.[17] and the epithelial component is the most commonly of conventional urothelial carcinoma. In some cases, malignant spindle cell component tends to occupy more than fifty percent of the tumor it is possible to lack any epithelial component, that will complicate the diagnosis. This pattern is rare and patients with sarcomatoid carcinoma usually presents with advanced stage and have worse prognosis as compared to conventional urothelial carcinoma. There is no optimal treatment option for this histomorphologic pattern of urothelial carcinoma because many patients develop metastasis after surgery. [14]

Now we discussed the neuroendocrine differentiation in the urothelial carcinoma. It is high grade variant of urothelial carcinoma. It includes small cell, large cell neuroendocrine carcinoma, well differentiated neuroendocrine carcinoma and paraganglioma. Small cell and large cell carcinoma arise from urothelial carcinoma and admixed either with the conventional carcinoma or any other morphologic pattern. Morphologically small cell carcinoma exhibits small cells with high nuclear to cytoplasmic ratio, nuclear molding abundant mitotic figures with necrosis and large cell carcinoma has larger cells with evident cytoplasm, finely stippled chromatin and prominent nucleoli. Overall survival rate is poor. Chemotherapy is the only established therapeutic regimen for treated neuroendocrine carcinomas.[8]

Quite a reasonable case of urothelial carcinoma is observed with definitive areas of squamous and glandular differentiation in high grade urothelial carcinoma and it should be distinguished from primary squamous cell carcinoma and primary adenocarcinoma.[9] The presence of in situ component of urothelial carcinoma indicated the exclusion criteria of primary squamous cell carcinoma or primary adenocarcinoma. As in the absence of any conventional urothelial carcinoma component, primary squamous cell carcinoma or adenocarcinoma should be considered. This pattern presented with worse prognosis and the only treatment option is new adjuvant therapy.[15] Various histomorphologic pattern along with the divergent histology is common in urothelial carcinoma and must be recognized quantified and reported accurately. There are still more fields of research regarding the biological predictive prognostic and treatment implications of urothelial carcinoma with histological variants. Proper recognition and consistent reporting of histomorphologic pattern in urothelial carcinoma is essential. For better defined treatment strategies as well as biomarkers of different variants of urothelial carcinoma more dedicated prospective clinical trials with definitive criteria, tumor registries data base recordings and biopsies are mandatory.

Cystoscopically resection remains the best treatment choice in noninvasive urothelial carcinoma and in some variants of urothelial carcinoma particularly in micro papillary, squamous, plasmacytoid and sarcomatoid. Neo adjuvant chemotherapy is in the chemo sensitive variants particularly in neuroendocrine and lymphoepithelioma like variants of urothelial carcinoma.

Recent research suggested that molecular composition of these urothelial carcinoma could be related to the expression of specific histomorphologic patterns and new subtypes could be identified with further investigation.

Methods

This study is descriptive study held in Pathology Department of Services Institute of Medical Sciences Lahore. We assessed the urothelial carcinoma in 193 cases comes from patients who underwent transurethral resection of bladder in 2013 to 2019 (07 years data). The specimen was retrieved from the files of the Histopathology Department of Services Institute of Medical Sciences. The cases were chosen to repre-

sent urothelial carcinoma along with its various variants to be assessed. Good presentation of morphology is the only criteria of selection. Cauterized and quantitatively inadequate material was excluded from the study. There were not consecutive cases. No patients reported a history of previous treatment. The tumors were diagnosed and reported along with their histological variants' counterpart.

Results

we examined different histological variants of urothelial carcinoma obtained from transurethral resection of bladder from 193 patients in the year of 2013 to 2019 in services hospital Lahore (**Figure 1**). In that study eighty eight (45.0%) cases were reported as urothelial carcinoma high grade and the remaining cases are represented as histomorphologic patterns of urothelial carcinoma. Fifty two (49%) cases were nested; three (2.8%) cases were urothelial carcinoma with neuroendocrine differentiation. Twelve cases (11.4%) were reported as sarcomatoid differentiation of urothelial carcinoma and twenty one cases (20.1%) were reported as urothelial carcinoma with squamous differentiation. Despite in apparent and recent rise in the incidence of variants of urothelial carcinoma the real epidemiology presentation and prognostic values are still not well established.[14] So the aim of our study is to better understand the increase in the load of various variants of urothelial carcinoma.

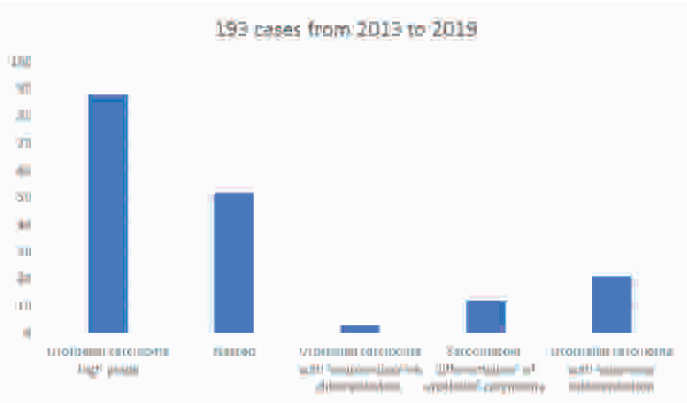

Figure 1: *Depiction of the Data through Histogram*

Discussion

To choose the better treatment modalities and improvement in the cases of urothelial carcinoma, we should identify and report of the various histomorphologic patterns accurately and it is crucial to identify precise risk stratification of patients with bladder cancer. The presence of some morphological variants such as sarcomatoid differentiation, plasmacytoid

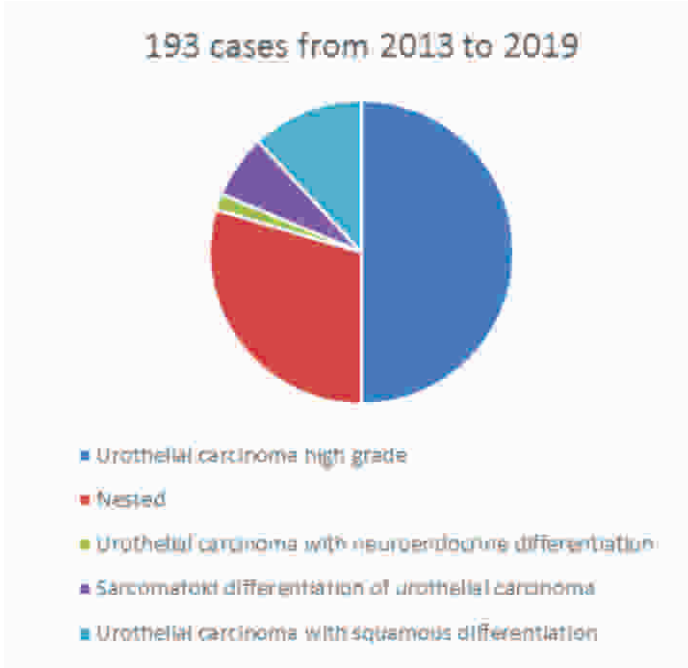

Figure 2: *Depiction of the Data through Pie Chart*

and nested in bladder carcinomas are more aggressive and at the time of presentation and often are in advanced stage of disease.

A single series of large cases has documented that many histomorphologic patterns are common in high grade urothelial carcinoma and that comprised forty percent of the cases in the series by Perez-Montiel D, 2006.[21] According to this study after squamous and glandular differentiation, sarcomatoid (7%) and micro papillary (3.7%) pattern were the common. Similarly, in our study 40% are of high-grade urothelial carcinoma and 11.4% is sarcomatoid variant but in contrast to this study nested variant is more common in our cases (49%) might be due to increase in incidence of this variants in our population as well as fail to collect data of reporting of micro papillary variant in subsequent other biopsies. Frequency of the various histomorphologic variants with respect to the conventional urothelial carcinoma is quite unavailable. Squamous differentiation is the second most common variant is seen in our cases (20%). The prognostic significance of squamous differentiation is unclear, although some studies of Budia Alba A in 1999, Zhai QJ in 2007 have suggested an adverse outcome.[2,17] Another study reveals that 60 to 70% cases were of nested variant of urothelial carcinoma[5,6,19,20,21] as in our study 49% nested variant. It is sufficiently clear that urothelial carcinoma has the ability for the divergent differentiation so for surgical pathologist it is important to be aware of this potential for multidirectional differentiation, as the correct characterization of tumors may have diagnos-

tic, therapeutic or prognostic implications significantly impacting on the management of the patient.

Conclusion

Upgrading in TURP procedures, devoted genitourinary pathologists and emerging genomic techniques for sub typing will lead to a better definition of each histomorphologic patterns of urothelial carcinoma along with related prognosis and treatment strategies.

Conflict of Interest: None

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Author's Contribution

KH: Interpretation, compiling & article writing
JA, LT: Interpretation, compiling of data
NI, SS: Interpretation, review of data
LR: Review of data