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STUDY OF HISTOMORPHOLOGICAL SPECTRUM OF TRANSURETHRAL RESECTED BLADDER TUMOURS: A SINGLE CENTRE EXPERIENCE FROM SOUTH INDIA

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Conflicts of Interest: Nil

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Abstract:

Introduction: Urinary bladder lesions can be both neoplastic and non-neoplastic. Incidence of bladder cancer varies in different countries and also in different regions of the same country.

Cystoscopic biopsy remains the mainstay for establishing bladder cancer diagnosis and also to know the morphologic grading and the staging of bladder cancer. Transurethral resection of bladder tumour (TUR-BT) is commonly done as a diagnostic as well as curative procedure in majority of bladder tumours.

Material & Methods: A total of 100 TUR-BT cases were studied from January 2017 to September 2019 at department of Pathology, Institute of Nephrourology. Samples sent in 10% formalin were routinely tissue processed and paraffin embedded,4-micron sections were taken and Hematoxylin and Eosin staining was done. PAS stain and ZN stain were done when indicated. Demographic data and histopathological diagnosis were retrieved from biopsy reports. Partial and radical cystectomy specimens were not included in the study.

Results: Most common age group affected was 6th decade. Male to female ratio of 1.5: 1.

91 cases out of 100 were neoplastic tumours, with remaining 9 cases of inflammatory/granulomatous lesions. Out of these 91 cases of tumours 10 were metastatic deposits from known cases of carcinoma cervix of the rest 81 cases of urothelial cancers, 39 cases(48.14%) were high grade papillary urothelial carcinoma(HGPUC),31 cases(38.27%) were low grade papillary urothelial carcinoma(LGPUC), ,4 cases (4.93%) of papillary urothelial neoplasm of low malignant potential(PUNLMP), 1 case(1.23%) of squamous cell carcinoma and 6 cases(7.40%) of poorly differentiated carcinoma.

Among 81 cases of neoplastic bladder tumours, 40 cases (49.38%) were non-invasive,17 cases (20.98%) were showing invasion into lamina propria (superficially invasive bladder cancer) and 19 cases (23.45%) showing invasion into muscularis propria (muscle invasive bladder cancer) and in the rest 5 cases (6.17%) invasion not identified.

Of the 36 invasive cases, 6 were showing associated divergent differentiation.

Conclusion: In the present study neoplastic lesions of the bladder were more common compared to inflammatory lesions with a male preponderance. High grade tumours were more common than the low-grade tumours. Invasive urothelial carcinomas were common than non-invasive. Bladder cancers are known for divergent differentiation like squamous, glandular, small cell, rhabdoid and microcystic variants and should be mentioned in histopathology report as some of the variants are aggressive and impact prognosis.

Keywords: Bladder tumour, Cystoscopic biopsy, India, TUR-BT, Urothelial carcinoma.

Introduction

Urinary bladder lesions can be both neoplastic and non-neoplastic. There are many variables in the incidence within a country as well in different geographical region. There is a wide variation in the incidence of urothelial cancer of the bladder with Western Europe and North America having a highest incidence with Eastern Europe and Asian countries having the lowest numbers.

Indian cancer registry states bladder cancer is the seventh most common cancer. Bladder cancer usually affects the elderly individuals even though few rare variants can be seen affecting children and young adults. In general, the incidence of bladder cancer is low in women.

Environmental risk factors account for most cases of bladder cancer. Bladder mucosa is exposed to potential carcinogens that are either excreted in the urine or activated from precursors in the urine. Chemical carcinogenesis is believed to be responsible for much of the burden of bladder cancer including the increased risk associated with cigarette smoking as well as varied industrial exposure. Cigarette smoking is the most important factor contributing to overall incidence of bladder cancer. Cystoscopic biopsy remains the mainstay for establishing bladder cancer diagnosis and also to know the morphologic grading and staging. Transurethral resection of bladder tumour (TUR-BT) is commonly done as

a diagnostic as well as curative procedure in majority of bladder tumours.

Material & Methods

A total of 100 transurethral resected bladder biopsies were studied from January 2017 to September 2019 at the department of Pathology, Institute of Nephrourology. It's a retrospective study. Samples sent in 10% formalin were routinely tissue processed and paraffin embedded, 4 to 5-micron sections were taken and Hematoxylin and Eosin staining was done. Sections were examined by two pathologists under the light microscope to document pathological diagnosis by consensus. PAS stain and ZN stain were done when indicated. Additional serial sections and deeper sections were taken when required. Demographic data and histopathological diagnosis were retrieved from biopsy reports. Partial and radical cystectomy specimens were not included in the study.

Results

Patient demographics

Total 100 transurethral resected bladder biopsies were included in the study period. Most common age group affected was 6thdecade (Table 1). Next common age group affected was 5th decade. Youngest patient affected was of age 23 years and oldest patient was of 82 years. Out of total 100 patients, 60 were males and 40 were females with a male to female ratio of 1.5: 1.

Histomorphological findings

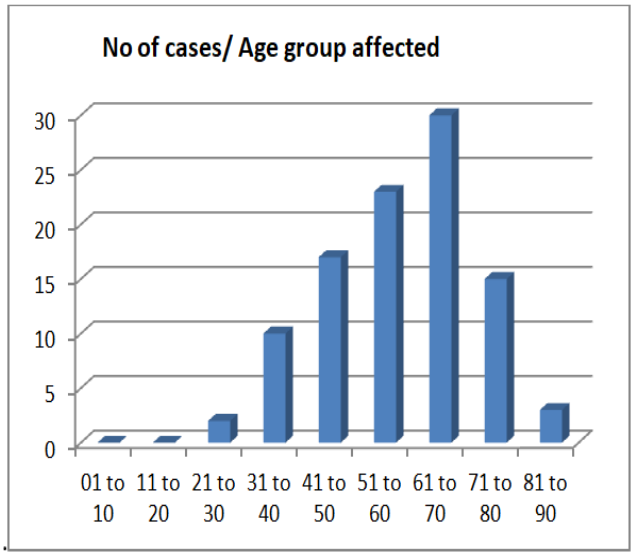
91 cases out of 100 were neoplastic tumours, with remaining 9 cases of inflammatory/granulomatous lesions (Table 2). Out of these 91 tumour cases,10 were metastatic deposits from known cases of carcinoma cervix. Among these 10 metastatic cases,8 were squamous cell carcinomas and 2 were undifferentiated tumours.

2016 WHO classification of tumours of urinary system and male genital organs,4th edition was used as reference for morphologic classification of urothelial tumours. Staging was done according to the American Joint Commission on Cancers (AJCC/TNM) staging manual (8th edition).

Of the 81 cases of urothelial bladder cancers, 39 cases(48.14%) were high grade papillary urothelial carcinoma(HGPUC, Figure 1),31 cases(38.27%) were low grade papillary urothelial carcinoma(LGPUC), 4 cases (4.93%) of papillary urothelial neoplasm of low malignant potential(PUNLMP), 1 case(1.23%) of squamous cell carcinoma and 6 cases(7.40%) were poorly differentiated carcinoma(Table 3).

Out of these 81 cases of neoplastic bladder tumour, 40 cases (49.38%) were non-invasive,17 cases(20.98%) were showing invasion into lamina propria(superficially invasive bladder cancer) and 19 cases(23.45%) showing invasion into muscularis propria(muscle invasive bladder cancer, Figure 2)and in the rest 5cases(6.17%) invasion was not identified out as both lamina propria and muscularis propria were not seen in tissue submitted(Table 4).

Of these 36 invasive cases (both superficial and deep invasive), urothelial carcinomas with variable differentiation was seen in 6 cases. These 6 included 2 cases of urothelial carcinoma with squamous differentiation, 1 case of urothelial carcinoma with glandular differentiation, 1 case with small cell carcinoma/neuroendocrine differentiation,1 with microcystic variant and 1 with rhabdoid differentiation.



Table/Chart 1: Number of patients affected with reference to age group.

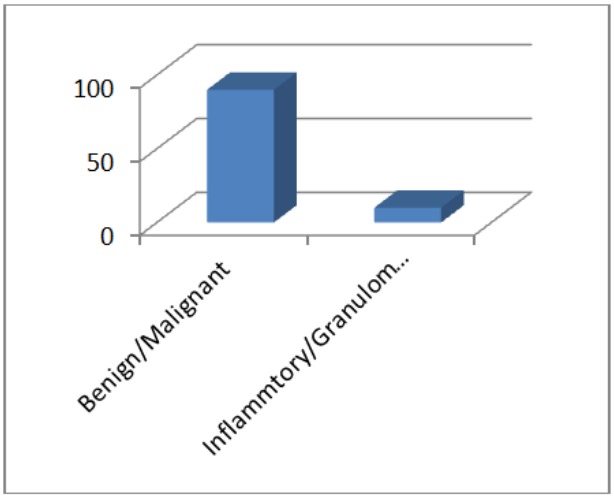


Table /Chart 2: Distribution of neoplastic versus non-neoplastic/inflammatory lesions.

Table 3: Histomorphological tumour types – as per 2016 WHO classification of urinary system and male genital organs.

WHO/ISUP grading of Bladder cancer	No of cases
High grade papillary urothelial carcinoma	39 (42.85%)
Low grade papillary urothelial carcinoma	31 (34.06%)
Papillary urothelial neoplasm of low malignant potential	4 (4.39%)
Squamous cell carcinoma	1 (1.09%)
Poorly differentiated carcinoma	6 (6.59%)
Metastatic tumours	10 (10.98%)

Table 4: Number of invasive versus non-invasive urothelial tumours – pathological staging.

Pathological staging of bladder cancer (pT)	No of cases
pTa - Non-invasive papillary carcinoma	40 (49.38%)
pT1 – Tumour invades subepithelial connective tissue	17(20.98%)
pT3 – Tumour invades muscularis propria	19(23.45%)

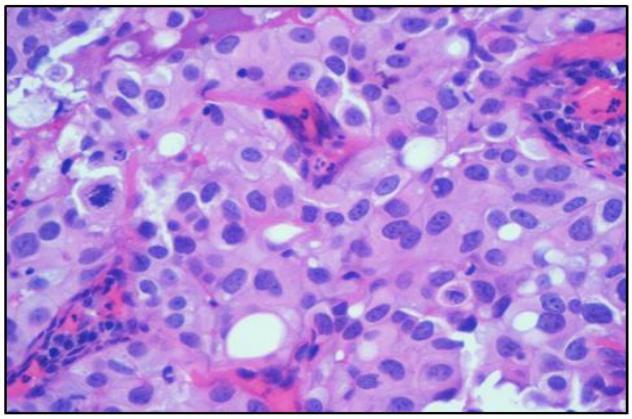


Figure 1: (40 x magnification, Haematoxylin and Eosin stain): High grade tumour showing pleomorphic hyperchromatic nuclei with prominent nucleoli and an atypical mitotic figure.

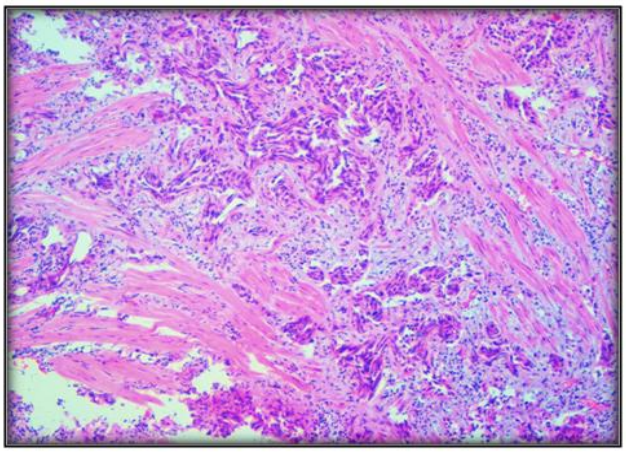


Figure 2: (10 x magnification, Haematoxylin and Eosin stain): HGPUC with clusters of tumour cells infiltrating into the muscular propria

Discussion

There are only few centres in India where high volumes of bladder cancers are diagnosed and treated. Ours is one such government institute– tertiary care referral centre for urology and nephrology, located in south India.

Urinary bladder and renal pelvis are the common sites of urinary tract tumours. Urothelial carcinoma is the most common tumour type accounting for 90% of all primary tumours of the bladder. Cystoscopy is an important tool in the diagnosis of urinary bladder carcinoma. Biopsy material obtained by the cystoscopy helps in accurately determining the histological grade and pathological stage as both are most important prognostic variables in bladder tumours [1]**.** Incidence of bladder cancer is more in men than the women. In the present study ratio of male to female is1.5 : 1 which is similar to study done by Anita Shah at al[2] where the authors reported bladder cancers were two times higher in men than in women i.e., 2.2 : 1.Similar findings were noted in a study done by Panchal Jaimin et al[3] who reported higher incidence of bladder carcinomas in males compared to females. Increase in prevalence of bladder carcinomas more in men may be attributed to the difference in smoking habits and occupational exposure to various chemical carcinogens [4]

Most common age group affected in present study was 6th decade which is in concordance with study done by Anita Shah et al [2] where authors reported highest number of cases (34%) in 6thdecade. In a study done by Panchal Jaimin et al [3] the most common age group affected was 5th decade.

In the present study majority of bladder cancers were neoplastic tumours(91%) and the rest being inflammatory/granulomatous lesions(9%).This is in correlation with the study done by Anita Shah et al[2] from Nepal where about 70% of cases were neoplastic and 30% were non neoplastic and also study by Yaavar shafi et al[5] from northern India(Kashmir valley)where about 95% of the cases were neoplastic with only 5% of cases of non-neoplastic/inflammatory lesions. This is also in concordance with study done by Thapa R et al [6] from Kathmandu, Nepal where about 70% were neoplastic and 30% were non neoplastic. In our study greater number of neoplastic cases may be due to the fact that because our institute is a super speciality referral centre for the entire state and other reason could be that the uncomplicated inflammatory cases may probably treated at primary and secondary centres. Among the inflammatory lesions in our study chronic non-specific cystitis was the common lesion attributing to 50% of non-neoplastic cases followed by case of cystitis glandularis and granulomatous lesion each and 2 cases of squamous metaplasia. This is in concordance with the finding by Yaavar shafi et al [5] where cystitis cystica

and inflammation comprised about 46% of the non-neoplastic cases. We had 1 case of non-caseating granulomatous lesion. We did Ziehl-Neelsen stain (ZN stain) to look for Acid fast bacilli which was negative. We also had 2 cases with squamous metaplasia but there was no history suggestive of bladder infection or bladder calculi in those 2 cases.

In the current study 40 cases (49.38%) were non-invasive,17 cases(20.98%) were showing invasion into lamina propria(superficially invasive bladder cancer) and 19 cases(23.45%) showing invasion into muscularis propria(muscle invasive bladder cancer) and in the rest 5 cases(6.17%) invasion was not identified as both lamina propria and muscularis propria were not seen in tissue sub mitted. This is in comparison with findings of the study done by Sushmita et al [1], wherein authors reported 11(39.29%) non-invasive cases,7(25%) cases with lamina propria invasion and 10(35.71%) showing invasion into muscularis propria**.** Ina study done by Panchal J et al[3], authors reported 53% of cases as non-invasive urothelial carcinomas and among the non-invasive carcinomas 35% were low grade and 65% were high grade tumours. In the present study all the non-invasive tumours were low grade. Both the treatment and prognosis vary for muscle invasive and non-invasive bladder tumours. In contrast with present study, Srikousthubha et al [7] in their study reported 87.5% of cases of non-invasive tumour. In one of the studies from Kathmandu, Nepal authors Pudasaini et al [8] muscle invasion was seen in 26.7% of the cases and there was no detrusor muscle in 33.3% of the urothelial tumour cases. It is always advisable that the deep biopsy when taken with part of muscle tissue after the superficial tumour has been resected must be sent separately in a different container for histopathological examination. In such cases identification of muscle invasion and reporting for the same will be more accurate. We would like to highlight the fact that if muscle tissue is not identified in the biopsy, comment about it should be made clearly in the report so that the call for repeat biopsy if needed can be taken by the treating Surgeon/Urologist if clinically indicated.

In the present study HGPUC was most common accounting for 42.85% of the cases followed by 34.06% cases of LGPUC. This is in concordance with study done by Aparna et al [9] and also Thapa R et al[5] where the authors reported 34% and 31% of HGPUC lesions and LGPUC cases of 23% and 50% respectively. Where as in contrast, study done by Yaavar shafi et al [5] authors reported 62% of cases of LGPUC.

We had two cases of HGPUC showing carcinoma in situ (CIS) changes in adjacent urothelium. CIS is defined as total replacement of urothelium by cells having cytological features of carcinoma but without invasion of basement membrane i.e. it's a flat lesion [10]. CIS changes in adjacent area indicate increased chances of recurrence and multifocality of the lesion**.**

Urothelial carcinomas with variant or divergent differentiation like nested, microcystic, microcapillary, lymphoepithelioma like, plasmacytoid, sarcomatoid, giant cell variant, lipid rich and poorly differentiated are not uncommon. In present study we had two cases of urothelial carcinoma with squamous differentiation and one case with glandular differentiation. Ina study done by Panchal Jet al [3] four cases were reported as urothelial carcinomas with squamous differentiation and one case of urothelial carcinoma with glandular differentiation. It is important here to mention that pure squamous cell carcinoma of the bladder is the carcinoma derived from urothelium with a histologically pure squamous cell phenotype. It is most commonly seen in infections like Schistosomiasis and in long standing cases of bladder calculi. The diagnosis of SCC of bladder is reserved for tumours with purely squamous elements, characterized by presence of keratin pearls and intercellular bridges. Squamous differentiation in bladder urothelial carcinoma should be mentioned in the report as it is more resistant to radiotherapy. In the present study we also had one case of urothelial carcinoma with small cell/neuroendocrine differentiation, one case of urothelial carcinoma with rhabdoid differentiation and 6 poorly differentiated/undifferentiated carcinoma cases. In one of the largest studies done by Muhammed Mubarak et al [4] from Karachi, Pakistan authors reported one each case of paraganglioma and small cell carcinoma,3 cases of embryonal rhabdomyosarcoma, 2 cases of sarcomatoid carcinoma and 3 cases of poorly differentiated carcinoma.

Primary adenocarcinoma of the urinary bladder is uncommon. Long standing intestinal metaplasia particularly in patients with bladder exstrophy is usually associated with adenocarcinoma.

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Conclusion

Cystoscopic biopsy remains the mainstay for establishing bladder cancer diagnosis and also to know the morphologic grading and staging. TUR-BT is commonly done as a diagnostic as well as curative procedure in majority of bladder tumours.

In the present study neoplastic lesions of the bladder were more common compared to inflammatory lesions with a male preponderance. High grade tumours were more common than the low-grade tumours. Invasive urothelial

carcinomas were common than non-invasive. At this juncture authors suggest that not all bladder biopsies include muscle tissue and hence depth of invasion cannot be made on histopathology slides. In such cases pathologists should clearly mention in the report about the absence of muscle tissue in the sample studied. So that a repeat biopsy including the muscle can be taken by the Surgeon/Urologist if indicated. Bladder cancers are known for divergent differentiation like squamous, glandular, small cell, rhabdoid and microcystic variants and should be mentioned in histopathology report as some of the variants are aggressive and can impact the prognosis.

References

1. Sushmita S, Girija SP, Patil SB. A study of histopathological spectrum of lesions in urinary bladder specimens. APALM 2018; 5(5):489-95
2. Anita S, Manglesh S, Ashok S, Ghanshyam S. Spectrum of lesions in urinary bladder - A histopathological study. JUCMS 2018;6(2), 24-27
3. Panchal J, Shreesha K.A gamut of histopathological lesions of carcinoma of urinary bladder – A study of 43 cases. Int J. Biomed Adv Res 2015;6(3): 212-19
4. Mubarak, M, Kazi J, Hashmi A, Hussain M, Naqvi S, Rizvi S. Urinary bladder tumours in Southern Pakistan: A histopathologic perspective. Middle East J Cancer 2014;5(3):167-73
5. Yaavar shafi, Danish Rafiq, Baba Iqbal Khaliq, Wajahat -un-Nazir, Naheena Bashir. Histopathological study of urinary bladder tumours in a tertiary care hospital. Int J Curr Res 2019; 11(3):2175-80
6. Thapa R, Lankhey M, Bhatta AD. Spectrum of histomorphological diagnosis in cystoscopic bladder biopsies. Journal of pathology of Nepal 2017;2(1),1062-65
7. Srikousthuba, Sukesh, Raghuveer C.V, Hingle S. Profile of lesions in Cystoscopic bladder biopsies-A histopathological study. J Clin Diagn Res 2013;7:1609-12
8. Pudasaini S, Subedi N, Prasad KBR, Rauniyar SK, Josi BR, Bhoomi KK. Cystoscopic bladder biopsies: A histopathological study. Nepal Med Coll J 2014;16(1);9-12
9. Aparna C, Thumma RR, Devi CP, Vanapalli SVR, Mounika TDN. Histopathological Spectrum of Urothelial Lesions – Experience of A Single Tertiary care institute. IJCMR 2016;3(6):1731 – 3
10. Farrow GM. Pathology of carcinoma in situ of the urinary bladder and related lesions. Cell Biochem Suppl 1992; 161:39-43