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Histopathological Gamut of Urinary Bladder Tumors: An Institutional Study

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Abstract: ***Introduction:*** *The present study was taken up to assess the incidence of different histological variants of bladder tumors, site, age and sex distribution, presenting symptoms and a brief comparison was done about the histopathological features of the tumors occurring in young and old individuals.* ***Material and methods:*** *The present study is a retrospective two year descriptive study conducted in the Department of Pathology, tertiary care hospital in Guntur. The biological materials included in the study were Trans-urethral resection of bladder tumor (TURBT) specimens, complete and partial cystectomies. The formalin fixed specimens were routinely processed and haematoxylin and eosin stained slides were retrieved from the departmental archives and reviewed.* ***Results:*** *The most common location for bladder tumors in the present study was lateral wall constituting 40.9% of the cases followed by posterior wall (20.4%), trigone (13.6%), neck (11.3%), anterior wall (9.1%) and ureteric orifice (4.5%).* ***Conclusion:*** *To conclude, urothelial carcinomas are rare and prognostically better in the age group below 40 years, as most present with non invasive low grade papillary urothelial carcinomas.*

Key Words: *TURBT, UROTHELIAL CARCINOMA, NILGPUC, ADENOCARCINOMA*

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I. Introduction:

Urinary bladder malignancies constitute world's seventh most common cancer[1]. There exists a considerable disparity in its incidence and mortality worldwide[2]. Epidemiological studies have shown that there exists a clear cut male preponderance and the most common age group being 65-70 years[3].

Urothelial carcinoma constitutes about 90% of all the bladder tumors. Other variants like squamous cell carcinomas and adenocarcinomas are relatively rare[3, 4]. Most patients are diagnosed with pre invasive or early invasive tumors, of which 50-70% commonly recur. Progression is however rare[3].

Risk factors include cigarette smoking[5, 6] occupational exposures to aromatic amines, arsenic, long term use of analgesic phenacetin[6], and radiotherapy for other childhood tumors, schistosoma infection and familial syndromes like Lynch Syndrome[7].

The most common presenting symptom is hematuria[8] which can range from microscopy to gross, based on the invasiveness of the tumor per se.

The present study was taken up to assess the incidence of different histological variants of bladder tumors, site, age and sex distribution, presenting symptoms and a brief comparison was done about the histopathological features of the tumors occurring in young and old individuals.

II. Material and methods:

The present study is a retrospective two year descriptive study conducted in the Department of Pathology, tertiary care hospital in Guntur. The biological materials included in the study were Trans-urethral resection of bladder tumor (TURBT) specimens, complete and partial cystectomies. The formalin fixed specimens were routinely processed and haematoxylin and eosin stained slides were retrieved from the departmental archives and reviewed. Clinical and histopathological data obtained were recorded and tabulated. The bladder tumors were categorized according to the WHO Classification, 2016[9]. Histological criteria for grading of tumors were also scrutinized. Age limit of 40 years was taken to classify the study cohort into younger and older group.

FIG- 1 : Low grade Non invasive papillary urothelial carcinoma

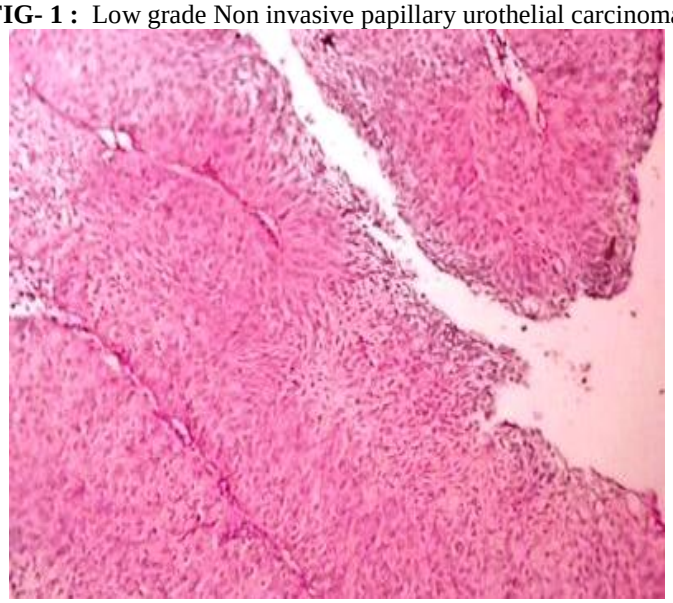

FIG-2: High grade non invasive papillary urothelial carcinoma

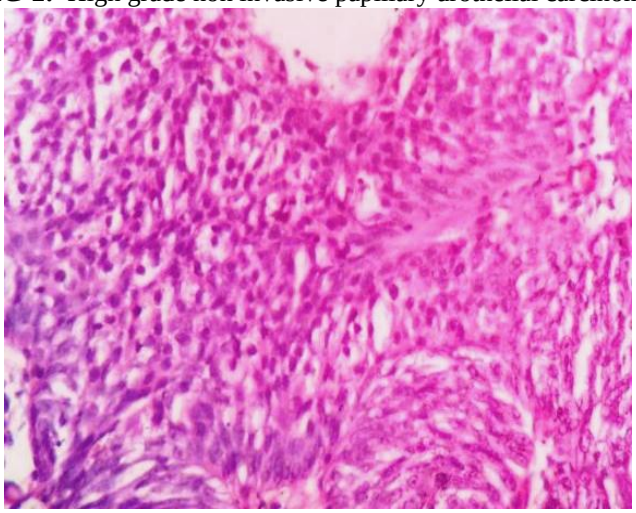

FIG-3 : Squamous cell carcinoma

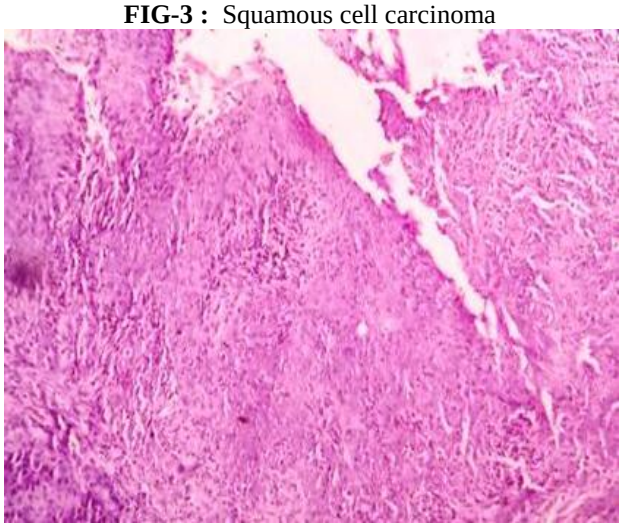

FIG-4 Clinical characteristics of the study cohort:

Characteristics	Number (%)
Age (years)	
21-30	2 (4.5)
31-40	2 (4.5)
41-50	4 (9.1)
51-60	10 (22.8)
61-70	18 (40.9)
71-80	6 (13.7)
81-90	2 (4.5)
Gender	
Males	36 (81.8)
Females	8 (18.2)
Presenting symptoms	
Hematuria	
Present	29 (65.9)
Absent	15 (34.1)
Frequency of micturition	
Increased	9 (20.5)
Normal	35 (79.5)
Abdominal pain	
Present	6 (13.7)
Absent	38 (86.3)
Pelvic mass	
Present	2(4.5%)
Absent	42 (95.5)
Location	
Lateral wall	18 (40.9)
Posterior wall	9 (20.5)
Trigone	6 (13.7)
Neck	5 (11.3)
Anterior wall	4 (9.1)
Ureteric orifice	2 (4.5)
History of tobacco use	
Currently smoking	24 (54.5)
Previously smoking	8 (18.2)
Never smoked	12 (27.3)

FIG-5 Histopathological distribution of the study cohort:

AGE (YEARS)	**NILGPUC**		**NIHGPUC**		**IUC**		**SCC**		**ADENOCARCINOMA**	
	M	F	M	F	M	F	M	F	M	F
21-30	1	1								
31-40	1	1								
41-50	2	-	-	1	-	-	1	-	-	-
51-60	6	-	-	2	-	-	1	-	-	1
61-70	6	-	6	-	5	-	-	1	-	-
71-80	4	-	2	-	-	-	-	-	-	-
81-90	-	-	1	-	-	1	-	-	-	-
	20	2	9	3	5	1	2	1	-	1
TOTAL	22		12		6		3		1	

FIG-6 Follow up of the patients with urothelial carcinoma:

	Non invasive		**Invasive urothelial carcinoma**
	LGPUC	HGPUC	
Mean follow up period	18 months	16 months	14 months
Alive with no recurrence	12	10	4
Alive with local recurrence	5	-	-
Alive with metastasis	1	-	1
Died of disease	-	2	1
Total	**18**	**12**	**6**

III. Results:

A total of 44 bladder tumors were reported in the above study period. The most common age group was 7th decade of life with male preponderance (male: female ratio= 4.5:1). The youngest patient in the cohort was a 26 years male who presented with dysuria and was diagnosed to have non invasive low grade papillary urothelial carcinoma, the oldest was a 85 year male presenting with gross hematuria and was diagnosed to have invasive urothelial carcinoma. The most common presenting symptom was hematuria constituting 65.9% of the cases, followed by increased frequency of micturition (20.4%) and abdominal pain (13.7%). 32 cases had a history of smoking tobacco and one case had a family history of bladder carcinoma.

The most common location for bladder tumors in the present study was lateral wall constituting 40.9% of the cases followed by posterior wall (20.4%), trigone (13.6%), neck (11.3%), anterior wall (9.1%) and ureteric orifice (4.5%).

Histologically, the most common tumor was low grade non invasive papillary urothelial carcinoma constituting 50% of cases (FIGURE 1), followed by high grade non invasive papillary urothelial carcinoma (27.2%) (FIGURE 2). Six cases of Invasive urothelial carcinoma, three cases of squamous cell carcinoma and one case of adenocarcinoma were also reported. Of the six invasive urothelial carcinomas diagnosed, one caseshowed invasion into lamina propria, four cases showed invasion into the muscularis propria and one case showed invasion beyond perivesical soft tissue. Of the eight female patients, six cases were found to have either high grade papillary urothelial carcinoma or other invasive carcinomas. Of the three squamous cell carcinomas (FIGURE 3) diagnosed one was well differentiated and the other two were moderately differentiated and all the three showed invasion into muscularis propria. A single case of adenocarcinoma was reported in the study period which occurred in a 54 year female patient who was a chronic diabetic and presented with recurrent urinary tract infection. This tumor also showed invasion into the muscularis propria.

When clinical and histological features of bladder tumors were compared in young and old patients, it was found that all the 100% of the young cases and only 45% of the old cases were diagnosed to have low grade non invasive papillary urothelial carcinoma. Gender incidence also varied appreciably between the two groups, which was 1:1 in the younger group compared to 5.7:1 in the older group. Two of the young patients had a history of tobacco smoking and one case had a family history of bladder carcinoma. 28 cases of the old group had a significant history related to tobacco smoking.

Follow up information was available only for 40 cases of the total study cohort with the mean follow up period being 18 months (Range: 6 months to 24 months). Of the 22 cases of low grade papillary urothelial carcinomas, it was found that all of them were alive during the follow up period of 18 months. However, 5 five cases had recurrence and one case was found to have progression to high grade and later invasive urothelial carcinoma, who underwent a cystectomy procedure, and has been disease free for now. Of the 12 high grade papillary urothelial carcinoma patients, 10 were alive after a mean period of 16 months, the remaining two died after developing secondary metastasis after a period of 7 months and 19 months respectively. Of the 6 invasive urothelial carcinomas 5 were alive after a mean period of 14 months, 2 had metastasis to lymph nodes and bone and one died of the disease 6 months post surgery.

IV. Discussion:

Incidence of urothelial carcinomas in young is relatively rare and it varies according to the criterion used to label as young. This incidence varies from 1 to 2.4% when younger than 40 years is used as criterion and 0.1 to 0.4% when younger than 20 years is used as the defining criterion[10, 11]. In the present study the incidence ratio between the younger and older groups was 10:1, which is similar to the study done by Manika Kundra et al[12], who quoted an incidence ratio of 10.1:1. The present study states that the sex incidence also varies in the young and old groups considerably and this observation is similar to that made by Stanton et al[13], who quoted a male to female incidence of 1.8:1 in the young.

75% of the female patients in the present study were diagnosed to have either high grade papillary urothelial carcinoma or invasive cancers. This could be explained by the delay in diagnosis due to lower suspicion of urothelial carcinoma in this gender and due to higher incidence of urinary tract infections.

Many studies have quoted that urothelial tumors of the young are relatively low grade and have better prognosis than that in the older groups[13]. We found that 100% of our young patients were diagnosed to have low grade papillary urothelial carcinoma, similar to the study done by Paner GP et al [14]. No patients in this age group died of the disease although one case developed recurrence of the tumor. When the older group was considered the incidence of low grade tumors was 45%, of which four cases had recurrence and one case showed progression to invasive carcinoma. Our results suggest that prognosis is better in the younger group and the incidence of recurrences do not differ much in the younger and older groups. These findings correlate well with that of Stanton et al[13].

Oncogenesis of urothelial carcinomas in the young is still unclear. However, most studies have shown that tobacco smoking and genetic factors play a critical role. In the present study 50% of the young cases have a history of smoking and one case had a family history of bladder cancer. Wan J et al have quoted a tobacco smoking incidence of 67% in the age group of 21-30 years and 96% in the age group of 31-40 years and Stanton et al have quoted an incidence of 58%. Genetic alterations occurring in the young and older group are diverse and different [15, 16].

Even though histopathological diagnosis of bladder carcinomas is not complicated, it is often deferred due to lack of suspicion of tumors in the young[17]. Moreover, urine cytology, a routinely performed investigation, is not very sensitive in diagnosing low grade tumors, which form the bulk in this age group.

The differential diagnosis include a wide range of metaplastic conditions like papillary cystitis, which can mimic low grade papillary tumors, florid cystitis glandularis which can mimic nested variant of invasive urothelial carcinoma. Grading of urothelial tumors has significant prognostic implication and hence it is essential to grade them using the present WHO 2016 guidelines. However, it is important to understand that the grade of the tumor may vary from area to area and hence differentiation may vary between TURBT specimen and surgical resection specimen of the same patient. Cheng L et al[18] consequently suggested that grading of urothelial carcinoma by methods that take into consideration this histopathological heterogeneity help in accurate stratification of tumors into different prognostic groups. With the emergence of molecular pathology, several authors like Bas WG et al[19] opined that molecular methods such as FGFR3 mutation status and immunohistochemical expression of MIB1 and P53 were better at grading the tumors as they were more reproducible than the pathologic grading systems.

Adenocarcinomas of urinary bladder are rare and constitute about 2% of all invasive tumors. In the present study a single case of adenocarcinoma was reported in a 54 year old female patient. The tumor grossly presented as a fungating mass covered with slimy mucinous material. The tumor cells showed invasion into muscularis propria. Follow up information of the patient was not available. However, most series report a poor prognosis of primary urinary bladder adenocarcinoma with a five year survival rate of 18%[20].

In the present study four cases of squamous cell carcinoma have been reported. Squamous metaplasia is a common feature in high grade urothelial carcinomas and hence the diagnosis of squamous cell carcinoma should be reserved only to cases which show solely features of squamous cell carcinoma with the background showing keratinizing squamous metaplasia[21].

V. Conclusion:

To conclude, urothelial carcinomas are rare and prognostically better in the age group below 40 years, as most present with non invasive low grade papillary urothelial carcinomas. In addition, the gender incidence is different in the two groups. Use of tobacco is an important risk factor in both the groups. It is important to meticulously categorize the tumors according to the grade and degree of invasion as there is a momentous difference in the prognosis and thus management of individual cases.

References:

[1]. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v 1.0, Cancer incidence and mortality worldwide: IARC cancer base no.11. Available from: http//globocan iarcfr: International agency for research on cancer.

[2]. Chavan S, Bray F, Lortet Tieulent J, Goodman M, Jemal A. International variations in bladder cancer incidence and mortality. Eur Urol 66:59-73. PMID: 24451595

[3]. Kirkali Z, Chan T, Manoharan M, Algaba F, Busch C, Cheng L, et al. Bladder cancer: epidemiology, staging and grading and diagnosis. Urology 66(6) suppl 1:4-34. PMID: 16399414.

[4]. Seigel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. CA Cancer J Clin 64:9-29. PMID: 24399786.

[5]. Pommer W, Bronder E, Klimpel A, Helmert U, Greiser E, Molzahn M.Urothelial Cancer at different tumor sites: role of smoking and habitual intake of analgesics and laxatives. Results of Berlin Urothelial cancer study. Nephrol Dial Transplant. 14:2892-7. PMID: 10570093.

[6]. Zeeger MP, Tan FE, Dorant E, Van Den Brandt PA. The impact of characteristids of cigarette smoking on urinary tract cancer risk: a meta analysis of epidemiologic studies. Cancer. 89:630-9. PMID :10931463.

[7]. Mueller CM, Caporaso N, Greene MH. Familial and genetic risk of transitional cell carcinoma of the urinary tract. Urol. Oncol, 26: 451-64. PMID: 1862223.

[8]. Davis R, Jones Js, Barocas DA, Castle EP, Lang EK, Leveillee RJ et al: American Urological Association. Diagnosis, evaluation and follow up of asymptomatic micro hematuria in adults:AUA guideline. J Urol. 188(6) suppl: 2473-81. PMID:23098784.

[9]. Holger Moch , Peter A Humphrey, Thomas M Ulbright , Victor E Reuter(Eds): WHO classification of tumors of the urinary system and male genital organs (4th edition). IARC: Lyon 2016.

[10]. Migaldi M, Rossi G, Maiorana G et al. Superficial papillary urothelial carcinomas in young and elderly patients: a comparative study. BJU Int. 2004;94(3):311–316.

[11]. Kutarski PW, Padwell A. Transitional cell carcinoma of the bladder in young adults. Br J Urol. 1993;72(5, pt 2):749–755.

[12]. Kundra M, Hemapant. Urinary Bladder Tumors: A comparative histopathological study in patients less than 40 years and more than 40 years Indian Journal of Pathology and Oncology, October-December 2017;4(4):507-510

[13]. Stanton ML, Xiao Li, Czerniak AB, Guo CC. Urothelial Tumors of the Urinary Bladder in Young Patients : A Clinicopathologic Study of 59 Cases. Arch Pathol Lab Med. 2013;137:1337–1341; doi:10.5858/arpa.2012-0322-OA

[14]. Paner GP, Zehnder P, Amin AM, Husain AN, Desai MM. Urothelial neoplasms of the urinary bladder occurring in young adult and pediatric patients: a comprehensive review of literature with implications for patient management. Adv Anat Pathol. 2011;18(1):79–89.

[15]. Wild PJ, Giedl J, Stoehr R, et al. Genomic aberrations are rare in urothelial neoplasms of patients 19 years or younger. J Pathol. 2007;211(1):18–25.

[16]. Owen HC, Giedl J, Wild PJ, et al. Low frequency of epigenetic events in urothelial tumors in young patients. J Urol. 2010;184(2):459–46.

[17]. Greenfield SP, Williot P, Kaplan D. Gross hematuria in children: a ten year review. Urology. 2007;69(1):166–169.

[18]. Cheng L, Neumann RM, Nehra A, Spotts BE, Weaver AL, Bostwick D. Cancer Heterogeneity and Its Biologic Implications in the Grading of Urothelial Carcinoma. CANCER (2000) 88: 7.

[19]. .Bas W.G. Rhijn V, Andre N. Vis et al: Molecular grading of Urothelial Cell Carcinoma with Fibroblast Growth Factor Receptor 3 and MIB-1 is superior to pathologic grade for the prediction of clinical outcome: *Journal of Clinical Oncology* 21, no. 10 (May 2003) 1912-1921. DOI: 10.1200/JCO.2003.05.073.
[20]. Anderstrom C, Johansson SL, von Schultz L.Primary adenocarcinoma of the urinary bladder. A clinicopathologic and prognostic study. *Cancer*. 1983; 52(7):1273-1280.
[21]. Sakamoto N, Tsuneyoshi M, Enjoji M.Urinary bladder carcinoma with a neoplastic squamous component: a mapping study of 31 cases. *Histopathology*. 1992; 21(2):135-141.

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