ORIGINAL RESEARCH PAPER

Histopathology

PREVALANCE OF UROTHELIAL CARCINOMA, ITS HISTOLOGICAL GRADE AND TYPE IN URINARY BLADDER OVER A PERIOD OF 2 YEARS: A STUDY IN A TERTIARY HOSPITAL IN CENTRAL INDIA

KEY WORDS:

Dr Varsha Verma* PG Resident Department Of Pathology, Gajra Raja Medical College Gwalior, Madhya Pradesh*Corresponding Author

Dr Reema Bhushan Assistant Professor Department Of Pathology, Gajra Raja Medical College Gwalior, Madhya Pradesh

Dr Sudha Iyengar Professor Department Of Pathology, Gajra Raja Medical College Gwalior, Madhya Pradesh

Dr Rajesh Gaur Professor & Head Department Of Pathology, Gajra Raja Medical College Gwalior, Madhya Pradesh

ABSTRACT

BACKGROUND:-Urinary bladder carcinoma is well known to show many histological divergent differentiation. The histological variants have important diagnostic, prognostic and therapeutic implications. The aim of the study was to find the prevalence of urothelial carcinoma in a tertiary care centre and to find the proportion of different histological grades and types of urothelial carcinoma. **MATERIAL AND METHODS:-** A retrospective monocentric study was done between April 2020 and April 2022 which includes 37 bladder biopsies which were received in the histopathology section of the Department of Pathology, Gajra raja medical college. Patients who refuse to give consent and those having cystitis were excluded from the study. **RESULTS AND OBSERVATIONS :-** Out of total 37 cases which were reviewed, the mean age was 62 years, with a male predominance (M:F ratio-3.16). Out of 37 cases, there were 8 cases each of high-grade urothelial carcinoma(21.6 %), high grade urothelial carcinoma with invasion (21.6 %) and high grade papillary urothelial carcinoma with invasion (21.6 %). There were 4 cases of high grade urothelial carcinoma with invasion with squamous differentiation (10.8 %), one case each of recurrent high grade urothelial carcinoma with invasion (2.7 %), well differentiated invasive glandular adenocarcinoma NOS (2.7%) and invasive micropapillary urothelial carcinoma with squamous differentiation (2.7 %), two cases each of low grade urothelial carcinoma - 2 cases (5.4 %), low grade papillary urothelial carcinoma (5.4%) and papillary urothelial neoplasm of low malignant potential (PUNLMP) (5.4 %). **CONCLUSION** Urinary bladder carcinoma is more common in male than females. Average age of presentation is 62 years in present study. High grade urothelial carcinoma (83.8 %) is more common compared to low grade (10.8%). H&E staining with ancillary techniques like immunohistochemistry or molecular it can be very effective in to analyse histological variants to better understand this invasive disease hence aiding in further management of patients.

INTRODUCTION

Urinary bladder carcinoma is well known for its many histological divergent differentiation.

About 80 % of urinary bladder cancer is a pure urothelial carcinoma, remaining 20 % have divergent histological variants[1-5].

The variant of urothelial carcinoma has important role in prognosis of the disease[6].

Urothelial neoplasms of urinary bladder may be subdivided into papillary (papilloma, low malignant potential and papillary carcinoma) and non-papillary (urothelial carcinoma in situ and invasive) categories. The neoplastic cells of typical or conventional pattern of invasive urothelial carcinoma are moderate to large size with moderate amount of pale to eosinophilic cytoplasm.Nuclear atypia is obvious and some cases may have bizarre hyperchromatic nuclei with marked anaplasia. Urothelial or transitional cells of urothelial carcinoma include the presence of longitudinal nuclear grooves, appreciable only in low grade tumours , absent to only focally present in high grade tumours[7]. The recognition of histological variants in urothelial carcinoma is important because some types may be associated with a different clinical outcome, some may have a different therapeutic approach or awareness of the unusual pattern may be critical in avoiding diagnostic misinterpretations[7]. Squamous cell carcinoma comprises of about 5% of all malignant bladder tumours and adenocarcinoma of the bladder is also rare[8].

MATERIAL AND METHODS

Present study has been conducted in the Department of Pathology, Gajra Raja Medical College, Gwalior, Madhya Pradesh, during the period April 2020 to April 2022. A total of 37 patients which were admitted in the Urosurgery Department were included in the study. The biopsy was sent in the Department of Pathology in Histology section Data pertaining to age, sex and other relevant clinical data was collected and compiled. Haematoxylin and Eosin (H and E) staining was done and cases were reported.

RESULTS

Cases were in between age 40 years to 75 years with average age of presentation being 62 years.

TABLE 1 – GENDER DISTRIBUTION

GENDER	NO OF PATIENT	PERCENTAGE
MALE	28	76%
FEMALE	09	24%

There were 28 male and only 9 females so male predominance (76%) was found in the present study compared to female (24%)(Table 1).

TABLE 2- Histological Grade

	No of sample	Percentage
HIGH GRADE	31	83.8
LOW GRADE	04	10.8
PAPILLARY UROTHELIAL NEOPLASM OF LOW MALIGNANT POTENTIAL (PUNLMP)	02	5.4

Out of 37 samples 31 were reported as High grade (83.8 %) , 04 were reported as Low grade (10.8%) urothelial carcinoma,02 were reported as Papillary urothelial neoplasm of low malignant potential (PUNLMP) (5.4 %)(Table 2).

TABLE 3- HISTOLOGICAL TYPE

CATEGORY	NUMBER OF CASES	
HIGH GRADE	UROTHELIAL CARCINOMA	8
	WELL DIFFERENTIATED INVASIVE GLANDULAR ADENOCARCINOMA NOS	1
	INVASIVE UROTHELIAL CARCINOMA	8
	INVASIVE PAPILLARY UROTHELIAL CARCINOMA	8
	RECURRENT WITH INVASIVE	1
	INVASIVE MICROPAPILLARY UROTHELIAL CARCINOMA WITH SQUAMOUS DIFFERENTIATION	1
	INVASIVE WITH SQUAMOUS DIFFERENTIATION	4
LOW GRADE	UROTHELIAL CARCINOMA	2
	PAPILLARY UROTHELIAL CARCINOMA	2
PAPILLARY UROTHELIAL NEOPLASM OF LOW MALIGNANT POTENTIAL (PUNLMP)		2

- Out of 37 cases in the present study, 31 cases (83.8%) were reported High grade urothelial carcinoma. Among them,
- 8 were high grade urothelial carcinoma
- 8 were invasive high grade urothelial carcinoma
- 8 were papillary with invasive high grade urothelial carcinoma(figure 1 and 2)
- 4 were invasive with squamous high grade urothelial carcinoma (figure 3 and 4)
- 1 was recurrent invasive high grade urothelial carcinoma
- 1 was invasive micropapillary squamous differentiation high grade urothelial carcinoma (figure 5 and 6)
- 1 was invasive adenocarcinoma high grade urothelial carcinoma(figure 7 and 8)
- 4 cases out of total 37 cases Low Grade Urothelial Carcinoma
- 2 were Low grade Urothelial Carcinoma.
- 2 were Low grade Papillary Urothelial Carcinoma (Figure 9 and 10).
- 2 were Papillary Urothelial Neoplasm of Low Malignant Potential (PUNLMP) (Figure 11 and 12) (Table 3)

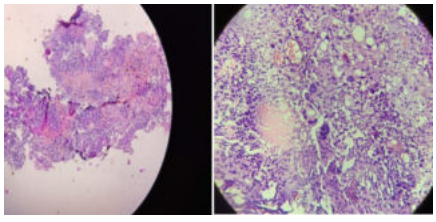

Fig. 1 :10x- High grade papillary urothelial carcinoma
Fig.2: 40x- High grade papillary urothelial carcinoma

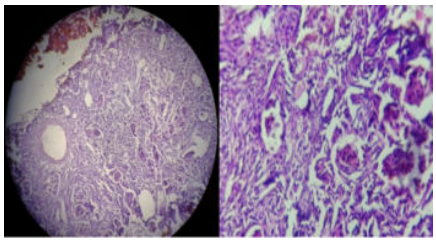

Fig. 3: 10x High grade urothelial carcinoma, with foci of squamous differentiation
Fig. 4 : 40x- High grade urothelial carcinoma with foci of squamous differentiation with invasion into muscle layer

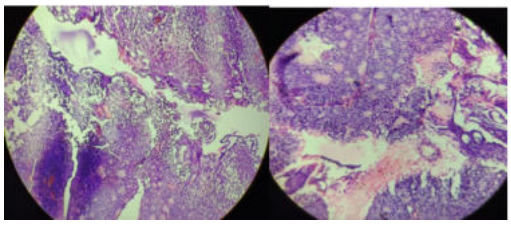

Fig.5 :10x Invasive Micropapillary High Grade Urothelial Carcinoma
Fig.6 :40x Invasive Micropapillary High Grade Urothelial Carcinoma

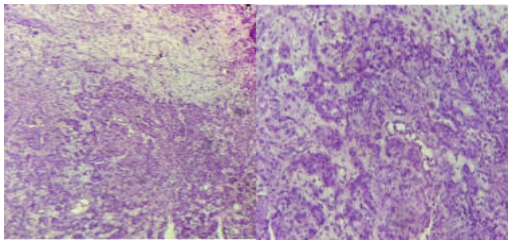

Figure 7: 10x-Well differentiated adenocarcinoma
Figure 8:40x- Well differentiated glandular Adenocarcinoma NOS with invasion into deep muscle, neoplastic cells

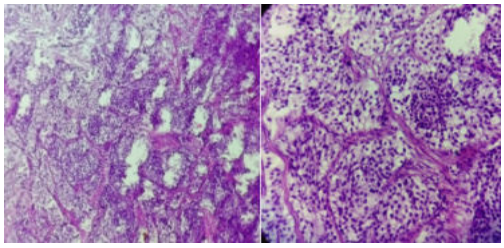

Fig. 9 : 10x- Low grade urothelial carcinoma
Fig. 10 : 40x- Low grade urothelial carcinoma No lamina propria/ deep muscle invasion

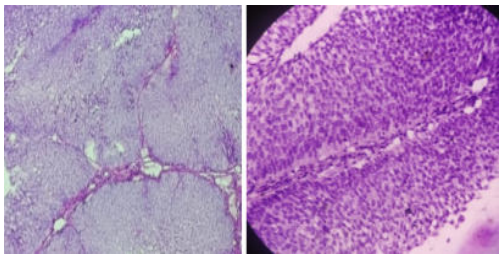

Figure 11:10x- Papillary urothelial neoplasm of low malignant potential
Figure 12:40x- Papillary urothelial neoplasm of low malignant potential (PUNLMP)

Discussion :-

Bladder cancer comprises a wide range of histological types[9]. Thirty seven cases were studied over a period of 2 year. Among them, 31cases were diagnosed as High-grade urothelial carcinoma. The mean age in present study was 62 years similar to studies done by Souli et al [10], Chalasani et al [11] and Gupta et al [12]. There was a male preponderance [76%] in present study ,similar to the studies done by Souli et al [10] Chalasani et al[11] and Gupta et al[12]. Pan et al [13] did study on 1515 cases of non-muscle invasive bladder cancer (NMIBC). There were 60% of cases in his study which were categorized as low grade. Zhang et al [14] found 56% of the superficial tumors in his study to be low grade, while 95% of the muscle invasive tumors were of high grade. In our study 6 cases were

non muscle invasive out of which 4 cases (66.6%) of the cases were reported as Low Grade, while 84 % (31 cases) were reported as High grade.

High grade urothelial carcinoma predominated in TURBT specimens (78%) in our study which is comparable to studies by Gupta P et al[12] and Mamoon N et al[15] but in some studies [16, 17] low grade carcinoma predominated. Cheng L et al [18](87.6%) found very high proportion of high grade carcinoma in his study. In present study, patient presented at late stages which may be due to lack of knowledge and awareness about disease. Previous studies [14,16,18,19] were done which found correlation between advancing tumor grade and muscle invasion which was also seen in the present study. Other studies [20-22] found that squamous differentiation was the most common subtype of urothelial carcinoma with divergent differentiation in his study. Present study showed squamous differentiation in 16 % cases (5 out of 31 cases of high grade cases). In study of Ertugul Sefik et al [23] ,the squamous differentiation rate was 12% , which is comparable to the finding of the present study (16 %). Previous studies quoted that adenocarcinoma comprises of 6-18 % cases of urothelial carcinoma [24]. In present study, there was one(2.7%) case of high grade adenocarcinoma. Micropapillary urothelial carcinoma is an aggressive variant of urothelial carcinoma with an estimated prevalence of 0.7-8% [25].The mean age of presentation is 66 years[26]. In present study, 2.7 % cases (1 out of 31 cases) of high grade tumours have invasive micropapillary variant similar to other studies. In the literature, urothelial carcinoma with variant histology cases varied between 7 and 81% [11]. Our findings support the report of Moschini et al who assessed 1067 radical cystectomy cases, observing squamous differentiation in 10.2% of cases [27].

CONCLUSION

Urinary bladder carcinoma is a common malignancy which is diagnosed at a relatively late stage when compared to the west. There are many histological variants of urothelial carcinoma. Squamous, glandular and micropapillary differentiation generally present at more advanced disease stage than conventional urothelial carcinoma resulting in worse patients outcomes. Early identification of histological variant and its grading and the use of new available techniques like immunohistochemistry or molecular can aid the physician in clinical decision making and can lead to better patient outcomes.

REFERENCES-

1. Moch H, Cubilla AL, Humphrey PA et al (2016) The 2016 who classification of tumours of the urinary system and male genital organs—part A: renal, penile, and testicular tumours. Eur Urol 70:93–105
2. Kaimakliotis HZ, Monn MF, Cary KC et al (2014) Plasmacytoid variant urothelial bladder cancer: is it time to update the treatment paradigm? Urol Oncol 32:833–838
3. Porten SP, Willis D, Kamat AM (2014) Variant histology: role in management and prognosis of nonmuscle invasive bladder cancer. Curr Opin Urol 24:517–523
4. Xylinas E, Rink M, Robinson BD et al (2013) Impact of histological variants on oncological outcomes of patients with urothelial carcinoma of the bladder treated with radical cystectomy. Eur J Cancer 49:1889–1897
5. Monn MF, Kaimakliotis HZ, Pedrosa JA et al (2015) Contemporary bladder cancer: variant histology may be a significant driver of disease. Urol Oncol 33(18):e15–2
6. Shah RB, Montgomery JS, Montie JE, Kunju LP (2013) Variant (divergent) histologic differentiation in urothelial carcinoma is under-recognized in community practice: impact of mandatory central pathology review at a large referral hospital. Urol Oncol 31:1650–1655
7. Dr MB Amin, MD, Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, 8700 Beverly Blvd. Suite 8728, Los Angeles, California 90048, USA.
8. Rosai J. Urinary tract. In: Rosai and Ackerman's Surgical Pathology .9th ed. Vol.1.Elsevier 2004:1327-1340.ISBN:978-81-8147-440-7.
9. Chasalani V,Chin JL,Izawa JL.Histological variants of urothelial bladder cancer and nonurothelial histology in bladder cancer.Can Urol Assoc J.2009:3:S193-S198.
10. Amine Souli, Tarik Karmouni, Khalid El Khader, Abdellatif Koutani and Ahmed Iben Attya Andaloussi, Histology of variants of urothelial carcinoma of the bladder: a Moroccan series of 39 cases (2021) 27:1
11. Chasalani V,Chin JL,Izawa JL.Histological variants of urothelial bladder cancer and nonurothelial histology in bladder cancer.Can Urol Assoc J.2009:3:S193-S198.
12. Gupta P,Jain M,Kapoor R Muruganandham K,Shrivastava A, Mandhani A. Impact of age and gender on the clinicopahological characteristics of bladder cancer. Indian J Urol 2009;25(2):207-10
13. Pan CC, Chang YH, Chen KK, Yu HJ, Sun CH, Ho DM. Prognostic significance of the 2004 WHO/ISUP classification for prediction of recurrence, progression, and cancer specific mortality of non-muscle invasive urothelial tumors of the urinary bladder : a clinicopathologic study of 1,515 cases. Am J Clin Pathol 2010;133:788-95
14. Zhang HZ, Wang CF, Sun JJ, Yu BH. A combined clinicopathologic analysis of 658 urothelial carcinoma cases of urinary bladder. Chin Med Sci J 2012;27:24-8
15. Mamoon N,Iqbal MA, Jamal S,Luqman M. Urothelial neoplasia of urinary bladder comparison of interobserver variability for WHO classification 1972 with WHO/ISUP Consensus Classification 1998. J Ayub Med Coll Abbotabad 2006;18(2).
16. Matalka I Bani-Hani K, Shotar A, Bani Hani O, Bani Hani I. Transitional cell carcinoma of the urinary bladder:a clinicopathological study. Singapore Med J 2008;49(10):790-4
17. Wen YC,Kuo JY, Chen KK, Lin ATL,Chang YH,Hsu YS, Chang LS. Urothelial carcinoma of urinary bladder in young adults- Clinical experience at Taipei Veterans General Hospital. J Chin Med Assoc. 2005 June;68(6):272-75.
18. Cheng L, Neumann RM, Nehra A, Spotts BE, Weaver AL, Bostwick DG.Cancer heterogeneity and its biologic implications in the grading of urothelial carcinoma. Cancer 2000;88:1663-70.
19. Ahmed Z, Muzaffer S, Khan M, Kayani N, Pervez S, Husseini A S and Hasan SH. Transitional cell carcinoma of the urinary bladder . A histopathological study. J Pak Med Assoc. Sep2002;52(9):396-8.
20. Humphrey PA et al. The 2016 WHO classification of tumours of the urinary system and male genital organs-part B: prostate and bladder tumours. Eur Urol. 2016;70(1):106-19.
21. Gluck G et al. Comparative study of conventional urothelial carcinoma, squamous differentiation carcinoma and pure squamous carcinoma in patients with invasive bladder tumors. J Med Life. 2014;7(2):211-4.
22. Kucuk U et al. Clinical, demographic and histopathological prognostic factors for urothelial carcinoma of the bladder. Cent European J Urol. 2015;68(1):30-6.
23. Ertugrul Sefik, Serdar Celik, Ismail Basmaci, Serkan Yarımoglu, Ibrahim Halil Bozkurt, Tarık Yonguc, Bulent Gunlusoy Bozyaka Training and Research Hospital, Department of Urology, Izmir, Turkey DOI: 10.4081/aiua.2018.3.172
24. Lopez-Beltran A et al. Variants and new entities of bladder cancer. Histopathology. 2019;74(1):77-96
25. Solomon JP et al. Challenges in the diagnosis of urothelial carcinoma variants: can emerging molecular data complement pathology review? Urology. 2017;102:7-16.
26. Samaratunga H, Delahunt B. Recently described and unusual variants of urothelial carcinoma of the urinary bladder. Pathology. 2012;44(5):407- 18.
27. Moschini M, Dell'Oglio P, Luciano' R, et al. Incidence and effect of variant histology on oncological outcomes in patients with bladder cancer treated with radical cystectomy. Urol Oncol. 2017;35:335-41.