

A Study of Histomorphological Spectrum of Urinary Bladder Lesions in a Tertiary Care Hospital

Preethy R¹, Thanga Raj², Mythili R³, Praba V⁴^{1,2,3}Assistant Professor, Department of Pathology, Government Kallakurichi Medical College, Kallakurichi⁴Professor and HOD, Department of Pathology, Government Kallakurichi Medical College Kallakurichi

Received: 25-01-2024 / Revised: 23-02-2024 / Accepted: 26-03-2024

Corresponding Author: Dr. Preethy R

Conflict of interest: Nil

Abstract:

Background: Diseases of the urinary bladder lesions can be neoplastic and non-neoplastic. Urothelial carcinoma is the commonest type accounting for 90% of all primary tumors of the bladder. Other epithelial bladder tumors include squamous cell carcinomas, mixed urothelial carcinoma with areas of squamous differentiation, adenocarcinomas and small cell carcinomas. Based on this aim of our study is to describe the histomorphological spectrum of urinary bladder lesions in TURBT and cystoscopic biopsy specimens and also to study the correlation of smoking habit with malignancies of the Urinary bladder

Methodology: This is a retrospective and prospective observational study of histomorphological spectrum of urinary bladder lesions undertaken in the department of pathology of a tertiary care teaching hospital over a period of 3 years, a total of 83 biopsies was done. A detailed clinical history was taken from the patient where special emphasis is laid on the smoking history. Patients of all ages with urinary bladder lesions attending department of urology who has undergone or undergoing TURBT/cystoscopic biopsy were included in the study, while Autolysed specimens and inadequate specimens were excluded.

Results: Among the study group coming to symptoms. 59 patients were presenting with haematuria, 65 patients had dysuria and 59 patients had abdominal pain. Out of 7 patients with benign lesions, none of them had history of smoking, whereas out of 76 patients with malignant lesions, 51 patients had history of smoking and 25 patients are non-smokers. 100% of the smokers were malignant, whereas 78.1% of the non-smokers were malignant. The difference in the malignancy rate between smokers and non-smokers were statistically significant with the p-value of 0.001. In this study, among 83 patients, histopathology examination of biopsies from 76 patients (92%) were reported as having malignant lesions and 7(8%) of them were reported as having benign lesions.

Conclusion: In our study most common bladder lesion was urothelial carcinoma. Out of total urothelial carcinoma cases, most common carcinoma was of high-grade papillary urothelial carcinoma presented with lamina propria and muscularis propria invasion. Pathological grade and muscle invasion are the most valuable prognostic predictors of survival. Hence, screening of all smokers above 40 years of age for bladder cancer has to be made mandatory. Increased awareness of smoking and its ill effects have to be promoted among the public.

Keywords: Urinary Bladder, Lesions, Smoking, Malignant.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Diseases of the urinary bladder lesions can be neoplastic and non-neoplastic. The neoplastic lesions are quite common. The non-neoplastic lesions include congenital anomalies, cystitis, malakoplakia, urachal lesions, tuberculosis, and metaplastic lesions like cystitis glandularis is squamous metaplasia and nephrogenic adenoma.

The precursor lesions of urothelial carcinoma include noninvasive papillary tumors and flat noninvasive urothelial carcinoma. The most common precursor lesions to carcinoma are noninvasive

papillary tumors, originating from papillary urothelial hyperplasia. The other precursor lesion to invasive carcinoma, flat urothelial carcinoma is referred to as carcinoma in situ.

Urothelial carcinoma is the commonest type accounting for 90% of all primary tumors of the bladder. Other epithelial bladder tumors include squamous cell carcinomas, mixed urothelial carcinoma with areas of squamous differentiation, adenocarcinomas and small cell carcinomas. As per Indian cancer registry data, it is the 9th most com-

mon cancer accounting for 3.9 % of all cancers. The association between some of the etiological agent like cigarette smoking, occupational carcinogens, and patients receiving radiation therapy are well established. Other risk factors include long term use of analgesics, heavy long term exposure to cyclophosphamide and schistosoma hematobium infections. The incidence of bladder cancer is higher in men than women with male to female ratio of 3:1. The most common age group affected ranges from 50 years to 80 years. [1-4]

The risk of recurrence and progression depends on tumor size, grade, stage, multifocality and associated dysplasia and / or carcinoma in situ in the surrounding mucosa. The prognosis of urothelial carcinoma depends mainly on histological grade and stage of the tumor at diagnosis. Invasive urothelial carcinoma is associated with a 30% mortality rate once the tumor invades into the lamina propria and 59% mortality rate when invades into muscularis propria. The papillary urothelial neoplasms of low malignant potential and low grade papillary urothelial cancer yield a 98% 10 year survival rate. High grade papillary urothelial carcinomas with invasion lead to death in about 25% of cases. [5,6] Based on this aim of our study is to describe the histomorphological spectrum of urinary bladder lesions in TURBT and cystoscopic biopsy specimens and also to study the correlation of smoking habit with malignancies of the Urinary bladder

Materials and Methods

This is a retrospective and prospective observational study of histomorphological spectrum of urinary bladder lesions undertaken in the department of pathology of a tertiary care teaching hospital over a period of 3 years, a total of 83 biopsies was done. After obtaining written and understandable consent, urinary bladder biopsies were taken in the urology department.

The biopsy is kept in 10% neutral buffered formalin immediately in a well closed container

and transported to the histopathology lab with adequate measures. A detailed clinical history was taken from the patient where special emphasis is laid on the smoking history. Patients of all ages with urinary bladder lesions attending department of urology who has undergone or undergoing TURBT/cystoscopic biopsy were included in the study, while Autolysed specimens and inadequate specimens were excluded.

The bladder biopsy specimens were received in Department of Pathology in 10% neutral buffered formalin. Specimens are left in the fixative for adequate time. After adequate fixation tissue processing is done as routine in the tissue processor, four to five micron thick sections are cut from paraffin blocks using microtome cutting and are subjected to Hematoxylin and Eosin staining. Data obtained are tabulated and statistical analysis is performed.

Results

A total of 83 bladder biopsies were received in the Department of Pathology during the study period, the mean age of the patients who had undergone the bladder biopsies (TURBT / Cystoscopic) in the department of urology was 61.13 years with the age ranging from 23 – 86 years. As per the biopsy results, the mean age of patients with benign lesions was 39.57 years (range: 23- 54years) whereas, the mean age of patients with malignant lesions was 63.11 years (range: 41- 86 years)

In this study, number of male patients who had undergone bladder biopsies were 68 (82%) and the number of female patients who had undergone the bladder biopsies were 15 (18%). Out of 76 patients with malignant lesions, 65 patients were males (86%) and remaining 11(14%) were females. Out of 7 patients with benign lesions, 3 (43%) were males and 4 (57%) were females. Among the study group coming to symptoms. 59 patients were presenting with hematuria, 65 patients had dysuria and 59 patients had abdominal pain.

Table 1: Distribution of samples according to smoking history

Smoking History	Malignant	Benign	p-value
Smokers	51 (100.0%)	0	0.001
Non-Smokers	25 (78.1%)	7 (21.9%)	

Out of 7 patients with benign lesions, none of them had history of smoking, whereas out of 76 patients with malignant lesions, 51 patients had history of smoking and 25 patients are non-smokers. 100% of the smokers were malignant, whereas 78.1% of the non-smokers were malignant. The difference in the malignancy rate between smokers and non-smokers were statistically significant with the p-value of 0.001.

Out of 83 biopsies, 81 were TURBT specimens (98%) and 2 were cystoscopic biopsy specimens (2%). In this study, among 83 patients, histopathology examination of biopsies from 76 patients (92%) were reported as having malignant lesions and 7(8%) of them were reported as having benign lesions. Out of 7 benign lesions, 6 (7%) of them had cystitis and cystitis glandularis. One (1%) had urothelial papilloma.

Among the 76 malignant cases, 50 cases (66%) were diagnosed as papillary urothelial carcinoma high grade with one showing squamous differentiation and 26 cases were diagnosed as papillary urothelial carcinoma low grade (34%). Out of 76 papillary urothelial carcinoma cases, 71 cases (95%) showed invasiveness. In 5 cases (5%) the sample did not show any invasion. Among the 71 cases with invasive tumours, 44 cases (62%) showed muscle invasiveness. In 27 cases (38%), there were only lamina propria invasion.

Discussion

This study conducted in the Department of Pathology, Coimbatore Medical College, included a total of 83 cases. The age ranged in the present study from 23 to 86 years with a mean age of 61.13 years.

As per the biopsy results, the mean age of patients with benign lesions was 39.5 years with the range of 23 – 54 years. The mean age of patients with malignant lesions was 63.11 years with the range of 41 – 86 years. This finding is similar to a study by Mojgan Karbakhsh et al [7] in 960 cases of urothelial carcinoma the peak incidence was seen at 62.14 years.

In the present study, the male to female ratio is 4:1, showing male predominance. Among 7 patients with benign lesions, 3 were males (43%) and 4 were females (57%). Out of 76 patients with malignant lesions, 65(86%) were males and remaining 11 (14%) were females. As per this study, male to female ratio for malignant lesions is 4:1. This observation is comparable to a study conducted by Johansson where the sex ratio was 3:1. Studies conducted by Rajesh Singh Laishram et al [8] (2012) showed a male predominance with male to female ratio of 2:1.

Among the 83 patients, 59 patients were present with hematuria, 65 patients were present with dysuria and 59 patients were present with abdominal pain. These features were comparable with previous studies by Kalpana et al [9].

Out of 83 patients studied, all 7 patients with benign lesions were non-smokers. Among the remaining 76 patients with malignant lesions, 51 of them were smokers and 25 of them were non-smokers which are statistically significant and show an almost double times increased incidence of urothelial carcinoma in patients who had history of chronic smoking. This is comparable with studies by Hartge P, Silverman D, Hoover R, et al. [10] which show increased risk of malignancy in smokers with men having 50- 65% and women having 20-30%.

Out of 83 biopsies studied, 81 biopsies were TURBT specimens and 2 biopsies were cystoscopic biopsy specimens. As per this study, we had re-

ceived only 7 biopsies with benign lesions like cystitis, cystitis glandularis and urothelial papilloma.

The biopsies were sent in most cases only to rule out carcinoma by the urologists due to unawareness of symptoms by the patient which is comparable with studies by Vaidya et al [11], Vaibhav Kumar Goyal et al [12]. Remaining all 83 malignant cases showed the morphology of papillary urothelial carcinoma with one showing squamous differentiation which is almost comparable with the study conducted by Vaibhav Kumar Goyal et al [12] which showed 96.8% incidence of urothelial carcinoma among malignant patients.

Among 76 malignant cases studied, 50 cases (66%) were high grade papillary urothelial carcinoma and 26 cases (34%) were low grade papillary urothelial carcinoma. This is comparable with results obtained by Mahesh Kumar et al [13]. The higher incidence of high grade tumors is likely due to late presentation of the patients, environmental or genetic factors which are yet to be understood.

Among the total 76 cases studied, 71 cases (95%) showed invasion and the remaining 5 (5%) cases were non-invasive. Out of 71 invasive tumors, 44 cases (62%) showed invasion into the muscularis propria and remaining 27 cases (38%) showed lamina propria invasion which is comparable with Vaibhav Kumar Goyal et al [12] which showed tumors with muscle invasion being 62.9% and Shah et al which showed muscle invasion of 69% [14].

Conclusion

In our study most common bladder lesion was urothelial carcinoma. Out of total urothelial carcinoma cases, most common carcinoma was of high-grade papillary urothelial carcinoma presented with lamina propria and muscularis propria invasion. Pathological grade and muscle invasion are the most valuable prognostic predictors of survival. There is almost double the time increased incidence of urothelial carcinoma noted among smokers than non-smokers. Hence, screening of all smokers above 40 years of age for bladder cancer has to be made mandatory. Increased awareness of smoking and its ill effects have to be promoted among the public.

References

1. Humphrey PA, Moch H, Cubilla AL, Ulbright TM, Reuter VE. The 2016 WHO Classification of Tumours of the Urinary System and Male Genital Organs-Part B: Prostate and Bladder Tumours. *Eur Urol.* 2016 Jul; 70(1):106-119.
2. Hinotsu S, Akaza H, Miki T, Fujimoto H, Shinohara N, Kikuchi E, Mizutani Y, Koga H, Okajima E, Okuyama A., Japanese Urological Association. Bladder cancer develops 6 years earlier in current smokers: analysis of bladder

- cancer registry data collected by the cancer registration committee of the Japanese Urological Association. *Int J Urol*. 2009 Jan; 16(1):64-9.
3. Pelucchi C, Bosetti C, Negri E, Malvezzi M, La Vecchia C. Mechanisms of disease: The epidemiology of bladder cancer. *Nat Clin Pract Urol*. 2006 Jun; 3(6):327-40.
 4. Cumberbatch MG, Rota M, Catto JW, La Vecchia C. The Role of Tobacco Smoke in Bladder and Kidney Carcinogenesis: A Comparison of Exposures and Meta-analysis of Incidence and Mortality Risks. *Eur Urol*. 2016 Sep; 70(3):458-66.
 5. Zeegers MP, Swaen GM, Kant I, Goldbohm RA, van den Brandt PA. Occupational risk factors for male bladder cancer: results from a population based case cohort study in the Netherlands. *Occup Environ Med*. 2001 Sep; 58(9):590-6.
 6. Ames BN, Kammen HO, Yamasaki E. Hair dyes are mutagenic: identification of a variety of mutagenic ingredients. *Proc Natl Acad Sci U S A*. 1975 Jun; 72(6):2423-7.
 7. Karbakhsh M, Dabbagh N, Shabani A, Tabibi A, Akhavidadegan H. Age at diagnosis in bladder cancer: does opium addiction play a role? *Asian Pac J Cancer Prev*. 2013; 14(8):4723-5.
 8. Laishram RS, Kipgen P, Laishram S, Khurajam S, Sharma DC. Urothelial tumors of the urinary bladder in Manipur: a histopathological perspective. *Asian Pac J Cancer Prev*. 2012; 13(6):2477-9.
 9. Gupta K, Grigoryan L, Trautner B. Urinary Tract Infection. *Ann Intern Med*. 2017 Oct 3; 167(7):ITC49-ITC64.
 10. Hartge P, Silverman D, Hoover R, Schairer C, Altman R, Austin D, Cantor K, Child M, Key C, Marrett LD, et al. Changing cigarette habits and bladder cancer risk: a case-control study. *J Natl Cancer Inst*. 1987 Jun; 78(6):1119-25.
 11. Vaidya S, Lakhey M, K C S, Hirachand S. Urothelial tumours of the urinary bladder: a histopathological study of cystoscopic biopsies. *JNMA J Nepal Med Assoc*. 2013 Jul-Sep; 52(191):475-8.
 12. Vaibhav Kumar Goyal, Surendra Kumar Prakash, Dharam Chand Kothari "Spectrum of lesions in Urinary bladder biopsies: Histopathological study" *International Journal of Dental and Medical Research* 2015; 1: 42-46.
 13. Mahesh Kumar U and B.R. Yelikal, Spectrum of Lesions in Cystoscopic Bladder Biopsies: A Histopathological study. *Al Ameen J Medical Sci* 2012; 5 (2):132-136.
 14. Shah ND, Weight CJ, Thompson RH, Wang JK, Karnes RJ, Han LC, Ziegenfuss JY, Frank I, Tollefson MK, Boorjian SA. Population-based trends in urinary diversion among patients undergoing radical cystectomy for bladder cancer. *BJU Int*. 2013 Aug; 112(4):478-84.