



UROTHELIAL LESIONS: CYSTOSCOPIC AND HISTOPATHOLOGICAL STUDY IN A TERTIARY CARE HOSPITAL IN HYDERABAD.

Pathology

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ABSTRACT

BACKGROUND: Neoplastic and non-neoplastic urinary bladder lesions are one of the main reasons for morbidity and mortality throughout the world. Aim of the present study was to analyze the cystoscopic findings, histopathological features and the frequency of different cystoscopic urothelial biopsies at a tertiary care hospital in Hyderabad.

MATERIAL AND METHODS: A two-year prospective study of the cystoscopic urothelial biopsies was carried out in the Department of Pathology at Princess Esra Hospital, Deccan College of medical sciences, Hyderabad. Patients complaining of hematuria and dysuria were subjected to cystoscopy and biopsies sent for histopathology.

RESULTS: Total 80 cystoscopic biopsies were evaluated. Hematuria was the most common presenting complaint predominantly affecting elderly males. Cystoscopic biopsies studied revealed 70 % neoplastic and 30 % non-neoplastic lesions. Among the neoplastic lesions, 41 % of low grade, 23.2% of Papillary Urothelial Neoplasm of low malignant potential (PUNLMP), 17.8 % of high grade urothelial Carcinomas, 7.1% each of Adenocarcinoma and papilloma and 3.6 % of Squamous cell carcinoma were reported. Of the Non-neoplastic lesions, 58.3% cases of Chronic nonspecific cystitis, 16.7% each of Cystitis cystica and Granulomatous Cystitis and 8.3% of squamous metaplasia was seen.

CONCLUSION: Our study has revealed that neoplastic lesions are more common. Papillary Urothelial Neoplasm of low Malignant potential was found in significant number which requires close follow up of these patients as these tumors tend to recur and progress to higher grade urothelial carcinomas.

KEYWORDS

Cystoscopy, Urothelial carcinoma, PUNLMP.

INTRODUCTION:

Diseases of the urinary bladder both non-neoplastic and neoplastic are responsible for significant morbidity and mortality¹. Despite the improved methods of diagnosis and treatment, they pose biologic and clinical challenges. Cystoscopy is the primary diagnostic tool for patients who are suspected of having bladder tumors, which allows a direct visualization of the bladder mucosa and take biopsies of the suspected lesions².

The non-neoplastic lesions especially cystitis constitute an important source of symptoms and signs. These diseases are more disabling than lethal. Bladder tumor is the seventh most common tumor worldwide. Urothelial carcinoma is the commonest type accounting for 90% of all primary tumors of the bladder³ They are an important cause of morbidity and mortality with the most common clinical sign being gross and microscopic hematuria in majority of the patients⁴. Male predominance is common worldwide with the risk factors being environmental factors, industrial exposure to aryl amines, long term use of analgesics, cigarette smoking and infestation with *Schistosoma hematobium*. Although progress has been made in the field of non-invasive imaging, histopathological analysis of biopsy material is the mainstay for cancer diagnosis and treatment⁴.

MATERIAL AND METHODS:

A prospective study was done over a period of two years in the Department of Pathology, Princess Esra Hospital, Deccan College of Medical Sciences, Hyderabad. All patients who visited Urology Outpatient Department were examined and related clinical histories of all these patients were recorded. Patients complaining of hematuria and dysuria were subjected to cystoscopy. Transurethral resection of bladder Tissue (TURBT) was done cystoscopically and the biopsies sent for histopathological examination. Routine processing was done starting from fixation, dehydration, embedding and section cutting. Staining was done by Hematoxylin & Eosin. The slides were examined and diagnosed according to WHO/ISUP classification (2004). Data was analyzed and tabulated for evaluation.

Inclusion Criteria

- All the cystoscopic biopsies received in the department of Pathology, Princess Esra Hospital, Hyderabad

Exclusion Criteria

- Autolyzed specimen

- Inadequate biopsies
- Cystectomy specimens

RESULTS:

The present study was conducted over a period of two years during which a total of 80 lesions were evaluated. Hematuria was the most common presenting complaint. The peak age of incidence of the lesions was 51-80 years contributing to 70 % of the cases with maximum number of cases in the sixth decade.

Table 1. Age distribution of Urothelial lesions

AGE DISTRIBUTION	NUMBER OF CASES	PERCENTAGE
0-10	02	2.8
10-20	02	2.8
20-30	08	8.3
30-40	02	2.8
40-50	06	8.3
50-60	16	16.7
60-70	22	27.8
70-80	18	25.0
80-90	02	2.8
>90	02	2.8
Total number of cases	80	100%

The male to female ratio was found to be 4.1:1. Of all the cystoscopic biopsies studied, 30 % (24 cases) were non-neoplastic lesions and 70 % (56 cases) were neoplastic lesions.

Table 2. Distribution of Urothelial lesions

TYPE OF LESIONS	NUMBER	%
NEOPLASTIC	56	70%
NON NEOPLASTIC	24	30%
TOTAL	80	100

Table 3. Distribution of Non neoplastic lesions of bladder

NON NEOPLASTIC LESIONS	NUMBER	%
Chronic nonspecific cystitis.	14	58.3%
Granulomatous cystitis	04	16.7%
Cystitis cystica	04	16.7%
Squamous metaplasia	02	08.3%
TOTAL	24	100

Out of 24 cases of Non-neoplastic lesions, Chronic nonspecific cystitis contributed to 58.3% (14 cases) followed by cystitis cystica and granulomatous cystitis reported in 16.7%(4 cases) each respectively. Squamous metaplasia was seen in 8.3 % (2 cases).

Of the 56 cases (70%) of neoplastic lesions, 58.9 % (33 cases) of urothelial carcinomas of varying grades were reported followed by 23.2% (13 cases) of Papillary Urothelial Neoplasms of low malignant potential ,7.1% (4 cases) of Adenocarcinoma and papilloma respectively and 3.8% (2 cases) of squamous cell carcinoma were reported. Out of 33 cases of urothelial carcinomas, 41.1 % (23 cases) were of low grade and 17.9 % (10 cases) were high grade urothelial carcinomas.

Table 4. Distribution of neoplastic lesions of bladder

NEOPLASTIC LESIONS	NUMBER	%
Papilloma	04	07.1%
Low grade urothelial neoplasms with low malignant potential	13	23.2%
Low grade urothelial carcinoma	23	41.1%
High grade urothelial carcinoma	10	17.9%
Adenocarcinoma	04	07.1%
Squamous cell carcinoma	02	03.8%
TOTAL	56	100

DISCUSSION:

The urinary bladder and renal pelvis are more common sites for urinary tract tumors than the ureters and urethra. Majority of urinary tract tumors are epithelial. Both benign and malignant tumors occur, the latter being more common⁴. Cystoscopy is the primary diagnostic tool in the diagnosis of urinary bladder carcinoma. The histopathological study of the cystoscopic biopsy not only gives the diagnosis but also provides the additional information to the urologist that can have impact on the treatment⁷.

In the present study 64 cases (80%) were male and 16 cases (20%) were female with a male to female ratio of 4.1:1. Similar finding was seen in several studies of cystoscopic biopsy⁵⁻⁸. Maximum number of cases were seen in 5th to 8th decade constituting to 70% of the cases. Mean age of the patient was found to be 60.2 which correlated with other studies^{5,10}. In our study hematuria was the most common clinical symptoms constituting to about 88% which correlated with the study of Ray⁹ et al who found that 91% of urinary bladder patients presented with painless hematuria.

Most common non-neoplastic lesions of the bladder biopsies studied showed chronic non-specific cystitis with histological variants like Granulomatous cystitis which together constituted to about 75% of the cases compared to the study done by SriKousthubha where 84% of the non-neoplastic lesions were inflammatory lesions¹.

In the present study,14 cases (58.3%) of chronic non-specific cystitis were studied, incidence of which were found to be between those studied by Srikoustubha et al¹ (71.4%) and Grandhi et al¹¹(43.7%). Most of them were catheterized and they showed thickened bladder walls on ultrasound and congested mucosa on cystoscopy. Microscopically, the urothelium was within normal limits in all the cases. The lamina propria showed edema and infiltration by chronic inflammatory cells.

Granulomatous cystitis was seen in 4 cases (16.6%) which correlated with the study done by SriKousthubha et al¹ where the incidence was found to be 14.2%. Granulomatous cystitis is seen as an erythematous or polypoidal inflammation on cystoscopy. Microscopy shows caseating or non-caseating granulomatous inflammation with epithelioid cells, histiocytes, giant cells and lymphocytes in the lamina propria of the bladder.

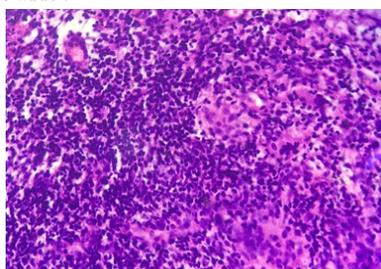


Diagram 1. Granulomatous cystitis

We had 4 cases (16.6%) of cystitis cystica which appeared as nodular, irregular mass on cystoscopy in the trigone area. Microscopically the urothelium showed a solid invagination into the lamina propria, some of them had lost connection with the surface urothelium.

Squamous metaplasia was seen in 2 cases (8.33%) which correlated with the study done by Mahesh Kumar et al³ which showed 10% of the cases to be of metaplasia.

In our study, 17 cases were benign lesions amongst 56 neoplastic lesions. Papillary urothelial neoplasms of low malignant potential were the commonest benign lesion with¹³ cases (23.21%) followed by Papilloma with 4 cases (7.14%) in our study.

PUNLMP, papillary urothelial neoplasm of low malignant potential is an entity which deserves a little discussion at this juncture. Incidence of these lesions was found to be similar to the study done by DrKarra Shilpa et al⁴ (20%) and Shah.et.al¹⁴ (15.8%). According to a study done by Xin-Ke Zhang et al¹⁵,PUNLMP tend to recur and the possibility of progression to higher grade is significantly higher. Similarly a study done by Fujii Y et al¹⁶ also revealed that the local recurrence rate of PUNLMP is higher. Hence a follow up of these patients is compulsory for recurrence and progression

It is defined as papillary urothelial tumor with abnormally thick urothelium, but lacking cytologic atypia. Cystoscopically these lesions are a little larger than papilloma, typically measuring less than 2cm. Microscopically these lesions have either thicker urothelium or diffuse nuclear enlargement than papilloma. Papillae are seen lined by thickened urothelium (more than seven cell layers) with a monotonous population of cells, often in a parallel pattern¹³.

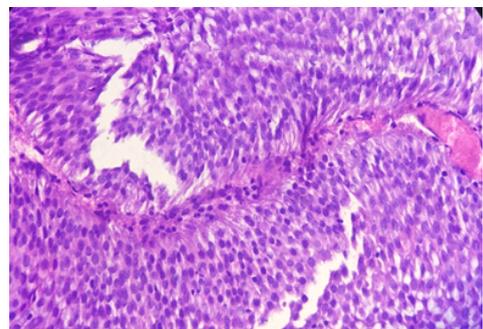


Diagram 2. Papillary urothelial neoplasm of low malignant potential

The incidence of papilloma were found to be similar to the study done by Shrestha EP et al¹² with 7.1% of the cases. Cystoscopically they were found incidentally as solitary tumors at the bladder of the neck. Microscopically Papillary fronds with fibrovascular stalks lined by normal-appearing urothelium lacking atypia is seen.

In the present study, Low grade papillary urothelial carcinomas constituted to about²³ out of 56 cases (41.07%) of the neoplastic lesions which correlated with the studies done by Mahesh Kumar et al³ (42.85%), Bhavana et al¹² (43.7%) and Shrestha EP et al¹² (44%).

Low grade papillary urothelial carcinoma is defined as a papillary neoplasm lined by urothelium with easily recognizable variation in cytologic features and characterized by an overall orderly appearance of the urothelium lining papillary fronds. The cells are evenly placed and cohesive with minimal nuclear atypia consisting of scattered hyperchromatic nuclei, infrequent mitotic figures and mild variation in size and shape¹³. Cystoscopically the tumors are usually solitary, but two or more lesions can be present.

Incidence of High grade urothelial carcinomas was found to be 17.85% in the present study which correlated with the study done by Pudasaini S et al⁷. However the present study was found to be contrary to that studied by Dr Karra Shilpa et al⁴, Mahesh Kumar et al³, Bhavana et al¹² and Shrestha EP et al¹² where the incidence was found to be more than 50%.

High grade papillary urothelial carcinoma is defined as a urothelial neoplasm exhibiting papillary fronds which shows a significantly disordered architectural and cytologic pattern with moderate cytologic

atypia. It contains cells that are dyscohesive with large hyperchromatic nuclei, high degrees of anaplasia and atypical mitotic figures. Architectural disarray with loss of polarity is a characteristic feature of these tumors¹³. Cystoscopic findings varying from papillary to solid sessile lesions, single or multiple.

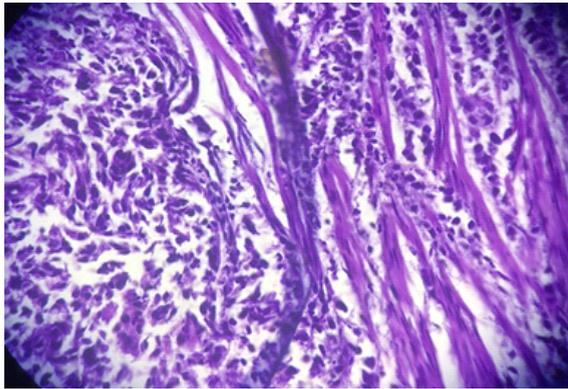


Diagram 3. High grade urothelial carcinoma

In this study, 2 cases (3.5%) of primary squamous cell carcinoma was recorded which correlated with the study done by Mahesh Kumar et al¹(3.3%). Cystoscopically they appear as a white, flaky and often exophytic mass. Microscopically keratin pearls and the presence of irregular nests of atypical squamous cells seen

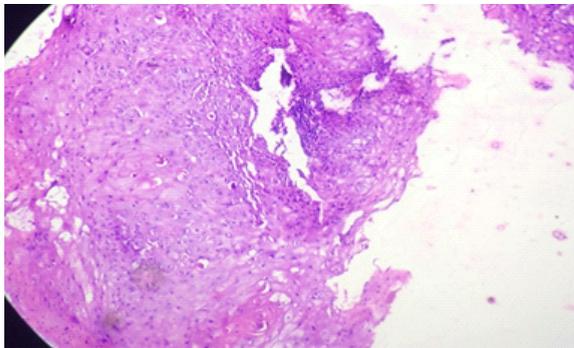


Diagram 4. Squamous cell carcinoma bladder:

There were 4 cases (7.14%) of Adenocarcinoma recorded which correlated with the study done by Pudaseni S et al¹(6.3%). Adenocarcinoma is an uncommon malignancy in the urinary bladder which may arise primarily in the bladder as well as secondarily from a number of other organs. Primary bladder adenocarcinoma exhibits several different growth patterns, including enteric, mucinous, signet-ring cell, not otherwise specified, and mixed patterns. We diagnosed our cases to be of enteric type. Cystoscopically it usually arises from the trigone and posterior wall and presents as a solitary papillary, sessile, solid, or ulcerating lesion. Microscopically they are similar to adenocarcinoma colon and is composed of intestinal-type glands with pseudostratified columnar cells and nuclear atypia. It may produce intracellular or extracellular mucin, and necrosis is not infrequent.

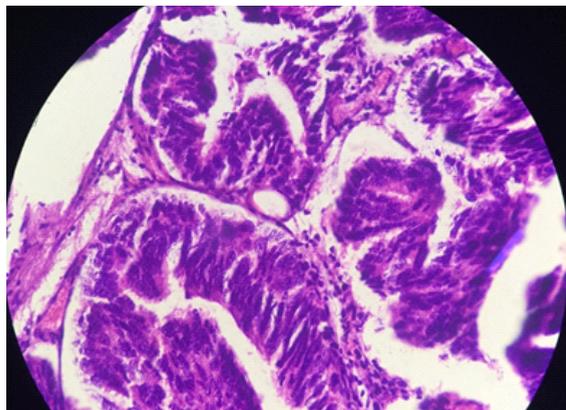


Diagram 5. Adenocarcinoma bladder:

CONCLUSION:

Our study has revealed that hematuria was the most common presenting complaint in bladder lesions with a male preponderance. In the present study chronic non-specific cystitis constitutes the bulk of the non-neoplastic lesions.

Bladder tumors are the commonest lesions seen in cystoscopic bladder biopsies which were of Urothelial origin. Low grade urothelial carcinomas were the predominant tumor type followed by papillary urothelial neoplasms of low malignant potential. PUNLMP deserves special mentioning here in that they are notorious for recurrences and may progress to higher grades if they recur. Hence patients have to be followed up for minimum 5 years for any recurrences or progression to urothelial carcinomas.

Urothelial carcinoma displays many forms, and some of these variant morphologies may pose diagnostic difficulties because of their similarity to other malignancies. Additionally, it is important to recognize the variants that are associated with different outcomes from conventional urothelial carcinoma. For these reasons, familiarity with the diverse morphology of urothelial carcinoma is not simply an academic exercise but is important in providing quality care for patients as they have prognostic significance.

Awareness is very much needed in the public about hematuria because they neglect it causing in an advanced stage of bladder cancer at the time of presentation. Cystoscopic studies and biopsies help in early detection of bladder neoplasms and they form the mainstay of the diagnosis and follow up.

REFERENCES

1. Srikousthuba et al., Profile of Lesions in Cystoscopic Bladder Biopsies: A Histopathological Study; J Clin Diagn Res. 2013; 8:1609-12.
2. Aparna C, Rayapa R, Thumma, Padmavathi D C, Jyothi V, Mounika T. Histological spectrum of urothelial lesions- experience of a single tertiary care institute. International Journal of Contemporary Medical Research 2016;3(6)1731-1733.
3. Mahesh Kumar U and B.R. Yelikar. Spectrum of Lesions in Cystoscopic Bladder Biopsies: A Histopathological study. AlAmeen J Medical Sci. 2012; 5:132-136.
4. Karra Shilpa et al., Histopathology of Urothelial Neoplasms-Tertiary Care Centre Study JMSCR Volume 05 Issue 02 February 2017.
5. Pudasaini S et al., Cystoscopic bladder biopsies: A histopathological study Nepal Med Coll J 2014; 16(1): 9-12.
6. Al- Samawi AS, Aulaji SM. Urinary bladder cancer in Yemen. Oman Med J 2013; 28: 337-40.
7. Viadya S, Lakhey M, KC S, Hirachand S. Urothelial tumors of the urinary bladder: a histopathological study of cystoscopic biopsies. J Nepal Med Assoc 2013; 52: 475-8.
8. Laishram RS, Kipgen P, Laishram S, Khurajam S, Sharma DC. Urothelial tumors of the urinary bladder in Manipur: a histopathological perspective. Asia Pacific Journal of Cancer Prevention. 2012; 13: 2477-9.
9. Ray D, Mondal R, Achryya S, De S, Mondal S. A retrospective study of bladder cancer and the impact of age, sex and smoking habits with related clinicopathological correlations in the tribal population of Bankura, WB, India. OISR J Dent Med Sci 2013; 10(4): 29-32.
10. Goyal VK, Vyas SP, Kothari DC Spectrum of Lesions in Urinary Bladder Biopsies: Histopathological Study. Int J Dent Med Res 2015;1(6):42-46.
11. Grandhi B, Sundara S, Byna, Shanthi V, Vydehi B V, Mohan N, GoelA, Histopathological Spectrum of Urothelial Lesions. e-ISSN: 2279-0853, p-ISSN: 2279-0861. Vol 15, Issue 6 Vol VI (June, 2016).
12. Shrestha EP, Karmacharya K., Profiles of histopathological lesions of urinary bladder: A five years study; Journal of Pathology of Nepal (2016) Vol. 6, 1001-1004
13. Ming Zhou, George J. Netto, JonathanI. Epstein Urothelial lesion. In: Uropathology: High Yield Pathology; Saunders 2012, p133-231.
14. Pooja Y. Shah, Monika Nanavati, Ravi G. Patel, Hansa M. Goswami. SPECTRUM OF LESIONS IN URINARY BLADDER -A HISTOPATHOLOGICAL STUDY. Int J Cur Res Rev | Vol 8 • Issue 4 • February 2016.
15. Xin-Ke Zhang, Ying-Ying Wang, Jie-Wei Chen, Bladder papillary urothelial neoplasm of low malignant potential in Chinese: a clinical and pathological analysis. Tao Qin Int J Clin Exp Pathol. 2015; 8(5): 5549-5555.
16. Fujii Y1, Kawakami S, Koga F, Nemoto T, Kihara K. Long-term outcome of bladder papillary urothelial neoplasms of low malignant potential. BJU Int. 2003 Oct;92(6):559-62.