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Original Article

Pathology Section

Profile of Lesions in Cystoscopic Bladder Biopsies: A Histopathological Study

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ABSTRACT

Aim and Introduction: Urinary bladder lesions, non-neoplastic and neoplastic, are collectively responsible for significant morbidity and mortality throughout the world. The present study aimed to study the histopathology of various lesions of the bladder through cystoscopic biopsies.

Material and Methods: The present prospective study aimed to study the histopathology of various lesions of the urinary bladder through cystoscopic biopsies. All patients who visited Urology Outpatients Department for haematuria and dysuria were subjected to cystoscopy.

Results: Histopathological examinations revealed an equal share of non-neoplastic lesions and neoplastic lesions. Amongst the non-neoplastic lesions, 84% were inflammatory lesions. Urothelial tumours (96%) formed the bulk amongst neoplastic lesions.

Conclusion: This article has stressed upon the importance of histopathological examinations in evaluating bladder pathologies.

Key Words: Bladder, Neoplastic, Urothelial lesions

INTRODUCTION

Urinary bladder lesions, non-neoplastic and neoplastic, are collectively responsible for significant morbidity and mortality throughout the world. Neoplasms of the bladder pose biologic and clinical challenges. Despite significant inroads into their origins and improved methods of diagnosis and treatment, tumours of the bladder continue to extract a toll in morbidity and mortality [1]. Bladder neoplasms account for 6% and 2% of the cancer incidences in men and women respectively. They are the second most common malignancy which is seen by urologists [2]. An accurate diagnosis of urinary bladder lesions requires simultaneous data from urology, radiology and surgical pathology labs. Cystoscopy is the primary diagnostic tool for patients who are suspected of having bladder tumours, which allows a direct visualization of the bladder mucosa and biopsies of the suspected lesions [3,4]. The present study aimed to study the histopathology of various lesions of the bladder through cystoscopic biopsies.

MATERIAL AND METHODS

The present prospective study aimed to study the histopathology of various lesions of the urinary bladder through cystoscopic biopsies. All patients who visited Urology Outpatients Department for haematuria and dysuria were subjected to cystoscopy. Biopsies were taken from the abnormal areas and tumours.The cystoscopic biopsies were fixed in 10% formalin for 12–24 hours.

The tissues were processed for paraffin blocking. Five micron sections were cut and they were stained with haematoxylin and eosin. The histological features were studied and relevant findings were noted.

RESULTS

A total of 53 cystoscopic biopsies were studied in a period 2 years. 3 biopsies were considered to be unsatisfactory. The biopsies were considered as satisfactory if they showed mucosa with lamina propria and without any crush artifacts. Twenty five cases (50%) had non-neoplastic lesions and 25 cases (50%) had neoplastic lesions [Table/Fig-1].

	No. of cases	Percentage
Non-neoplastic	25	50%
Neoplastic	25	50%
Total	50	100%

[Table/Fig-1]: Lesion wise distribution of 50 cystoscopic biopsies

Of the 25 non-neoplastic lesions, 21 cases (84%) were inflammatory lesions, 2 cases (08%) came under the category of tumour like lesions and 2 cases (08%) came under the category of epithelial abnormalities. Among the 21 inflammatory lesions, 15 cases (71.4%) were of chronic non-specific cystitis (polypoid type), 3 cases (14.28%) were of tubercular cystitis and one case (4.76%) each was of eosinophilic cystitis, haemorrhagic cystitis and follicular cystitis.

In the present study, chronic, nonspecific form of cystitis (polypoid type) was the commonest form of cystitis. 2 cases of tumour like lesions included 1 case each of malakoplakia and an inflammatory psuedotumour. 2 cases of epithelial abnormalities included 1 case each of Von Brunn's nest with cystitis cystica and squamous metaplasia.

Amongst the 25 neoplastic lesions which were observed, 24 cases (96%) were urothelial neoplasms and 1 (04%) was squamous cell carcinoma.

Urothelial neoplasms were by far the commonest neoplasms (96%). Of the 24 cases of urothelial neoplasms, 3 cases (12.5%) were invasive urothelial neoplasms and 21 cases (87.5%) were non-invasive urothelial neoplasms [Table/Fig-2].

	No. of cases	Percentage
Invasive	03	12.5%
Non-invasive	21	87.5%
Total	24	100%

[Table/Fig-2]: Distribution of Invasive and Non-invasive Urothelial Neoplasms

Thus, non-invasive neoplasms were more frequent than the invasive urothelial carcinomas (probably because of early detection by cystoscopic biopsies).

Amongst the 3 cases of invasive urothelial carcinomas, 2 were of the typical invasive urothelial carcinomas and 1 case was of an infiltrating urothelial carcinoma with a squamous differentiation.

Out of 21 cases of noninvasive urothelial carcinomas, low grade non-invasive papillary urothelial carcinoma (PUCLG) constituted 15 cases (71.42%), high grade papillary urothelial carcinoma (PUCHG) constituted 05 cases (23.80%) and papillary urothelial neoplasm with a low malignant potential (PUNLMP) constituted 01 case (4.76%). No case of papilloma was noted.

Lateral wall was the most common area of the bladder (64%) which was affected and the least common sites which were affected were dome (4%) and ureteric orifice (4%).

The age distribution of the urothelial neoplasms is shown in [Table/Fig-3].

	Urothelial Neoplasms					Squamous cell carcinoma
	Invasive		Non-invasive			
	Typical	With Squamous differentiation	PUCHG	PUCLG	PUNLMP	
20-29						
30-39						
40-49				1(4%)		
50-59			2(8%)	7(28%)		
60-69	2(8%)	1(4%)	2(8%)	7(28%)	1(4%)	
70-79			1(4%)			
80-89						1(4%)

[Table/Fig-3]: Age-wise distribution of bladder neoplasms in the present study

Most of the patients who had neoplasms were in the age group of 60–69 years and papillary urothelial neoplasms of low and high grades were seen in an earlier age group (50–59 years) also, in addition to the 60–69 years age group. The youngest patient who had a papillary urothelial neoplasm was 46 years old and the oldest patient was 79 years old. The only case of squamous cell carcinoma was 85 years old. (which was relatively later than the urothelial carcinoma).

Out of 50 cases which were studied, 33 patients (66%) were males and 17 (34%) were females.

Of the 24 cases of urothelial neoplasms which were studied, 20 were males and 4 were females. The only case of squamous cell carcinoma was a male [Table/Fig-4].

	Urothelial Neoplasms				Squamous Cell carcinoma
	Non-invasive			Invasive	
	Punlmp	Punlg	Punhg		
Male	1	13	4	2	1
Female	-	2	1	1	-

[Table/Fig-4]: Gender wise distribution of bladder neoplasms

All the 24 cases of urothelial neoplasms which were studied, presented with haematuria. Cystoscopically, 21 cases showed a papillary exophytic growth and 3 cases showed solid lesions. All the 3 cases which showed solid lesions were found to be invasive neoplasms microscopically.

DISCUSSION

Cystoscopy is the primary diagnostic tool for patients who are suspected of having bladder tumours, which allows a direct visualization of the bladder mucosa and biopsies of the suspected lesions [3]. While most of the lesions are fairly easy to identify, occasionally, there can be diagnostic difficulties. The role of the pathologist is not just limited to giving a diagnostic label, but also to giving additional information that can have an impact on the treatment [5].

In the present study, 15 cases of chronic non-specific cystitis, whose ages ranged from 28 years to 76 years, were studied. 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 oedema and infiltration by chronic inflammatory cells.

All the 3 cases of tuberculous cystitis showed ulcerations with the characteristic granuloma of epithelioid cells, histiocytes, Langhan's giant cells, and lymphocytes. Two cases showed caseation necrosis. This correlated with the findings of Young et al., [5].

Sarma [6] stated that follicular cystitis is a term which is used to describe the presence of lymphoid follicles with germinal centres in the urinary bladder.

In one case of follicular cystitis, in the present study, dense aggregates of lymphoid follicles with germinal centres were seen in the lamina propria.

Hellstorm et al., [7], in their study, observed that a bladder inflammation with a striking infiltrate of eosinophils, occurs in two settings: in association with allergic diseases or without an allergic association, but usually in association with bladder injuries.

The only case which was studied was that of a biopsy from a catheterised 32 year female, which showed numerous eosinophils which were admixed with neutrophils, with congested vessels in the lamina propria. The overlying mucosa was normal.

Reuter stated that haemorrhagic cystitis is microscopically characterized by marked oedema and haemorrhage throughout the lamina propria [8].

In the present study, the biopsy from one case of haemorrhagic cystitis showed extensive haemorrhage in the lamina propria.

Malakoplakia occurs most frequently in the urinary bladder, where it is visible as yellow white soft raised plaques on the mucosal surface [7].

In the present study, one case of Malakoplakia was encountered, which showed M G bodies and numerous histiocytes infiltrating the lamina propria.

Edward Jones [9] studied 75 cases of inflammatory pseudotumours, which had a female to male ratio of 2:1.

In the present study, there was one case of a inflammatory pseudotumour. Its biopsy showed proliferation of the blood vessels with infiltration of histiocytes, neutrophils and eosinophils. Plump spindle cells with vesicular nuclei were seen in fascicles and they were scattered singly.

In the present study, one case of Von Brunn's nest with cystitis cystica was noticed in a 39 year old male, in the region of trigone, in which the urothelium showed a solid invagination into the lamina propria. Some of them had lost connection with the surface urothelium. Few cell nests showed central cystic spaces which were lined by cuboidal epithelium.

Also, one case of squamous metaplasia was seen in a 33 year old female, in the region of trigone. The biopsy showed a non keratinizing, stratified, squamous epithelium. The cells appeared to be glycogented, with clear cytoplasm [Table/Fig-5].

A vast majority of tumours of the urinary bladder are of epithelial origin, which arise from the urothelium, the specialized, transitional type of epithelium, that lines the bladder.

Approximately 90% of malignant bladder tumours are transitional cell carcinomas. The remaining 10% comprises all other types of carcinomas [8].

	Papilloma	Papillary neoplasm of low malignant potential	Low-grade papillary carcinoma	High-grade papillary carcinoma
Architecture				
Papillae	Delicate	Delicate. Occasional Fused	Fused, branching and delicate	Fused, branching and delicate
Organization of cells	Identical to normal	Polarity identical to normal. any thickness cohesive	Predominantly ordered, yet minimal crowding and minimal loss of polarity. Any thickness. Cohesive	Predominantly disordered with frequent loss of polarity. Any thickness. Often discohesive
Cytology				
Nuclear size	Identical to normal	uniformly enlarged	Enlarged with variation in size	Enlarged with variation in size
Nuclear shape	Identical to normal	Elongated, round-oval, uniform	Round-oval. Slight variation in Shape and contour	Moderate-marked pleomorphism
Nuclear chromatin	Fine	Fine	Mild variation within and between cells	Moderate-marked variation both within and between cells with hyperchromasia
Nucleoli	Absent	Absent to inconspicuous	Usually inconspicuous	Multiple prominent nucleoli
Mitoses	Absent	Rare, basal	Occasionally	Usually frequent
Umbrella cells	Uniformly present	Present	Usually present	May be absent

[Table/Fig-5]: Histologic features of urothelial papillary lesions [4].

In the present study, neoplastic lesions were noticed in 25 of the 50 cases, which constituted 50%. Of the 25 cases, 24 cases (96%) showed features of urothelial neoplasms and one case showed features of pure squamous cell carcinoma (4%).

Wynder and Goldsmith [10] observed that 75% of patients presented with superficial (non-invasive) disease, while 20% and 5% presented with invasive and metastatic diseases respectively.

In the present study, 87.5% patients presented with superficial (non-invasive) disease, while 12.5% patients presented with invasive disease.

Pauwells et al., [11] studied 168 carcinomas and they found a distribution of 8% grade I, 69% grade 2, and 23% Grade 3 urothelial carcinomas (WHO 1973). This, according to the WHO 2004 classification, is 8% papillary urothelial neoplasms with a low malignant potential, 69% low grade papillary carcinomas and 23% high grade papillary urothelial carcinomas.

In the present study, papillary urothelial neoplasms with a low malignant potential constituted 4.76% cases. Low grade papillary urothelial carcinomas constituted 71.40% cases. High grade papillary urothelial carcinomas constituted 23.80% cases.

Grignon et al., [3] found that the median age at diagnosis of urothelial neoplasms was 65 years.

In the present study, a majority of the cases which were diagnosed as urothelial neoplasms (13 cases) belonged to the age group of 60-69 years and the median age was 65 years.

In the study which was done by Oosterhuis et al., [12] on a total of 359 consecutive patients, 295 men (82%) and 64 women (18%) had primary non-invasive transitional cell carcinoma.

In the present study, out of 24 cases of urothelial neoplasms, 20(83%) were males and 4(17%) were females, with a male to female ratio of 5:1.

Stephenson et al., [13], in their study which was done on 914 cases of bladder carcinomas, found that carcinoma of the lateral wall accounted for 37.1% cases, carcinoma of the posterior wall accounted for 17.9% cases, that of the trigone accounted for 12.6% cases, that of the neck accounted for 11.1% cases, that of ureteric origin accounted for 9.8% cases and those of the dome and anterior wall accounted for 7.7% and 3.8% cases.

In the present study, lateral wall was the most common site (64%), followed by posterior wall (28%), dome (4%) and ureteric orifice (4%).

The criteria which were considered for the diagnosis of bladder carcinomas were those which were outlined by Epstien et al., [14] in The Bladder Concensus Committee WHO/ ISUP and WHO 2004.

The following features were observed in the present study:

A papillary architecture, with the increase in number of cell layers of urothelium ranging from 8-16 layers.

Preservation of superficial umbrella cell layers in most of the low grade neoplasms and their loss in most of the high grade neoplasms.

Loss of polarity of the nuclei was seen in the lower 2/3rd layers in low grade carcinomas, and throughout the thickness in high grade lesions.

Nuclear membranes were highly irregular in higher grade lesions.

Mitotic figures were limited to lower layers in low grade neoplasms and they were found throughout the thickness of epithelium in the higher grade neoplasms.

Necrosis was found in most of the cases of invasive and high grade neoplasms.

The invasive urothelial carcinomas were found to show small nests and sheets of tumour cells beneath the muscularis mucosa. These cells had vesicular nuclei, alterations in the chromatin texture and mitotic figures.

SUMARY AND CONCLUSION

In this study, 53 cystoscopic biopsies were studied during a period of 2 years. Non neoplatic lesions were as common as neoplastic lesions (50%). Most of the non-neoplastic lesions were of inflammatory origin. Chronic non-specific cystitis (predominantly polypoid) formed the bulk of the non-neoplastic lesions. Tuberculous cystitis accounted for a significant percentage of inflammatory lesions (14.8%). A great majority of the neoplastic lesions (96%) were of urothelial origin, while squamous cell carcinomas accounted for only 4% cases. Tumour like conditions like inflammatory pseudotumours and malakoplakia were encountered. Amongst the urothelial neoplasms, a majority were non-invasive papillary urothelial neoplasms (87.5%). Invasive papillary urothelial neoplasms accounted for 12.5% of the cases. All urothelial neoplasms were more common in males. Cystoscopic studies and biopsies help in an early detection of bladder neoplasms and they form the mainstay of the diagnosis and follow up.

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