

Usefulness of Bladder Biopsy

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It is not uncommon to find discrepancy between cystoscopic observations and histological findings, particularly in non-neoplastic diseases and at times, in neoplastic conditions. However, histological confirmation is a must to formulate the ultimate management protocol. It is commonly observed that gross visualization of a condition during the procedure can contradict the ultimate histopathological outcome.

The main objectives are to determine the indications and the histological outcome of cystoscopic biopsy of the urinary bladder and to compare histological outcome with the gross findings at cystoscopy.

This is a retrospective and descriptive study. This study was conducted in the section of Urology at B and B Kathmandu University Hospital, Gwarko, Lalitpur, Nepal. Data were collected from January 2005 from December 2008.

In the last four years (Jan 2005- Dec 2008), two hundred and forty-four patients underwent cystoscopic evaluation along with bladder biopsies for various reasons. Out of 134 cases of suspected bladder cancer at cystoscopic examination, histology was confirmatory only in 76 cases. Out of 42 cases of suspected tuberculosis at cystoscopy, only 11 were confirmed histologically whereas the rest were found to have various form of cystitis. Out of 108 cases of histologically confirmed neoplasia, there were 94 papillary urothelial tumors, 4 non-invasive urothelial carcinoma, 7 carcinoma in situ (CIS), 2 verrucous carcinoma and 1 squamous cell carcinoma.

Bladder biopsy may have a limited value in the diagnosis of genitourinary tuberculosis. Patients with hematuria and normal cystoscopic findings should be biopsied and followed up clinically. Proper sample handling and retrieval of adequate tissue are important in order to avoid false negative results.

Keywords: cold punch, cystoscopy, hematuria, lower urinary tract infection, resectoscope.

It is not uncommon to find discrepancy between cystoscopic observations and histological findings, particularly in non-neoplastic diseases and at times, in neoplastic conditions. Histological confirmation is a must to formulate the ultimate management strategies. It is quite commonly observed that gross visualization of a condition during the procedure can contradict the ultimate histopathological outcome. We have reviewed 244 cases of bladder biopsies and have tried to assess the usefulness of bladder biopsy in urological diseases by comparing the clinical diagnosis with histological observations.

Materials and Methods

Two hundred and forty four bladder biopsies were done from January 2005 till December 2008. Biopsies were taken either by a resectoscope or cold punch biopsy forceps and patients were followed up with biopsy reports. Biopsy reports were studied in detail and cystoscopy was repeated whenever required.

Results

Diseases of urinary bladder were common in males aged between 40-60 years and in females, between 20-40 years. Lower urinary tract symptoms (LUTS) in the form of irritative or obstructive symptoms were the common symptoms of bladder pathologies. Along with LUTS, hematuria was a pertinent symptom, where cystoscopic evaluation, whenever applicable, is a must. Hematuria along with LUTS were the most common symptoms for neoplastic as well as non-neoplastic

pathologies.

In last four years (Jan 2005- Dec 2008), two hundred and forty-four patients underwent cystoscopic evaluation along with bladder biopsies for various reasons. Majority of the bladder biopsy specimens were from subjects aged between 60-70 years of age (27.04%). Age and sex distribution are shown in **Table 1 and Figure 1**. The youngest and the eldest subjects were aged 5 and 95 years, respectively.

Age interval	Number	Percentages (%)
<10	5	2.04
11-20	4	1.63
21-30	17	6.96
31-40	35	14.34
41-50	28	11.47
51-60	33	13.52
61-70	66	27.04
71-80	35	14.34
>80	21	8.60
TOTAL	244	100

Table 1: Age distribution of the cases

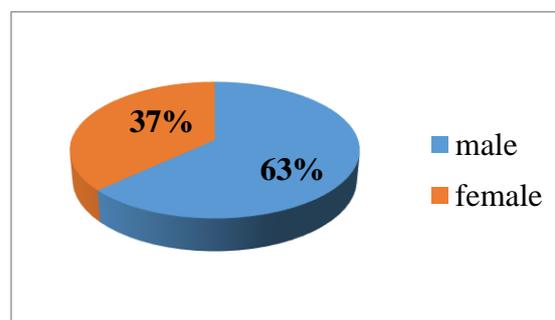


Figure 1: Sex distribution of the cases

Provisional diagnosis on the basis of cystoscopic findings

One hundred and fifty two patients presented with hematuria; 87 had various features of lower urinary tract symptoms (LUTS) and 5 patients had retention of

urine. The youngest one was a 5 years old boy who presented with features of recurrent urinary tract infections (UTI) and admitted to having loss of weight and appetite as well. His cystoscopic examination revealed features of cystitis and histology also confirmed non-specific cystitis.

The eldest subject was 95 years of age and he presented with LUTS and microscopic hematuria. Histological examination of his bladder biopsy specimen revealed papillary urothelial bladder tumor (Table 2, 3).

Findings at cystoscopy	Number	Percentages (%)
Superficial bladder cancer	132	54.1
Invasive bladder cancer	2	0.08
Tuberculosis	42	17.2
Cystitis	66	27.0
CIS	2	0.08
Total	244	100

Table 2: Cystoscopic findings

In the group with neoplasia, cystoscopy showed single or multiple, sessile or papillary growths, or polypoidal thickening of mucosa. In the invasive bladder cancer group, thickened bladder wall along with papillary lesions or solid bladder lesions were seen at cystoscopy. In the tuberculosis group, the patients had radiological evidence of pulmonary Kochs together with cystoscopically-visualized tubercles (single or multiple) or ulcers on the mucosa. In the cystitis group, there were bullous oedema and redness or congestion of the mucosa. In the CIS group, all patients had

hematuria with grossly abnormal non-inflamed bladder without any obvious specific lesion.

Histological findings	Total	Percentages (%)
Papillary urothelial tumor	94	38.4
Non-specific cystitis	68	27.9
Tuberculosis	11	4.5
Follicular cystitis	9	3.7
Granulomatous cystitis	9	3.7
Acute cystitis	9	3.7
Normal histology	9	3.7
Haemorrhagic cystitis	8	3.3
CIS	7	2.9
Papillary cystitis	4	1.6
Squamous metaplasia	4	1.6
Non-invasive urothelial carcinoma	4	1.6
Cystitis cystica	3	1.2
Verrucous carcinoma	2	0.8
Squamous papilloma	1	0.4
Von brun nest	1	0.4
Squamous cell carcinoma	1	0.4
Total	244	100

Table 3: Histological diagnosis

The cystoscopic findings were compared with histological reports. Out of 134 cases

with bladder growths suspected to be bladder cancer at cystoscopy, histology confirmed the diagnosis in only 76 cases. Twenty-two cases were histologically confirmed as transitional cell cancer (TCC), that were initially suspected to be cystitis at cystoscopy. Out of 66 cases of suspected cystitis at cystoscopy, only 35 cases were confirmed histologically. Among the remaining 31 cases, histology revealed 22 to be TCC, 2 as tuberculosis, 2 verrucous carcinoma, 1 squamous papilloma, 1 squamous cell carcinoma, 1 squamous metaplasia and 2 as carcinoma in situ. Out of 42 cases of suspected tuberculosis at cystoscopy, only 11 were proven histologically whereas the rest were found to have various form of cystitis. Out of 108 cases of histologically-confirmed neoplasia, 94 were papillary urothelial tumor, 4 were noninvasive urothelial carcinoma, 7 were CIS, 2 were verrucous carcinoma and there was 1 was squamous cell carcinoma.

Discussion

Papillary urothelial tumor appears to arise from papillary urothelial hyperplasia.¹ Lesions demonstrate a range of atypia. Tuberculous cystitis tends to involve the bladder adjacent to the ureteral orifices, and it is presumably secondary to renal tuberculosis.²

In “follicular cystitis”, lymphoid follicles with germinal centers are present in the wall of urinary bladder. The term is a misnomer because it doesn’t necessarily indicate inflammation and sometimes, it is seen in repeated transurethral biopsies or after installation of intravesical chemotherapeutic agents or BCG.²

Intravesical administration of BCG can result in granulomatous cystitis. The granulomas usually are situated in the superficial one-third of lamina propria and are associated with an intense lymphocytic infiltrate.³

Most cases of cystitis take the form of nonspecific acute or chronic inflammation of the bladder. However, hemorrhagic cystitis is characterized by marked edema and hemorrhage throughout the lamina propria, along with extensive ulceration and fibrinopurulent exudate.²

CIS (Carcinoma in situ) refers to a nonpapillary (flat) mucosa in which the normal urothelium has been transformed into or replaced by cancer cells that have not invaded through the basement membrane.²

In case of squamous metaplasia, urothelium frequently undergoes either squamous or glandular metaplasia, presumably as a response to chronic inflammatory stimuli such as urinary tract infection, calculi, diverticulae, or frequent catheterization. It is a common finding in women and is responsive to estrogen production.²

When the cells lining the cyst maintain a transitional appearance, the condition is called cystitis cystica.³ Verrucous carcinoma is a variant of squamous carcinoma which is very low grade, orderly carcinoma that is clinically indolent but capable of invasion and causing death.²

Squamous papilloma is characterized by a proliferation of mature and benign appearing squamous epithelium surrounding a central fibrovascular core.²

Von brun nest is a focal proliferation of the basal layer of the transitional epithelium, which produces buds that later become

solid nodules³. Squamous cell carcinoma constitutes 2 to 7% of urothelial cancers and 1 formation of a pearl, intercellular bridges and keratotic cellular debris are hallmarks.² In this study, hematuria, increase in urinary frequency, dysuria were the most common symptoms for neoplastic as well as non-neoplastic diseases. Diagnosis of genitourinary tuberculosis is rather difficult, as the patients clinically manifest late, only after extensive damage of the genitourinary system. Bladder biopsy is one of the means of diagnosis. In the present series, histology was confirmatory in 11 (26.19%) out of 42 suspected cases. The failure to detect tuberculosis on histology in spite of cystoscopic evidence of tubercles, could be due to sampling error or tendency to over diagnose the entity. Thus, bladder biopsy may have a limited value in the diagnosis of genitourinary tuberculosis.

Follicular cystitis, a variety of chronic cystitis, characterized by the presence of reactive follicles in the submucosa, was also mistaken for tuberculosis at cystoscopy. In four patients presenting with hematuria only and in whom cystoscopy was non-contributory, histology showed transitional cell carcinoma in two of them while cystitis glandularis and squamous metaplasia were revealed in one each. Squamous cell was found to be present in one patient, a known case of neurogenic bladder who was on suprapubic catheterization, though it was suspected to be a case of cystitis at cystoscopy. Prolonged use of indwelling catheter in neurogenic bladders can lead to squamous metaplasia as well as squamous cell carcinoma.⁴

Patients with hematuria and normal cystoscopic findings should be biopsied and

then, followed- up clinically. Out of 132 cases of obvious papillary bladder tumor, only 88(66.66%) cases were confirmed as papillary urothelial tumor. The rest of the 6 cases of histologically- confirmed papillary urothelial tumors were suspected to have merely cystitis and tuberculosis. This could be due to sampling error as dysplasia is known to occur in the vicinity of malignant urothelium,⁵ or it could be due to excessive electro-coagulation of papillary tumor during resection, distorting its architecture.

Conclusion

Along with adequate tissue sampling, good handling and proper retrieval of tissue sample is the key to achieve maximum true-positive results during bladder biopsy. Histological outcome of suspected genitourinary tuberculosis at cystoscopy correlates poorly with the gross findings. Hence, other factors like clinical correlation, urine for AFB (acid fast bacilli) culture and PCR (polymerase chain reaction) should be taken into consideration whenever there is a strong clinical suspicion.

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