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Efficacy of voided urinary cytology and ultrasonography compared to cystoscopy in the detection of urinary bladder cancer



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KEYWORDS

Urinary bladder cancer;
Cytology;
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Abstract

Introduction: Painless hematuria is the presenting symptom in 85–90% of patients with bladder cancer.
Objectives: To evaluate the efficacy of voided urinary cytology and ultrasonography in the diagnosis and follow up of bladder cancer compared to cystoscopy as a gold standard with reference to its grade. To recommend a protocol that improves the overall sensitivity and specificity of detection of new cases and recurrence in the follow up of patients with bladder cancer.
Subjects and methods: A prospective analysis of patients with painless hematuria and follow up patients of bladder cancer was done. They were subjected to voided urinary cytology and ultrasonography. The results were compared with the inferences drawn from cystoscopy and histopathological examination of the resected tumor, wherever applicable.
Results: The sensitivity of urinary cytology and ultrasonography was 13.33% and 66.67%, respectively, compared to cystoscopy as a gold standard, whereas the specificity of urinary cytology and ultrasonography was 100% and 93.33%, respectively. Cytology was positive only in high grade cases.
Conclusions: Voided urinary cytology can be omitted as a screening test. Ultrasonography can be recommended as the initial imaging investigation for detection of bladder carcinoma in patients presenting with hematuria and for follow up of bladder carcinoma patients.

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Introduction

Bladder cancer is the fourth most common cancer in men and the ninth most common cancer in women [1]. The commonest histological variant is transitional cell carcinoma (TCC) and accounts for more than 95% of all the cases of bladder cancer [2,3].

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Painless hematuria is the presenting symptom in 85–90% of patients with bladder cancer [4]. The workup of suspected bladder cancer should include cytology, a cystoscopy, and an upper tract study. The most important modality for detection of bladder tumor in a new patient with hematuria or a known patient of bladder cancer is cystoscopic evaluation followed by histopathological examination of resected tumor, if present.

Although cystoscopy is the gold standard for the detection of bladder cancer, the false negative results associated with cystoscopy can range from 10 to 40%. Lesions of Carcinoma in situ (CIS) may escape detection even by cystoscopy [5,6]. Also tumors of the upper tract and very small bladder tumors at relatively less optimally visualized areas on cystoscopy may be missed.

To overcome this, voided urine cytology is used as an adjunctive test in identifying occult cancers that may be missed on cystoscopy. It can identify exfoliated cells from both normal and neoplastic urothelium and may be useful in detecting cancer in symptomatic patients and assessing response to treatment. Detection rates are high for tumors with high grade and stage as well as CIS [7,8]. Cytology is illustrative of the problems of non-invasive screening. Poorly differentiated tumors have a 20% false-negative detection rate, whereas well-differentiated tumors have up to an 80% false-negative detection rate. Cytology, however, remains the preferred bladder tumor marker for specificity [9].

Bladder cancer may also be detected by various imaging techniques. CT urogram is the imaging modality of choice to detect bladder masses. Large tumors can also be detected on ultrasonographic study of the KUB region, in which case cystoscopy may be planned with transurethral resection of bladder tumor.

The aim of our study was to evaluate the efficacy of voided urinary cytology and ultrasonography in the diagnosis and follow up of bladder cancer compared to cystoscopy as a gold standard with reference to its grade and to devise a protocol that improves the overall sensitivity and specificity of detection of new cases and recurrence in the follow up of patients with bladder cancer.

Subjects and methods

In this study, a prospective analysis of new and follow up patients under evaluation for bladder cancer was done at urology center of Command Hospital (EC), Kolkata from Feb 2013 to July 2014. Sixty (60) patients being evaluated for Carcinoma Bladder both freshly detected and those on follow-up were included as per convenience sampling after obtaining their informed written consent.

Inclusion criteria were (1) patients of painless hematuria on evaluation for bladder cancer, and (2) known patients of bladder cancer under follow up. Following categories of patients were excluded from the study: (1) patients with major co-morbidities requiring acute intensive medical care, (2) patients with major psychiatric illnesses, (3) benign inflammatory or infectious conditions of bladder, (4) renal or bladder calculi, (5) foreign body (stent or nephrostomy tube), (6) other genitourinary cancer, (7) recent instrumentation, (8) bleeding disorders, (9) bowel interposition.

The study was approved by the ethical committee of the institute. Demographic profile of patient's such as name, age, sex, etc. was

recorded. Under structured pro forma in depth history of the patients was taken to note the indication for which patient was being evaluated for Carcinoma Bladder and the duration of illness in known cases of Carcinoma Bladder. Any past or concomitant co morbidity was noted. Detailed clinical examination including vital parameters recording was done. Abdomen was examined thoroughly to look for any abnormality like swelling, tenderness, lump, etc. with special reference to suprapubic region.

All patients fulfilling the inclusion criteria were subjected to freshly voided urinary cytology with 100 ml of random urine samples on three consecutive days. A well mixed sample of urine (12 ml) was centrifuged in a centrifuge tube for 5 min at 1500 rpm and supernatant was poured off. The tube was tapped at the bottom to resuspend the sediment in 0.5 ml of urine. One drop of this sediment was placed on a glass slide and smear was made, which was fixed and stained with Pap stain. Another drop was placed on a separate slide and stained with Leishmann-Geimsa stain. The slides were examined immediately under the microscope using first the low power and then the high power objective. Malignant transitional cells were seen having pleomorphic hyperchromatic nuclei, high nucleus: cytoplasmic ratio and moderate amount of cytoplasm. Imaging of the KUB region in the form of ultrasonographic study was done in all cases prior to cystoscopy. CECT/IVU was done as and when indicated. Ultrasonography was performed with Logiq P5 with an electronic curved array transducer available in the radiology department. Patients were asked to present with a full bladder. Ultrasound examination of the KUB region was performed on all patients. The bladder was imaged with transverse and longitudinal scans with the patient in the supine position. Scanning was performed both pre and post micturition.

This was followed by cystoscopy with transurethral resection of lesions, if found and their histopathological examination. The bladder was evacuated before cystoscopy. Under local anaesthesia with the patient in lithotomy position, after proper cleaning and draping, a Karl Storz 19 Fr rigid cystoscope with 30° lens was introduced with prophylactic antibiotic cover and the entire urinary bladder was inspected systematically. The tumor(s) if found was mapped diagrammatically over the data collection sheet. If tumor was found on cystoscopy or in patients with tumor visible during ultrasonography, transurethral resection of bladder tumor was done under spinal anaesthesia (under general anaesthesia, if growth was on lateral bladder wall to avoid obturator jerk during surgery). A 26 Fr continuous flow rotating sheath resectoscope was used and the tumor was completely resected, proper haemostasis was done and resected tissue was sent for histopathological examination. Finally examination under anaesthesia was done again for clinical staging. A 3-way Foley's catheter (22Fr) was placed per urethrally and irrigation with normal saline was started if hematuria was present.

The results were compared with the inferences drawn from cystoscopy and histopathological examination of the resected tumor, wherever applicable. Histologically confirmed urothelial carcinoma was graded according to WHO/ISUP consensus classification [10]. The findings were analyzed in terms of sensitivity, specificity, positive predictive value and negative predictive value of voided urine cytology and imaging in the diagnosis of Carcinoma Bladder with respect to grade keeping cystoscopy as the gold standard. The results were collected, evaluated, calculated, tabulated and statistically ana-

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