

Significance of urine cytology in diagnosis of urothelial carcinoma of urinary bladder , Cytopathological correlation.

Zainab Khalid Al-Mukhtar¹, Saba Ali Abd Alkareem², Issraa Ali Husein³

1,3 Department of Pathology and Forensic Medicine, College of Medicine, University of Baghdad, Baghdad, Iraq

2 Department of Pathology , Ghazi Alhariri for surgical specialties ,Baghdad Medical city ,Iraq.

zainabks48@gmail.com

Abstract

Background: Urothelial carcinoma is the most widespread histological type of malignancy affecting urinary bladder, the study aimed to examine different histopathological findings in different bladder lesions and their correlation with exfoliative urine cytology. **Material and Methods:** This study was run on 96 patients, clinically diagnosed or suspected to have urothelial carcinoma of the urinary bladder be present at urologic sector in Gazy Al Hariri educational hospital for surgical specializations in Baghdad Medical City. Urine cytology smears from all these patients were studied. Cytological findings were correlated with histopathological findings. **Results:** revealed that bladder tumors were commonly seen in males with average age of presentation being the fifth decade, the most common type of carcinoma seen was low-grade urothelial carcinoma-noninvasive type. Urine cytology was positive in 71.43% patients. **Conclusion:** Urine cytology has a sensitivity and specificity of acceptable accuracy in the diagnosis of cancer of the urinary bladder, and it provides a good implement to determine the degree of tumor, especially high-grade. . But, it must be reported in a background of full clinical information and must always be followed by histopathological examination.

Keywords: Urine cytology, Invasive urothelial carcinoma, low-grade noninvasive urothelial carcinoma.

Introduction:

Urinary bladder carcinoma is the most common type of malignancy affecting the urinary tract. Urothelial carcinoma is the most prevalent type of carcinoma, responsible for about 90 percent of bladder cancers [1&2]. In Iraq, malignant tumors of the urinary bladder are the sixth most prevalent malignancy and hold the second place in men [3].Painless hematuria, irritative voiding and obstructive symptoms are the most common presenting signs of bladder cancer [4&5], It is widely seen in males in the 6th and 7th decades, cigarette smoking is the most significant established risk factor [6]. Others involve occupational exposure to certain chemicals, use of certain drugs such as cyclophosphamide, pelvic radiation, chronic bladder infection / irritation, hereditary, personal or family history of bladder cancer [7].Diagnosis of urothelial neoplasm is established on the clinical imaging findings, study of urine cytology & histopathological examination.[8]. Nearly 70% of bladder urothelial carcinomas are non-muscular invasive tumors (TA / T1), which are categorized as low-grade urothelial carcinoma (LGUC)) , they have a good

prognosis, but in around 10–15 % of cases they can be associated with recurrence and development to high-grade urothelial carcinoma (HGUC). The remaining 30% are muscle-invasive with pathologic stage is equal to or more than (T2), which are classified as high-grade histologically and are associated with worse overall survival than LGUC [9&10]. Voided Urine Cytology is simple, inexpensive, standard noninvasive method or minimally invasive with easy access to the specimens & It has significant impact in early detection, monitoring, reducing cancer related morbidity and mortality & management of bladder urothelial neoplasm [11&8]. It also had high sensitivity for detection, prognosis & tumor progression of urothelial carcinoma, especially the high grade one [12]. These patients need more aggressive follow-up, cystoscopy, biopsy, and staging. Bladder biopsy whether transurethral resection of bladder tumor (TURBT) or cystoscopic stays the gold standard for histopathological diagnosis, staging urothelial cancer of the bladder and treating non-muscle invasive bladder cancer [13]. In this study, we point to evaluate the diagnostic yield of urine cytology and comparing it with histopathological findings in different urinary bladder lesions along with grade and type of bladder growth among Iraqi patients coming to the outpatient clinic at Gazy Al Hariri hospital for surgical specializations, Baghdad, Iraq.

Material and Methods:

In this retrospective study of urine cytology reports for 96 patients with clinical and radiologic diagnosis of bladder lesions attending to urologic department in Gazy Al Hariri teaching hospital for surgical specializations in Baghdad Medical City during the period from January to November 2019, In the cytopathologic department of the same hospital, the clinicopathologic information were obtained after ethical approval from the patients, including age, gender, clinical indication for urine cytology, cytologic smears were reexamined by three pathologists and The cytological diagnosis was classified into three categories depend on the cellular morphology.

96 formalin fixed paraffin embedded tissue blocks of the same patients, These were collected from the archived materials in the histopathology department of Gazy Al Hariri teaching hospital for surgical specializations at Baghdad, These paraffin blocks represent the cases of cystoscopic and transurethral resection biopsies, also the clinicopathological parameters such as age, sex, histological/morphological grades were obtained from the available histopathologic reports.

one section of 5 Mm thickness was taken from each block and stained by hematoxylin and eosin (H&E) then reestimate for the histologic grades of the tumor and depth of invasion by three pathologists, histological diagnosis of the lesions were made according to the WHO classification of tumors of the urinary tract. [14]

Histopathological diagnosis was regarded the gold standard, and urine cytology findings were correlated and compared with the histopathological findings of biopsies.

Results and discussion:

In our study, there were 63 (73.3 %) male and 23 (26.7 %) were female [Table 1]. Age of the patients varied from 32 to 85 years with a maximum number of patients falling between 53 and 88 years. Out of 86 cases, 72 cases (83.7 %) were above 55 years.

Table (1): Gender Distribution

Sex	Number of cases (%)
Male	63 (73.3 %)
Female	23 (26.7 %)
Total	86

The most common complaints are gross or microscopic hemorrhage seen in 54 patients (62.7 %) Retention of urine, dysuria & urgency were seen in 26 patients (30.2 %). 6 (7 %) of patients with no presenting symptoms but they a known case of urothelial carcinoma and now on follow up.

A total of 84 patients were diagnosed as urothelial neoplasm (97.6%). Two cases were diagnosed as primary squamous cell carcinoma of the urinary bladder.

The major histopathological diagnosis of urothelial carcinoma is noninvasive papillary urothelial carcinoma low grade, seen in 51 patients, followed by invasive urothelial carcinoma -high grade seen in 23 patients. Non Invasive high grade urothelial carcinoma is noticed in 9 patients. Only 1 case is papillary urothelial lesion of undetermined malignant potential was diagnosed .[Table 2].

Table 2: Distribution of Histopathological Diagnosis

Histopathological diagnosis	Number of patients (%)
High grade noninvasive carcinoma	9 (10.46)
Low grade noninvasive carcinoma	51(59.30)
Invasive carcinoma	23(26.74)
Squamous cell carcinoma	2(2.32)
Papillary urothelial lesion of undetermined malignant potential	1(1.16)

In the present study, cystoscopic findings revealed lateral wall as the most common site in 41% of the cases followed by posterior wall and trigone of the urinary bladder .

Urine cytology was given as positive for malignant cells in 60 cases. In our study, malignancy was not recognized in 24 histologically confirmed cases. In 4 cases, atypical cells were given on cytology smears and further investigations were recommended. In which one prove to be urothelial papilloma , one was papillary urothelial neoplasm of low malignant potential and two were of low -grade urothelial carcinoma. Of the whole of detected malignant urothelial lesions,20 cases were of invasive urothelial neoplasm and 7 cases were of high -grade noninvasive urothelial neoplasm and 29 cases of low -grade noninvasive urothelial carcinoma [Table 3].

Table 3: Correlation of Cytological diagnosis with Histopathological Diagnosis

Cytological diagnosis (%)	Histopathological diagnosis	Number of cases
Positive for malignant cells	Invasive urothelial carcinoma	20 (33.33)
Positive for malignant cells	High - grade noninvasive	7 (11.66)
Positive for malignant cells	Low - grade noninvasive	29 (48.33)
Positive for atypical cells	PUNLUMP 1 case - low - grade noninvasive 2cases urothelial papilloma 1 case	4 (6.66)

Bladder cancer in Iraq has shown a pattern similar to that in western world, where urothelial Carcinoma is the dominant histological type & constitute more than 90 % of all primary malignant urinary bladder tumors .[15]

Contrary to studies that worked in Iraq previously in which reveal the squamous cell carcinoma is the most predominant histopathologic type carcinoma in bladder due to decrease in the incidence of bilharziasis , which is the most common predisposing factor for squamous cell carcinoma.[16&17]

In the current study, exfoliative urine cytology and bladder biopsies of 84 patients with bladder growth were reviewed. Of these 72.6 % were male and 27.4 % were female. Male to female ratio was 2.6:1. This is in agreement with the earlier studies published.[18]

Bladder cancer is more prevalent in males due to different lifestyle-associated risk factors such as smoking and occupational exposure. Although more in males, muscle-invasive bladder cancers are more common in females.[19] Urinary bladder tumors are commonly seen in 5th–8th decade of life.[20]

In the present study, 96 cases (96.46%) cases were above 55 years. This is in correlation with other studies mentioned in the literature. [21]

The average age of patients with urothelial carcinoma was 58 year, which is much lower than the mean age reported in the literature outside Iraq [22] . But like the studies done by Iraqi authors ,this may be explained by a great increase in the smoking habit, urothelial carcinogens exposure is due to frequent wars and in increase activity in industries. [23,24]

The most common presenting complaint counted in this study was hematuria seen in (52.8%) of the total, followed by dysuria, Urgency and frequency , this result was equated with results get by many authors [25,26].

Histopathological examination was done in all 96 patients. A total of 84 patients were diagnosed as urothelial carcinoma. In Which most of them was noninvasive papillary urothelial carcinoma seen 72.6% of the cases [figure 1], while the Invasive urothelial carcinoma was seen in 27.3% of patients[figure 2]. This is similar with the other studies published in the literature.[27,28]

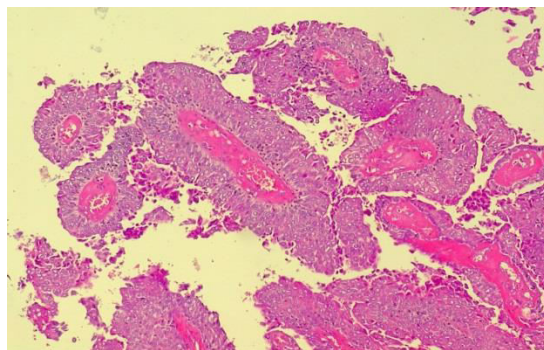


Figure 1: Low-grade noninvasive urothelial carcinoma, (H and E, ×200)

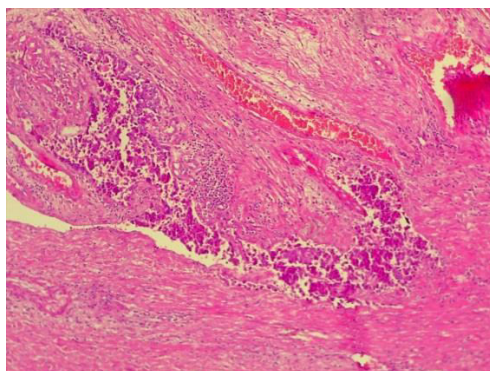


Figure2: Invasive urothelial carcinoma, (H and E, ×200)

Of 96 patients, urine cytology smears were reported as benign in (34.5%) of patients , 4 patients were reported as positive for atypical cells, in Which cytological changes override those described as for benign cellular changes but does not certified for malignancy. Positive for malignancy was reported in 60 patients (57.6 %).the cytological findings of malignancy were seen like nuclear enlargement, high nucleocytoplasmic, hyperchromasia, and prominent nucleoli .[figure 3]

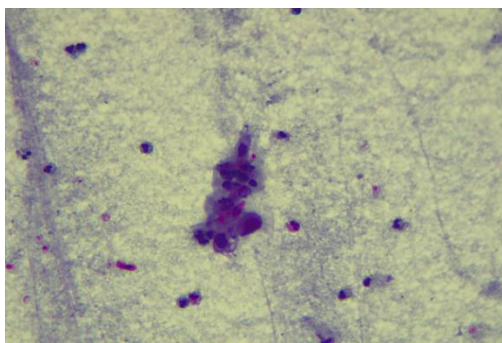


Figure 3: Papanicolaou stain urine cytology (×400) showing atypical urothelial cells with high nuclear–cytoplasmic ratio, hyperchromatic nuclei, and prominent nucleoli.

Accuracy of diagnosing malignancy by cytology is highly variable and determined by grade of tumor, processing and type of the sample, and proficiency of the cytopathologist. Diagnosis is more difficult in cases of low-grade noninvasive carcinoma as the sensitivity of detection of malignant cells is very low.[29]

Various problems experienced while reporting exfoliative urine cytology like scant cellularity and cellular degeneration before fixation. false positivity results can be seen in cases of infections, previous instrumentation, and intravesical therapy.

Urine cytology should always be reported in a background of complete clinical information, radiologic findings and followed by histopathological examination for urinary bladder tumor.

Conclusion:

The urine cytology had a good sensitivity, specificity and an overall accuracy in the diagnosis of urothelial carcinoma of urinary bladder, especially in high grade neoplasm. Cytological findings must always be harmonize with clinical, radiologic findings and in combination with histopathological findings and immunohistochemistry stainings as an ancillary studies.

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