Original Article

An appraisal of urine cytology in the diagnosis of transitional cell carcinoma of the urinary bladder

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Summary:

Background: *Urine cytology has an acceptable sensitivity, & specificity that justifies its use in the current diagnostic protocol.*
In Iraq transitional cell carcinoma (TCC) constitute about 62.1 % of bladder cancer (which ranks the third according to the results of Iraqi Cancer Registry 1995-1997). Urine cytology used in the primary
diagnosis, follow up, and in the screening programs of asymptomatic but high-risk patients.
Patients and methods: *This study was conducted on 93 patients, diagnosed or clinically suspected to have TCC of the urinary bladder attending to the Urological department in AL-Kadhimiya Teaching Hospital, AL-Yarmouk Teaching Hospital, and Baghdad Medical City. During the period from July 2004to July 2005. 76 were males & 17 were females.*
Urine cytological examination was done to those patients using two types of stain (hematoxylin and eosin, and papanicoloau stain) to detect malignant cells with the identification of the degree of differentiation, if possible, the cytological findings were correlated with the histopathological findings. And the cytological findings compared regarding each type of stain.
Results:. *Mean age of the patients was 59 year. Male:female ratio was 4.4:1. Main clinical presentation was hematuria (45.8%) of the total.*
Urine cytological examination has a sensitivity of 87.7%, specificity of 100% with an overall accuracy of 78% in the detection of TCC of urinary bladder. The main chief complaint of patients with TCC was haematuriawitch constitute 45.8% of the total. The percentage of highgrade cases in urine cytology was higher than that in histopathology.the percentage of cases of TCC diagnosed by papanicoloau stain was more than that diagnosed by H & E (73.24% by pap stain versus 70.42% by H&E).
Conclusion: *Urine cytology has an acceptable sensitivity, specificity and an overall accuracy in the diagnosis of TCC of urinary bladder, and it offers a good chance for determination of the grade of the tumor especially in high grade tumor. Pap stain was better in the diagnosis of TCC.*

Introduction:

Bladder cancer in Iraq ranks the third after breast cancer & lung cancer. It is the second in men, & the sixth in women. The most common histological type of bladder tumor is TCC (62.1%), followed by squamous cell carcinoma (25.2%

Urine cytology is an established diagnostic procedure in the primary diagnosis, in the follow up, monitoring of patients with known & treated disease, & in screening programs of asymptomatic but high risk patients. Urine cytology has an acceptable sensitivity & specificity, it is easy, cheep, quick, repeatable, and readily accepted by the patients (4's)

Swedish investigators have used cytological technique to assess the grade of TCC depending on the cytological criteria.

TCC, have three grades:

Grade I: urine samples are more cellular than normal. The cell clusters are irregular with ragged border, mild atypia, N/C ratio is approximately 37(the normal ratio is 12).

Grade II: urine samples are more cellular, more striking nuclear abnormalities, moderate degree of atypia, and N/C ratio is approximately 42.

Grade III: highly cellular urine samples, sometimes minute tissue fragments. The nuclei are more than twice the size of normal nuclei, & greater degree of atypia. More RBC, necrotic debris, & leukocytes.

Material and methods:

From July 2004 to July 2005, 93 patients, 33 of them has a diagnosis of TCC of the urinary bladder (confirmed by histopathological examination) & 60 suspected to have TCC attending the department of urology in the AL-Kadhimiya Teaching Hospital, AL-Yarmook Teaching Hospital, & Baghdad

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15-30 ml of urine was obtained from those selected patients. Urine samples were collected in plastic container, samples were processed within two hours. If delay in processing of the specimen is anticipated an equal amount of 50% ethyl alcohol. was added to the specimen. The samples .were centrifuged at (1500) for 20 minutes & four smears from the sediment were prepared, & two slides stained with H& E, and the other two stained with pap stain.

Smears, which were stained examined & cellular findings, were classified as follows:
1- Negative for malignancy, (including dysplasia).
2- Positive for malignancy, (with identification of grade if possible). Statistical analysishad had been made using sensitivity, specificity, and accuracy of urine cytological.. examination in the detection of malignancy.

Results:

93 cases suspected to have or diagnosed as TCC were subjected to urine cytological examination. 71 cases were proved to have TCC by histopathology, six cases had squamous cell carcinoma (SCC) & 16 cases were negative for malignancy. SCC cases were excluded from the study. Of this 71 case, 58 were male, 13 cases were female.

Table (1) An age distribution of 58 male patients with TCC of the urinary bladder

Age of the patients (years)	No. of patients
25-33	1
34-42	3
43-51	14
52-60	15
61-69	14
70-78	9
79-87	2

Table (2) An age distribution of 13 female patients with TCC of the urinary bladder

Age of the patients(year)	No. of patients
50-55	3
56-61	3
62-67	0
68-73	5
74-79	2

(Table 3): The most fre went complaint of patients

The complaints	% of total
Haematuria	45.80
Frequency of urination	10
Dysuria & urgency	14.50
Retention of urine	6.80
Constitutional s & s*	4.50

**** Signs & symptoms***

(table 4): the results of urine cytotogical examination of 87 patients suspected to have or diagnosed as TCC.
****sensitivity was 87.6%, specificity was 100%.***

The results	No. of patients
'true positive	52
False negative	19
True negative	16
False positive	0
Total	87

Table (5): The no. of patients according to cytological grade of the true ositive atients 52 cases with TCC of the urina bladder.

Grade	Total no. of patients	No. of male patients	No. of female patients
Low	11	10	1
Intermediat	11	7	3
High	30	24	6

Table (6) :the no. of patients according to cytological grade of the false negative patients (19) with TCC of the urinary bladder.

Grade	Total no. patients
Grade I	7
Grade 1-I1	8
Grade III	4

Table (7): A comparison between cytological and histopathological results re ardin the rade of 52 true ositive cases .

Grade,	No. of cases diagnosed by	No. of cases diagnosed
Low	11	5
Intermediat	11	14
High	30	33

Table (8): A comparison between cytological results using II & E stain and the results usin a stain.

No. of cases	H & E	Pap stain
1 case	Moderate dysdplasia	TCC (low grade)
1 case	Severe dysplasia	TCC (low grade)

Discussion:

Bladder cancer in Iraq has displayed a pattern similar to that in western world, where TCC is the predominant histological type & constitute more than 62.1% of all primary malignant urinary bladder tumors. Previously SCC was the predominant histological type in Iraq. This change in the pattern may be explained by the improvement in the standafd of living and education, that resulting in a decline in the incidence of bilhariziasis which is the most common predisposing factor for SCC (6,7).

The mean age of patients with TCC was 59 year, which is much lower than the mean age mentioned by other authors outside Iraq (&1°). This may be explained by a profound increase in the smoking habit, industrial exposure to urothelial carcinogens, and the carcinogens exposure due to frequent wars (11).

The male: female ratio was found to be 4.4:1, which is rather similar to the ratio obtained by other studies (9,10).

On reviewing the main chief complaint of the patients (table 3) included in this study we found that, haematuria was the most common clinical presentation which constitute 45.8% of the total, this result consistent with results obtained by many authors (12).

In this study the sensitivity was 87.6%, and the specificity was 100% (table 4). This result is in concordance with results obtained by other studies, which were show, a sensitivity range between 34.2%- 92.4%, and a specificity range between 88.1%-100%(13-16)

In this study the false negative results were recorded in 21.8%, several factors may contribute to this (16"19):

1- The sensitivity of diagnosis depends on the histological type, and the grade of the malignancy.

2- Marked infection and hemorrhage may mask the picture.

3- Inadequate urine sample, as in case of collapsed bladder.

On reviewing the histopathological diagnosis of these 19 false negative cases (table 5): 7 cases were grade I, 8 cases were grade I-II, and 4 cases were grade III. So we conclude that the sensitivity is lower in higher grade.

In table (6) we found that the number of true positive cases which were of low grade in cytological examination was (5), while it was higher (11) in histopathological examination. The number of highgrade cases was higher in cytological examination (33 in cytological examination versus 30 in histopathological examination). This could be explained by: that the urine usually has a low acidic pH and a high content of urea and other organic components, therefore it is not isotonic, so the urine is not a hospitable medium for desquamated cells, which are often poorly preserved, and sometimes difficult to asses on microscopically examination.

Table (8) shows that two cases of TCC were diagnosed as moderate and severe dysplasia when stained by H& E, while they were diagnosed as TCC when stained by PAP stain. This could be explained by the fact that the PAP stain results in well stained nuclear chromatin, differential nuclear counterstaining, and cytoplasmic transparency.

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