

Utility of Urine Cytology in Urinary Tract Neoplasm with Histopathological Correlation

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ABSTRACT

Background: Urinary bladder tumor is the sixth most common tumor diagnosed worldwide. Urine cytology is an important screening tool of patients for urothelial carcinoma (UC) and follow-up of patients with treated disease. The aim of this study to determine the sensitivity of urine cytology in detection of urinary tract neoplasms with its clinical and histopathological correlation.

Material & Methods: A five years prospective study includes 73 cases of urine cytology from January 2014 to December 2018 at a tertiary care hospital in the Department of Pathology. Urine cytology slides were reviewed and were correlated with histopathological diagnosis.

Results: Out of 73 cases, histopathological follow up received only in 43 cases. Out of that, 33 were male and 10 were female. Male to female ratio is 3.3:1. Maximum age incidence was found 5th-6th decade. Hematuria was most common and presenting complaint found in 90% of cases. Urothelial carcinoma was most common neoplasm comprising for 87.5% of bladder tumors, Squamous cell carcinoma comprising 7.5%. The overall urine cytology sensitivity combining with the positive and suspicious result was 77.5%.

Conclusion: Urine cytology, despite its variable sensitivity remains a useful tool in evaluating suspected urothelial malignancies. Positive urine cytology requires confirmation with cystoscopy and biopsy before instituting any form of definitive therapy and a negative cytology does not always exclude malignant disease.

Keywords: Urothelial carcinoma, Urine cytology.

INTRODUCTION

Urothelial carcinoma (UC) is the second most common malignancy of the urogenital system, following prostate cancers in male, ranking 11th in incidence in global cancer statistics. [1] Around 75% of patients present with early, 20% with higher tumor stage, and 5% with metastatic disease. Disease recurs in overall 70% of treated patients, with 30% of these patients developing metastatic disease. [2] Urinary bladder tumor is thrice as common in males as compared females and is usually seen in patients over 50 years of age. [3] Cigarette smoking is the most common etiological factor associated with urinary bladder tumors. [4] Other etiological factors associated with urothelial carcinomas are exposures to aryl amines, *Schistosoma haematobium* and long-term use of analgesics. [5] Cystoscopy is the most widely and routinely used procedure for diagnosis. But cystoscopies are not carried out in every Centre, are not cost effective to every patient as well as lesion like carcinoma in situ can be missed. While urine cytology is a far more superior in cost-effectiveness, very simple, rapid and non-invasive and can be repeated without discomfort. Cell can be obtained from area inaccessible to biopsy like renal pelvis. The diagnostic potential of urine cytology lies in its high specificity which ranges between 58% to 95%, however the sensitivity is not that impressive which is reported to be in the range of 48% to 80%. [6-9]

AIMS AND OBJECTIVES

The aim of the study was to find out the incidence and etiological agent of urinary tract neoplasm. To determine the sensitivity of urine cytology in detection of urinary tract neoplasm with its clinical and histopathological correlation.

MATERIALS AND METHODS

A Prospective study of urine cytology with its clinical and histopathological correlation of urinary tract neoplasm was carried out from January 2014 to December 2018 at a tertiary care hospital in the Department of Pathology. The clinical details, age, sex, and imaging details were obtained. Three consecutive urine samples were included in the study. Samples were centrifuged at 1000 rpm for 3 min and stained with Papanicolaou stain.

Cytology smears were divided into three categories based on the cellular morphology. Biopsies were fixed in 10% formal saline and hematoxylin and eosin staining was done. Lesions were classified according to the WHO classification of tumors of the urinary tract. The cytological findings were compared and correlated with histopathological findings.

RESULTS

We have studied the urine cytology in 73 admitted patients. Reports of the cytological examination were given as positive, suspicious, negative. (Table 1) Typing of Urothelial, Squamous or Adenocarcinoma was given whenever possible. Urine cytology was positive in 49 cases, suspicious in 10 cases and negative in 14 cases even after multiple examinations.

Table 1: Results of Urine cytology.

Urinary tract neoplasm	Total no cases (%)	Urine cytology		
		Positive	Suspicious	Negative
Urinary Bladder tumors	70 (95.89%)	49 (70%)	10 (14.28%)	11 (15.71%)
Pelvic-ureteric tumors	2(2.74%)	0	0	2 (100%)
Urethral tumor	1(1.37%)	0	0	1 (100%)

Out of 73 cases, histopathological follow up received only in 43 cases. Youngest patient in our study was 9 years and oldest was 70 years. Maximum age incidence was found 5th-6th decade. (Table 2) Out of 43 cases, 33 were male and 10 were female. Male to female ratio is 3.3:1.

Almost all patients with urinary bladder tumor presented with one or more features of bladder irritation. Hematuria was most common and presenting complaint

found in 90% of cases. Only one patient of ureteric malignancy who presented as lump in abdomen with no urinary complaints which was diagnosed as synovial sarcoma immuno-histochemically. In case of urethral tumor patient came with complaint of difficulty in micturition which was clinically suspected as prostatomegaly. In our study there was not a single person working in chemical Industries. Most common occupation was farming.

Table 2: Age incidence in Urinary tract neoplasm.

SN	Urinary tract neoplasm.	0-20 yrs	21-30 yrs	31-40 yrs	41-50 yrs	51-60 yrs	61-70 yrs	Total
	Urinary Bladder tumors							
1.	Leiomyoma	1	-	-	-	-	-	1
2.	Urothelial carcinoma	-	1	5	7	15	7	35
3.	Squamous cell carcinoma	-	1	-	1	1	-	3
4.	Adenocarcinoma	-	-	-	1	-	-	1
	Pelvic-Ureteric tumors							
5.	Synovial sarcoma	1	-	-	-	-	-	1
6.	Low grade urothelial carcinoma	-	-	-	-	-	1	1
	Urethral tumors							
7.	Mucinous adenocarcinoma	-	-	-	1	-	-	1
	Total	2	2	5	10	16	8	43

In our study, urinary bladder tumor comprises 40 cases (93.02%) while pelvic-

ureteric tumor constitutes 2 cases (4.65%) and only 1 case (2.32%) of urethral tumor of

all. (Table 3) Histopathological study were done, where Urothelial carcinoma seen in 35 cases, Squamous cell carcinoma in 3 cases and one each of adenocarcinoma and leiomyoma of bladder. So Urothelial carcinoma was most common neoplasm comprising for 87.5% of bladder tumor, Squamous cell carcinoma comprising 7.5% and least common adenocarcinoma and leiomyoma accounting for 2.5%. From 40

cases of urinary bladder tumor, urine cytology was positive in 25 cases and suspicious in 6 cases and negative in 9 cases. The overall sensitivity combining with the positive and suspicious result was 77.5%. From 35 cases of Urothelial carcinoma, urine cytology were positive in 65.7% and in 14.3% wear suspicious for malignant cell and only in 22.9% cases diagnosis of malignancy was not possible.

Table 3: Histopathological correlation with Urine cytology.

Histopathological Diagnosis	Total no cases (%)	Urine cytology		
		Positive	Suspicious	Negative
Urinary Bladder tumors	40	25 (62.5%)	6 (15%)	9 (22.5%)
1.Urothelial carcinoma	35(87.5%)	23 (65.7%)	5 (14.3%)	8 (22.9%)
2.Squamous cell carcinoma	3(7.5%)	2 (66.6%)	1 (33.3%)	0
3.Adenomacarcinoma	1(2.5%)	-	-	1(100%)
4.Leiomyoma	1(2.5%)	-	-	1(100%)
Pelvic-ureteric tumors	2			
1.Low grade urothelial Carcinoma	1	0	0	1
2.Synovial sarcoma	1	0	0	1
Urethral tumor	1			
1.Mucinous adenocarcinoma	1	0	0	1

Urothelial neoplasm are graded according to WHO into four categories of papilloma, papillary neoplasm of low grade malignant potential (PUNLMP), low grade Urothelial carcinoma (LGUC) and high grade papillary carcinoma (HGUC). In our study 1 case was PUNLMP and 14 cases were of low grade papillary carcinoma and 20 cases of high grade papillary carcinoma. Urine cytology result was negative in case of PUNLMP. Out of 14 cases of LGUC (Figure 1) 50% cases give positive result, 14. 29% were suspicious and 35.71% give negative results for malignant cells. But in HGUC urine cytology give better results

than the low grade. Out of 20 cases HGUC (Figure 2), 16 cases (80%) were positive and 3 cases (15%) were suspicious and only 1 case (5%) was negative for malignant cells on urine cytology.

In 3 cases of SCC (Figure 3), 2 have shown cytological features of SCC and 1 case suspicious of malignancy. While in one case of adenocarcinoma, there was dense inflammatory background and occasional epithelial cells without atypia on cytology. In leiomyoma report was normal. In low grade urothelial carcinoma of pelvis and in urethral adenocarcinoma urine cytology results were negative.

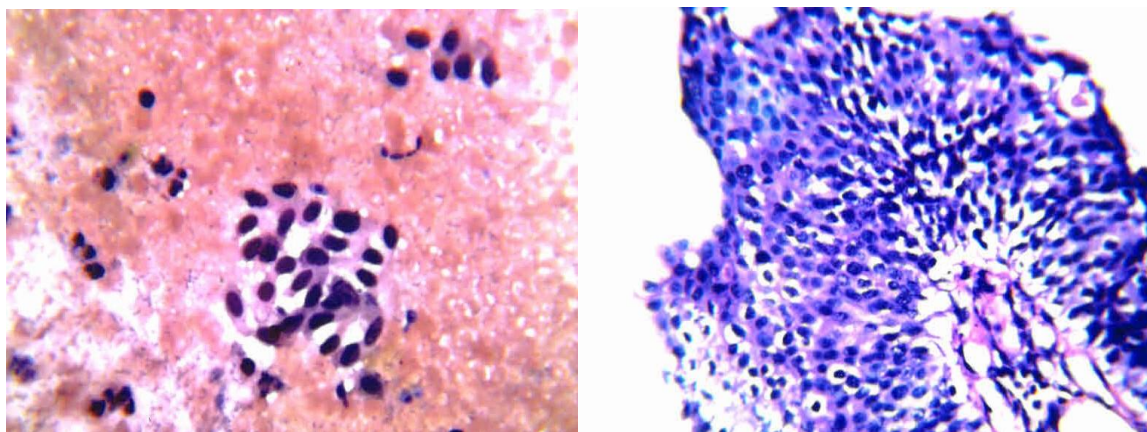


Figure 1: Low grade urothelial carcinoma, urine cytology (PAPX40) and (H & E X40)

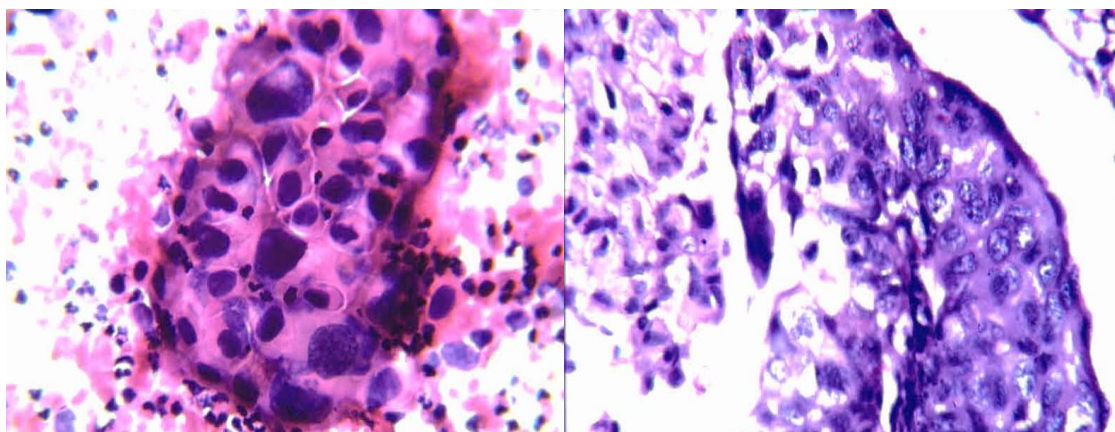


Figure 2: High grade urothelial carcinoma, urine cytology (PAPX40) and (H & E X40)

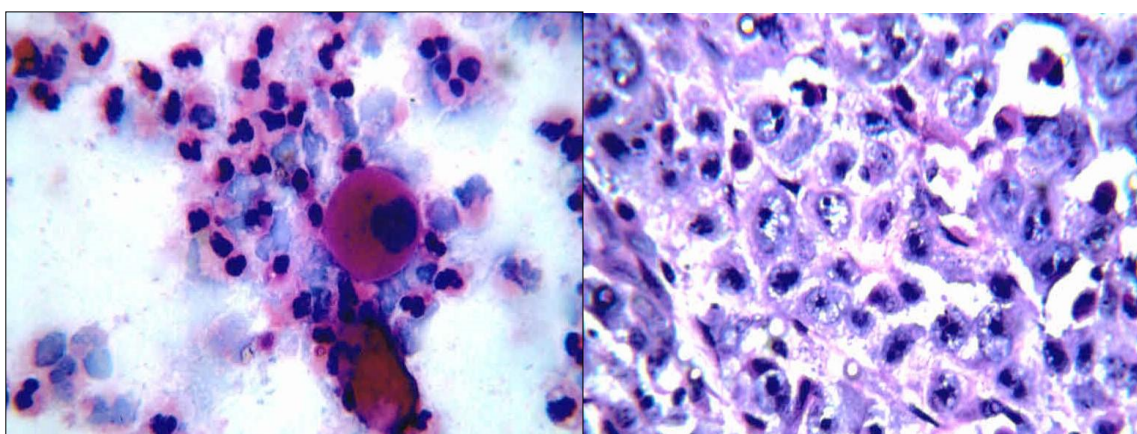


Figure 3: Squamous cell carcinoma, urine cytology (PAPX40) and (H & E X40)

DISCUSSION

Urinary bladder tumor is the sixth most common tumor diagnosed worldwide. Diagnosis of urothelial neoplasm is based on the clinical imaging findings, histopathological examination and study of urine cytology. Urine cytology is a well-established and useful diagnostic as well as screening tool for urinary bladder tumors. However, sensitivity is more in high-grade urothelial tumors. The sensitivity and specificity of urine cytology in high-grade urothelial tumor is 90%. Urine cytology has been faced with numerous challenges one of which is lack of agreed diagnostic criteria and terminology when compared to other cytology such as for breast and thyroid. [10]

In our study maximum cases were in 6th decade. The male to female ratio was 3.3:1 in our study while in Chawla et al study [11] it was 3:1. Male preponderance was distinctly evident our study, also correlate with the most of other studies. [12]

Almost 90% of our patient presented with hematuria with or without other symptoms of bladder irritation which was well correlate with Ghazizadeh et al [13] and Uchida et al [14] studies who reported hematuria as a commonest presenting symptoms. In our study, 25 out of 35 cases of Urothelial carcinoma were chronic heavy cigarette smokers for duration of 25 to 30 years. Abraham M. et al [15] indicate a direct relationship of cigarette smoking with bladder cancer in men who has smoked cigarette for a period of 30 years or longer.

We have found 87.5% cases Urothelial carcinoma, in Chawla et al study [11] it was 97.3%. Thus the present study correlate with other studied showing Urothelial carcinoma as a most common type of bladder tumor. Our study gives higher incidence of high-grade tumors which is in correlate to Rai S et al study [16] and contradiction to Chawla et al study [11] where Grade 2 tumors were common. According to a study conducted by Ajmera

S et al, [12] the most common histological diagnosis was non-invasive papillary urothelial carcinoma, high grade seen in 29.1% patients which is in contradiction with the our study. Probably this may be due to tertiary referral centre where high grade and high stage tumours are referred. In present study out of 70 cases of bladder tumors, histopathological study was done in 40 cases of which 35 were Urothelial carcinoma in that urine cytology was positive in 65.71% and suspicious in 14.28% and negative in 20%. In some study suspicious results were included in positive and in that case sensitivity approaches to 80%. The present study correlates with the studies of Chautard D et al [17] and Ravi et al [18] with increasing grade of tumor chances of detection of malignant cell increases. The high rate of detection of HGUC on cytology is attributed to the fact that shedding of dyscohesive malignant cells in urine is greater in HGUC compared with LGUN. Accuracy of diagnosing malignancy by cytology is highly variable and depends on the presence of diagnostic yield, processing of the sample, and expertise of the cytopathologist. Diagnosis is all the more difficult in low grade non-invasive carcinoma as the sensitivity of detection of malignant cells is very low. [19] Urine cytology should always be reported in a background of detailed clinical information and followed by histopathological examination for urinary bladder tumor.

CONCLUSION

Urine cytology, despite its variable sensitivity remains a useful tool in evaluating suspected urothelial malignancies. It is used as a complement but not replacement for cystoscopy and biopsy. Therefore positive urine cytology requires confirmation with cystoscopy and biopsy before instituting any form of definitive therapy and a negative cytology does not always exclude malignant disease.

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