



ORIGINAL RESEARCH PAPER

PATHOLOGY

CYTOHISTOLOGICAL STUDY OF URINARY BLADDER NEOPLASMS

KEY WORDS: urine cytology, bladder neoplasm, cytohistological correlation.

Dr. S. Sasikala

M.D, Associate Professor, Department Of Pathology, Government Stanley Medical College, Chennai, Tamilnadu, India.

Dr. I. Vijay Sathish Kumar*

M.D, Associate Professor, Department Of Pathology, Government Stanley Medical College, Chennai, Tamilnadu, India. *Corresponding Author

ABSTRACT

Introduction: Urine cytology has an important role in the multidisciplinary diagnostic approach to bladder cancer. It is used for screening, diagnosis and follow-up of urinary tract neoplasm.

Aim: To study the value of urine cytology in the diagnosis of bladder cancer and to correlate it with histopathology.

Method: Voided urine cytology of 54 patients who had symptoms suggestive of bladder tumour or were under follow up for bladder cancer was done. Subsequently, biopsy of these patients was correlated with cytology.

Results: 67% of bladder cancers were diagnosed by voided urine cytology. The sensitivity was 67% and the specificity was 56%. 65% of cytological diagnosis correlated with histo-morphological diagnosis.

Conclusion: Urine cytology is a simple test that can be used for screening, diagnosis and follow up of urinary bladder neoplasms. The accuracy is more with high grade tumours.

INTRODUCTION

Urine cytology has an important role in the multidisciplinary diagnostic approach to bladder cancer. Voided Urine cytology is a simple, safe, non-invasive, inexpensive screening test that can be used in remote areas of the country. Cytology can classify and grade the malignancy. As the entire mucosa can be sampled by cytology, the occult urothelial malignancies which cannot be detected by cystoscopy can be detected by cytology. Urine cytology plays an important role in detecting in-situ malignancies and the recurrent malignancies in patients who are under follow up. It can also detect persistent tumour after transurethral resection. Urine cytology also has a prognostic value. Patients with negative cytology have a low risk of recurrence while high grade cytological abnormalities predict an aggressive tumour course.¹

Cystoscopy and cytology are complementary studies. As cystoscopy cannot explore the whole bladder epithelium and cannot diagnose all in-situ cases or lesions of upper urinary tract, it must be combined with urine cytology. The accuracy of urine cytology is high in diagnosing high grade carcinomas with cytohistological correlation reported as high as 98%.²

Even though a variety of newer diagnostic techniques like flow-cytometry, molecular biology have been applied to increase the diagnostic accuracy, the urine cytology remains indispensable in the diagnosis of bladder neoplasm. Hence we carried out this study.

AIMS AND OBJECTIVES:

To study the value of urine cytology in diagnosing bladder cancer and to correlate urine cytology with histopathology of bladder neoplasms.

MATERIALS AND METHODS.

This study was conducted in a tertiary care hospital in Tamilnadu, India over a period of 2 years. Voided urine samples were collected from 54 patients who had symptoms suggestive of bladder tumour or were being followed after treatment for bladder cancer. The patients were in the age group of 28 to 85 years. Three random freshly voided urine samples were collected, avoiding early morning urine. Smears were prepared after centrifugation and were fixed in 95% isopropyl alcohol. Then the slides were stained using Haematoxylin and Eosin stains and Papanicolaou stain. Then the slides were analysed under light microscopy. From these 54 patients, histopathology material was obtained either from TURBT (Transurethral resection of bladder tumour) specimen, cystoscopic biopsy or radical cystectomy specimens. Specimens were fixed in 10% formalin, processed, sectioned and stained with Haematoxylin and Eosin stains. Cytology smears were reported

either as negative for malignancy or positive for malignancy. Positive cases were graded into low grade malignancy and high grade malignancy. Histopathology slides were reported as either no malignancy or low grade papillary urothelial carcinoma or high grade papillary urothelial carcinoma. Then the cytohistological correlation was done.

RESULTS:

Among the 54 cases studied, 37 cases were in the age group of 50-69 years. Among 54 cases, histologically proven bladder tumor cases were 45, out of which 44 occurred in males. Among the 54 cases, cytology showed malignancy in 34 cases and 20 cases were negative for malignancy. Regarding histopathology out of 54 cases 45 showed malignancy which included 21 cases of low grade papillary urothelial carcinoma and 24 cases of high grade papillary urothelial carcinoma. Histopathology was negative in 9 cases.

Among the 20 cytologically negative cases, histopathology showed malignancy in 15 cases which included 10 low grade papillary urothelial carcinoma and 5 cases of high grade papillary urothelial carcinoma. Urine cytology in correlation with histopathology for 54 cases is shown in table 1.

TABLE 1. CYTOLOGY IN CORRELATION WITH HISTO PATHOLOGY.

HISTOLOGY	CYTOLOGY		TOTAL
	POSITIVE	NEGATIVE	
LOW GRADE	11	10	21
HIGH GRADE	19	5	24
NEGATIVE	4	5	9
TOTAL	34	20	54

Among the 54 cases, true positives [TP] were 30, false positives [FP] were 4, false negatives [FN] were 15 and true negatives [TN] were 5 (Table-2).

TABLE 2. PREDICTION STATISTICS TABLE FOR CYTOLOGY AND BIOPSY CORRELATION.

CYTOLOGY	BIOPSY		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	30[TP]	4[FP]	34
NEGATIVE	15[FN]	5[TN]	20
TOTAL	45	9	54

Specificity of urine cytology = $TN / (TN + FP) = 56\%$.

Sensitivity of urine cytology = $TP / (TP + FN) = 67\%$

High grade tumours had high correlation whereas low grade tumours had a poor correlation. Out of 24 histologically proven high grade cases, 19 (79%) were detected cytologically.

Chart 1. Efficacy Of Urine Cytology In High Grade Tumours

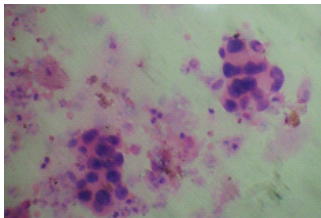
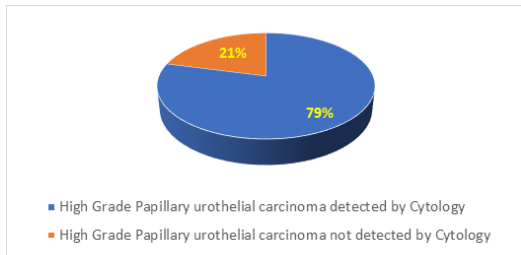


Fig.1: Smear from urinary sediment of high grade papillary urothelial carcinoma showing large cells with pleomorphic, hyperchromatic nuclei. H&E. 400x. Out of 21 histologically proven low grade cases, 11 (52%) were detected cytologically.

Chart 2. Efficacy Of Urine Cytology In Low Grade Tumours

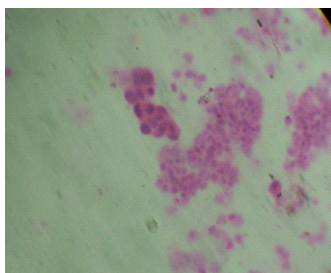
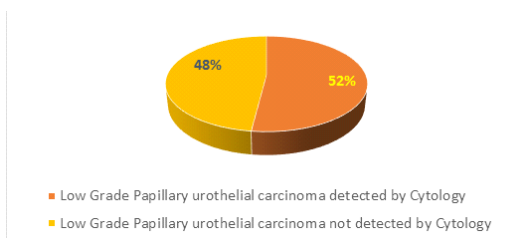


Fig2: Smear from urinary sediment of low grade papillary urothelial carcinoma. H&E. 400x.

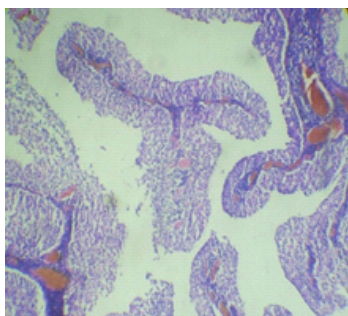
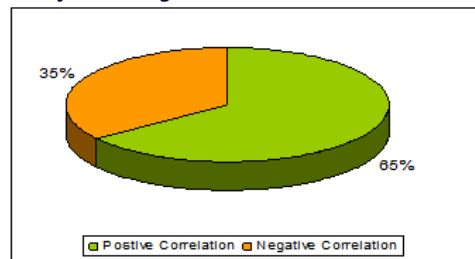


Fig. 3: Histology of low grade papillary urothelial carcinoma. H & E. 100x. Overall cytohistological correlation was 65%.

CHART 3. Cytohistological correlation



Overall histologically confirmed papillary urothelial carcinoma cases occurred in 45 patients of whom 30 (67%) were diagnosed cytologically.

DISCUSSION

Voided urine cytology is the only non-invasive method used for screening, diagnosis and follow up of tumours of lower urinary tract. Literature review showed that most of the patients with bladder neoplasm are older than 50 years of age. In our study, 34 patients were over 50 years of age. The sensitivity and specificity of voided urine cytology in the studies conducted by the various authors are shown in the table 3.

Table 3. The Sensitivity And Specificity Of The Voided Urine Cytology In Various Studies.

S.NO	Author	Sensitivity	Specificity
1.	M.N.EL-Bolkainy ³ 1980	44.7 to 97.3% with mean of 73.8%	88% to 99.5% with mean of 97.1%
2.	Uma A. Shenoy et al ⁴ 1985	85%	99%
3.	Asitava Mondal et al ⁵ 1992	92%	88%
4.	Misra V et al ⁶ 2000	47.37%	41.18%
5.	V. Poulakis et al ⁷ 2001	62%	96%
6.	A. Saad et al ⁸ 2002	48%	87%
7.	Planz B et al ⁹ 2005	38%	98.3%

Our study showed a sensitivity of 67% and specificity of 56% for voided urine cytology. Overall cytohistological correlation was 92% in the study conducted by William M. Murphy et al¹⁰, 74% in the study conducted by Uma A Shenoy et al⁴, and it varied from 20% to 92.8% in the study conducted by DiBonito L et al.¹¹ It was 59.8% in the study conducted by Raab et al.¹² In our study, the overall cytohistological correlation was 65%. Consistent with previously published data, our study showed higher diagnostic accuracy with high grade tumours. In our study 79% of high grade tumours were detected by cytology but only 52% of the low grade tumours were detected by cytology.

Cystoscopy and cytology are complimentary studies.⁹ The low grade tumours that may be difficult to diagnose cytologically are usually easy to diagnose cystoscopically. In our study, out of 10 low grade tumours which were falsely diagnosed as negative in cytology, 8 showed cystoscopically diagnosable growth.

In our study, 4 cases showed false positive cytology. 2 out of these 4 cases received radiation in the past and the radiation induced changes were falsely diagnosed as high grade urothelial carcinoma. So it is essential that the cytologist be informed whether [and when] previous radiotherapy has been given to the patient, as insisted by P.N. Cowen.¹³ In other 2 cases, cystoscopy showed no growth and biopsy was negative. There after patients could not be followed up. As stated by David M Schwalb et al¹⁴ inadequate follow up may be the cause for false positivity.

TABLE 4. False positive rates reported by various authors compared with our study

S.no	Author	False positivity (%)
1	M.N.EL.BOLKAINY	1.5%
2	UMA A.SHENOY ET AL	11%
3	EDWARD M MESSING	1-12%
4	OUR STUDY	12%

False positive cases may develop tumours in subsequent years and therefore needs repeated examination of urine for malignant cells. In our study, 15 cases showed false negative cytology. Out of these 15 cases, histology showed low grade tumour in 10 cases, and this may be due to exfoliation of non-diagnostic cells from low grade tumours. Histology showed high grade tumours in 5 cases which showed heavy inflammatory background in cytology which masked the tumour cells.

CONCLUSION

Voided urine cytology is an aid in the diagnosis and in the follow-up of bladder tumours. It also has prognostic value. Positive cytology identifies patients at high risk. The accuracy is more with high grade tumours. Previous therapy reduces the diagnostic accuracy. Inadequate follow up and previous therapy led to false positive cytology. Cystoscopy is more useful in diagnosing low grade tumours which were missed by voided urine cytology. Voided urine cytology is a valuable adjunct in the evaluation of urologic patients as it is a simple, non-invasive test with good diagnostic accuracy.

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