Evaluation of the Efficacy of Post Prostatic Massage Urine Cytology in Diagnosis of Various Prostatic Lesions with Cytohistological and Clinical Correlation

Monisha Choudhury, Savita Agarwal
Department of Pathology, Lady Hardinge Medical College, New Delhi, Department of Pathology, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, Uttar Pradesh, India

Abstract

Background: Elderly men are at high risk of various prostatic diseases carrying high morbidity and mortality rates. For screening large populations, there is a need for a simple, reliable, and noninvasive test with high sensitivity and specificity. Exfoliated prostatic cancer cells can be harvested by prostatic massage and subjected to cytologic examination and molecular tests. Aims: This study was undertaken to evaluate the morphology of various prostatic lesions on post prostatic massage urine cytology and correlate cytologic, histologic, and clinical findings. It was further proposed to establish the diagnostic accuracy of post prostatic massage urine cytology in different prostatic lesions. Materials and Methods: Totally, 100 cases including 50 cases each from study group and control group were subjected to post prostatic massage urine cytology and correlated with clinical and histological findings. Results: Five out of 50 cases were diagnosed as prostatic carcinoma, of which 60% were clinically detected. Diagnostic accuracy by histology and cytology independently was 80%, and 20% remained false negative by each technique. On combining both the techniques, diagnostic accuracy was 100%. For nine cases each of prostatitis and nodular hyperplasia diagnosed clinically, the diagnostic accuracy by cytology was 100 and 66.6%, respectively. 62% (31) cases were diagnosed as nodular hyperplasia including 22 (44%) cases of nodular hyperplasia with prostatitis. Conclusion: Collection of urinary specimens after prostatic massage provides adequate samples for cytological examination and carries great importance in establishing the preoperative morphologic diagnosis in cases of malignancy, prostatitis, and prostatic calculi.

Keywords: Nodular hyperplasia, prostatic carcinoma, prostatitis, tuberculosis, urine cytology

INTRODUCTION

Presenile and senile men are at high risk of various prostatic diseases which carry high morbidity and mortality rates and pose diagnostic difficulties. Often a morphological confirmation is required to substantiate the clinical diagnosis. Carcinoma of the prostate is the commonest malignancy affecting males and is the second most common cause of cancer-related deaths in males.[1] Incidence of carcinoma prostate increases with age and 30% cases are detected between 30 and 49 years and 64% cases are detected between 60 and 70 years; hence screening for all men is recommended after 50 years of age.[2] For screening a large population, there is a need for a simple, reliable, and noninvasive test with high sensitivity and specificity. Prostatic cancer cells have increased tendency to exfoliate and these cells can be harvested by prostatic massage and subjected to cytologic examination and various molecular tests.[3] Exfoliated cells represent the disease status of entire gland and hence this method can be used for the detection of various benign and malignant processes affecting the prostate. This study was undertaken to evaluate the morphology of various prostatic lesions on post prostatic massage urine cytology and to correlate cytologic, histologic, and clinical findings. It was further proposed to establish the diagnostic accuracy of post prostatic massage urine cytology for different prostatic lesions, particularly for the preoperative diagnosis of carcinoma, in symptomatic patients.

**Address for correspondence:** Dr. Savita Agarwal, Department of Pathology, Uttar Pradesh University of Medical Sciences, Saifai, Etawah - 206 130, Uttar Pradesh, India.

E-mail: savvymedico@gmail.com

Access this article online

Quick Response Code:

Website: www.jcytol.org

DOI: 10.4103/JOC.JOC_130_16

How to cite this article: Choudhury M, Agarwal S. Evaluation of the efficacy of post prostatic massage urine cytology in diagnosis of various prostatic lesions with cytohistological and clinical correlation. J Cytol 2017;34:212-6.
Materials and Methods

The present prospective study was carried out in the Department of Pathology and Department of Surgery at Lady Hardinge Medical College New Delhi on 100 cases in which study group and control group comprised 50 cases each. Control group comprised cases who presented with complaints other than those related to genito-urinary system.

In all the cases, detailed history and clinical examination was conducted. Based on clinical and rectal examination, 50 cases of study group were divided under following subgroups: Group I – Prostatitis (9 cases), Group IIa – Nodular hyperplasia with prostatitis (16 cases), Group IIb – Nodular hyperplasia (16 cases), Group III – Suspicious for carcinoma (6 cases), and Group IV – Carcinoma (3 cases).

Pre and post massage urine samples were collected and subjected to routine biochemical and microscopic examination. Urine culture was done in selected cases only. Detailed hematological investigations, serum alkaline and acid phosphatase, were measured. X-ray chest and abdomen, intravenous pyelogram, and endoscopy were done as per clinical indication.

After evacuating the bladder, prostatic massage was carried out on all cases by Fergusson and Gibson technique and first 10 ml of voided urine was collected in plastic centrifuge tubes. In cases with urinary retention, both pre and post massage urine samples were collected. Urine samples were centrifuged at 1500 rpm for 5 min and sediment was spread on the glass slides and fixed in equal parts of ether and 95% alcohol for 30 min and subjected to Papanicolaou staining. Surgical or needle biopsy specimen of the prostate gland was obtained in 38 out of 50 cases. Cytologic and histopathologic diagnosis was established without the knowledge of other.

Results

Age range in the study group varied from 30 to 90 years. Age distribution of various subgroups is shown in Table 1. Majority of the patients presented with symptoms of frequency with nocturia, dysuria, and retention of urine. Hematuria and pain in lower abdomen were present in some cases with prostatitis or concurrent vesicle calculi.

Per rectal examination findings of 50 cases of study group are shown in Table 1 and no abnormality was observed in control group. Examination of pre prostatic massage urine sample was performed in all 100 cases. Significant findings are shown in Table 1. Albuminuria was not observed in control group and

| Group | Clinical diagnosis, number of cases (% age) | Age range (years) | Prostate on per rectal examination | Significant radiological finding | Significant urinary finding (pre prostatic massage sample) | Significant urinary finding (post prostatic massage sample) |
|-------|-------------------------------------------|------------------|----------------------------------|--------------------------------|----------------------------------------------------------|---------------------------------------------------------|
| I     | Prostatitis, 09 (18)                      | 30-60            | Small to moderately enlarged, tender | 1 case - ureretic calculi | In all cases - Trace to 1+ albumin, Pus cells – 3-10/hpf | Cytology smears of all cases showed prostatic cell degeneration, cytoplasmic vacuolization, and cytolysis [Figure 1a] along with fair number of neutrophils in 8 (88.9%) out of 9 cases. All 16 cases showed prostatic epithelial cells in groups and sheets with slight nuclear enlargement, degenerative changes, and vacuolization [Figure 1b] along with significant number of neutrophils, macrophages, and lymphocytes. |
| IIa   | Nodular hyperplasia with prostatitis, 16 (32) | 40-50           | Moderate to large size, elastic, nodular, tender | 3 cases - vesicle calculi | In all cases - Trace to 1+ albumin, Pus cells 3-10/hpf | Prostatic epithelial cells were uniform in size and shape and displayed mosaic pattern. Nuclei were slightly enlarged with uniform distribution of the chromatin and no visible nuclei [Figure 1c]. Five cases showed significant number of neutrophils and two cases showed corpora amylacea. |
| IIb   | Nodular hyperplasia, 16 (32)             | 50-80            | Moderate to large size, elastic, nodular | 1 case - ureretic calculi | 1 case - Trace to 1+ albumin, 5 cases - Pus cells 3-10/hpf | One case showed malignant prostatic cells in groups having scant cytoplasm, and large hyperchromatic nuclei with coarsely clumped chromatin. Two cases showed numerous corpora amylacea and concretions with fair number of inflammatory cells. Another case showed inflammatory cells with foreign body giant cells. |
| III   | Suspicious for carcinoma, 06 (12)        | 40-80            | Moderately enlarged, firm to hard, not fixed | 2 cases - healed tubercular lesion in lungs, 2 cases prostatic calculi | 5 cases - Trace to 1+ albumin, 2 cases - Pus cells 3-10/hpf | One case showed features of undifferentiated carcinoma [Figure 2a]. One case showed features of well-differentiated adenocarcinoma with well-formed acinar pattern [Figure 2b]. Third case showed presence of malignant cells having high nucleocytoplasmic ratio and marked nuclear pleomorphism. |
| IV    | Carcinoma, 03 (06)                       | 50-80            | Small to moderately enlarged, hard, nodular, fixed in 2 cases | 1 case - osteoblastic secondaries in sacrum | 3 cases - Trace to 1+ albumin, Pus cells 3-10/hpf | 1 case showed features of undifferentiated carcinoma [Figure 2a]. One case showed features of well-differentiated adenocarcinoma with well-formed acinar pattern [Figure 2b]. Third case showed presence of malignant cells having high nucleocytoplasmic ratio and marked nuclear pleomorphism. |
none of the cases in the study and control group had urinary sugar or ketone.

Urine culture was performed in 35 cases of study group showing significant number of pus cells and *Escherichia coli*, *Streptococcus pyogenes*, *Klebsiella*, and *Pseudomonas aeruginosa* were the various organisms grown in different subgroups.

Alkaline phosphatase levels were slightly elevated [15–17 King Armstrong (KA) units] in three cases of carcinoma prostate. Acid phosphatase levels were raised in two cases of carcinoma with values of 5 and 7 KA units.

Post prostatic massage urine samples were subjected to cytological examination in all 100 cases. 41 out of 50 (82%) study cases were adequate. Smears from all the cases were assessed for cellularity, pattern of cells, type of epithelial cells – prostatic, transitional, squamous and seminal vesicle, inflammatory cells, and other components – sperms, red cells, calculi, and corpora amylacea.

Cytological examination in the study group demonstrated – prostatitis 14 cases (28%), granulomatous prostatitis 1 case (2%), prostatic calculi 2 cases (4%), nodular hyperplasia with prostatitis 10 cases (20%), nodular hyperplasia 10 cases (20%), prostatic carcinoma 4 cases (8%), and inadequate in 9 cases (18%).

Nine out of 50 control cases showed an occasional benign prostatic epithelial cell, transitional cells, and few lymphocytes and rest were inadequate.

| Table 2: Correlation of clinical and cytological diagnosis with histopathology |
|---------------------------------------------------------------|
| **Histopathological diagnosis, no. of cases (%)** | **Clinical correlation** | **Cytological correlation** |
| | Correlated no. of cases (%) | Not correlated, no. of cases (%) | Correlated, no. of cases (%) | Not correlated, no. of cases (%) |
| Tubercular prostatitis 2 cases (4%) | - | 2 (100) | - | 2 (100) |
| Nodular hyperplasia with prostatitis 22 cases (44%) | 16 (72.7) | 6 (27.3) | 10 (45.5) | 12 (100) |
| Nodular hyperplasia 9 cases (18%) | 9 (100) | - | 6 (66.7) | 3 (33.3) |
| Carcinoma prostate 4 cases (8%) | 3 (75) | 1 (25) | 3 (75.0) | 1 (25) |
| Normal prostatic tissue 1 case (2%) | - | 1 (100) | - | 1 (100) |
| Total 38 (76%) | 28 (73.7) | 10 (26.3) | 20 (52.6) | 18 (47.4) |

**Discussion**

A high percentage of carcinoma is known to remain asymptomatic and hence remain undiagnosed until it has transgressed the bounds of surgical removal and cure. A preoperative morphological diagnosis in such cases and in early suspicious lesions would be invaluable in ruling out the possibility of malignancy and helping us in guiding the treatment. Conditions involving the prostate are usually diagnosed by digital examination. A needle biopsy can provide a morphological diagnosis in symptomatic patients but this technique is not simple and involves a certain degree of risk, and moreover, it has the potential to miss the lesion. Several methods for sampling prostate are in use,
alkaline phosphatases. Cytologically, these cases showed fair confirmed radiologically and had normal levels of acid and belonging to clinically suspicious group. Both the cases were Diagnosis of prostatic calculi was made in two cases (4%) by culture, and polymerase chain reaction of prostatic fluid. confirmed by demonstration of acid fast bacilli on prostatic tissue, occur following miliary tuberculosis and the diagnosis can be infection of prostate causing granulomatous prostatitis can had taken irregular antitubercular treatment. Mycobacterial prostatitis. Both the cases had past history of tuberculosis and from clinically suspicious group were reported as tubercular cancer study. Granulomatous prostatitis may clinically mimic prostatic by culture, and polymerase chain reaction of prostatic fluid. measurement of telomerase activity, nucleolar prominence. Few molecular techniques, such as protoporphyrin IX fluorescence are also being developed for detection of prostatic carcinoma on ThinPrep® as described by Tyler et al.[12] and demonstration of and 92% negative predictive value for detecting prostatic cancer by this technique. Important diagnostic features of prostatic adenocarcinoma on ThinPrep® as described by Tyler et al.[12] are clustering, high nuclear to cytoplasmic ratio, and nucleolar prominence. Few molecular techniques, such as measurement of telomerase activity,[12] and demonstration of protoporphyrin IX fluorescence are also being developed for detection of prostatic carcinoma cells in urinary sediments.[13]

Hence cytology of the prostate is a valuable adjunct to the clinical diagnosis. It has been found to be of great importance in establishing the preoperative morphologic diagnosis in cases of malignancy, prostatitis, and prostatic calculi. Collection of the urinary specimen after prostatic massage for cytology is a simple, safe office procedure, which provides adequate samples for cytological examination.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.
REFERENCES

1. Jemal A, Murray T, Samuel A, Ghafoor A, Ward E, Thun MJ. Cancer statistics, 2003. CA Cancer J Clin 2003;53:5-26.
2. Botchkina GI, Kim RH, Botchkina IL, Kirshenbaum A, Frischer Z, Adler HL. Noninvasive detection of prostate cancer by quantitative analysis of telomerase activity. Clin Cancer Res 2005;11:3243-9.
3. Magri V, Cariani L, Bonamore R, Restelli A, Garlaschi MC, Trinchieri A. Microscopic and microbiological findings for evaluation of chronic prostatitis. Arch Ital Urol Androl 2005;77:135-8.
4. Hessler D. Diagnosis of chronic prostatitis: Urinary cytology following prostatic massage. Helv Chir Acta 1981;48:401-4.
5. Nickel JC. The pre and post massage test (PPMT): A simple screen for prostatitis. Tech Urol 1997;3:38-43.
6. Tekin A, Yuksel A, Tekin S, Gumrukcu G, Aslan AR, Sengor F. Post-prostatic massage examination for prediction of asymptomatic prostatitis in needle biopsies: A prospective study. J Urol 2009;182:564-8.

7. Oppenheimer JR, Kahane H, Epstein JI. Granulomatous prostatitis on needle biopsy. Arch Pathol Lab Med 1997;121:724-9.
8. Domingue GJ, Hellstrom WJ. Prostatitis. Clinical Microbiol Rev 1998;11:604-13.
9. Kulchavenya E, Brzhatyuk E, Khomyakov V. Diagnosis and therapy for prostate tuberculosis. Ther Adv Urol 2014;6:129-34.
10. Varo Solis C, Hens Perez A, Bachiller Burgos J, Figueroa Murillo E. Prostatic exfoliative cytology obtained from urine samples after massage. Initial results. Actas Urol Esp 2002;26:398-406.
11. Tyler KL, Selvaggi SM. Morphologic features of prostatic adenocarcinoma on ThinPrep® urinary cytology. Diagn Cytopathol 2011;39:101-4.
12. Meid FH, Gygi CM, Leisinger HI, Bosman FT, Benhattar J. The use of telomerase activity for the detection of prostatic cancer cells after prostatic massage. J Urol 2001;165:1802-5.
13. Nakai Y, Anai S, Kuwada M, Miyake M, Chihara Y, Tanaka N, et al. Photodynamic diagnosis of shed prostate cancer cells in voided urine treated with 5-aminolevulinic acid. BMC Urol 2014;3:59.