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# Cytopathological Evaluation of Prostatic Lesions

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***Abstract:*** *The objectives of the present study was to evaluate cytomorphology of prostatic lesions on fine needle aspiration (FNA) smears, & to correlate between the cytomorphology by FNA and histological examination of the core needle biopsy & resected prostatic tissue. This study was conducted on 125 patients from the general surgery and urosurgery departments. Male patients with clinical or radiological diagnosis of prostatomegaly and patients with biochemical assay findings were selected for the study. FNA smears using Franzén guide cannula, were made & stained with May Grünwald Giemsa and Papanicolaou stains. Postoperative tissue specimen obtained were formalin fixed, processed, sectioned and stained with Haematoxylin & Eosin. Of the 125 cases, non-malignant cases constituted 81.6 % of the total cases studied, of which benign nodular hyperplasia of prostate constituted 80 %, and 18.4% of the total cases were malignant. The results were based on cyto & histomorphological observation.*

*In countries economically compromised as ours, fine needle aspiration cytology (FNAC) of prostate both as screening and as a preliminary diagnostic tool for suspected prostatic cancer can be recommended as it is a simple, sensitive cost effective way to exclude malignancy in the prostate. The high levels of FNAC accuracy for prostatic cancer detection shown by the present study coupled with the low procedure risk supports the value of prostatic FNAC as a good alternative to core biopsies when used in conjunction with DRE, and serum PSA levels.*

***Key words:*** *Prostate, FNAC, BHP, Prostatic adenocarcinoma & PIN*.

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## I. Introduction:

The term prostate was originally derived from the Greek word "Prohistani", meaning, " to stand in front of ", and has been attributed to Herophilus of Alexandria who used the term in 335 B.C to describe the organ located "in front of the urinary bladder[1].

Prostate, a fibro muscular glandular organ situated deep in the male pelvic cavity, is affected by inflammation, cystic lesions, benign nodular enlargement and tumours. Of these, benign nodular enlargement or benign hyperplasia of prostate (BHP), is far most common. In the recent years, carcinoma of the prostate is extremely common and a major and escalating international health problem. It is the second leading cause of cancer death in males in the western world[2] and therefore merits consideration.

The standard workup for the diagnosis of prostatic pathologies includes a comprehensive history, physical examination including digital rectal examination (DRE), relevant laboratory investigations, uroflowmetry and appropriate imaging studies. Now there are various modalities, which can directly evaluate the prostate. They include, transrectal fine needle aspiration cytology (FNAC) and tissue needle biopsy. The same can be done under digital or transrectal ultrasonographic (TRUS) guidance. Of these, FNAC has drawn attention, as it is a diagnostic modality which helps lower the costs of preoperative work-up and hospitalization and at the same time provides results with high sensitivity and specificity. This technique of FNAC of the prostate was introduced by Franzén, Giertz and Zajicek in 1960[3].

Three methods are currently available for the detection and clinical diagnosis of prostatic lesions; digital rectal examination, measurement of serum prostatic specific antigen (PSA) levels and transrectal ultrasonography. Each method alone has limited sensitivity and specificity, but a combination of three, has significantly improved the cancer detection rate[4]. If cancer is suggested by one or more of these diagnostic methods, preoperative confirmation of the diagnosis is the next step. This can be done by fine needle aspiration (FNA) for cytological diagnosis or transrectal core needle biopsy for histological examination[4].

Currently the transrectal ultrasonography-guided biopsies using the 12-core (or more) biopsy schemes is the current modality of choice for preoperative diagnosis of prostatic pathologies owing to its advantages. Nevertheless, there are many advantages of transrectal FNAC that warrants its use in the assessment of prostatic

pathologies – especially as the first line of investigation. TRUS plays an important role in the evaluation of the prostate when malignancy is suspected[5].

Preoperative FNAC of prostate is of value in patients when a carcinoma may be missed by transurethral resection, which usually does not include subcapsular parts of the gland, the site of predilection for carcinoma. FNAC is also useful for preoperative tissue diagnosis and staging of malignancy, in the diagnosis of disseminated cancer and in patients with debilitating diseases. In older patients, who are not candidates for radical surgery transrectal FNA is the method of choice of investigation[4]. FNAC prostate is recommended in patients with advanced cancer, where it can be used to follow the response and to monitor the chemotherapeutic dose levels[6].

The procedure of FNAC can be carried out as an out door procedure, is easier to perform, results in lower morbidity, no special preparation, no anesthesia is required, access to radiological equipment is not necessary and the complications of the procedure are minimum and rare. High sensitivity, specificity, and efficacy account for its reliability.

The main problem is the distinction of well-differentiated carcinoma from basal cell hyperplasia and prostatic intraepithelial neoplasia (PIN) on FNAC. PIN is a premalignant proliferation where the cellular arrangement shows preservation of duct and gland architecture along with progressive disruption of the basal cell layer with increasing grades, while invasion of the stroma is lacking. However, immunohistochemical (IHC) stains may be a useful adjunct in differentiating PIN from invasive adenocarcinoma. The basal cell IHC markers like high molecular weight cytokeratin (HMWK) & p63, that highlight basal cells are found in benign glands, but are absent in adenocarcinoma of the prostate. Alpha methylacyl Co A racemase (AMACR), another IHC marker will stain the cytoplasm of adenocarcinoma cases of the prostate[7- 9]

Complications of FNAC are very minimal and rare. Apart from epididymitis, transient haematuria, haemospermia, and transient fever, very rarely cancer seeding (spread) has been observed.

## II. Aims and Objectives

The objectives of the present study was to evaluate cytomorphology of prostatic lesions on fine needle aspiration (FNA) smears, & to correlate between the cytomorphology by FNA and histological examination of the core needle biopsy & resected prostatic tissue.

## III. Materials and Methods

The study, 'Cytopathological evaluation of prostatic lesions' was conducted in 125 subjects from general & urosurgical departments in a private hospital of Kolkata after informed consent of the patients. The selected male patients, had any one or more of the following:

- Clinical diagnosis of prostatomegaly
- Positive radiological or biochemical assay finding i.e. PSA > 4ng/ml
- Obstructive symptoms like difficulty in voiding, urinary retention, frequency of urination, hesitancy or dysuria or any sexual symptoms.

Patients with symptomatic febrile prostatitis were excluded from the study.

The patients were initially screened with digital rectal examination (DRE), serum prostate specific antigen (PSA) and a routine ultrasonography (USG) done whenever feasible. FNAC, Core biopsy and examination of the resected prostate done as and when applicable. The selected patients were referred to the department of pathology for an FNAC and before undergoing the test, patients were asked to abstain from alcohol, aspirin, and nonsteroidal anti-inflammatory drugs (NSAIDs) and refrain from sexual intercourse for five days. They were asked to take one fleet enema the night before the procedure. An oral antibiotic (usually Ciprofloxacin) was prescribed for 3 days, starting the day before of the procedure. DRE done, then using the Franzén guide cannula, a 20 cc syringe with the FNAC handle was used to make several passes for the desired aspirate, preferably from any hard part of the prostate, if felt. The patients were educated on the minor complications, which could arise such as haematuria, dull ache in the perineum or hemospermia.

The aspirates were then put on labeled 75 x 25 mm glass slides and smears drawn. Wet smears were put in 95 % ethanol for fixation for Hematoxylin & Eosin (H&E) and Papanicolaou (PAP) stains and others air-dried for May Grünwald Giemsa stains (MGG).

The tissue specimens when received were fixed in 10 % formalin, appropriately processed, made into blocks, sectioned & stained with H&E.

The points of cytological examination included adequacy of specimen, cellularity, architecture, cytoplasmic & nuclear details, background & any other additional points noted.

Histopathological examination of the core biopsy material & prostate specimen done. Gleason Score was assigned to all the dignosed adenocarcinomas.

## IV. Observations and Results

In one hundred and twenty five patients that were evaluated prospectively, it was tried that each of them have an FNAC before a core biopsy or prostatectomy.
The findings have been tabulated as follows:

**Table 1:** Distribution of nature of prostatic lesions

| CASES | No. OF CASES | PERCENTAGE |
|---|---|---|
| **BHP** | 100 | 80.0 % |
| **Malignancy** | 23 | 18.4 % |
| **Others** | 02 | 01.6 % |
| **TOTAL** | **125** | **100 %** |

**Table 2:** Age distribution in BHP and Prostatic malignancy

| AGE GROUP (YEARS) | NO. OF BHP | % OF BHP | NO. OF CA | % OF CA |
|---|---|---|---|---|
| **≤45** | 02 | 01.96 | 01 | 04.34 |
| **46 – 50** | 02 | 01.96 | 00 | 00.00 |
| **51 – 55** | 07 | 06.86 | 01 | 04.34 |
| **56 – 60** | 10 | 09.80 | 02 | 08.70 |
| **61 – 65** | 21 | 20.59 | 06 | 26.09 |
| **66 – 70** | 29 | 28.44 | 04 | 17.39 |
| **71 – 75** | 15 | 14.71 | 03 | 13.05 |
| **76 – 80** | 07 | 06.86 | 02 | 08.70 |
| **≥81** | 09 | 08.82 | 04 | 17.39 |
| **TOTAL** | **102** | **100** | **23** | **100** |

**Table 3:** Comparative study of Cytological and Histopathological Evaluation†

| CASES | CYTOPATHOLOGY | CORE Bx | TISSUE HISTOPATHOLOGY |
|---|---|---|---|
| **BHP** | 83 | 87 | 100 |
| **Malignancy** | 10 | 18 | 20 |
| **Inadequate/Not done** | 32 | 19 | 03 |
| **Others** | - | 01 | 02 |
| **TOTAL** | **125** | **125** | **125** |

† PIN has been included in the malignant group & the 'others' group includes prostatic infarct/ acute prostatitis/ abscess

**Table 4:** Comparative study of Cytopathology and Core Biopsy in diagnosis of Prostatic Carcinoma

| EVALUATING STATISTICS | CYTOPATHOLOGY % | CORE Bx % |
|---|---|---|
| **SENSITIVITY*** | 42.85 | 89.47 |
| **SPECIFICITY#** | 98.61 | 98.85 |
| **POSITIVE PREDICTIVE VALUE#** | 90 | 94.44 |
| **NEGATIVE PREDICTIVE VALUE#** | 85.54 | 97.72 |
| **PERCENTAGE OF FALSE POSITIVE#** | 01.38 | 01.14 |
| **PERCENTAGE OF FALSE NEGATIVE*** | 57.14 | 10.52 |
| **ACCURACY*** | 42.85 | 88.23 |

*$\chi^2$ = p significant $\leq 0.001$ #$\chi^2$ = p insignificant

**Table 5:** Comparative study of Cytopathology and Core Biopsy in diagnosis of Benign Prostatic Lesions

| EVALUATING STATISTICS | CYTOPATHOLOGY % | CORE Bx % |
|---|---|---|
| **SENSITIVITY*** | 98.61 | 98.85 |
| **SPECIFICITY+** | 42.85 | 89.47 |
| **POSITIVE PREDICTIVE VALUE*** | 85.54 | 97.72 |
| **NEGATIVE PREDICTIVE VALUE*** | 90 | 94.44 |
| **PERCENTAGE OF FALSE POSITIVE+** | 57.14 | 10.52 |
| **PERCENTAGE OF FALSE NEGATIVE*** | 01.38 | 01.14 |
| **ACCURACY#** | 69.6 | 98.85 |

*$\chi^2$ = p insignificant +$\chi^2$ = p significant $\leq$ 0.001 #$\chi^2$ = p significant $\leq$ 0.01

## V. Discussion

Prostate cancer one of the most common malignancy in men and the the present study has been undertaken to evaluate the usefulness and accuracy of transrectal FNAC in comparison with the core tissue biopsy and postoperative prostatectomy tissue specimen.

According to this study, as indicated by data in Table , BHP was the most common prostatic lesion constituting 80 % of the total lesions.

Besides the only case of metastatic transitional cell carcinoma (TCC) from the bladder and three cases of PIN, all the other malignant lesions were adenocarcinomas. Though PIN is a premalignant condition; in our study we have considered it under the malignant category.

Table 2 reveals that most of the cases of BHP belong to 66 – 70 years and most of the cases of malignancy by histopathology belong to 61 – 65 years accounting for 28.44 % & 26.09 % respectively. The youngest patient with BHP being 39 years and the oldest being 90 years. The youngest patient having carcinoma prostate was 45 years and the oldest 85 years.

Table 3 shows that by FNAC evaluation, eighty-three cases turned out to be BHP, ten malignant and thirty-two cases were inconclusive. Needle core biopsy showed that, eighteen cases were malignant (including two cases of PIN). Histopathological examination of resected prostate, showed hundred cases of BHP, and twenty malignancies and one case each of prostatic infarct and prostatic abscess.

From table 4 & 5, it is evident that the sensitivity of core biopsy is the higher than FNAC in the diagnosis of prostatic carcinoma. However, in specificity core biopsy and FNAC are almost comparable. Also that the percentages of false negative are much higher in FNAC, though that of false positive is nearly the same as that of core biopsy. However, in benign cases, sensitivity of both FNAC & core biopsy is comparable, but the specificity of core biopsy is much higher. A low sensitivity in diagnosing of prostatic carcinoma by cytopathology could be attributed to the fact that there was a lack of experience in interpreting the smears and the high number of inadequate material.

It is to be noted that cytosmear interpretation should be done carefully as aspirated rectal mucosa may be misinterpreted as adenocarcinoma by inexperienced pathologists. Diagnostic pitfalls exist and it is not possible to distinguish high-grade prostatic intraepithelial neoplasia (PIN) and carcinoma cytologically. Also regenerative atypia in prostate, rectal mucosa or cells from seminal vesicles and well-differentiated carcinoma can pose diagnostic difficulties. Small foci of carcinoma can be missed by the needle or tumour cells may be very few for comment in desmoplastic stroma.

As tumor grading, based on patterns of prostate carcinoma done by Gleason's scoring on histological sections have a significant impact on patient prognosis and on determining patient therapy, and so, cytological diagnosis is poorly accepted.

## VI. Conclusion

In conclusion, FNAC of the prostate is a simple, sensitive & cost effective way to exclude malignancy in the prostate. The high levels of FNAC accuracy for prostatic cancer detection coupled with the low procedure risk as shown by the results of the present study, supports the value of prostatic FNAC as a good alternative to core biopsies when used in conjunction with DRE, and serum PSA levels.

Following this case study, in countries economically compromised as ours, FNAC of prostate both as screening and as a preliminary diagnostic tool for suspected prostatic cancer is recommended. However, there should be no hesitancy whatsoever in sampling or requesting for a core biopsy whenever there is a discrepancy between the cytological findings and clinical suspicion of malignancy.

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