

FINE NEEDLE ASPIRATION CYTOLOGY OF LESIONS OF PROSTATE GLANDS AND ITS CORRELATION WITH ITS HISTOPATHOLOGY

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ABSTRACT

Aspiration cytology specimens were obtained from 100 patients of prostatic enlargement by transrectal route. The cytological findings were correlated with histopathology. Diagnostic accuracy on aspiration cytology was 98%. There was no false positive diagnosis. Diagnostic yield of fine needle aspiration cytology and fine needle biopsy of prostatic lesions are very important diagnostic method for both palpable and non-palpable malignant lesions of prostate. Objective of this prospective study is to analyse the diagnostic yield of FNAC of all prostatic lesions. Prostatic lesions are in most cases diagnosed clinically by digital examination but well-differentiated adenocarcinoma which appeared in nodular form or in focal region can be missed. FNAC can give more accuracy for support of proper diagnosis of prostate lesions. In the early developing stage or in some of its localized expressions may pose diagnostic difficulties. A total of 100 patients subjected FNAC of prostatic lesions over a three years period (2013-2016). All FNAC reports were correlated with histopathology reports. All 100 cases of prostatic enlargement were available.

KEYWORDS : Fine Needle Aspiration Cytology, Benign Prostatic Hyperplasia, Adenocarcinoma of Prostate

It is often difficult for the examining finger in the rectum to decide whether the enlargement is due to benign or malignant or inflammatory conditions of the prostate such as chronic inflammation, both specific and non-specific, prostatic abscess, calculi, benign hyperplasia and carcinoma of the prostate.

Prostatic obstruction must be diagnosed as early as possible so that a definite treatment can be instituted to relieve the patient of symptoms and also to prevent the sequelae of the obstruction, such as changes in the bladder, ureters and kidneys due to retrograde reflux and to avoid the most troublesome urinary infection due to stasis and ultimate renal failure which may end fatally.

It is not an uncommon experience of the surgeon and the pathologist to find an unsuspected carcinoma in the tissue, removed under the clinical diagnosis of benign hyperplasia. As Grabstald (1957) said "It is tragically apparent that normal prostates were removed because of suspected carcinoma and because of the lack of adequate method of pre-operative diagnosis".

Early and accurate diagnosis is essential for affective surgical treatment. This necessity for early diagnosis demands a search for a method which will enable early recognition of the cause of the obstruction, particularly malignancy. Various methods of diagnosis such as rectal examination, estimation of acid phosphatase and alkaline phosphatase, cytological examination of prostatic smears ect. are all non-specific and inadequate revealing the exact nature of pathology.

Indications for prostate gland FNAC

- Palpable nodules.
- Focal or diffuse stony indurations
- Patients older than 75 years with PSA >30 ng/ml or with PSA >20 ng/ml and suspicious digital rectal examination.
- Pathological fracture even if the prostate has been deemed benign on palpation.
- Control of the effect of hormonal treatment.
- To establish prostate origin in metastatic carcinomas of unknown primary.
- Guideline for the use of digitally guided tFNA and Us-guided TNCB have been proposed.

Determination of histological nature of the lesion is the only positive method of establishing a definitive diagnosis. A suitable and simple technique of obtaining biopsy material or aspiration materials from the prostate for definitive diagnosis is essential. Fine needle aspiration cytology provides an excellent, safe, and reliable method of diagnosis and at the same time sufficient tissue can be procured.

Every hard prostate is not a carcinoma. Although the impressive teaching dictum is it is carcinoma until proved otherwise, at the same time every firm or soft prostate is not free from carcinoma. This necessity for early diagnosis demands pre-operative Fine needle aspiration cytology.

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Fine needle aspiration cytology of prostate gland was first used by Ferguson in 1930.

Since then its importance has grown. The present study has been undertaken with the objective of early detection by aspiration biopsy cytology and results were compared with histopathology.

MATERIALS AND METHODS

All the 100 cases of prostate enlargement (prostatic obstruction) were subjected to FNAC using 80 mm long spinal needle (210 to 22 gauge).

The procedure has been performed transrectally. The patient stands bent over the examining table or lies in his dorsal lithotomic or left lateral position. The spinal needle with obturator is held to the gloved index finger with its point just proximal to the finger tip. The needle then is advanced directly into the palpable prostatic lesion. Finally the obturator is removed, a 20 cc. Disposable syringe is attached and negative pressure is applied while the needle is manoeuvred within the nodule. Smears are made gently on the slides and fixed immediately in 90% alcohol or absolute alcohol and stained by the Papanicolaou method.

The diagnostic criteria and for differentiation of degree of carcinoma which have been used are according to Epstein and others.

Stains which are used 1- Papanicolaou method, 2- May Grunwal (Giemsa's stain (MGG))

Papanicolaou Method

16 steps for this staining, these are mentioned below :-

- Fix the smear in equal part of 95% alcohol and ether. then
- Hydrate the smear in decreasing concentrations of alcohol (taking to water) 80%, 70%, 50% (6 dips in each) then
- Rinse gently in distilled water (rough handling over the slide may wash off the specimen materials from the slide) then
- Stain in diluted Harris's haematoxylin then
- Gently rinse in the distilled water. then
- Dip in 0.25% HCl 6 times or in 0.5% HCl 3 times.

- Place in running tap water for 5 minutes (run the water gently: be careful that cells do not wash off). This will wash off the acid thoroughly and blue the nuclei.
- Check the slides under the microscope to see if the nuclei are adequately stained. If over stained, decolorize again in acid-alcohol and if pale (under stained), return to haematoxylin stain, continue the process until the nuclei are distinct, and the cytoplasm of the cells is clear and light blue in colour.
- Dehydrate the slides by running through: Distilled water 50%-70%-80%-95% alcohol (6 dips in each) then
- Stain in OG 6 for 2 minutes. then
- Rinse in 95% alcohol, 3 changes (in three separate containers), 6 dips in each. then
- Stain in EA-36 for 2 minutes. then
- Rinse in 95% alcohol (3 separate changes) then
- Dehydrate by passing through absolute alcohol (2 changes) then
- Clear by rinsing in a mixture of absolute alcohol and xylene (6 dips in each)
- Mount in per mount (DPX)

Result Shows Nuclei

Blue with clear sharp details.

Cytoplasm varying shades of pink, blue, yellow, green-grey. If the contrast is unsatisfactory, decolorize in acid alcohol, wash thoroughly in tap water and repeat the staining procedure, increasing or decreasing the staining time as deemed appropriate.

May Grunwal (Giemsa's) stain (MGG)

Staining Method

Dry the film in the air, then fix by immersing in a jar of methanol for 10-20 minutes. Transfer to staining jar containing May-Grünwald's stain freshly diluted an equal volume of buffered water. After the films have been allowed to stain for 15 minutes, transfer them without washing to a jar containing Buffered water and rapidly wash in three or four changes of water and finally allow to stand undisturbed in water for a short time (usually 2-5 minutes) for differentiation to take place. This is controlled by inspection of the wet slide under the low power of the microscope. When differentiation is complete, stain the slides upright to

dry. When thoroughly dry, cover the films by a rectangular No-1 cover- glass, using for this purpose a mount, Cedar-wood oil may be used.

Result shows - Nuclei - dark pinkish in colour and Cytoplasm Light Eosinophilic in colour.

RESULTS

In Benign prostatic hyperplasia (figure 1)

Smears revealed Monolayered sheets of glandular epithelial cells and distinct cell membranes with low N:C ratio, evenly distributed, uniform, rounded nuclei bland granular chromatin, tiny nucleoli/chromocenters and Coarse intracytoplasmic granules (Variable). In Prostatitis (figure 2) Many inflammatory cells, polymorphs, lymphocytes and macrophages and mild epithelial atypia are present. In Granulomatous prostatitis, Presence of epithelioid granulomas and Obvious caseous necrosis are seen. Epithelial atypical cells in Granulomatous prostatitis show a typical basophilia in DQ stained smears. This basophilia is not seen in prostate carcinoma cells.

In Adenocarcinoma of prostate (figure 3 and 4) Cell cell rich smears (If derived from a solid carcinoma nodule) decreased cell cohesion, variable numbers of single cells are present in poorly differentiated carcinoma (figure 4) cell cohesion are more in grade 1 (figure 3).

Three dimensional clusters, microacini. Interconnected large mono- or bilayered sheets with honeycomb pattern (well-differentiated carcinoma fig. 3). Indistinct cell membranes, with high N:C ration. Nuclear

and nucleolar enlargement ; variable pleomorphism.

Intracytoplasmic granules only rarely present. Positive staining for PSA and/or PSAP, absence of cytokeratin positive basal cells.

Magnification of Photographs

High power - 40x x 10 x = 400x magnification.

- i- 400x, PAP stain.
- ii- 400x, Giemsa's stain.
- iii- 400x PAP stain.
- iv- 400x PAP stain.

Diagnostic criterias, which have been used are according to Orell & sterrett's Fine needle Aspiration cytology, Male and female genital tract, 13th chapter, 2012;5th ed: p 339-346.

Other diagnostic criteria for differentiation of degree of carcinoma, on the basis of cytological features, are according to statements of Bentley et al 's (1988).

OBSERVATION

The study of 100 cases of prostatic obstruction admitted in Dr. Bidhan Chandra Roy Hospital Haldia- 721645 and I Q city medical college Hospital, Durgapur- 713206 WB and Varun Arjun medical college and Rohilkhand Hospital, Banthra shahjahanpur, up, pin code- 242307, from period 2013-2016. All investigations show the highest incidence of prostatic enlargement in 6 th decade followed by 5 th decade and least in the 3 rd to 4 th decade. All the patients were admitted with complains of acute retention retention with overflow, burning in micturation,

Table 1 : Showing DRE Based Diagnosis of BPH, BPH with Chronic Prostatitis

Diseases	No. of Cases	Percentage
BPH	88 Cases	88%
BPH with chronic prostatitis	2 Cases	2%
Prostatic carcinoma	10 Cases	10%

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dysuria, frequency of micturation and haematuria. Out of the 100 cases, 92 patients (92%) presented with frequency of micturation then 90% of acute retention with dysuria. Haematuria was found in few cases (6%). 16 patients (16%) presented with retention with overflow.

In all age group, the maximum duration of illness was found 10 months in 2% cases and minimum duration was 10 days in 12 % cases. The maximum cases (54%) were detected in between 1-3 months. Clinically 90% were diagnosed as benign prostatic hyperplasia on the basis of rectal digital examination. The prostates were smooth, convex and typically elastic, firm in consistency.

On the digital rectal examination (DRE) are shown in table 1. Total 100 cases of prostatic enlargement---shows below diagnosed by DRE.

10% cases were diagnosed clinically as carcinoma prostate /suspicious/inconclusive/under investigation , on the basis of irregular indurated and characteristically stony hard in consistency with obliteration of median sulcus.

All the benign enlargement, the lateral lobes were enlarged in their size and some cases were having median

groove obliterated. 16 cases were atypical and its consistency were hard.

Out of 6 cases of carcinoma prostate, 4 cases were obtained with suspicious limit of acid phosphatise for carcinoma prostate and 2 cases obtained were having acid phosphatise more than 5 KA unit.

After all the examination and investigations, all cases were diagnosed by FNAC, out of 100 cases, 46 % were Benign prostatic hyperplasia, 26% cases were Benign prostatic hyperplasia with chronic prostatitis. 20% cases were BPH with acute prostatitis and finally 6 % cases were diagnosed as carcinoma prostate. All cases were proved histopathologically. Two cases were due to inadequate tissue obtained (BPH diagnosed in FNAC and BPH with chronic prostatitis diagnosed in histopathological findings). Overall the series shows 98% accuracy after comparing to histopathological findings.

Age incidence in study group for prostatic enlargement (table 2).

The highest incidence of prostatic enlargement is seen in 6th decade followed by 5th decade and least in 3rd decade.

Table 2 : Showing Percentage of Prostatic Enlargement in Different Age Group

Age in years	Number of Cases	Percentage
1- 31 - 40	2	2 %
2- 41 - 50	14	14 %
3- 51 - 60	26	26 %
4- 61 - 70	32	32 %
5- 71 - 80	20	20 %
6- 81 - 90	6	6 %
Total	100 Cases	

Table 3 : Showing Level of Acid Phosphatise in Prostatic Enlargement

Range of acid phosphatase UI/L	Number of Cases	Percentage
2.5 - 5.0	6	6 %
5.1 - 7.5	20	20 %
7.6 - 9.5	66	66 %
9.6 - 11.0	4	4 %
11.1 - 11.5	2	2 %
11.6 - above	2	2 %

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Range of serum acid phosphatase in all 100 cases mentioned in table 3.

Out of 100 cases, 96 % showed acid phosphates in normal range (2.5 to 11 UI/L) 4% showed higher level. The maximum number 66% fall in the range of 7.6 to 9.5 UI/L. blood urea levels were done at the time of admission The maximum 90% cases whose blood urea were in normal range, and 10% cases revealed above 40mg %.

Prostate Cancer is the leading cancer in older men. when detected early (organ confined), it is potentially curable by radical prostatectomy. Therefore, early detection is important and PSA is widely used for this purpose. It is considered one of the most promising tumour markers available.

In 1979, Wang and co-workers purified a protein from prostatic tissue and called it prostatic specific antigen. PSA is found in normal, benign, hypertrophic, and malignant prostatic tissues.

Low concentration of PSA is found in the sera from women as well as in the nipple aspirate fluid.

PSA is an extremely useful tumour marker and is used to detect and monitor treatment of prostate cancer.

PSA value tests done for all cases of (100 Cases) prostatic enlargement.

All benign prostatic hyperplasia (BPH, BPH with chronic prostatitis and BPH with acute prostatitis)

revealed increased level above normal range in few cases between 4.0 to 14 ng/ml. and All 6 prostatic carcinoma revealed high level 40- 60 ng/ml.

FNAC done on all 100 cases of prostatic enlargement (table 5).

(Inconclusive due to inadequate material obtained, BPH were diagnosed in FNAC but histopathological findings revealed BPH with chronic prostatitis).

DISCUSSION AND CONCLUSION

Serum Acid phosphatase is not a reliable method in diagnosing early and locally extending malignant conditions of prostate.

Diagnosis done by digital rectal examination is correct when compared to FNAC reports upto 50% in overall. 50% cases were missed, mainly due to focal involvement by inflammation (acute and chronic) and malignancy.

Benign prostatic hyperplasia is usually associated with chronic prostatitis. Clinically it is missed when compared with FNAC reports.

Table 4 : Showing PSA Level in All Cases

Prostatic Diseases	Test Result (range) of PSA
1. BPH	Between 1.0 to 10.0 ng/ml
2. BPH With Chronic Prostatitis	Between 1.0 to 12.0 ng/ml
3. BPH With Acute Prostatitis	Between 4.0 to 14.0 ng/ml
4. Prostatic Carcinoma	Between 40.0 - 60.0 ng/ml

Table 5 : Showing Comparison Study and Accuracy of Prostatic Enlargement Between Diagnosed Done By FNAC and Approved by Histopathological Examination

Diseases	Number of Cases	Percentage
1. Benign Prostatic Hyperplasia	46 Cases	46 %
2. BPH With Chronic Prostatitis	26 Cases	26 %
3. BPH With Acute Prostatitis	20 Cases	20 %
4. Carcinoma Prostate	6 Cases	6 %
5. Inconclusive	2 Cases	inconclusive
Total	100 Cases	98 %

Table 6 : Showing Total Accuracy of FNAC on Prostatic Enlargement

Diseases	Number of Cases	Diagnosed and Approved by Histopathology
1. Benign Prostatic Hyperplasia	46 Cases	Approved Byhistopathology
2. BPH With Chronic Prostatitis	26 Cases	Approved Byhistopathology
3. BPH With Acute Prostatitis	20 Cases	Approved Byhistopathology
4. Carcinoma Prostate	6 Cases	Approved Byhistopathology
5. 2 cases due to inadequate material obtained , BPH were diagnosed in FNAC but histopathological findings revealed BPH with chronic prostatitis		

Overall accuracy was 98% found in 100 cases of prostatic enlargement when compared with histopathological findings.

The duration of symptoms was short (10 days to 2 months) in malignant condition in comparison to benign hyperplasia.

Dysuria, frequency, thinness of stream and poor force are the early symptoms of prostatic obstruction. Acute retention is the presenting symptoms (complaint) in majority of cases.

Transrectal fine needle aspiration and US guided THCB using automated biopsy devices have a high and essentially equal accuracy in diagnosing prostate cancer. The most common cause of a false negative FNA is an inadequate sample.

All cases were diagnosed by FNAC, out of 100 cases, 46 % were Benign prostatic hyperplasia, 26% cases were Benign prostatic hyperplasia with chronic prostatitis. 20% cases were BPH with acute prostatitis and finally 6 % cases were diagnosed as carcinoma prostate. All cases were proved histopathologically. Two cases were inconclusive due to inadequate tissue obtained. Overall the series shows 98% accuracy after comparing to histopathological findings.

It is accepted that aspiration biopsy is a technique with minimal complications that can give a definitive diagnosis of malignancy (Esposti et al, 1968). Reports of false negative cases are very less. This limitation is inherent in any technique that involves sampling of a small lesion by small biopsy in a large organ.

Alfthan et al (1970) and Hendry & Williams (1971) had observed overall accuracy of 95% in FNAC of prostatic lesions. Overall accuracy in the present series shows 98 %.

Prostatitis is the major source of false suspicious diagnosis and it may be missed in FNAC in diagnosis of the prostatic enlargement. It may be because the area of needle aspiration is limited and needle has not touched the infiltrated area.

False positive results may be due to contamination, dysplasia, and therapy induced alterations.

Diagnosis by digital rectal examination is correct when compared to FNAC upto 90% in all benign and malignant cases of prostatic enlargement. Benign prostatic hyperplasia is usually associated with chronic prostatitis.

It is concluded that fine needle aspiration cytology is easiest, accurate and quick diagnostic procedure and may be performed in all the cases of prostatic enlargement.

Smears from BPH contain a few cohesive aggregates of cells with frank atypia that may represent PIN. Basal cells or atypical hyperplasia and can be mistaken for malignancy. The presence of nuclear enlargement in some cells should not lead to the diagnosis of carcinoma since they may correspond to focal atypical hyperplasia. PIN should not be diagnosed by tFNA alone. The term 'atypical cells' when the atypia and cellularity are below the requirements needed to reach a confident diagnosis of malignancy and submit the patient for systemic TNCB. Histology of these cases always reveal either high grade PIN or low grade carcinoma. Pathologists should refrain from making a definitive diagnosis of malignancy when the smears contain only a small proportion of cells with malignant features.

Contamination of samples by epithelial cells from the rectal mucosa is common when tFNA is performed by an inexperienced operator.

Isolated tall cylindrical cells, palisaded rows, glandular structures and goblets intermingled with mucin and rectal content indicate rectal mucosal origin. Rectal cells lack intracytoplasmic granules.

In advertment aspiration of the seminal vesicle may yield large atypical cells that may mislead the unwary into an erroneous diagnosis of poorly differentiated carcinoma. Large hyper chromatic, often multilobated, Pleomorphic, even bizarre nuclei are seen. Coarse intracytoplasmic granules of lipofusin which stain dark green- blue with DQ, brown with PAP or H&E, quite different from the secretory granules of prostate epithelium, dense aggregates of basophilic amorphous materials and spermatozoa in background indicate origin from seminal vesicle. Ganglion cells may mimic malignant cells.

Nuclear overlapping, anisonucleosis, occasionally striking atypia, naked nuclei and some acinar formation may result in a false positive diagnosis.

Transitional cell carcinoma may invade the prostate from the urinary bladder or it may arise from periurethral ducts within the prostate itself. Coexistence of transitional cell carcinoma and adenocarcinoma of the prostate is not rare. It is important to distinguish transitional cell carcinoma from adenocarcinoma, since the former does not respond to hormonal treatment.

The distinction from prostatic adenocarcinoma is essential. Cells from a prostatic adenocarcinoma of comparable differentiation show a lesser degree of nuclear pleomorphism, the nuclei are paler, vesicular, and the cytoplasm is indistinct and fragile. The nuclei are also fragile and some are smudged. Microacini can nearly always be found in adenocarcinoma except in truly anaplastic tumours. Palisading at the periphery of cell aggregates from a transitional cell carcinoma should not be mistaken for glandular differentiation. Immunostaining for PSA, PSAP, 34βE12, Uroplakin III and p63 is helpful in difficult cases, although interpretation may be troublesome.

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