HISTO-PATHOLOGICAL STUDY OF 100 CASES OF PROSTATIC NODULES

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ABSTRACT:

Objective: This study is planned to evaluate the histological lesions of prostatic specimens and it's correlation with the clinical data. **Materials and Methods:** The present study is a prospective study, undertaken in the Department of Pathology, Mahatma Gandhi Medical College, Jaipur, Rajasthan, during the period of July 2010 to May 2012. This study was conducted on 100 prostatic specimens referred to department of pathology. Brief clinical data were noted from the case records, which included the age, presenting symptoms, DRE findings, serum PSA levels and clinical diagnosis. All the prostatic specimens were subjected to H&E, **AgNOR** staining method. **Results:** Out of 100 cases studied, commonest pathology encountered was benign lesion constituting 92% and malignant lesions were 08%. Out of 92 cases of benign lesions, 70 cases (63.64%) were diagnosed as nodular hyperplasia without prostatitis, 20 cases(17.69%) were diagnosed as nodular hyperplasia with prostatitis & graulomatous prostatitis and squamous metaplasia in 01 case and clear cell hyperplasia in 01 case. Clinical diagnosis of prostatic carcinoma was made in 08 cases which correlated histologically. Gleason's score of 7 was seen in 75% of the cases and 6 was seen in 25% cases. Mean AgNOR count in benign and malignant lesions were 1.57±0.13 and 4.8±0.2 respectively. **Conclusion:** Prostatic carcinoma shows heterogeneity of differentiation, nuclear anaplasia, cytoplasm, functional differentiation and DNA content. There is a need for research on all aspects of this disease. Further refinement of diagnostic techniques and the development of new therapeutic modalities for the treatment of systemic disease.

Keywords: nodular hyperplasia ,graulomatous prostatitis, squamous metaplasia,Adenocarcinoma,

INTRODUCTION:

Prostatic disease is responsible for significant morbidity and mortality in men, throughout the world. **(1)** Recently there is considerable change in the understanding of many prostatic diseases. Accurate diagnosis of prostatic disease frequently requires simultaneous data from clinical chemistry, imaging techniques and surgical pathology laboratory.**(2)** Even following detailed histopathologic examination of biopsy tissues, taken from precisely defined micro-anatomic sites within the prostate, informed opinions as to the diagnostic or prognostic significance of particular morphologic features, frequently remain controversial, to the extent that

distinction of benign from malignant neoplastic disease may not be possible.**(3)**

Several risk factors have been implicated in causation of prostate cancer but none has been proved to be causative.

The strongest risk factors for the development of prostate cancer are advancing age, race, hereditary, hormonal activity and two premalignant conditions prostate intraepithelial neoplasia (PIN) and atypical adenomatous hyperplasia.**(4)**

The clinical importance of recognizing PIN is based on its strong association with prostatic cancer. It coexists with cancer in more than 85% of cases.**(5)** There is little evidence that nodular hyperplasia or atrophy is directly related to the genesis of prostatic adenocarcinoma.

Gleason devised a system of pathological classification of prostatic carcinoma that combines clinical staging with histological grading and a prognostic score yielded. Gleason's grading and PSA level are important markers for estimating prognosis of prostatic cancer.**(6)**

This study will be done to evaluate the spectrum of histo-pathological lesions in prostatic specimens using PSA level, Gleason's grading, AGNOR score and special stains wherever required.

The subject of prostatic disease is fraught with doubts, uncertainties and apparent contradictions. This has prompted to take up this study.

MATERIAL AND METHODS

The present study is a prospective study, undertaken in the Department of Pathology, Mahatma Gandhi Medical College, Jaipur,

Rajasthan, during the period of July 2010 to May 2012. This study was conducted on 100 prostatic specimens referred to department of pathology.

Brief clinical data were noted from the case records, which included the age, presenting symptoms, DRE findings, serum PSA levels and clinical diagnosis.

Following inclusion and exclusion criteria are adopted in this study. **Inclusion criteria :**All types of prostatic specimens including TURP and prostatectomy are considered in this study.

Exclusion criteria: Inadequate biopsies and poorly preserved prostatic specimens are excluded.

All the prostatic specimens were subjected to a careful and detailed gross examination. 10% formalin fixed and paraffin embedded tissue sections from these specimens were used for microscopic study. 4-6μ thick sections being prepared and stained routinely with H&E.

H&E stains were studied and classified into various benign and malignant lesions.

Different types of carcinoma were analysed under light microscope. Histologic grade for each type of adenocarcinoma using the VACURG, Gleason grading system and Gleason's histologic scores were noted. Associated prostatic tissue changes like tumor invasion, PIN and other prostatic lesions were also analysed.

AgNOR staining method was done for every case and mean AgNOR count calculated. In all specimens, 100 nuclei of each lesions were examined using a 100x oil immersion objective and a 10x ocular. Lesional nuclei were taken at random for the counting procedure. Careful focusing allowed the nucleolar organizer regions (NOR) to be visualized as black dots arranged

both in clusters and clumps and as individual "satellites" within the cell nucleus. To assess the reproducibility of the counting procedure, all counts were repeated.

Other special stains like Alcian blue pH-1, PASd, and Ziehl Neelsen were performed wherever necessary.

All the specimens were subjected to a detailed study with special reference to the features mentioned in the proforma and the staining of the histological sections was done using standard procedures.

Statistical analysis:

Results are presented as Mean ± SD and range for quantitative data and number and percentages for qualitative data. Group-wise comparisons were made either by student t- test or Mann- Whitney test whichever was appropriate. P value of 0.05 or less was considered for statistical significance.

RESULTS

A prospective study to evaluate the various histological lesions in prostatic specimens was undertaken. The following are the salient observations noted in this study.

Out of 100 cases studied, commonest pathology encountered was benign lesion constituting 92% and malignant lesions were 08%.Majority of specimens were TURP (97%) followed by prostatectomy (03%) specimens.Benign lesions were common in age group of 61-70 years with commonest symptoms of frequency, hesitancy and nocturia.

Digital rectal examination finding showed firm nodule in 90 cases and hard consistency in 10 cases. In benign cases, serum PSA was normal in 48.6% cases. Modest elevation (4.1 – 10ng/ml) was seen in 34.3% cases and marked elevation (>10ng/ml) in 17.14% cases. In malignant cases, modest elevation was seen in 20% cases and marked elevation in 60% cases.

Out of 92 cases of benign lesions, 70 cases (63.64%) were diagnosed as nodular hyperplasia without prostatitis, 20 cases(17.69%) were diagnosed as nodular hyperplasia with prostatitis & graulomatous prostatitis and squamous metaplasia in 01 case and clear cell hyperplasia in 01 case.

Clinical diagnosis of prostatic carcinoma was made in 08 cases which correlated histologically. Incidence of carcinoma was 08% and peak age group affected was between 61-70 years with commonest symptoms of hesitancy, nocturia and frequency. Hematuria was significantly associated with malignant lesions.

Histologically, all the malignant lesions encountered were adenocarcinoma of prostate. The commonest pattern seen were acinar followed by arrangement of tumor cells in cords, sheets and cribriform pattern. Gleason's score of 7 was seen in majority of the cases (75%).Gleason score of 6 was seen in 25% cases.

The mean AgNOR counts were higher in cases of malignant lesions as compared with benign lesions. Occasionally, there was a fine background precipitate of silver granules in some tissue sections which could be easily differentiated by its random distribution and smaller size. The mean AgNOR counts were: granulomatous prostatitis 1 .4 $\pm$ 0. 1, metaplasia 1.5, NH with or without prostatitis 1.57 $\pm$ 0.13 and prostatic adenocarcinoma 4.7 $\pm$ 0.3.

Table -1 Final histopathological diagnosis

Final histopathological diagnosis	No of cases	%
1. NH		
a) Without prostatitis	70	70
b) With prostatitis	17	17
c) Granulomatous prostatitis	03	03
2. Clear cell hyperplasia	01	01
3.Squamous metaplasia of urothelium	01	01
4. Adenocarcinoma	08	08

Table -2. Mean AgNOR count in prostatic lesions

Prostatic Lesions	Mean AgNOR ISD
1. Granulomatous prostatitis	1.4 ± 0.1
2- Metaplasia	1.5
:L NH with or without prostatitis	1.57 ± 0.13
4 Adenocarcinoma (Gleason Score 6)	4.5 ± 0.1
S. Adenocarcinoma (Gleason Score 7)	4.8 ± 0.2

The pooled mean AgNOR count for the benign prostatic lesions was 1.57 ± 0.13 which was significantly lower than that of the prostatic adenocarcinomas ($p<0.001$) which was highly significant.

DISCUSSION

Prostatism is a common malady in the geriatric age group. BPH and carcinoma of the prostate are increasingly frequent with advancing age. Prostatic specimens thus constitute a good percentage of surgical pathology workload.**(7)** The various histological appearances of BPH and prostatic adenocarcinoma are well known and have been described and illustrated extensively in the literature.**(8)** This study was undertaken to evaluate the various histological lesions in the prostatic specimens.

In this study, 100 prostatic lesions were analysed. The present study showed that majority, 92% of cases were benign lesions, followed by 08% of cases of adenocarcinoma. In a study, Mittal et al showed 92.98% of cases of benign lesions followed by 7.02% of malignant cases.**(7)**

In the present study, the incidence of benign lesions was 92%. NH alone was noted in 70% of cases, out of which majority of cases were encountered in the 6th and 7th decade. The decline in the number of cases beyond the age of

80 years may reflect the average life span of people in our country.

The present study showed 01 case of squamous metaplasia of urothelium in addition to NH and 1 case of clear cell hyperplasia along with NH together accounting for 2 % of total cases studied. However study by Mittal et al showed metaplastic epithelium in 10.27% of cases.**(7)**

In the present study, out of 100 cases, 20 cases had prostatitis. In a study by Stillwell et al, 25 cases of prostatic abscess showed sheets of neutrophils in and around the acid.**(9)** In cases of chronic non-specific prostatitis, lymphocytes, plasma cells and macrophages were seen. Bostwick in his study has reported more cases of chronic abacterial as compared to bacterial prostatitis.**(10)**

In the present study, 3 cases of granulomatous prostatitis (3%) were noted, out of which 1 case showed evidence of caseation with granulomas and 2 without caseation. Ziehl Neelsen stain for AFB was positive in 1 case. Mittal et al, showed granulomatous inflammation in 1.6% of his cases.**(7)**

In a study of 200 cases of granulomatous prostatitis, non-specific granulomatous prostatitis was seen in 138 cases (69%), 49 cases were post biopsy granulomas (24.5%), 7 cases were due to tuberculosis (3.5%) and 6 cases were systemic granulomatous disease (3%).**(11)**

In the present study, the prevalence of carcinoma prostate was 08%. This is rather low compared to most reported series and there is wide variation in the incidence rate of prostate cancer in different parts of the world.**(7)** The prevalence rate of 08% observed in present study is comparable with study by Murali et al,which showed a prevalence rate of 8.56%. The increased incidence of prostatic carcinoma in developed countries is attributed to the extent of diagnosis of latent cancers by screening of asymptomatic individuals and also to the risk of the disease associated in these countries.**(12)**

Direct comparison of total rates of prostatic carcinoma in different series may be misleading. There is a great discrepancy between the high frequency of prostatic carcinoma revealed at autopsy and the occurrence of carcinoma which has been clinically suspected. In clinically manifested carcinoma, the tumor is generally larger than in the latent one, but the histological features are essentially the same.**(7)**

In the present study, peak incidence of prostatic carcinoma was seen in age group of 61-70 years. Many recent studies show a higher incidence of prostatic carcinoma in the age group of 61-70 years. In the present study, 08 cases of adenocarcinoma prostate were seen accounting for 08% of the cases.

All these 08 malignant cases were graded using Gleason's scoring system. Majority of our cases showed moderate to poor differentiation. Gleason score of 7 was the commonest pattern seen in 75% of cases. Gleason score of 6 was the next commonest pattern seen in 25% of cases. In present study, low grade adenocarcinoma was not detected probably as these lesions were asymptomatic.

In a study by Bob Djavan et al, the incidence of carcinoma was 22% Mean age of patient was 67 years and mean Gleason score was 6.**(13)**

PSA is elevated by any change that destroys the normal architecture of the prostate which allows diffusion of protease into the microvascular circulation.**(14)**

NH is a common cause of serum PSA elevation and accounts for 60-70% of cases. Studies of patients with histologically confirmed NH have shown that 21-86% have elevated serum PSA levels. The degree of elevation is modest (4.1--10 ng/ml).**(15)**

According to a study on chronic prostatitis, serum PSA was high in 99% of cases. Prostatic manipulations including cystoscopy, needle biopsy causes marked elevation of serum PSA levels. Whereas digital rectal examination, prostatic massage and ultrasonography have minimal effects on serum PSA levels in most patients.**(16)** Acute urinary retention also elevates the serum PSA values.**(17)** In the present study, 3 cases of prostatic carcinoma showed PSA levels > 20ng/ml, however 2 cases had PSA levels <10ng/ml. This is attributed to study in which prostate cancers detected at lower PSA levels are more likely to have a small volume and are of low grade.**(18)**

AgNOR in normal cells are usually tightly aggregated within one or two nucleoli, making individual AgNORs indiscernible. An increase in the mean AgNOR count of a cell population could be result of

a) Cell proliferation causing nucleolar disaggregation and making individual AgNOR detection easier.

b) Defect of nucleolar association resulting in AgNOR dispersion.

c) Increase in ploidy, resulting in a real increase of AgNOR bearing chromosomes.

d) Increase in transcriptional activity.**(19)**

Theoretically, neoplastic cell populations could show any or all of the above defects and therefore demonstrate increased AgNOR counts. In prostate lesions many studies have shown a significantly increased proportion of proliferating cells in malignant lesions compared to that of benign hyperplasia, the greatest proliferative indices are noted in high grade carcinomas .

Thus, AgNOR numbers increase with more aggressive, higher grade prostate lesions.**(19)**

In present study, mean AgNOR counts progressively increased from NH to carcinomas. Furthermore, the mean AgNOR counts of carcinomas were significantly different from those in benign conditions and no overlap in count was seen between these conditions.

In the present study, mean AgNOR counts of intermediate grade tumor (Gleason score-6) was 4.5 ± 0.1 and high grade tumor (Gleason score7) was 4.8 ± 0.2 which correlated with conventional histological grade.

The counts were higher in high grade tumor compared to low count in intermediate grade tumor. Similar observations were seen in different studies.(19,20)

CONCLUSION

Mean AgNOR counts of malignant lesions are significantly higher when compared to benign lesions and correlated with histologic grade of tumor. Combined staging, grading and follow-up study are required to obtain best predictive values.

Another obstacle is several forms of therapy may significantly alter the normal and diseased prostatic tissue, making the assessment difficult. Further, immunohistochemistry and molecular genetic analysis are suggested. Screening protocols and awareness programs need to be instituted.

Prostatic carcinoma shows heterogeneity of differentiation, nuclear anaplasia, cytoplasm,

functional differentiation and DNA content. There is a need for research on all aspects of this disease. The ultimate conquest of prostatic carcinoma will require substantial advances in our understanding of the cause of this tumor, further development and refinement of diagnostic techniques and the development of new therapeutic modalities for the treatment of systemic disease.

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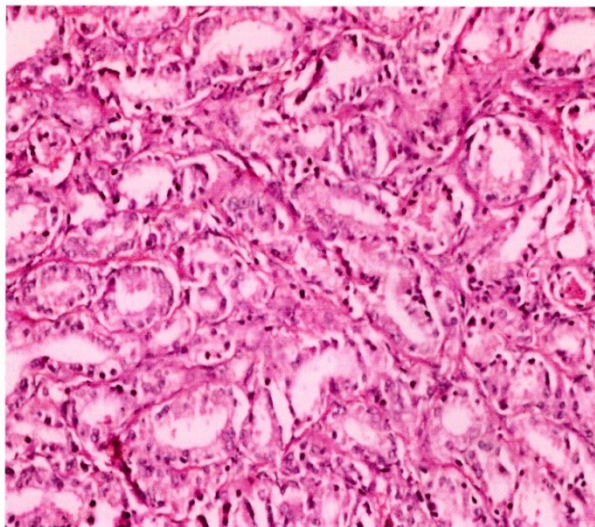
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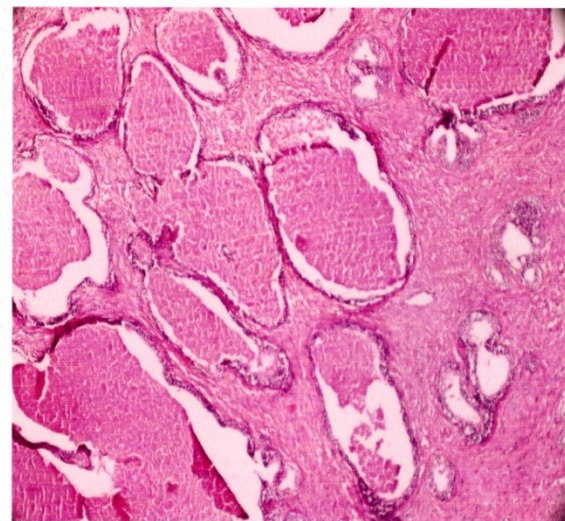
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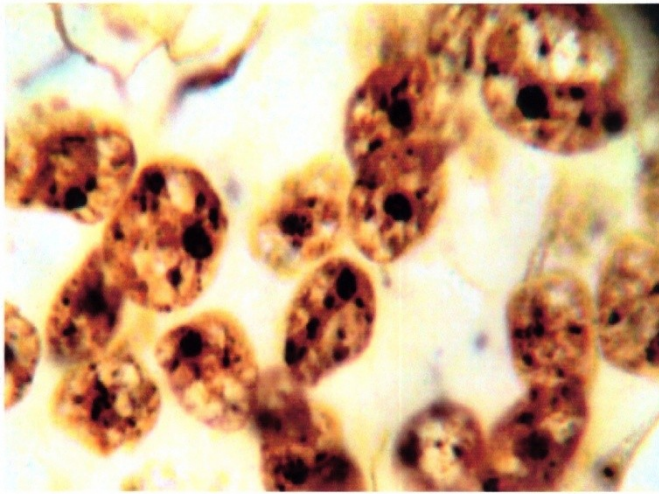
Fig 1

Prostatic adenocarcinoma (H & E 40x)

Fig.2

Prostatic adenocarcinoma showing necrosis (H & E 40x)

Fig.3

Adenocarcinoma of the prostate showing numerous AgNOR dots per nucleu