Original Research Paper Anatomy

Histological changes in the prostate of geriatric age group and associated clinical complaints.

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ABSTRACT Advancing age is associated with increasing disability and functional impairments which may be contributed by functional decline in cardio- vascular, pulmonary, musculo-skeletal, other systems and organs of human body. Prostatism is a common malady in the geriatric age group. Benign hyperplasia and carcinoma of the prostate are increasingly frequent with advancing age and are uncommon before the age of 40. The only clearly defined risk factors for benign hyperplasia of prostate are age and the presence of circulating androgens

KEYWORDS : prostate, geriatric age, histological features, clinical complaints.

Introduction:

Ageing is the progressive, universal decline first in functional reserve and then in function. It is heterogeneous; it varies widely in different individuals and in different organs within a particular individual. Ageing is not a disease; however, the risk of developing disease with age is increased and population worldwide is ageing (1).

Advancing age is associated with increasing disability and functional impairments which may be contributed by functional decline in cardio- vascular, pulmonary, musculo-skeletal, other systems and organs of human body(2)..The prostate is a pyramidal fibromuscular gland which surrounds the prostatic urethra from the bladder base to the membranous urethra and itself surrounded by thin but tough connective tissue capsule (3).

Interestingly abnormal growth of the prostate is only experienced by the humans and dogs and why other mammals are spared is a mystery (4). The histological changes due to disease processes and the inevitable effect of ageing simultaneously and so intricately coexist in the prostate tissues that the study of prominent histological changes of senescence become of great importance in diagnostic pathology(5). Many of these age-dependent changes, particularly the development of diffuse atrophy of prostatic acini, are probably caused by a decline in circulating testosterone with ageing in most rat strains **(6)**. A broad spectrum of benign lesions has been described in the prostate. These include benign prostatic hypertrophy/hyperplasia, prostatitis, tumor like condition of prostate, necrotic glands, stromal reparative changes, different types of epithelial hyperplasia, a typical adenomatous hyperplasia, prostatic intraepithelial neoplasia and miscellaneous conditions like infarcts, squamous metaplasia etc. (7,8).

Prostatism is a common malady in the geriatric age group. Benign hyperplasia and carcinoma of the prostate are increasingly frequent with advancing age and are uncommon before the age of 40. The only clearly defined risk factors for benign hyperplasia of prostate are age and the presence of circulating androgens. Benign hyperplasia of prostate does not develop in men castrated in early life (9). Therefore in the light of growing knowledge about prostatic lesions, it is necessary to periodically review known benign lesions in order to know the incidence of these lesions, to better define the morphology of these lesions.

Aims and objectives:-

To study different Histological changes in the prostate of geriatric age group with clinical complaints of the patients.

Material and methods:-

The present study was a prospective study of prostate specimens (Prostatectomy and transurethral resection of prostate) received in the department of Pathology for a period of one year, carried out in the Department of Anatomy, Government Medical College Jammu from October 2011 to September 2012. Prostate specimens were collected from the Department of Pathology which was submitted there by the Department of Surgery, Govt. Medical College Jammu. This study included 39 cases that were evaluated on the basis of the histological findings.

These prostate specimens were divided into two groups as per age

Group A = 61-75 years

Group B = 76 and above.

Transurethral resection of prostate (TURP) chips and prostatectomy specimens were taken for the study. In this study of one year, maximum numbers of patients were in the age group A (61-75 years) i.e. 30 cases, Age group B (more than 75 years) had only 9 cases so total of 39 cases from Pathology Department were studied.

Histological results were obtained only after surgery and their clinical complaints were taken prior to surgery

These prostate specimens were fixed in 10% buffered formalin followed by routine paraffin embedding, haematoxylin and eosin staining and microscopic examination. A detailed histological examination of haematoxylin and eosin stained sections of each group was evaluated .

Photographic documentation had been done for important finding.

Various parameters of each case were included in the study like age, clinical features, surgical details and various histological changes were observed.

Almost all the patients admitted with the lower urinary tract symptoms (LUTS) had prostatic lesions, which were age related and ultimately progressed to the pathological lesions.

Clinical Presentation:

Clinical Presentation of the 39 patients suffering from the prostate ailments was lower urinary tract symptoms (LUTS) that included:

Obstructive or voiding symptoms:
Hesitancy, poor flow, intermittent stream, dribbling, sensation of poor bladder emptying, episode of near retention and acute retention.

Irritative or storage symptoms:
Frequency, nocturia, urge, urge incontinence and nocturnal incontinence.

The most common presentation was obstructive symptoms i.e. 26 cases (71.15%) and rest had irritative symptoms i.e. 13 cases (28.95%). Highest cases of obstructive symptoms presented with hesitancy in 12 cases (30.5 %) followed by poor flow in 8 cases (24.4%). Among irritative symptoms, frequency was the most common i.e. 6 cases (11%).

Table I: Showing details of the Presenting Symptoms.

S.No.	Obstructive Symptoms	Number of cases	Percentage (%)
1.	Hesitancy	12	30.5
2.	Poor flow	8	24.4
3.	Intermittent stream	2	5.08
4.	Dribbling	1	1.69
5.	Sensation of poor bladder emptying	1	3.38
6.	Episode of near retention and acute retention	2	5.08
	TOTAL	**26**	**71.1**

S.No.	Irritative Symptoms	Number of cases	Percentage (%)
1.	Frequency	6	13.55
2.	Nocturia	3	8.47
3.	Urge	2	3.38
4.	Urge incontinence	1	1.69
5.	Nocturnal incontinence.	1	1.69
	TOTAL	**13**	**28.9**

OBSERVATIONS:-

Group A (61 years to 75 years) There was marked proliferation of both glandular and stromal tissue in twenty four cases suggestive of nodular hyperplasia of prostate. Papillary infoldings were seen only in areas of glandular hyperplasia. Corpora amylacea was present in almost all acini which were made up of concentric lamellas, glands having large and irregular lumens were also seen (Fig 1, 2).

Few slides show aggregation of lymphoid tissue (Fig 3). Three cases showed that the basal layer of the glands proliferated and thick protruding into the lumen in a peripheral palisading manner with retention of overlying secretary luminal epithelium suggestive of basal cell hyperplasia. One case in this age group also showed that acinar unit was distended by the proliferation of bland looking clear cells which had papillary or cribriform arrangement (Fig 4). In three out of thirty cases, there was presence of single layered cell lining with complete absence of basal cell layer, nucleomegaly and presence of large nucleoli, suggesting adenocarcinoma of prostate (Fig.5).

Myxoid change in stroma and abscess formation was also seen in few cases (Fig. 6 , 7) . In single case of this group, cells were characterized by clear cytoplasm and nuclear displacement. These cells diffusely infiltrated the prostatic stroma. These findings were suggestive of signet ring cell carcinoma (Fig. 8).

In another single case, adjacent to the necrotic or infarct area, there was squamous cell metaplasia which simulate with basal cell hyperplasia lesion, but here cells had more cytoplasm and more distinct borders than basal cells of basal cell hyperplasia (Fig.9).

In one case, the architecture of the prostate was effaced by the dense sheets- like aggregation of histiocytes (Van-Hansemann cells) admixed with lymphocytes and plasma cells. Intracellular and extracellular Michaelis – Gutmann bodies were seen. These findings were suggested of Malakoplakia (Fig. 10).

In single case there were multiple clear spindle shaped areas within the lumen of the much dilated or atrophied glands, these were cholesterol clefts or crystals (Fig. 11).

Table II: Different Histological Findings in the age group of 61 – 75 years.

Different Histological Findings	No. of Cases
Benign hyperplasia of prostate	24
Atrophy	20
Prostatitis	10
Basal cell hyperplasia	3
Adenocarcinoma	3
Myxoid stroma	3
Prostatic abscess	2
Signet ring cell carcinoma	1
Squamous cell metaplasia	1
Malakoplakia	1
Cholesterol crystals	1

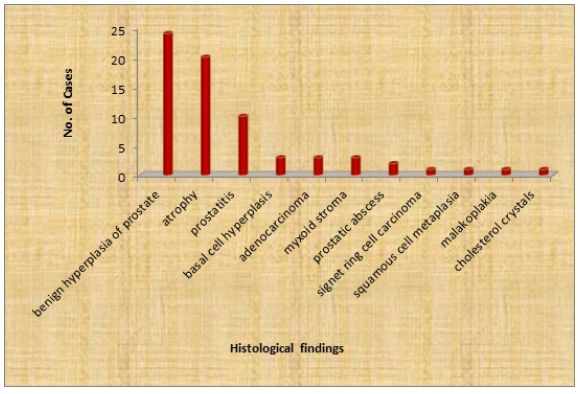

Fig. I: Bar chart of different histological findings in the age group of 61 – 75 years

Group B (more than 76 years
The microscopic observation of all the prostatic specimens of this age group showed marked proliferation of stroma and glandular tissue. Marked atrophy and dilatation of glands was seen. The papillary infoldings were absent. The lumen was large and irregular. There was abundant amount of secretion and corpora amylacea (Fig12).

Two cases showing the inflammation also had infiltration of neutrophils and macrophages, both within and outside (Fig 13).
One case also showed proliferation of basal layer, suggestive of basal cell hyperplasia (Fig.14).

In two cases, there was loss of basement membrane with cellular atypia in the glands. Acini were packed together with fused glandular pattern. Thus the histological pattern observed is of adenocarcinoma (Fig.15).

Table III: Different Histological findings in the age group more than 76 years.

Different Histological Findings	No. of Cases
Benign hyperplasia of prostate	7
Atrophy	7
Adenocarcinoma	2
Inflammation	2
Basal cell hyperplasia	1

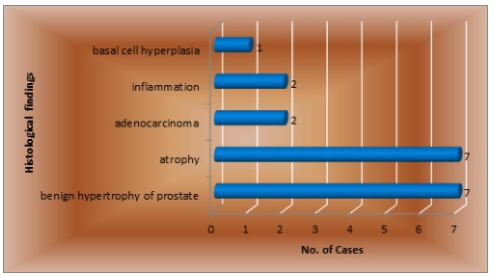

Fig. II: Bar chart of different histological findings in the age group more than 76 years.

DISCUSSION

In the age group of Group-A (60-75 years) there was marked proliferation of both glandular and stromal tissue in twenty four cases (80% cases) suggestive of nodular hyperplasia of prostate in this study. Stromal hyperplasia lesions were well demarcated from surrounding prostatic tissue but were not encapsulated; cells were arranged in fasciculated or whorled pattern. Papillary infoldings were seen only in areas of glandular hyperplasia and these infoldings decreases with age. Corpora amylacea was present in almost all acini. These findings are consistent with the study of **Mohammed *et al* 2003 (10)** who showed that the mean age of benign hypertrophy of prostate was 63.7 years, and 88% of them had a glandulostromal histological pattern. Present study findingsare also in accordance with **Di Silverio *et al* 2003 (11)** study in which the mean patient age for benign hyperplasia of prostate was 68.85+/-7.67 years. Frequency of the benign hyperplasia of prostate in the present study was consistent with finding of **Harbitz and Haugen 1972 (12)** in which benign nodular hyperplasia was the most frequent histological pattern encountered (80.1 per cent) before the age of 70. Similar findings were also observed by **Shapiro 1992 (13)** who demonstrated that the relative proportion of the epithelium and stroma were related to the development of symptomatic benign hyperplasia of prostate.

Twenty cases (67 percent) in the present study showed atrophy of the glands having low cuboidal to flattened cells with scanty cytoplasm. These finding are in accordance to **Moore 1936(14)** who found that there was a strong correlation with age and, according to his study, prostatic atrophy was initiated during the 5th decade and continued as a progressive process into the 8th decade.
In the current study there was lymphocytic infiltration in the prostate suggestive of inflammation , these findings are similar with the study of **Truce *et* al 1999(15)** and **Asgari and Mohammadi 2011(16)**

Three cases (10%) in the present group showed acini which were arranged in a back to back fashion having only single cell layer suggestive of adenocarcinoma of prostate and corpora amylacea was absent. These finding are in accordance to the **Mittal *et al* 1989(17)** study, who noted that the incidence of carcinoma was low (7.02%) and Corpora amylacea were conspicuously absent in carcinoma. Also study reported by **Tavora and Epstein 2008 (18)** showed that the mean age of the patient was 68 years who suffered from adenocarcinoma. Signet ring carcinoma, variant of prostate carcinoma was observed in 1.7% cases which histologically coincide with the findings of **Fletcher 2000 (19)** that showed that these tumor cells (signet ring cells) diffusely infiltrate the prostatic stroma.

Five cases in this group (16%) evaluated as basal cell hyperplasia were present in association with benign hyperplasia of prostate. These finding are in accordance to **Cleary *et al* 1983 (20).**

In the present study under this group myxoid change was seen in three cases (10%) of the benign hyperplasia of prostate. These lesions are similar to study of **Manzarbeitia *et al* 2010 (21)**.

All the cases above 76 years (Group B) of age showed marked proliferation of stroma and glandular tissue with diffuse atrophy and dilatation of glands. Papillary infolding was absent. The lumen was large and irregular. There was abundant amount of secretion and corpora amylacea. These findings are consistent with the study of **Price *et al* 1990 (22)** Incidence of nodular prostatic hyperplasia are in accordance to the study of **Bushman 2009** (23) which revealed that by the eighth decade, over 90% of males will have prostatic hyperplasia and also to the study of **Harbitz and Haugen 1972 (12)** which showed that after the age of 70 years, benign nodular hyperplasia was observed in practically all cases. Two cases in this study show features of inflammation , these findings are consistent with the study of **Nielsen *et* al 1973 (24) and Kohnen and Drach 1978** (25)One case showed proliferation of basal layer, suggestive of basal cell hyperplasia. Same finding were also studied by **Cleary *et al* 1983(20)** on men above the age 60 years and observed that all had benign hyperplasia of prostate in addition to basal cell hyperplasia

In two cases there was loss of basement membrane with cellular atypia in the glands and nuclei were hyperchromatic and large with nucleoli. Acini were packed together with hardly any stroma in between. Thus the histological pattern was suggestive of adenocarcinoma. These histological findings are same as studied by **Harbitz and Haugen 1972 (12)** who found that after the age of 80 years, 52 % carried carcinoma. Same higher incidence was studied by **Bostwick *et al* 2004 (26)** and found prostatic adenocarcinoma in 80% of men more than 80 years old.

CONCLUSION : In the geriatric age group the common clinical presentation was obstructive symptoms present in 71.1% of the cases followed by irritative symptoms which constituted 28.9% of the cases. Common symptoms presented were hesitancy followed by poor flow and frequency

79 % of the cases show histological features of benign hyperplasia of prostate. Atrophy of prostate gland seen in 69% of cases. Inflammatory changes seen in 30% of cases. Percentage of basal cell hyperplasia and adenocarcinoma is 10 and 12 respectively.7.5% of cases show myxoid stroma and 5% show features of prostatic abscess. Signet ring carcinoma, squamous cell metaplasia, Malakoplakia each share equal percentage of 2.5.

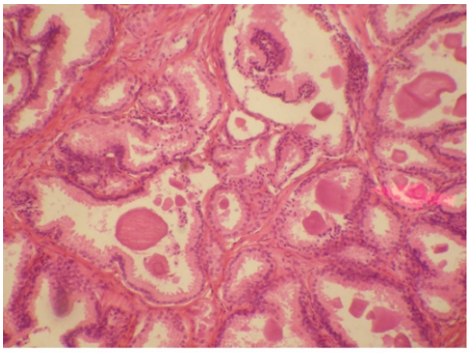

FIG 1. PHOTOMICROGRAPH OF PROSTATE GLAND SHOWING GLANDULAR HYPERPLASIA WITH LESS PAPILLARY INFOLDINGS AND PRESENCE OF CORPORA AMYLACEA. (H & E STAIN 200X)

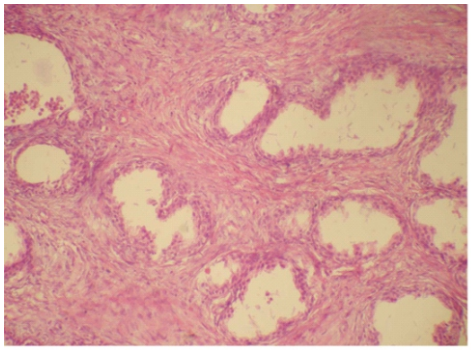

FIG 2; PHOTOMICROGRAPH OF PROSTATE GLAND SHOWING GLANDULARSTROMAL HYPERPLASIA (H & E STAIN 200X)

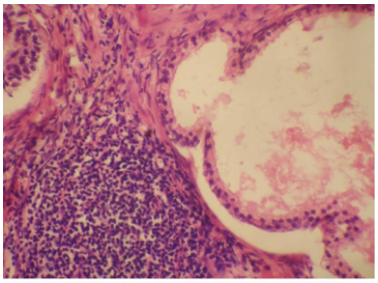

FIG 3. PHOTOMICROGRAPH OF PROSTATE GLAND SHOWING ISOLATED STROMAL LYMPHOID AGGREGATE. (H & E STAIN 400X)

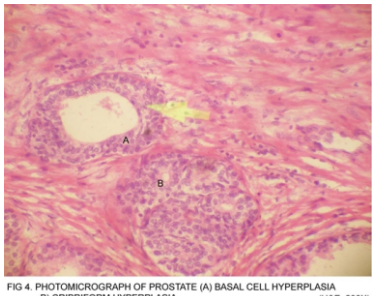

FIG 4. PHOTOMICROGRAPH OF PROSTATE (A) BASAL CELL HYPERPLASIA B) CRIBRIFORM HYPERPLASIA. (H&E, 200X)

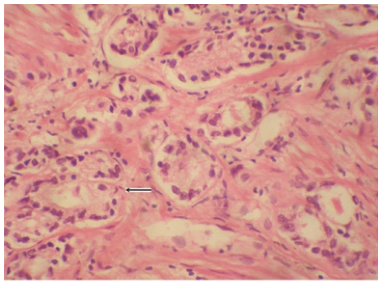

FIG 5. PHOTOMICROGRAPH OF PROSTATIC ADENO CARCINOMA SHOWING CLOSELY PACKED SINGLE GLANDS (H & E STAIN 400X)

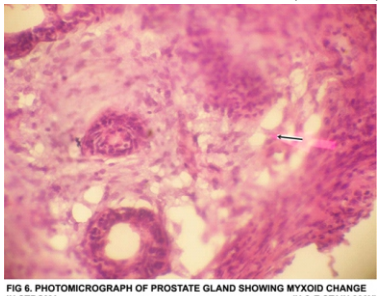

FIG 6. PHOTOMICROGRAPH OF PROSTATE GLAND SHOWING MYXOID CHANGE IN STROMA. (H & E STAIN 200X)

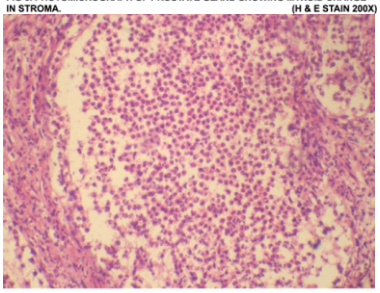

FIG 7. PHOTOMICROGRAPH OF PROSTATE GLAND SHOWING ABSCESS FORMATION (H & E STAIN 200X)

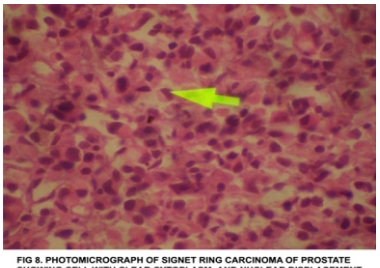

FIG 8. PHOTOMICROGRAPH OF SIGNET RING CARCINOMA OF PROSTATE SHOWING CELL WITH CLEAR CYTOPLASM AND NUCLEAR DISPLACEMENT. (H & E STAIN 400X)

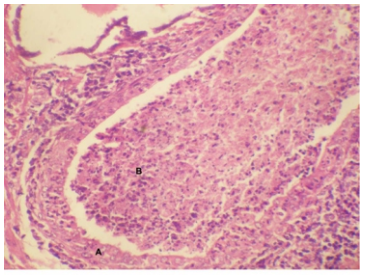

FIG 9. PHOTOMICROGRAPH OF (A) SQUAMOUS CELL METAPLASIA OF PROSTATE GLAND WITH (B) NECROSED AREA. (H & E STAIN 200X

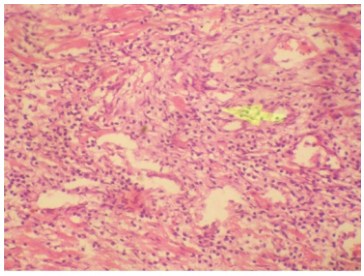

FIG 10. PHOTOMICROGRAPH OF PROSTATE GLAND SHOWING MALAKOPLAKIA (H & E STAIN 200X)

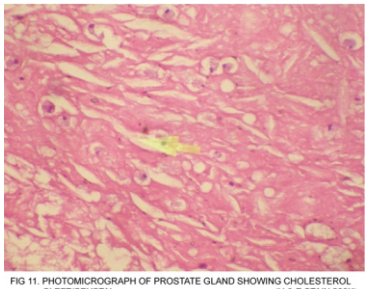

FIG 11. PHOTOMICROGRAPH OF PROSTATE GLAND SHOWING CHOLESTEROL CLEFT/CRYSTAL. (H & E STAIN 200X)

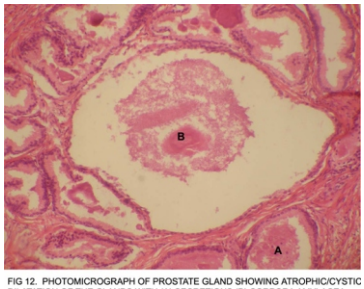

FIG 12. PHOTOMICROGRAPH OF PROSTATE GLAND SHOWING ATROPHIC/CYSTIC DILATATION OF THE GLANDS WITH (A) SECRETIONS (B) CORPORA AMYLACEA. (H & E STAIN 200X)

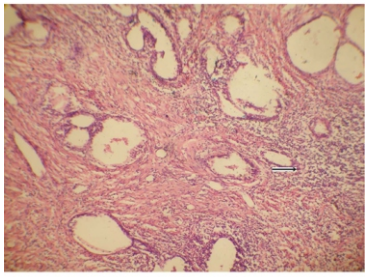

FIG 13. PHOTOMICROGRAPH OF CASE OF BENIGN HYPERPLASIA OF PROSTATE GLAND SHOWING LYMPHOCYTIC INFILTRATE (INFLAMMATION). (H & E STAIN 100X)

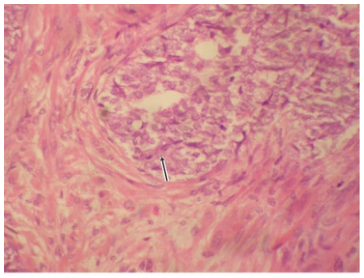

FIG 14. PHOTOMICROGRAPH OF BASAL CELL HYPERPLASIA OF PROSTATE GLAND SHOWING PROLIFERATION OF BASALOID CELLS IN SOLID NESTS AND TUBULES WITH PERIPHERAL PALLISADING. (H & E STAIN 400X

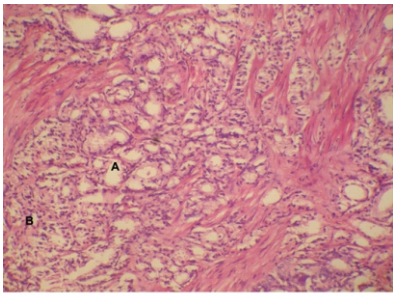

FIG 15. PHOTOMICROGRAPH OF PROSTATIC ADENOCARCINOMA (A) CLOSELY PACKED SINGLE GLANDS (B) FUSED GLANDULAR PATTERN.
(H & E STAIN 100X)

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