

Research Article

A histological study of prostate

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ABSTRACT

The work of anatomists and pathologists in the role of study of prostate has been significant. Starting from earlier times till modern time, the study of prostate has been a dynamic one and the basic anatomical knowledge of the prostate has undergone much change apart from the new techniques, micro invasive procedures and the chemotherapeutic approach for various disorders of the gland. The present study was based on the microscopic examination of Prostatic tissue of individuals with individual tissues of different age groups. The present study involved 40 cases which were further subdivided into various age groups and characteristic histological changes were noted. The study presents an assessment of age changes in prostate in elderly in Kashmiri population with pathological significance. Besides the histological study is of great importance in staging of diseases of prostate and especially in modern era where the incidence and prevalence of prostatic diseases is on rise.

Keywords: Prostate, Adenocarcinoma, Prostatitis, Staging, Capsule, Corpora amylacea, Ducts, Zones

INTRODUCTION

The work of anatomists and pathologists in the role of study of prostate has been significant. Starting from earlier times till modern time, the study of prostate has been a dynamic one and the basic anatomical knowledge of the prostate has undergone much change apart from the new techniques, micro invasive procedures and the chemotherapeutic approach for various disorders of the gland.¹

Most of the organs undergo atrophy with increasing age but most of the times prostate undergoes hyperplasia which is of clinical relevance. The changes occur at both microscopic level as well as macroscopic level. My study was aimed at looking into histological changes and accompanying other related changes which might come during the course of the study.

In the modern era, especially in the elderly males, the geriatric age group, people come with complaints of the

prostate gland. The frequency of the prostate disorders has been on the increase and disorders such as prostatitis, Benign Prostatic Hyperplasia and Prostatic Cancer have been on the rise.

To study the various changes the prostate undergoes during its development as the age passes by is a topic of immense interest and I have made an attempt to study the same.

Most of the complaints to a doctor are because of problems in the abdomino pelvic region. It has been found that of all the cases in out patients department 75 percent people complain of symptoms in the region of abdomen and pelvis.²

Especially in case of males the complaints in the pelvic region are comparable to females. As we have predominantly symptoms related to ovaries and cervix in case of females similarly we have growing concerns problems concerning prostate in males. Being a very

important organ of the male genito urinary system and the rapid progress made in the field of Anatomy, Histology, Pathology Surgery, Radiology the finer details about the organs makes our study more interesting and mind absorbing.

Histology of Prostate

The Prostate is a glandular organ.

The gland is a fibromuscular glandular organ.

We can see prostatic urethra, colliculus seminalis and the utriculus as well.

The glandular element is in the form of alveoli as tubules of small, multiple irregularly branching alveolar glands. These alveoli may contain Corpora Amylacea or prostatic concretions. These glands are embedded in a fibromuscular stroma smooth muscle fibres collagenous and elastic fibres are seem to be distributed throughout the gland.

The prostate can be divided into the outer larger zone and the inner smaller zone

The outer zone is composed of large branched glands and is a site for cancer.

The inner zone is composed of sub mucosal glands and is a site for Benign Prostatic Hyperplasia.

Histological examination is important for prostatic disorders because

- Different Disorders can be diagnosed with best possible accuracy. It surpasses all other methods by having the highest diagnostic accuracy.
- Differential diagnosis is sometimes based on histological findings only.
- Differentiating acute from chronic conditions.
- For evaluating grades of tumors.
- For evaluating response to therapy.
- For staging of diseases.
- For evaluating metastasis.
- For differentiating benign lesions from malignant lesions.
- As an adjunct for devising appropriate treatment options along with other diagnostic procedures.
- For determining relapse due to failed treatment regimens.
- To study tissues at a genetic/ molecular level, i.e. hormonal receptor studies, Immunological assays, DNA assays, Enzyme assays, PCR assays.

METHODS

The present study was based on the microscopic examination of prostatic tissue of individuals with individual tissues of different age groups.

The present study involved 40 cases which were further subdivided into various age groups.

The cases were divided into four different age groups namely:

- Group A 45-55 years
- Group B 56-65 years
- Group C 66-75 years
- Group D 76 onwards.

All of the Patients were males and the distribution of cases was irrespective of religious criterion i.e. there was a random selection of cases as far as the religion was concerned.

The observations were made from the prostate specimen collected and then through the proper histological technique the tissue was processed upto the stage of observation under microscope.

Group A	10 Prostate specimen
Group B	10 Prostate specimen
Group C	10 Prostate specimen
Group D	10 Prostate specimen

Group A

Normal Histology	9 slides
BPH	1 slide

Group B

Normal Histology	8 slides
BPH	2 slides

Group C

Normal Histology	7 slides
BPH	2 slides
Chronic Prostatitis	1 slide

Group D

Normal Histology	7 slides
BPH	2 slides
Chronic Prostatitis	0slide
Adeno carcinoma Prostate	1 slide

RESULTS

The microscopic examination of prostatic tissue of different age groups showed that the Prostate tissue in contrast to other organs shows hyperplasia instead of atrophy and that as the age increases there is more proliferation of fibro- musculo glandular tissue producing increase in the size of prostate which manifests itself in the form of Benign Hyperplasia of Prostate. With increase in the age it seems that the level of hormonal; stimulation increases or the response of the tissues to the hormones increases. At a molecular level the growth factors cause an increase in cellular elements to a varying degree.

In cases of prostatic tissues showing normal histology the intact capsule, absence of cells characteristic of prostatic inflammation, absence of cells having atypical characters such as abnormal shape and size, abnormal nuclei was characteristic. The amount of fibrous tissue, muscular tissue as well as the glandular element differs and most of the tissues showed mixed elements on the whole and proliferation of single element was not common as is the case with normal histology of prostate. However with increasing age the important components tend to increase in amount and people of younger age had less proliferation as compared to older age signifying that the fibromuscular glandular element increases with increase in age. The normal male prostate gland is composed of a mixture of glands and intervening fibro muscular stroma, in about equal proportions. Normal prostate is composed of a mixture of glands lined by tall columnar cells with in foldings and the intervening fibro muscular stroma, in about equal proportions, as seen here at medium power. Corpora amylacea are concretions that occur in benign prostate glands

Normal prostate has glands and intervening fibromuscular stroma. The tall columnar cells of the glands are surrounded by a thin myoepithelial cell layer.

Components of normal histology

Intact capsule
No Inflammatory infiltrate (absence of neutrophils/ Lymphocytes)
Normal shape/ size of epithelial cells
Normal nuclear characteristics
Non Proliferation of extra fibrous/ muscular/ glandular element

In Group A microscopic evaluation of the prostate was more or less normal in most of the cases. In one case, the evaluation showed benign hyperplasia of the Prostate in which there was an increase in the muscular and the fibrous element of the tissue. However the glandular element was not significantly increased. The capsule was intact in all the observations of Group A. There was no

gross change in the cellular architecture in case of normal observations. However in case of hyperplasia of prostate the glands were slightly altered in shape. The glands of the peripheral zone lined by columnar epithelium are clearly seen. The relative lengths of their ducts were longer and they were branched. The glands of the central and transitional zones were seen to be shorter and unbranched

In Group B microscopic evaluation of the prostate was again more or less normal in most of the cases (8 cases) . In two cases, the evaluation showed Benign Hyperplasia of the Prostate in which there was a moderate increase in the muscular and the fibrous element of the tissue which was more than that seen in Group A. However the glandular element was not significantly increased .the capsule was intact in all the observations as of Group A. There was no gross change in the cellular architecture in case of normal observations. However in case of Hyperplasia of Prostate the glands were moderately altered in shape. The glands of the peripheral zone lined by columnar epithelium are clearly seen. The relative lengths of their ducts were longer and they were branched. The glands of the central and transitional zones were seen to be shorter and unbranched

In Group C microscopic evaluation of the prostate was again more or less normal in most of the cases (7 cases). In two cases, the evaluation showed Benign Hyperplasia of the Prostate in which there was a moderate increase in the muscular and the fibrous element of the tissue which was more than that seen in Group A and B. However the glandular element was not significantly increased .the capsule was intact in all the observations as of Group A and B. There was no gross change in the cellular architecture in case of normal observations. However in case of Hyperplasia of Prostate the glands were moderately altered in shape. The glands of the peripheral zone lined by columnar epithelium are clearly seen. The relative lengths of their ducts were longer and they were branched. The glands of the central and transitional zones were seen to be shorter and unbranched

In one case by chance there was a chronic infiltrate suggesting the diagnosis of Chronic infection of the prostate (Chronic Prostatitis).

Here the capsule was intact. The fibrous element, the muscular and the glandular elements were normal and there was no apparent change I the distribution of these three constituents of the prostate gland apart from the cells.

In Group D microscopic evaluation of the prostate was again more or less normal in most of the cases (7 cases). In two cases, the evaluation showed Benign Hyperplasia of the Prostate in which there was a moderate increase in the muscular and the fibrous element of the tissue which was more than that seen in Group A. However the glandular element was not significantly increased .the

capsule was intact in all the observations as of Group A. There was no gross change in the cellular architecture in case of normal observations. However in case of Hyperplasia of Prostate the glands were moderately altered in shape. The glands of the peripheral zone lined by columnar epithelium are clearly seen. The relative lengths of their ducts were longer and they were branched. The glands of the central and transitional zones were seen to be shorter and unbranched

One observation of infiltration of malignant cells into the prostatic tissue was found. As the prostate is a glandular structure consisting of the ducts and the acini, therefore the histological pattern is that of an Adeno carcinoma. The changes occurring in the cells are the loss of basement membrane with the cellular atypia becoming more and more prominent and at a stage of progressive development solid sheets of carcinomatous cells can be seen.

At high magnification, the neoplastic glands of prostatic adenocarcinoma are still recognizable as glands, but there is no intervening stroma and the nuclei are hyper chromatic

DISCUSSION

Patients having inflammation of the prostate present like any other UTI. Diagnosing Prostatitis is not that easy for a physician

Sometimes prostate can get inflamed but the patients won't complain of any sign and symptom till late until finally he develops a picture suggestive of prostatitis especially chronic prostatitis with features of dysuria, pain in the pelvic region, pyrexia. The prostate retains its histological structure apart from the fact that it gets studded with chronic inflammatory infiltrate and if left as such prostatic abscess can follow. However in clinical cases the rate of chronic prostatitis turning into prostatic abscess was found to be insignificant apart from patients on immunosuppressive therapy or having immunodeficiency syndromes such as HIV infections.

In prostatitis the capsule was intact. The fibrous element, the muscular and the glandular elements were normal and there was no apparent change in the distribution of these three constituents of the prostate gland apart from the cells. Foci of inflammation can be seen on histology and depending on the grade of inflammation variable amount of prostatic tissue can be involved.

In certain unfortunate conditions there is profound increase in the glandular element progressing to latent carcinoma of prostate and then to full-fledged carcinoma.

In cases of benign hyperplasia of the prostate, patients present with either obstructive symptoms or irritative symptoms. Obstructive symptoms present with decreased flow, hesitancy, poor urinary stream or acute obstruction

or anuria while as those with irritative symptoms present with increased frequency of micturition and nocturia. They can be having concurrent detrusor instability or associated bladder problems. From the per rectal examination, often an enlarged prostate is noticed but with features different from malignancy .PSA levels can be elevated moderately.

Besides USG will confirm the grade of Prostatic enlargement as BHP Grade I, II, or III.

Macroscopically As well there will be an increase in the size of the gland, but the size of the gland does not always indicate the clinical severity of prostatic obstruction. In fact it is the amount of projection of the median lobe of prostate projecting into the bladder which determines the symptomatology of prostatism.

Histologically there is a moderate increase in the muscular and the fibrous element of the tissue which is more in elderly age groups than that seen in younger ones. However the glandular element there is no gross change in the cellular architecture in case of normal observations. However in case of Hyperplasia of Prostate the glands were moderately altered in shape. The glands of the peripheral zone lined by columnar epithelium are clearly seen. The relative lengths of their ducts were longer and they were branched. The glands of the central and transitional zones were seen to be shorter and unbranched

Excessive stimulation by steroids or increased response to steroids has been the main cause of hypertrophy of the prostate. Many drugs in the market presently available for the treatment of hypertrophy of prostate depend upon their ability to wave off the stimulus for prostatic growth. The role of DHT in benign hyperplasia of prostate is directly supported by the fact that 5 alpha reductase inhibitors directly inhibit prostatic growth. As a result nowadays many drugs based on this physiological effect of 5 alpha reductase activities are used to reduce the size of enlarged prostate with considerable success.

Finasteride which is a competitive inhibitor of the enzyme 5 alpha reductase type 2 and specific for the male urogenital tract is used. It markedly reduces circulating and prostatic dihydrotestosterone levels.

It markedly reduces prostate size and as far as the urinary peak flow rates are concerned, they are increased. The latest research on Prostatic diseases lately is going on in:

- Muscarinic Receptor antagonists
- Endothelin Receptors
- Nitric oxide donors
- Purino receptors
- Vanaloid receptors

The normal prostatic tissue undergoes immense changes due to hormonal stimulation and as the age increases.

There appears to be a proliferation of all the three elements (fibrous, muscular and the glandular element). However in some cases there is more proliferation of one element than the other.

We can have mixed response as well. However it is seen that in certain cases we usually have the dominant proliferation of one element. Associated with these changes we also have the increase in the concretions i.e. the corpora amylacea tends to increase in Number as the age grows. There tends to be more concentration of prostatic secretions which in due course tend to become calcified to produce these atypical bodies characteristic of prostate. The size of corpora amylacea however did not vary much.³ The irregularity of corpora amylacea as per the variation in shape and size does not in any case effect the overall clinical or prognostic significance of the prostatic diseases. These are present in normal senile older men as well.

Also the fibrous tissue is laid in irregular pattern as can be the case with muscular element giving the appearance of nodularity to the BHP. That is how the cases of BHP can be diagnosed by per rectal examination of the male patients by peculiar feel of the enlarged prostate and the associated nodularity of the gland. In some cases of Prostatic Cancer also there might be nodularity of the Prostate which indirectly implies the predominance of fibrous proliferation of the gland as compared to glandular proliferation at the microscopic level.

In some cases there is excessive proliferation of the epithelial/ glandular elements which in some cases remains confined to only a part of prostate forming small foci of Prostatic cancer within a normal prostate and the condition is called latent cancer of prostate.

This has been found to be of common occurrence. The picture resembles islands of neoplastic tissue embedded within an otherwise normal gland.

These isolated neoplastic tissues however can enlarge and involve widespread parts of the gland and evolve into full fledged cases of cancer prostate.

However in some cases this glandular proliferation is more extensive involving major parts of prostate forming the adenocarcinoma prostate which can produce both localized effects as well as metastatic effects. However rarely squamous cell tumors, transitional tumors as well as carcinosarcoma have been reported.

Reported subtypes of Cancer Prostate

1	Adeno carcinoma
2	Squamous cell carcinoma
3	Transitional cell carcinoma
4	Carcinosarcoma

The response of chemotherapy to these different tissues is different. This is again based on the histological subtype as well as the stage of cellular differentiation. Even the response to radiotherapy, external beam therapy, interstitial therapy, and surgery vary. As far as the differentiation of cells is concerned, poorly differentiated cells don't respond well and are associated with poor prognosis and five year survival rates are not good.

However in these cases the response to therapies is limited by the patients' tolerance and the adverse effects of the therapeutic agents as well. A proper evaluation of the patient as far as the blood counts, renal function tests, liver function tests, chest X ray, and other baseline tests are considered is taken into account.

In case of metastatic spread of the disease to other pelvic organs or vertebrae or abdominal organs, a conservative approach is taken as the benefits of conservative treatment outweigh any intervention on the whole.

The effects can be in the form of bladder outlet obstruction as well as spread to Bones especially the Vertebrae, Pelvis in the form of osteoblastic secondaries as compared to osteolytic lesions of other organs. The route of spread to the vertebral column is through the Batesons vertebral venous plexus which is a common route of metastasis.

The increase in the number of cases received daily in the hospitals as far as BHP, Cancer of Prostate seems to be a problem of major concern not only in developed countries but in underdeveloped country of ours as well. A need for urgent readressal to the patient's complaints as well as the importance of biopsy and histopathological examination of the tissue is important in the management of the problem. The histopathological examination can aid the physician/ Surgeon to give the exact details about the possibility of cure, Effective therapy, and staging and most importantly the prognosis of the patients' condition.

By knowing the normal first we can comment on abnormal. In this study we have been simultaneously examining the normal as well as abnormal tissues and come out with a conclusion that there is change in the normal cellular architecture with the increasing age in the Prostatic tissue.

The study of not the gland only but the prostatic fluid and subsequent research on the composition of this fluid with high concentrations of prostaglandins, fructose, spermine, zinc, fibrinolysin, fibrinogenase, acid phosphatase and ascorbic acid. Other locally acting peptides found to be secreted by the prostatic epithelium and the mesenchymal stromal cells were epidermal growth factor, insulin like growth factors, basic fibroblast growth factor and transforming growth factors.²⁵

The elaboration of Prostate Specific antigen (PSA) (562) which is a 30 k DA serine protease and its elevation in

case of prostatic cancer especially proved to be significant as a screening test for prostate Cancer. Its function is to facilitate liquefaction of semen normally and its normal range was found to be upto a highest level of 4 nmol/ml.

With the advent of more precise techniques, serial monitoring of PSA levels, PSAD, PSA velocity levels, histological techniques, the mortality and associated morbidity has reduced to considerable levels.²⁹

Newer techniques such as reverse transcriptase polymerase Chain reaction (RT-PCR), Trans Rectal Ultrasound (TRUS) have added additional diagnostic specificity.

CONCLUSION

Hence we can conclude that the histological examination of prostate gland is of utmost importance and a guide to the approach towards the patient's problem and his therapy. By studying the variation from normal to abnormal, we can to a great extent confirm or refute his presenting complaint. In case of him having a diseased state we can confirm his disease and once confirmed we can predict his chances of survival /outcome with a great deal of reliability. By saying so we don't mean that each and every one can be diagnosed with histological techniques to an exact 100 percent accuracy but our efforts to reach to a specific diagnosis can be accomplished by a multimodality approach through a combination of investigations in which histological examination will always have an immense and primary role to play not only for prostatic disorders but for other organ pathologies as well.

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