Original Article

Microscopic Anatomy of Aging Human Prostate Histological Architecture of BPH

Muhammad Amin, Shaista Ali and Samar Ashraf

Objective: To study the histological architecture of aging human prostate.
Methods: To study the histological architecture of aging human prostate. Materials and methods: Twenty samples of chips of human prostate (transitional zone) were collected from patients of benign prostatic hypertrophy (BPH), by transurethral resection of prostate (TURP) performed at Urology Department of Mayo Hospital Lahore. The parenchyma and stroma of the transitional zones of aging prostate specimens were analyzed qualitative & quantitative.
Results: Luminal dimensions of acini in transitional zone of aging prostate were significantly increased and height of the secretory epithelial cells (EH) was significantly reduced & they became cuboidal to flattened. Both inter-acinar smooth muscle (SM) and collagen fibers (CF) were increased between widely apart acini in BPH.a
Conclusions: The considerable increase in the luminal dimensions of the acini and significant reduction in the height of epithelial cells of acini along with remarkable increase in both inter-acinar muscle and collagen fibers are the hallmarks of BPH, and it signifies that both stromal and glandular elements were involved in BPH.
Keywords: luminal dimensions, BPH, transitional zone, TURP, parenchyma, stroma

Introduction

The prostate is the largest accessory reproductive gland of male, which is exceptional due to its potential to grow with age and has direct and indirect effects to the quality of an individual's life. Its role in sexual, reproductive, and lower urinary tract function is very important. However, its parenchyma related to reproductive functions and stroma associated with bladder function, are dispensable.[1] The parenchyma of the prostate gland comprises of branched tubuloacinar glands of varying sizes while the stroma contains smooth muscle cells and abundance of collagen fibers. As the age advances noncancerous enlargement of the prostate glandBenign Prostatic Hypertrophy (BPH) occurs in almost all men.[2,3] This enlargement is a fibromyadenoma resulting from nodular overgrowth of glandular epithelium and fibromuscular tissue. It is usually harmless but often can lead to lower urinary tract symptoms or problems in urination called prostatism.[4,5]

In general the effect of nodular overgrowth of parenchyma and stroma is a microscopic enlargement of the prostate gland without any clinical manifestations. The process of budding and branching continues within the nodule, and adjacent ducts become stimulated and incorporated into the process as well. Microscopic nodules develop into macroscopic nodules. As this process occurs, the original anatomy of the prostate gland becomes markedly distorted.[6]

It has been seen that clinical manifestation of BPH does not necessarily follow histological BPH. Microscopic BPH with no detectable prostatic enlargement can be found in men as young as 25 - 30 years and the prevalence is approximately 10% for that age range. There is a steady increase in incidence of histological evidence of BPH with age to 50% by the sixth decade (51 60 years) and to almost 90% in men aged > 80 years. Although almost all men will ultimately develop histological BPH, half will develop macroscopic BPH and only half of patients with macroscopic BPH will develop clinical BPH.[1,2,6.]

McNeal found that benign prostatic hyperplasia nodules were found to originate within the tissue that lies proximal to the verumontanum of the prostatic urethra and in proximity to the cylindrical sphincter around the bladder neck. This is known as the transitional zone of the prostate. BPH nodules may also arise from periurethral tissue immediately adjacent to urethra and inside the internal urethral sphincter. It is postulated that BPH arising from the transitional zone, developed earlier and consisted predominantly of epithelium i.e. glandular element. They are usually larger and form the main mass of BPH tissue, while the nodules originating from the periurethral zone tend to have a later onset and were smaller, fewer in number, and mostly composed of stromal components of fibromuscular tissue. It appears that the nodules originating from the

periurethral gland serve as the origin of the so-called median lobe as they grow and expand into the least resistant area i.e. into the orifice of the bladder. The glands of the transitional zone intrude into the bladder and produce the commonly observed circular intravesical prostate, compressing other prostatic regions, mainly the prostatic urethra.[7,8]

The knowledge of the histological elements of normal prostate and the changes occurring in these elements in BPH might contribute to understanding the genesis of this pathological condition, and help to choose better therapies among the several alternatives available. Currently there is still controversy about the main elements involved in prostate enlargement in BPH, i.e. whether there is an epithelial origin (ducts or acini) overgrowth or a proliferation of stromal component. Nevertheless, to date there are few quantitative studies of the changes in the glandular components in BPH.[9-11]

Methods

In this study, the glandular and the stromal component of transitional zone of aging human prostate were observed. Twenty samples of chips of human prostate (transitional zone) were collected from patients of benign prostatic hypertrophy (BPH), by transurethral resection of prostate (TURP) performed at Urology Department of Mayo Hospital Lahore. The specimens were immediately placed in 10% neutral buffered formalin for 48 hours. Tissue samples from hypertrophic prostates were processed for paraffin embedding. Five-micron thick sections were stained with Hematoxylin & Eosin and Masson's trichrome stains to study parenchyma and stroma qualitatively & quantitatively. Three random readings per slide of the luminal dimension (longitudinal as well as transverse), the height of acinar epithelium was measured by using ocular micrometer and multiplied by calibration factor. Numbers of smooth muscle fibers and collagen fibers were counted per high power field at 40 x. Patients with bladder outlet obstruction having raised PSA (prostate specific antigen) levels were excluded from the study.

Results

Data collected through the specified self-designed performa was entered into SPSS version 26 and analyzed descriptively. In descriptive analysis means and standard deviations were computed for all quantitative variables e.g. luminal longitudinal dimension, luminal transverse dimension, number of acini, height of epithelial cells, number of muscle fibers and collagen fibers. In Aging Human prostate, acini were larger in size. Secretory cells were small and luminal border was smooth and did not project inside the lumen. Nuclei were uniformly basal in position and darkly staining with scanty cytoplasm. The height of the epithelial cells lining the acini was reduced and they became cuboidal to flatten. **(Table-1, Fig-1 & 2).** The mean±SD of the luminal longitudinal dimensions (LLD) and the luminal transverse dimension (LTD) was 0.3582±0.08252 mm and 0.2989±0.07271 mm respectively. The mean±SD of the height of epithelial (EH) cells was 0.0077±0.00178 mm. The mean±SD number of smooth muscles fibers (SM) and collagen fibers bundle (CF) per high power field was 46.62±1.785 and 44.78±1.559 respectively **(Table-2, Fig.-3)**

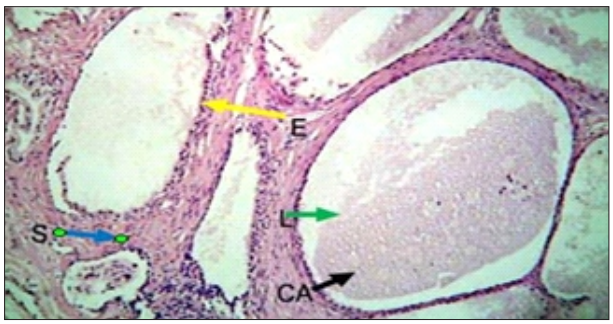

Fig.-1: Microphotograph showing histological features of aging human prostate (BPH). (Eosin and Hematoxylin).

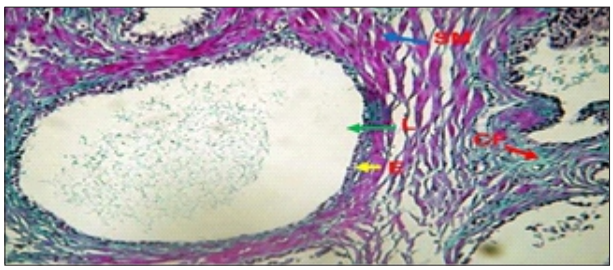

Fig.-2: Microphotograph showing histological features of aging human prostate (BPH). (Masson's Trichrome).

Table-1: iQualitative description of aging human prostate (BPH).

Tissue	Uniformity	Shape	Parenchyma (Acini) Size	Secretory cells	Basal cells	Stroma Compact/ loose
Transitional zone of aging human prostate (BPH)	Uniform	Rounded	Large	Cuboidal to flat	Present	Compact

Table-2: Quantitative descriptions of aging human prostate (BPH).

Variables	Benign Prostatic Hypertrophy
Mean luminal longitudinal dimension (mm)	0.3582±0.08252
Mean luminal transverse dimension (mm)	0.2989±0.07271
Mean number of acini	1.81±0.335
Mean epithelial hight (mm)	0.0077±0.00178
Mean number pf smooth muscle fibers	46.62±1.785
Mean number of collagen fibers	44.78±1.559

Discussion

Many workers were interested in histological composition of BPH and they found that two main components of the human prostate i.e. the fibro-muscular stroma and the glandular or epithelial component were involved in BPH that produced changes in prostatic histological architecture resulting in formation of nodules.[10] There is an age dependent trend towards prostate glandular dilation and prostate enlargement. Benign Prostatic Hypertrophy, an extremely common disorder in men aged > 50 years, develops in transitional zone and periurethral gland region of the prostate. Untegasser and his workers considered that aging and androgen were the main factors for the development of benign prostatic hyperplasia.[4]

In this study the histomorphometric changes of BPH were observed in aging human prostates and it was found that there were some important architectural and cytological changes in BPH. Some authors did not consider the prostate as histologically heterogeneous gland while in 1997 McNeal observed that anatomically prostate was heterogeneous gland of specific histological features. This may explain the different results for histological components found in aging prostate by various authors.[7,12]

In present study, the architectural changes were depicted in acinar luminal dimensions (LLD and LTD) and it was found that the mean values of the LLD & LTD were significantly increased in BPH (Table 2). This increase in the luminal dimensions of acini might be the result of simultaneous increase in the luminal volume and decrease in the height of epithelial cells (EH). The height of epithelial cells lining the acini was reduced and the cells became flattened. A significant decrease in the mean height of epithelial cells was seen in BPH (Table 1). Enlarging hyperplastic nodule of prostate might be related to the ductal obstruction that lead to stasis of secretions in acini of prostate and changes in the lumens of acini. These variations were apparent in BPH as cystic acinar alterations secondary to obstruction. The decrease in epithelial height with cells becoming cuboid or even flattened in acini might be related to compression and might progress to significant atrophy of the glandular component. It was also observed that the luminal dimension and the height of the cells decreased, the luminal dimension increased. The presence of prostatic concretions (corpora amylacea) was probably a consequence of congestion and secretory stasis. Our findings were consistent with Babinski et al 2001 who reported that in patients with BPH there was a significant decrease in epithelial height.[13]

Some previous quantitative data suggested that the stroma was the major component involved in BPH. All these studies which were focusing on stromal growth, did not refer to simultaneous or secondary changes in the number and form of the hyperplastic acini, although in some other studies there were comparisons between the epithelial and prostatic volume.[14] In this study, the stroma of aging human prostate i.e. BPH, data showed a significant increase in both smooth muscles and collagen fibers. The above mentioned findings also showed that there were both stromal as well as glandular changes occurred in BPH. These observations were similar to that of Babinski et al 2001 and McNeal JE 1978 who found that the transitional zone hyperplasia was predominantly glandular whereas nodules of the periurethral zone were stromal in origin and the glandular hyperplasia resulted as the budding of new glands from pre-existing ducts, with the creation of new glandular architecture. This could be due to re-awakening, which was explained as stromal-epithelial interactions in which epithelial cells were stimulated in some way by prostatic stroma to induce growth. Our descriptions were consistent with that of Diokno and Mc Neal, while these were dissimilar from Schuster and Schuster.[18] Who measured the relative amount of epithelium, muscle, connective tissue and lumen in BPH obtained by transurethral resection of prostate (TURP) and correlated their findings with prostate size. He also described that in BPH, there was significantly more adenomatous changes in epithelium and lumen, as compared to fibromuscular component, while we claimed that there were hyperplastic as well as hypertrophic changes in BPH of our patients. Our findings were also contradicted from that of Marcio et al, who observed the same findings in their study as did the Schuster and Schuster but the findings disagreed with those of Chagas MA *et al* and Deering *et al*.. who found no relationship between percentage stroma and

specimen size. They studied that the largest component of hypertrophy was stroma and the major component of the stroma was the non muscular part i.e. connective tissue involved in BPH.

acini were distinctly increased while the height of epithelial cells of acini in BPH is reduced. Both inter-acinar muscle and collagen fibers are increased in BPH. It signifies that both stromal and glandular elements are involved in BPH.

Conclusions

From above discussion, it can be concluded that in aging prostate (BPH) the luminal dimensions of the

Deportment of Anatomy
KEMU/ Mayo Hospital ,Lahore.
www.esculapio.pk

References

1. Diokno AC. Benign changes in the prostate with aging. Br J Urol. 1998 Dec; 82 Suppl 1:44-6.
2. Fujikawa S, Matsuura H, Kanai M, Fumino M, Ishii K, Arima K. Natural history of human prostate gland: Morphometric and histopathological analysis of Japanese men. Prostate. 2005 Dec 1; 65(4):355-64.
3. Oesterling JE. Benign prostatic hyperplasia. Its natural history, epidemiologic characteristics, and surgical treatment. Arch Fam Med. 1992 Nov; 1(2):257-66.
4. Untergasser G, Madersbacher S, Berger P. Benign prostatic hyperplasia: age-related tissue-remodeling. Exp Gerontol. 2005 Mar; 40(3):121-8.
5. Pfeiffer GM, Giacomarra M. Benign prostatic hyperplasia. A review of diagnostic and treat- ment options. Adv Nurse Pract 1999 Apr; 7(4):31-6; quiz 7-8.
6. Oesterling JE. The origin and development of benign prostatic hyperplasia. An age-dependent process. J Androl 1991 Nov-Dec; 12(6):348-55.
7. .McNeal JE. Origin and evolution of benign prostatic enlargement. Invest Urol. 1978 Jan;15(4):340-5.
8. McNeal J. Pathology of benign prostatic hyperplasia. Insight into etiology. Urol Clin North Am. 1990 Aug;17(3):477-86.
9. Babinski MA, Chagas MA, Costa WS, Sampaio FJ. Prostatic epithelial and luminal area in the transition zone acini: morphometric analysis in normal and hyperplastic human prostate. BJU Int. 2003 Oct;92(6):592-6.
10 Cadeddu JA, Pearson JD, Lee BR, Landis P, Partin AW, Epstein JI, et al. Relationship between changes in prostate-specific antigen and the percent of prostatic epithelium in men with benign prostatic hyperplasia. Urology. 1995 May;45(5):795-800.
11. Lepor H, Wang B, Shapiro E. Relationship between prostatic epithelial volume and serum prostate-specific antigen levels. Urology. 1994 Aug;44(2):199-205.
12Shapiro E, Becich MJ, Hartanto V, Lepor H. The relative proportion of stromal and epithelial hyperplasia is related to the development of symptomatic benign prostate hyperplasia. J Urol. 1992 May;147(5):1293-7.
13. Chagas MA, Babinski MA, Costa WS, Sampaio FJ. Stromal and acinar components of the transition zone in normal and hyperplastic human prostate. BJU Int. 2002 May;89(7):699-702.
14. Marks LS, Treiger B, Dorey FJ, Fu YS, deKernion JB. Morphometry of the prostate: I. Distribution of tissue components in hyperplastic glands. Urology. 1994 Oct;44(4):486-92.
15. Deering RE, Bigler SA, King J, Choongkittaworn M, Aramburu E, Brawer MK. Morphometric quantitation of stroma in human benign prostatic hyperplasia. Urology. 1994 Jul;44(1):64-70.
16. [Schuster GA, Schuster TG. The relative amount of epithelium, muscle, connective tissue and lumen in prostatic hyperplasia as a function of the mass of tissue resected. J Urol. 1999 Apr;161(4):1168-73.
17. [Eri LM, Svindland A. Can prostate epithelial content predict response to hormonal treatment of patients with benign prostatic hyperplasia? Urology. 2000 Aug 1;56(2):261-5.
18. McNeal JE. Normal histology of the prostate. Am J Surg Pathol. 1988 Aug;12(8):619-33.