A Brief Overview of Non-Neoplastic Lesions of the Prostate

Noha Said Helal
Department of Pathology, Theodor Bilharz Research Institute, Egypt

Abstract
Prostatitis occurs in approximately 10% to 15% of men and is classified into four categories: acute bacterial, chronic bacterial, chronic prostatitis/chronic pelvic pain syndrome and asymptomatic. A brief summary of non-neoplastic lesions of the prostate are discussed in the report.

Keywords: Prostatitis; Adenosis; Hyperplasia; Stroma

Introduction
The prostate gland is an accessory sex gland, apricot-sized, located underneath the bladder and surrounding the prostatic urethra. It is composed of glands and ducts arranged in a lobular fashion within a fibro-muscular stroma. Anatomically; it is composed of transition zone: which is 2 pear shaped lobes, surrounding proximal urethra; central zone: which surrounds transition zone to angle of urethra to bladder base; and peripheral zone: which rises from apex posterior to base, and surrounds transition and central zones. The normal prostate weighs between 7 g and 16 g [1,2].

Prostatitis
Prostatitis occurs in approximately 10% to 15% of men and is classified into four categories: acute bacterial, chronic bacterial, chronic prostatitis/chronic pelvic pain syndrome and asymptomatic [3].

Compared to prostate cancer and BPH, prostatitis is more likely to affect younger men, 18 to 50 years of age. Patients who undergo needle core biopsies of the prostate for elevated Prostate-Specific Antigen (PSA) levels show evidence of prostatitis on histology in approximately 27% of the cases [4]. Most have chronic inflammation, followed by acute inflammation, and rarely, granulomatous inflammation. Microscopically, prostatitis usually appears as a localized process involving a small number of ducts or acini. Inflammatory cells are a mixture of lymphocytes, plasma cells, and histiocytes (Figure 1) [5].

Granulomatous prostatitis
Granulomatous prostatitis is a distinctive form of prostatitis that can be mistaken for carcinoma. It is sub-classified into: infectious granulomas, Nonspecific Granulomatous Prostatitis (NSGP), post-biopsy granulomas, and systemic granulomatous prostatitis. NSGP is a rare disorder, but it is the most common granulomatous prostatitis seen on needle biopsy [6].

Granulomas are localized collections of activated macrophages (epithelioid histiocytes), usually surrounded by a collar of lymphocytes. The activated macrophages may fuse to form multinucleated giant cells [7].

Xanthogranulomatous prostatitis
Xanthogranulomatous prostatitis is a rare form of idiopathic granulomatous prostatitis that is characterized by lobulocentric accumulation of mixed inflammatory cells incorporating lymphocytes, plasma cells, and sometimes polymorphs with eosinophils. Specifically, there are numerous foamy macrophages or cholesterol-laden histiocytes admixed with other inflammatory cells. These histiocytes may occur in sheets, giving a pale appearance on low-power microscopy [7].

Malakoplakia
Malakoplakia is a rare specific variant of granulomatous prostatitis that is associated with a defective intracellular lysosomal digestion of bacteria. Usually, it is caused by E. coli and other gram-negative bacteria [8]. Histologically, it is characterized by diffuse sheets of macrophages/ von Hansemann cells (ovoid histiocytes), lymphocytes, plasma cells, and neutrophils. The macrophages characteristically contain intracytoplasmic Michaelis-Gutmann bodies, which are sharply demarcated, concentrically laminated, spherical, basophilic inclusions 2 μm to 10 μm in diameter, which represent calcified bacterial debris. Michaelis-Gutmann bodies can also be extracellular [9].

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*Corresponding author: Noha Said Helal, Department of Pathology, Theodor Bilharz Research Institute, El-Nile Street, Warrak El-Hadar, Imbaba, Po Box 30, Giza 12411, Egypt, Tel: +20-2-25401019; Fax: +20-2-35408125; E-mail: nohasaidhelal@yahoo.com
Prostatic Gland Atrophy

Atrophy of the prostate is a common process that is mostly found in older patients. It is more frequent in the peripheral zone. Four main subtypes are recognized: simple atrophy, cystic atrophy, post-atrophic hyperplasia, and partial atrophy. Combined patterns are common [10].

Simple atrophy appears as a well-circumscribed area of glands usually involves an entire lobule, although isolated acini may be affected. The acini are small showing scant cytoplasm and decrease in the height of the epithelial cells. They may be cystic with flattened epithelium (cystic atrophy) (Figure 2). The surrounding stroma may show fibrosis, while post-atrophic hyperplasia consists of small crowded acini arranged in a lobular configuration often surrounding a central dilated duct. In both simple atrophy and post-atrophic hyperplasia the glands appear basophilic. The stroma in atrophy is altered by a pale fibrosis with periacinar collagen deposition. Partial atrophy differs from simple atrophy and post-atrophic hyperplasia as it can show a more disorganized diffuse growth pattern and glands do not have the typical atrophic basophilic appearance and appear as a focus of crowded glands with pale scant cytoplasm [11].

Benign Prostatic Hyperplasia

Benign Prostatic Hyperplasia (BPH) is a common urologic condition caused by increase in cell number, and increase in weight of the prostatic gland, which commonly occurs in older men and is often accompanied by lower urinary tract symptoms. The etiology of BPH is multifactorial and includes environmental and genetic factors. Chronic inflammation of the prostate is thought to play a role in the genesis of BPH [12].

Nodule formation is the hallmark of prostatic hyperplasia that arises predominantly in the transition zone and histologically, nodules composed of proliferation of either pure stromal cells (Figure 3A) or both epithelial (glandular) and stromal cells [8]. The glandular component of BPH is made up of small and large acini, some showing papillary in folding and projections (Figure 3B). The luminal epithelial cells are tall columnar cells with pale-staining granular cytoplasm. Basal cells are variably seen, ranging from difficult-to-detected to hyperplastic. The stroma consists of smooth muscle and fibrous tissue. Lymphocytes and plasma cells are often present around the hyperplastic glands [13]. Immunohistochemically, the pattern of staining of BPH is similar to that of normal prostatic glands. The basal cells stain positively for High-Molecular-Weight cytokeratin (HMWCK), p63, and cytokeratin CK5/6. The secretory cells are PSA and PSAP positive [8].

Basal cell hyperplasia

Basal cells are a normal constituent of benign prostatic glands, located in the outermost layer [14]. Basal cell hyperplasia is occasionally a component of nodular, glandular and stromal hyperplasia, or benign prostatic hyperplasia, which arises in the transition zone in the prostate [15].

Histologically, appears as small, generally solid nests of benign-appearing epithelial cells with a somewhat clear cytoplasm. A range of growth patterns includes acinar, cribriform/pseudo-cribriform, and solid patterns or mixtures of these patterns (Figure 4). Nuclear enlargement, hyperchromasia, and nucleolar prominence are seen in the variant designated as atypical basal cell hyperplasia [8]. It is divided into usual basal cell hyperplasia, atypical basal cell hyperplasia, atrophy-associated basal cell hyperplasia, and adenoid cyst-like hyperplasia [16]. Immunohistochemically, they stain for p63 and HMWCK, which is helpful in differentiating benign glands from neoplasia.

Figure 2: Prostate atrophy: variable sized glands, lined with flat epithelial cells with scant cytoplasm (hematoxylin-eosin, X20).

Figure 3A: Benign prostatic hyperplasia: proliferation of fibro-muscular stroma (hematoxylin-eosin, X20).

Figure 3B: Benign prostatic hyperplasia: A mixture of variable amounts of prostatic glands and stroma (hematoxylin-eosin, X20).

Figure 4: Basal cell hyperplasia: nests of basal cells (hematoxylin-eosin, X20).
and high-grade prostatic intraepithelial neoplasia from prostatic adenocarcinoma [14].

**Adenosis**

Adenosis, also known as atypical adenomatous hyperplasia, is one of the most common lesions that may be confused with prostatic carcinoma. It is characterized by a well-circumscribed nodule of small, closely-spaced glands within the prostate, predominantly arising in the transition zone.

Features that distinguish adenosis from prostatic adenocarcinoma are the infiltrative pattern of adenocarcinoma [16]. By definition, the basal cell layer in adenosis is fragmented, with some small acini completely lacking basal cells. Immunohistochemical staining with HMWCK demonstrates the absence of basal cells in about one-half of all glands. Cytologically, the luminal cells have cytoplasm that is pale and clear to granular and round to oval nuclei, usually with inconspicuous nucleoli [17].

**Sclerosing adenosis**

Sclerosing adenosis is a rare benign lesion arising in the transition zone of the prostate, characterized by well-circumscribed nodules composed of small glandular structures, separated by a dense cellular and myxoid spindle cell stroma [18]. The nodules contain both a continuous basement membrane and a layer of basal cells. The latter are immunoreactive for keratin, S-100 protein, and smooth muscle actin, suggesting myoepithelial differentiation. The spindled stroma, basal and myoepithelial cells, and lack of appreciable nuclear atypia are useful in distinguishing sclerosing adenosis from adenocarcinoma. However, in some cases, there can be significant cytologic atypia (atypical sclerosing adenosis) mimicking carcinoma [8].

**Prostatic Gland Metaplasia**

A variety of metaplastic changes can be seen in the prostate, including transitional cell metaplasia, mucinous metaplasia, squamous metaplasia, and eosinophilic metaplasia. Transitional metaplasia can be a pitfall for high-grade prostatic intraepithelial neoplasia and is distinguished by the presence of nuclear elongation and grooves, as well as inconspicuous nucleoli [16]. Mucinous metaplasia is seen in benign processes, including atrophy, transitional cell metaplasia, basal cell hyperplasia, prostatrophic hyperplasia, and nodular hyperplasia. Squamous metaplasia occurs in normal prostatic glands, as well as in a variety of reactive settings such as adjacent to prostatic infarcts and in hormonally treated prostates [19].

**Mesonephric Remnant/Mesonephric Remnant Hyperplasia/ Mesonephric Adenoma**

Mesonephric remnants are mesonephric duct vestiges that can be identified histologically in the prostate, prostatic urethra, and seminal vesicle [20].

Mesonephric remnant hyperplasia is well documented in the female genital tract but is an uncommon incidental histological finding in the prostate and periprostatic tissue, being composed of small glandular structures lined by a single layer of cuboidal cells, usually with dense eosinophilic intraluminal secretory material [21].

Despite its earlier designation as nephrogenic adenoma, this lesion is thought to arise from metaplasia of the underlying urothelium. The lesion has been associated with radiation, surgery, stones, instrumentation, intravesical thiopeta and Bacille Calmette-Guérin (BCG), and renal transplantation [22]. Histologically, it includes four patterns: tubular, cystic, polypoid-papillary, and diffuse. It composed of small, solid to hollow tubules, arranged in a lobular appearance, lined by low columnar or cuboidal epithelial cells, with thickened hyaline sheath around some tubules and occasional eosinophilic secretions. It may extend into underlying smooth muscle. Cytoplasmic staining for HMWCK is found in more than half of cases [23].

**References**