

Original Research Paper

Pathological and Immunohistochemical Findings of Prostate Glands from Clinically Normal Dogs

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Abstract: To investigate the incidental histopathologic findings in clinically normal dogs and determine the immunohistochemical expression of several tissue-specific differentiation markers. The University of Mosul's animal research ethical committee authorized this study (UoM.Dent/A.DM.L.1/22). Seven samples were obtained from the veterinary hospital in cooperation with the College of Dentistry. Dogs with two detectable testicles were considered intact. Dogs with a history of clinical signs of prostatic or lower urinary tract disease were dismissed from the study. Sections were cut at 5µm, and then hematoxylin and eosin staining procedures were applied. Immunohistochemistry was performed following the manufacturer's protocol for each antibody. Typical prostatic glandular features lined by simple columnar epithelial cells with apical intracytoplasmic eosinophilic granules were detected, which represent a major basic protein. Additionally, despite a lack of gross lesions, 13 types of microscopic lesions were identified. Infiltration by lymphocytes and plasma cells was the most frequent, in 85.71% (6/7) of samples. Atrophied glands and congested blood vessels were noticed in 71.42% (5/7). Intraluminal glandular hyperplasia, epithelial vacuolar degeneration, and increased fibrous tissue were detected in 57.14% (4/7). Increased interstitial stroma was found in 42.85% (3/7). Polypoid projections, hyaline cast deposition, cystic alveoli, and epithelial lining deterioration play a significant role in the inflammatory process, prostate concretions and capsule thickening were rarer abnormalities. P63, cytokeratin 8, and high molecular weight cytokeratin were used to target normal prostate gland cells in clinically normal mixed-breed dogs. We also investigated the expression of BCL-2 and P53, which have been recorded in human prostatic cancer. P63 was detected in all samples and CK8 was detected in 7/8 samples. No samples had immunoreactivity for BCL-2 and P53. Prostate samples from normal dogs show a spectrum of lesions, with a majority of samples having lymphoplasmacytic inflammation. IHC found weak to strong P63 immunoreactivity and strong CK8 immunoreactivity, with no reactivity for P53, BCL-2, and HMWC. All statistical work, both descriptive and inferential, was accomplished in JMP Pro 16.1. Analyzing with a chi-squared test. By showing similar lesions to those seen in humans, even in normal cases, these results further suggest that dogs may be a suitable model for human prostatic illness. Also, caution is warranted while looking for small neoplasms, as these lesions may hide small neoplasm foci.

Keywords: Canine Prostate Gland, Histopathology, Immunohistochemistry, P63, BCL-2, P53, HMWC, CK8

Introduction

Dogs as a Model

The prostate, a bilobed oval accessory sex gland in adult male dogs' pelvic cavity, excretes seminal plasma components. Leis-Filho and Fonseca-Alves (2018). The utilization of the canine prostate as an animal model is prevalent in the preclinical assessment of novel therapeutic treatments (Sun *et al.*, 2017b). The dog is a natural model for studying human disorders since it closely resembles that of humans, and also, serves as a disease model for research, eliminating the necessity of creating synthetic illness models (Gilmore and Greer, 2015). The canine and human prostate share a comparable ovoid, bilobed morphology and are both located adjacent to the bladder, surrounding the proximal urethra (Ryman-Tubb *et al.*, 2022). Dogs are not only useful models for molecular studies with naturally occurring prostate cancer but also for treatment efficacy (Kobayashi *et al.*, 2018). Protein networks (PTEN, MDM2, AR, and P53) influence cancer therapies as they are crucial to the development of human prostatic cancer. Because tumors occur spontaneously in dogs, they have been considered good models for comparative oncology. However, there is significantly less information available about protein expression in canine tumors (Rivera-Calderón *et al.*, 2016). Studies of normal and malignant tissue are often supplemented by immunohistochemistry using antibodies against intermediate filament proteins (Grieco *et al.*, 2003). The University of Mosul's animal research ethical committee authorized this study. (UoM.Dent/A.DM.L.1/22).

Frequent Pathologic Features in Dogs

Dogs frequently exhibit spontaneous Benign Prostatic Hypertrophy (BPH), which, other than chimpanzees and macaques, are the only non-human species to produce this condition (Sun *et al.*, 2017b; Steiner *et al.*, 1999; Mubiru *et al.*, 2008). Prostate hyperplasia in older males is common and is assumed to afflict all older intact canines Leav *et al.* (2001). Proliferative prostatic lesions often occur in dogs and are associated with both androgen hormone levels and age (Fonseca-Alves *et al.*, 2013). Prostatitis, prostatic cysts, prostatic neoplasia, and benign prostatic hyperplasia are the most prevalent disorders that affect the canine prostate (Smith, 2008). Physicians have found that the number of lesions that can develop in the prostate gland presents a major challenge in the detection of prostatic cancer, as sampling artifacts may mask small foci of neoplasia due to adjacent disease (Wei, 2010).

Immunohistochemistry Markers in Prostate Tissues

For more than 20 years, pathologists have relied heavily on Immunohistochemistry (IHC), which is still the method

that they employ most commonly, however, only a small number of prognostic indicators were routinely evaluated in all patients, but an increasing number are becoming a regular component of clinical sessions. Immunohistochemistry (IHC) is employed for the identification of distinct cellular components, such as basal and myoepithelial cells (Fitzgibbons and Cooper, 2009). This technique aids in the determination of malignancy and/or invasion, as well as the diagnosis of infectious diseases. However, the significance of IHC in predictive marker testing, which involves the selection or exclusion of patients for specific therapies, is increasingly gaining prominence and frequency. (Fitzgibbons and Cooper, 2009; De Matos *et al.*, 2010). In normal canine and human prostatic ducts and alveoli, basal cells and luminal cells are two distinct kinds of epithelial cells (Brawer *et al.*, 1985). It has been documented that some cytokeratin's are expressed differently in the human prostate's luminal and basal cells (Sherwood *et al.*, 1991); for instance, CK 8 is expressed by luminal cells (Grieco *et al.*, 2003) and basal cell layer positive for P63 can be seen in human normal prostatic tissues. When prostatectomy specimens are examined, the biomarkers P53 and BCL-2 are significant for predicting the recurrence of prostate cancer, however, this is not evident with immunohistochemistry labeling of smaller prostate biopsies. More research is needed to determine if this variation is due to sampling error or the varied nature of prostate tumors (Stackhouse *et al.*, 1999). Both PC and a normal prostate express BCL-2 family protein (Ali and Kulik, 2021). BCL-2 proteins in prostate cancer have not been extensively studied in response to anti-cancer therapy and anti-apoptotic pathways (Ali and Kulik, 2021). In the course of typical prostate growth and differentiation, basal cells proliferate, expressing more luminal markers than basal Cell markers (CK18) and eventually merely luminal markers (De Godoy Fernandes *et al.*, 2021).

Prostate diseases are common in older healthy dogs. No breed-significant predilections for the prostatic disease have been identified, although some breeds of dogs, such as German shepherds and Dobermans, appear to have a high incidence of prostatic disease (Canine and Feline Theriogenology (VetBooks, 2010). The natural history and etiology of prostatic diseases associated with aging, such as Benign Prostatic Hyperplasia (BPH), is still unclear (Steiner *et al.*, 1999). Prostate-Specific Antigen (PSA) is commonly used in monitoring Benign Prostatic Hyperplasia (BPH), prostatic neoplasia, and prostatitis because of significant increases in the bloodstream at the onset of these disorders. Although canine prostate-specific esterase, a serine protease, is the primary secretory product of the canine prostate gland, Prostate-Specific Antigen (PSA) cannot be detected in dogs (Bell *et al.*, 1995). While CPSE is elevated in cases of prostatic disease, it does not differentiate between inflammation, neoplasia, or hyperplasia. Similarly, PSA

testing has low sensitivity and specificity, and more studies are needed to better understand the biological factors that influence PSA serum levels (Mubiru *et al.*, 2008). Given the similarity of canine disease to human disease, studies in canine prostatic disease may be helpful in determining biomarkers with better specificity than PSA in the future. Therefore, the aim of this research is to look into any unexpected histopathological findings in dogs with normal clinical conditions and find out whether any tissue-specific differentiation markers were immunohistochemically expressed.

Materials and Methods

Samples

The current work was conducted on seven male dogs, with samples collected from August 2021 to February 2022 from the necropsy unit of the veterinarian educational institution at the College of Veterinary Medicine of the University of Mosul. The glands were resected at the time of necropsy from healthy male mixed-breed dogs euthanized for reasons unrelated to prostatic or urinary tract disease. Dogs ranged from 1.8-10 years old and from 17.8-41.1 kg. At the moment of euthanasia, dogs with two detectable testicles were considered intact. Dogs with a history of clinical signs of prostatic or lower urinary tract disease were dismissed from the study. All specimens were inspected grossly to identify any lesions and to check for any differences in the size, color, and texture of the prostate. Specimens were then collected, chilled, and transferred to the lab. The study followed ethical standards for animal research UoM.Dent/A.DM.L.1/22.

Histopathology and Immunohistochemistry

Hematoxylin and eosin were used to stain the samples after they had been fixed in 10% neutral buffered formalin for 48 h. Tissue sections were prepared for immunohistochemistry by being dewaxed in xylene, rehydrated in ethanol, and washed in phosphate-buffered saline. To inhibit endogenous peroxidase activity for 30 min, a hydrogen peroxide-methanol solution (3%) was applied. After that, tissue samples were frozen for 60 min at 25°C. After that, the sections underwent an overnight incubation with primary antibodies at 4°C. Primary antibodies included rabbit anti-human P53 polyclonal antibody (PA5-88098, Thermo Scientific, Wilmington, DE, USA) at a dilution of 1:100, targeting P53 protein which is a transcription factor that may trigger the expression of several target genes and regulates the cell cycle, apoptosis and genomic stability (Wang *et al.*, 2023), rabbit anti-human Cytokeratin 8 (Ck8) polyclonal antibody (PA5-29607, Thermo Scientific, Wilmington, DE, USA) at a 1:2000 dilution, which can effectively differentiate between basal cells and luminal cells within human

prostate tissue; rabbit anti-human BCL-2 polyclonal antibody (Product # PA5-114899) at a dilution of 1:100, which is the main procedure via which cells undergo death. This event is subject to significant regulation by the BCL-2 family of proteins, encompassing either pro-apoptotic or pro-survival proteins (Hafezi and Rahmani, 2021). Rabbit polyclonal antibody to P63 (ab216493, Abcam Cambridge UK) 1:200, aim for the expression of nuclear P63 in both luminal and basal cells (Fonseca-Alves *et al.*, 2018) and cytokeratin, High Molecular Weight (HMWC) Monoclonal mouse antibody, Clone 34βE12, Agilent, US), which specifically identifies basal cells, has recently been demonstrated in academic institutions for the purpose of diagnosing prostate cancer (Kahane *et al.*, 1995).

The sections were washed three times, then treated with poly-HRP goat anti-mouse IgG (dilution 1:200, Wuhan Biotech, China) for 60 min at 37°C. An avidin-biotin combination was used for detection. The sections were dehydrated and covered after being stained with hematoxylin for 60 sec.

Statistical analysis

JMP Pro version 16.1 was utilized to perform descriptive and inferential statistics. Using chi-square analysis, a significant difference between lesion frequencies was examined. At a p-value of 0.05, the results were significant. JMP Pro 16.1 Software, SAS Institute Inc., Cary, North Carolina, United States of America, 2021.

Results

Hematoxylin and Eosin Findings

Microscopic examination revealed typical simple columnar epithelial cells form glandular structures with eosinophilic cytoplasmic granules, besides acinar and cystic epithelial cells (supplementary data Figs. 3-4 and Table 3). There was no evidence of neoplasia in any of the seven samples. Typical prostatic glandular features lined by simple columnar epithelial cells with apical intracytoplasmic eosinophilic granules were detected. Additionally, despite a lack of gross lesions, 13 types of microscopic lesions were identified (Fig. 1) representing the frequently observed lesions. "Lymphoplasmacytic infiltration" was the most frequent, seen in six (85.71%) out of the seven samples. Prostatitis was the most frequent histologic finding in our population of healthy dogs. Atrophied glands and congested blood vessels were noticed in 71.42% (5/7). Intraluminal glandular hyperplasia, epithelial vacuolar degeneration, and increased fibrous tissue were detected in 57.14% (4/7). Increased interstitial stroma was found in 42.85% (3/7). Polypoid projections, hyaline cast deposition, cystic alveoli, epithelial lining deterioration, prostate concretions, and capsule thickening were rarer abnormalities. Lesions frequencies are summarized in Table 1.

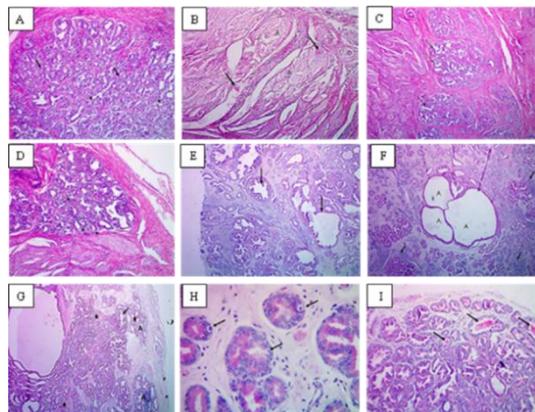


Fig. 1: Interstitial infiltration of lymphocytes and desquamation of glandular epithelial H and E 100×; (A) Smooth muscle, and fibrous tissue hyalinization and hyaline cast deposition) H and E 100×; (B) Cystic alveoli H and E 100×; (C) Vacuolar degeneration of epithelial lining of both glandular epithelia and urethra H and E 100×; (D) Chronic prostatitis, large alveoli with intra luminal hyperplasia of glandular epithelium H and E 100×; (E) Infiltration of lymphocytes in the prostatic stroma (arrows) cystic glandular structure (letter). (Cystic dilatation) H and E 100×; (F) Necrosis of epithelial lining (arrows). Subscapular infiltration of lymphocytes (letter), thickening prostatic capsule (head arrows) congested blood vessels (star) cystic glandular structure (Cystic dilatation) H and E 40×; (G) Vacuolation of epithelial cells lining the glands H and E 400×; (H) Prostatic concretions, H and E 100× (I)

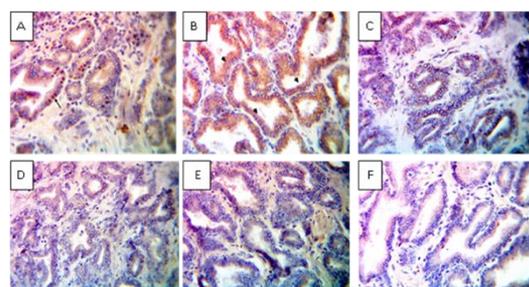


Fig. 2: Basal cells creating a discontinuous layer of nuclear P63 expression. 400×; (A) Weak cytoplasmic expression of CK8 in luminal cell layers 400×; (B) Weak cytoplasmic expression of CK8 in luminal cell layers 400×; (C) The negative reaction of HMWC 400X; (D) Negative IHC expression of P53 in a normal prostate gland 400×; (E) Negative immunohistochemical expression of BCL-2 in a normal prostate gland 400× (F)

Table 1: Number of lesions detected in each case

Cases	Number of lesions
1	6
2	4
3	2
4	8
5	9
6	9
7	5

Table 2: Immunohistochemistry results

Case numbers	Basal cell markers		Luminal cell Markers	Markers detected in Human PC	
	P63	HMWC		P53	BCL-2
1	+	-	CK8	-	-
2	+	-	+	-	-
3	Weak (±)	-	-	-	-
4	+	-	Weak (±)	-	-
5	Weak (±)	-	+	-	-
6	+	-	+	-	-
7	Weak (±)	-	Weak (±)	-	-

Immunohistochemical Findings

Our immunohistochemistry results confirm previous findings. The normal prostate glands (all 7 cases) had discontinuous weak to strong nuclear P63 expression. Currently, the relevance of P63 positivity in dogs is unknown. Negative immunoreactivity for both P63 and HMWC for luminal cells is also similar to previous work. Normal alveoli and duct luminal cells abundantly expressed CK8 and some cases showed weak cytoplasmic expression of CK8 in luminal cell layers. This is comparable to the CK8 immunoreactivity of luminal cells via expressed luminal markers (CK8, CK18) in mature rats and human prostates and similar to that found in normal dog prostates.

However, all seven samples lacked HMWC expression in basal cells, likely due to the discontinuous pattern of basal cells in dogs compared to a continuous pattern in humans. P53 and BCL-2 expression was lacking in both basal and luminal cells in all samples. (Table 2) summarizes the IHC results for all marker reactions in normal canine prostatic luminal and basal cells. All seven normal prostate glands expressed nuclear P63 only in basal cells, which formed a disconnected layer. Normal alveoli and ductal cells abundantly expressed CK8 and some cases showed weak cytoplasmic expression of CK8 in luminal cell layers. All seven samples lacked immunoreactivity for HMWC in basal cells. Basal and luminal cells were negative for both P53 and BCL-2 immunoreactivity in all samples (Fig. 2).

Discussion

The current research aimed to investigate the incidental histopathologic findings in clinically normal dogs and determine the immunohistochemical expression of several tissue-specific differentiation markers. Prostatic problems in dogs are difficult to identify in the initial stages and are typically only noticed when advanced, as they are asymptomatic at the time of initiation (Alonge *et al.*, 2018; Johnston *et al.*, 2000). These difficulties might impact the study's findings by scanning more dogs and we might find a correlation between the type of lesions and the predicted disease. While dogs may have an enlarged prostate without

symptoms, delayed diagnosis typically occurs after clinical signs due to an enlarged gland (Russo *et al.*, 2012), when affected dogs have a normally shaped, painless gland, making diagnosis difficult (Smith, 2008). Prostate sampling is necessary to definitively diagnose prostatic conditions and rule out alternative illnesses, such as neoplasia (Lea *et al.*, 2022). About 50% of dogs may have histologic alterations at the age of 4-5 years and by the age of eight, more than 90% may have these abnormalities. The prevalence of prostatic problems in healthy dogs has been found to be 0.3%, with the exception of prostatic neoplasia (Polisca *et al.*, 2016). Lymphoplasmacytic infiltration was the most frequent finding. This result agrees with the chronic prostatitis cases documented by Christensen (2018), which discovered an abundance of macrophages together with plasma cells and lymphocytes. Occasional information of prostatitis in neutered male dogs usually involves a history of recent castration prior to the onset of symptoms (Christensen, 2018). Prostatitis was the most frequent histologic finding in our population of healthy dogs and is similar to that described previously (Palmieri *et al.*, 2022). This inflammatory process may be asymptomatic or a key sign of preclinical disease, particularly in the acute phase once neutrophils penetrate the interstitium and glandular acini lumen (Palmieri *et al.*, 2014; 2019a; Palmieri and Riccardi, 2013; Cowan *et al.*, 1991) Atrophied glands and congested blood vessels were detected in five samples (71.42%) and were usually associated with inflammation. Glandular atrophy may explain why some chronic prostatitis conditions do not show an enlargement of prostate glands (Christensen, 2018) despite large numbers of lymphocytes suggesting inflammation (Palmieri *et al.*, 2019a). Increased interstitial prostatic stroma was found in three samples (42.85%), which agrees with Berry *et al.* (1986) who found a significant quantity of fibromuscular stroma separating the non-secretory branching duct systems in the canine prostate in cases with atrophy. Intraluminal glandular hyperplasia, epithelial vacuolar degeneration, and increased fibrous tissue were detected in four samples (57.14%). This is the most common condition in intact male dogs (Palmieri *et al.*, 2022) and is correlated with aging and sex hormone imbalance (Sun *et al.*, 2017a-b; Berry *et al.*, 1986; Palmieri *et al.*, 2019b) As early as 2-3 years old, dogs can develop glandular hyperplasia, which is characterized by a consistent glandular expansion of the prostatic alveoli, an increase in papillary infoldings and an increase in columnar secretory cells. Leav *et al.* (2001); DeKlerk *et al.* (1979). The ultrasound examination occasionally fails to accurately detect the initial phases of clinical Benign Prostatic Hyperplasia (BPH). Nonetheless, it is worth noting that a considerable proportion (14%) of dogs

classified as normal exhibited a notably extensive presence of polycystic parenchyma, characterized by many cavities smaller than 5 mm dispersed throughout the parenchyma (Lévy *et al.*, 2014). Other less frequent abnormalities identified by microscopic examination were polypoid projections, hyaline cast deposition, cystic alveoli, desquamation, and loss of the epithelial lining as well as prostatic concretions and thickening of the capsule as noticed by Berry *et al.* (1986). In comparison to histologically normal tissue, glandular hyperplasia definitely increases the density of the secretory epithelium and this result is also linked to an increase in androgen receptors. Cysts were seen along with exacerbated hyperplasia in the gland and the alveoli were enlarged and packed with eosinophilic material, which agrees with previous studies (Berry *et al.*, 1986; Sun *et al.*, 2017a; Palmieri *et al.*, 2022). Prostatic chronic inflammation appears to steer to proliferative atrophy of the prostate gland (De Godoy Fernandes *et al.*, 2021). This indicates that the origin of this disorder can be related to the excessive proliferation of basal cells, which is triggered by the persistent inflammatory process (Nascente *et al.*, 2022).

There was no evidence of neoplasia in any of the samples examined. This may be due to the fact that all dogs involved in this research were intact, as previous work by Sorenmo *et al.* (2003) suggests that testicular hormones may affect the development of cancer by altering the environment in the prostate³³. Additionally, dog prostate cancer is an infrequent ailment, representing less than one percent of all cancer cases identified in canines (Stans, 2020). Negative immunoreactivity for both P63 and HMWC for luminal cells is also similar to previous work, which is important in which understanding the formation and progression of prostate cancer involves the recognition of stem cells and the differentiation programs that govern the normal prostate epithelium (Grisanzio and Signoretti, 2008). Carcinogenesis depletes the basal cell layer and human prostatic cancer cells lack p63 positivity (Fonseca-Alves *et al.*, 2018) besides reacting negatively in normal luminal human prostate cells (Fonseca-Alves *et al.*, 2018). Basal cell markers are not applicable to PC analysis in veterinary medicine since the basal cell layer is arranged discontinuously in a normal canine prostate (Fonseca-Alves *et al.*, 2018).

Both p53 and BCL-2 are significant for predicting the recurrence of prostate cancer in humans. Previous work in dogs suggests these are less helpful in dogs (Ali and Kulik, 2021). We found no evidence of expression of either in these samples; however, the small number of samples limits our sensitivity in detecting weak or infrequent expression. In normal human prostates, p53 was only weakly nuclear immunoreactivity expressed

in a few numbers of dispersed epithelial cells (Pagliarone *et al.*, 2016). Other markers, such as cytokeratin 5, NKX 3.1, AR, PSA and chromogranin, may be helpful in future studies for prostates in both animals and humans.

Conclusion

Prostate samples from clinically normal dogs show a spectrum of lesions that we were able to identify about 13 types of microscopic lesions with a majority of samples having lymphoplasmacytic inflammation followed by atrophied glands and congested blood vessels, then intraluminal glandular hyperplasia, epithelial vacuolar degeneration and increased fibrous tissue with different percentages. These results provide additional evidence that dogs are a good model for human prostatic disease, as they demonstrate similar lesions to those found in humans. The utilization of this approach can prove to be highly advantageous in the development of treatments that aim to target diseases that are common to both species, such as cancer.

IHC found weak to strong P63 immunoreactivity and strong CK8 immunoreactivity, with no reactivity for P53, BCL-2, and HMWC same reaction behaves exactly as its human counterparts. It also indicates caution is warranted when searching for small neoplasms, as these lesions may mask small neoplastic foci. Finally, this study confirms that without any symptoms of prostatic diseases intact male dogs could reflect the same specific defects that could be found in both humans and dogs. This study will take us to further investigation in the future to include specific markers for such lesions. Addition markers would help to find a relation between those types of lesions in both dogs and humans such as NKX 3.1 which has been documented in many neoplastic and non-neoplastic tissues. Furthermore, scanning of distinct types of lesions and their relation to promote cancers. The target of our study was dogs since the absence of clinical signs might hide a serious disease, which could be irreversible and will not be treated easily. Additionally, our findings can be used to begin rational, preventative, and therapeutic efforts in symptomatic dogs having frequent lesions that could be hidden in normal dogs and humans.

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Author's Contributions

Firas Mohammed Abed: Study conception and design, analysis, interpretation of results and drafted manuscript preparation. Revised it critically for important intellectual content.

Asseel Mohammed Rahawi and Ahmed Nazar Abduljawaad: Data collection analysis and interpretation of results. Revised it critically for important intellectual content. Approved the version to be published.

Hadil Basim Al-Sabaawy: Data collection analysis and interpretation of results. Drafted manuscript preparation. Revised it critically for important intellectual content. Approved the version to be published.

Michael James Dark: Study conception and design, data collection, analysis and interpretation of results and manuscript preparation. Drafted manuscript preparation. Revised it critically for important intellectual content.

All authors reviewed the results and approved the final version of the manuscript.

Ethics

This article is characterized by its originality and includes previously unpublished content. The corresponding author affirms that all co-authors have thoroughly reviewed and endorsed the work and that no ethical concerns were encountered throughout the research process.

Conflict of Interest

The authors have declared no conflicts of interest.

Approval

The University of Mosul's Ethical Committee for Animal Research approved this study. (UoM.Dent/A.DM.L.1/22) for the period extended from November 30, 2021, to December 31, 2022.

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Supplementary Data

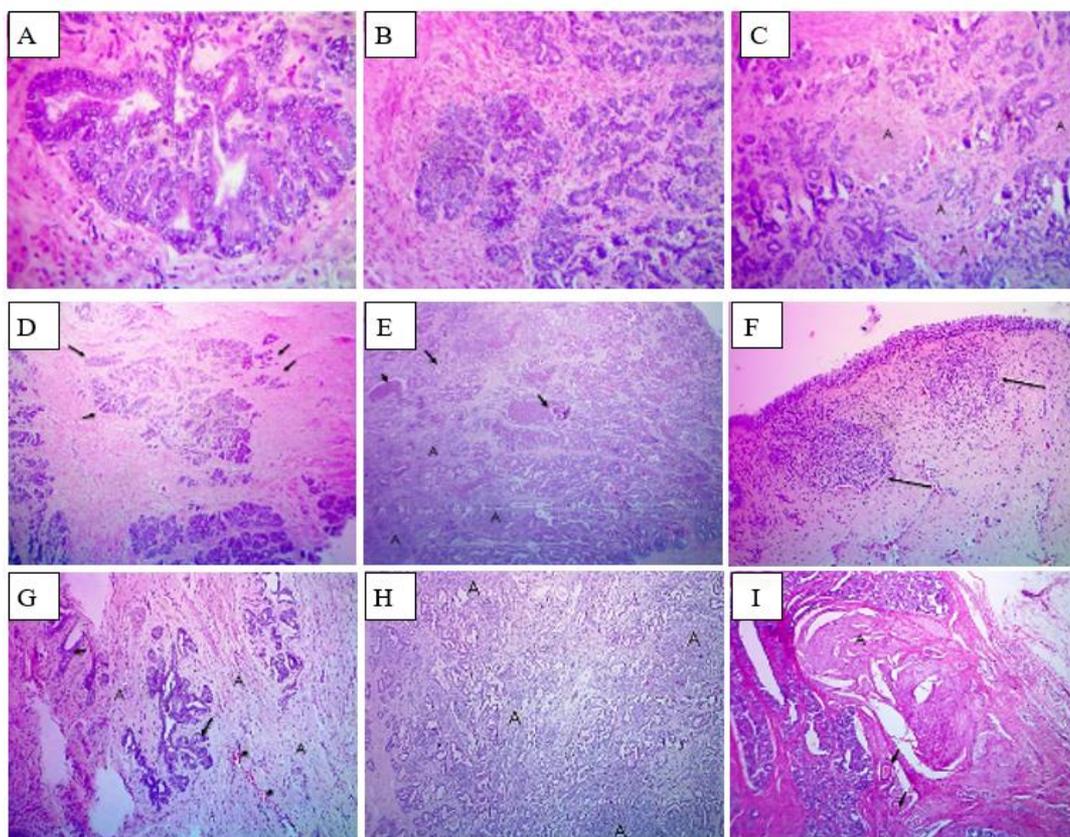


Fig. 3: Glandular structures lined by simple columnar epithelial cells with obvious eosinophilic granules in their cytoplasm and acinar with cystic epithelial cells. H and E 400× (A); Benign prostatic hyperplasia H and E 100× (B); Diffused fibroconnective tissue in replacement of the glandular structures (letters) H and E 40× (C); Hormonal atrophy with a relative increase of interstitial stroma. (arrows) H and E 40× (D); Hormonal atrophy with a relative increase of interstitial stroma. Infiltration of inflammatory cells, (letters) necrotic glands, and desquamation of epithelial linings (arrows) H and E 40× (E); Multifocal lymphoplasmacytic infiltration of inflammatory cells in prostate stroma H and E 100× (F); Hormonal atrophy with a relative increase of interstitial stroma (letters) with vacuolar degeneration of glandular epithelial (arrows), and congested blood vessels (arrows head) H and E 100× (G); proliferative inflammatory atrophy with severe lymphoplasmacytic inflammation surrounding the acinus, multifocal, lymphoplasmacytic prostatitis, note the markedly inflamed prostatic stroma H and E 40× (H); fibrous displacement of prostatic stroma (letter) and congested blood vessels (arrows) H and E 100× (I)

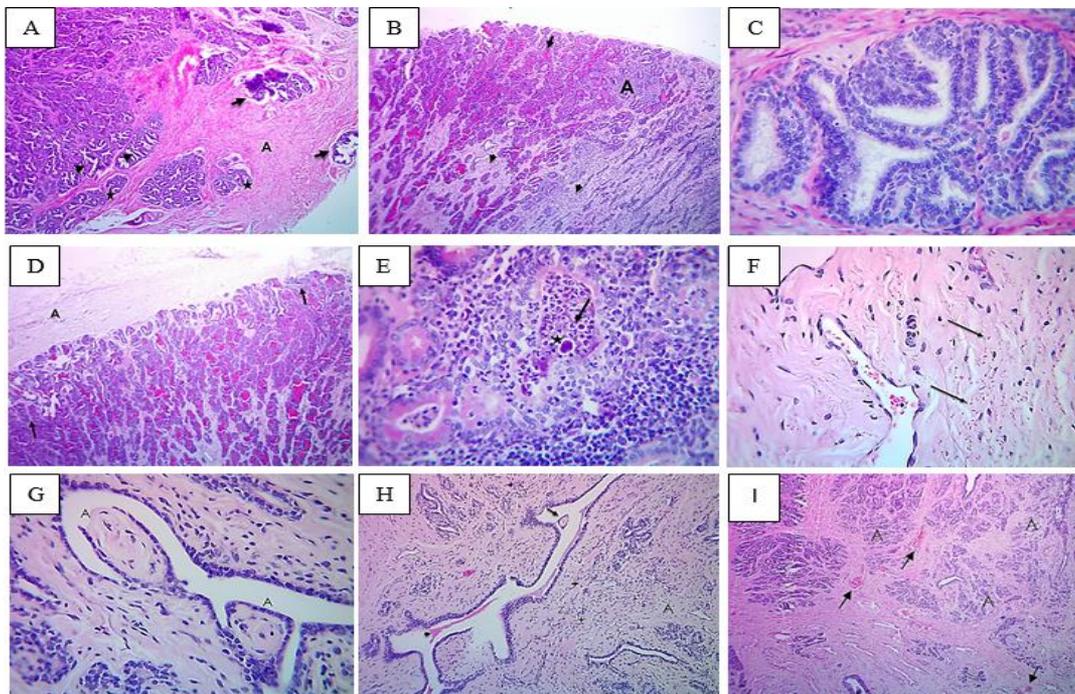


Fig. 4: Necrosis of some prostatic glands (arrow), hyperplasia of the glandular epithelium (head arrow), increase fibrous tissue stroma (letter), atrophy of some prostatic glands H and E 40× (A); Intestinal infiltration of lymphocytes (letter), presence of prostate concrete (arrow), increase fibrous tissue stroma (head arrow) H and E 40× (B); Intra luminal hyperplasia of glandular epithelium. H and E 400× (C); Subcapsular infiltration of lymphocytes (arrows). Thickening of the prostatic capsule (letter). H and E 40× (D); Infiltration of neutrophils (arrow), hyaline cast depositions (Star) H and E 400× (E); Extravasated RBCs (stars) in the prostatic stroma (arrow), H and E 400× (F); Polypoid projections in urethral ducts. H and E 400× (G); Polypoid projections in urethral ducts (arrow), presence of prostatic concrete (Head arrow) with increased fibromuscular stroma (letter) extravasated RBCs (stars) in the prostatic stroma, H and E 40× (H); Necrosis of some prostatic glands (arrow), hyperplasia of the glandular epithelium (head arrow), increase fibrous tissue stroma (letter), atrophy of some prostatic glands H and E 40× (I)

Table 3: Summary of lesions in each case

Cases	Pathological Findings
1	Fibromuscular hyperplasia Congested blood vessels Fibrous tissue displacement Increase fibrous tissue represented by increased mitotic activities.
2	Benign hyperplasia of epithelial lining glands Hormonal atrophy with a relative increase of interstitial stroma. Prostates showed atrophied glands admixed with glandular hyperplasia lined with interstitial fibrosis
3	Infiltration of mononuclear inflammatory cells. Proliferative inflammatory atrophy
4	Fibrous displacement of prostatic stroma, congested blood vessels, deposition of hyaline cast, interstitial infiltration of lymphocytes. Destruction of glandular epithelium and desquamation of glandular epithelial. Cystic alveoli were seen in some glands. The atrophied gland was identified, smooth muscle fiber hyalinization. Mass destruction of glandular epithelium. Polypoid projection in the glandular duct. Congested blood vessels. Interstitial edema in fibrous tissue in prostatic stroma. Prostatic concrete is seen as well. Vacuolar degeneration of epithelial lining of both glandular epithelia and urethra
5	Chronic prostatitis, large alveoli with Intra luminal hyperplasia of glandular epithelium, infiltration of lymphocytes in the prostatic stroma, cystic glandular structure (cystic alveoli). Destruction and necrosis of epithelial lining urethral ducts. Subcapsular infiltration of lymphocytes as well as thickening of the prostatic capsule, congested blood vessels with the presence of prostatic concretions, vacuolation of epithelial cells lining the glands, and infiltration of neutrophils (bizarre cells). Hyalin cast depositions
6	Intestinal infiltration of lymphocytes, presence of prostate concrete, increase fibrous tissue stroma, necrosis of some prostatic glands, hyperplasia of glandular epithelium, congested blood vessels, atrophy of some prostatic glands, Subcapsular infiltration of lymphocytes as well as thickening of prostatic capsule
7	Intra luminal hyperplasia of glandular epithelium, thickening of the prostatic capsule, polypoid projections in urethral ducts, increase fibromuscular stroma, extravasated RBC in the prostatic stroma, interstitial infiltration of lymphocyte