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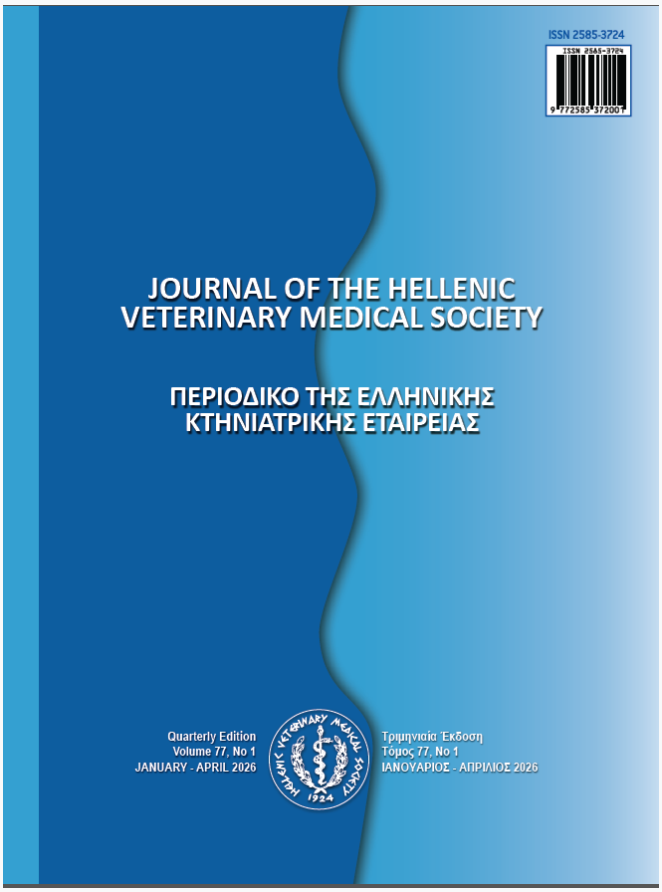

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Case report
Κλινικό περιστατικό

A case report of acinar type prostate cancer with urogenital differentiation in a Terrier dog

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ABSTRACT: In this presentation, a case of cystic adenocarcinoma of the prostate in a 13-year-old Terrier male dog is described pathologically. The patient was brought to the Selcuk University Veterinary Faculty animal hospital with complaints of cross-walking for two months, urinary incontinence and paralysis in the last two days. After the physical examination, the total prostate was removed by mass surgery and sent to the pathology laboratory. The prostate was found to be red, sticky, necrotic, and measuring 4 x 7 x 9 cm when viewed macroscopically. Tissue sections prepared after routine tissue processing procedures were stained with Hematoxylin Eosin (HE) and immunohistochemically (IHC) using PCNA antibody. Under a microscope, it was possible to identify acinar/tubular structures made of atypical tumor cells with or without many central lumens. It was realized that certain tumor cells had vacuoles in their cytoplasm and displayed squamous differentiation. Tumor cells with localized intracytoplasmic eosinophilic bodies (Melamed-Wolinska) were also detected. In some parts of the tumor, epithelial cells embedded in the stroma were seen in the form of "signet ring". In the immunohistochemical staining of prostate sections with PCNA antibody, severe immunoreactivity was observed in tumor cells. As a result of all these, a rare diagnosis of acinar type prostate adenocarcinoma with urogenital differentiation was made.

Keyword: Acinar; Adenocarcinoma; Differentiation; Prostate; Urogenital

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INTRODUCTION

The canine prostate is an oval-shaped, bilobed gland that surrounds the male urethra at the bladder outlet and is androgen-dependent. The canine prostate surrounding the urethra in the center and is bordered by a thin capsule of fibrous tissue. The canine prostate is anatomically, histologically, physiologically and functionally similar to the human prostate. (Ryman-Tubb et al., 2022).

Prostate adenocarcinoma is rare, extremely aggressive and malignant tumor of male dogs. In necropsy investigations, its frequency was reported to be 0.2-0.6%, and the age at diagnosis ranged from 5 to 17 years. Several investigations have determined that there is no evidence to imply that castration influences the development or course of the disease. (Bell et al., 1991; L'Eplattenier et al., 2006; Obradovich et al., 1987). However, some studies demonstrate that castrated male dogs have a higher incidence of prostate adenocarcinoma than uncastrated male canines (Johnston et al., 2000). Prostatic carcinoma is androgen-independent and metastasizes fast in 70-80% of cases (Sun et al., 2017). Systemic disease was seen in 29% of dogs with a clearly relevant prostate disease, lower urinary tract disease in 41%, gastrointestinal tract abnormalities in 28%, and locomotor problems in 13% (Krawiec & Heflin, 1992). It has been reported that Doberman, beagle, German short-hair, Scottish terrier, Shetland sheepdog, Airedale terriers are genetically predisposed to prostate adenocarcinoma (Krawiec & Heflin, 1992). Prostate adenocarcinomas are aggressive and it has been found that prostate adenocarcinomas frequently metastasize to various organs such as the pelvic and sublumbar lymph nodes, bones, and brain. It has been reported that mortality is high in prostate adenocarcinoma (Maxie, 2015).

Macroscopically, the prostate may appear asymmetrical and irregular. Microscopically, severe fibrosis is evident against tumor cells and the neoplasm is usually fairly firm (Meuten, 2020). Cyst formation in association with the neoplasm is common. Most prostates with carcinoma also appear to contain areas of hyperplasia (Maxie, 2015).

Prostatic urothelial carcinoma develop from urothelial cells of the prostatic urethra or periurethral ducts. Neoplastic cells have been reported to have plenty eosinophilic cytoplasm, hyperchromatic nuclei and a high mitotic index. Melamed-Wolinska bodies, which are intracytoplasmic eosinophilic bodies, have been found to be a crucial morphological characteristic in the identification of urothelial cell tumors (Palmieri et al., 2019). Signet ring cells, which are cells with cytoplasmic vacuoles, are another factor supporting the prostatic urothelial cell tumors diagnosis (Palmieri et al., 2022).In the acinar type of tumor, it contains microacini of various sizes and is within the fibromuscular stroma of a sclerotic structure (Lai et al., 2008).

This case report aims to contribute to the field of Veterinary Oncology through histopathological and immunohistochemical identification and typing of prostate adenocarcinoma.

CASE HISTORY

The patient was submitted to the Selcuk University Veterinary Faculty animal hospital with complaints of cross-walking for two months, urinary incontinence and hindlimb paralysis in the last two days. After the physical examination, the total prostate was removed by mass surgery and submitted to the pathology laboratory. The patient was discharged after the operation but animal owner reported to the veterinarian of our hospital that the dog died a week later.

HISTOPATHOLOGICAL METHOD

Tissue samples were fixed with 10% formol. Following routine tissue processing with the Leica TP1020 tissue tracking device, the tissues were embedded in paraffin. Hematoxylin-Eosin (HxE) staining was performed by taking 5 µm thick tissue sections from paraffin blocks. After staining, the preparations were examined under an Olympus BX51 light microscope and their photographs were taken (Olympus DP12, Tokyo, Japan).

IMMUNOHISTOCHEMICAL (IHC) METHOD

Fixe 5 µm thick tissue sections taken from the prostate for IHC staining were stained with the Bond™ polymer refine detection (Leica DS9800) kit procedure in an immunohistochemistry staining device (Leica, Bondmax). Prior to rehydrating in graded alcohols (Merck), tissues had been initially deparaffinized with temperature and dewax solution (Bond™, Leica AR9222). After each stage, sections were washed for at least three minutes in distilled water using washing solution (Bond™, Leica, AR9590). Following that, epitope uptake from the temperature source (Epitope 1 antigen retrieval solution, Bond™,

Leica, AR9961, citrate buffer, pH: 6, 100°C, 20 min) was applied to these sections according to the primary antibody properties used. Peroxidase block was applied to remove peroxidase activity. Post-primary and polymer applications were performed after reaction with proliferating cell nuclear factor antibody (PCNA, 1:100, Dako Denmark, M0879]) at room temperature. Following a five-minute incubation with 3,3'-Diaminobenzidine (DAB) at room temperature, sections were washed with distilled water before being contrast stained with Mayer Hematoxylin. Photographed after viewing sections with a binocular light microscope (Olympus BX51, Tokyo, Japan).

Macroscopically**;** it was observed macroscopically that the prostate was 4 x 7 x 9 cm in size, red in color and firm. Asymmetry was detected in the prostate (Figure 1.A). Necrotic areas and gelatinous spongy appearance were determined on the cross-sectional surface of the prostate (Figure 1.B).

Microscopically; numerous acinar/ductal structures, some of which had lumens, were identified microscopically, formed by atypical tumor cells (Figures A-D). Mucus was observed in some acini, and neoplastic cells were found to be embedded in a dense fibrous stroma. Intracytoplasmic eosinophilic bodies (Melamed-Wolinska) were detected in some tumor cells (Figure B). In some parts of the tumor section, the cells with a vacuole in the cytoplasm were detected, in the form of a "signet ring", embedded in the stroma, showing squamous differentiation in some places (Figure A-C). Perivascular mononuclear cell infiltration was also detected in the sections. Locally a small number of apoptotic cells and dense mitotic figures were seen (Figure A-C). In addition to these, cystic cavitations were detected as well as intense hyperplasia in the prostatic glands.

In the immunohistochemical staining of prostate sections with PCNA antibody, severe immunoreactivity was observed in tumours cells (Figure D).

DISCUSSION

Castration is not thought to be associated with prostate adenocarcinoma (Obradovich et al., 1987). However, one studies have reported a greater risk of prostate adenocarcinoma in castrated dogs compared to uncastrated male dogs (Johnston et al., 2000). The observation of prostate adenocarcinoma in an uncastrated male dog in this case supports the view that this may not be directly related to castration. On the other hand, the opinion that although the prevalence in dogs is quite low, it has a high fatality course and is mostly observed in older ages (Obradovich et al., 1987) was confirmed by our study.

In cases of prostate adenocarcinoma, it is recorded that the prostate may be macroscopically asymmetrical and irregular shaped (Maxie, 2015). The macroscopic asymmetry of the prostate seen also in this case; It is compatible with the view (Palmieri et al., 2022) that the prostate can enlarge asymmetrically and irregularly in prostate adenocarcinomas independent of invasion to circumambient organs.

Microscopically, in the present case, it was determined that acinar/ductal type prostatic adenocarcinoma findings came to the fore with the observation of numerous microacini structures formed by atypical tumor cells within the fibromuscular stroma of scirous structure. In addition to these findings,

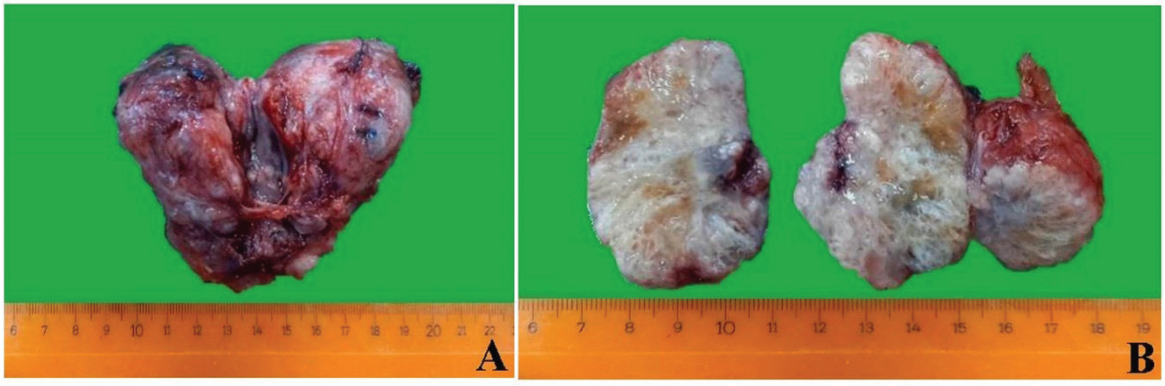

Figure 1. Macroscopic view of the prostate, **A:** Enlargement and asymmetrical appearance in the prostate, **B:** Necrotic areas and gelatinous spongy appearance on the cross-sectional surface of the prostate.

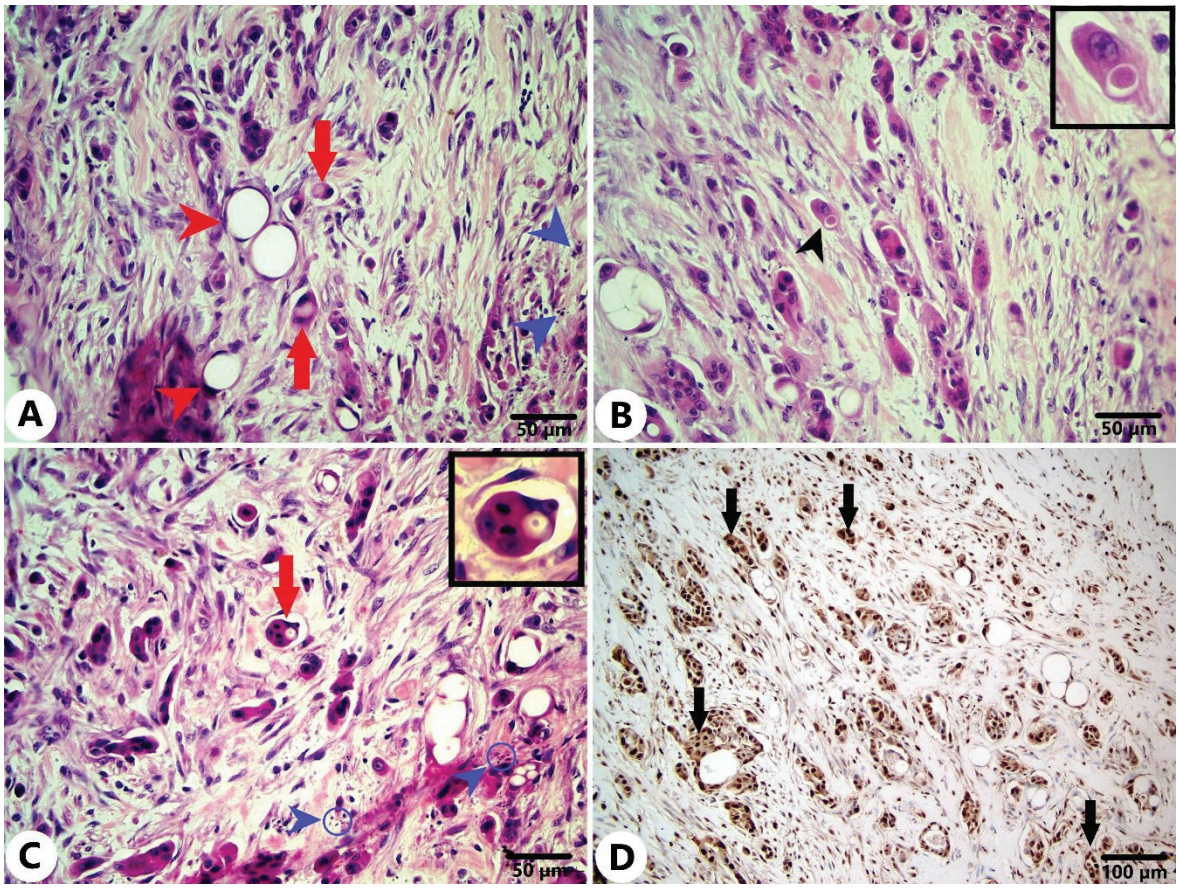

Figure 2. Histopathological and immunohistochemical findings of the tumor, **A:** Acinar formation within dense fibrous stroma (red arrowheads), apoptotic bodies (blue arrowheads), signet -cells shaped tumor cells (red arrow) x 40, HE, **B:** Intracytoplasmic eosinophilic inclusion bodies (Melamed Wolinska) (black arrowhead, inset) x40, HE, **C:** Signet-ring tumor cell and mitotic figure (red arrow, inset), apoptotic bodies (blue arrowhead) x 40, HE, **D:** PCNA positive immunoreactivity in tumor cells (black arrows), x 20, IHC.

tumor cells with intracytoplasmic eosinophilic bodies and locally cells with squamous differentiation in the form of "signet ring" and vacuoles in their cytoplasm were detected. It has been reported that intracytoplasmic eosinophilic bodies so called ''Melamed-Wolinska bodies'' and the cells with cytoplasmic vacuoles in the form of signet-ring are an important morphological feature in the diagnosis of urothelial cell tumors (Palmieri et al., 2022). When all these findings were evaluated together, it was concluded that a mixed form of prostatic adenocarcinoma and prostatic urothelial carcinoma was formed as phenotype in the present case. In addition, it was thought that hyperplasia and cancer may develop simultaneously, as in this case, and it would be beneficial to consider both in prostate enlargements.

One of the key molecules determining whether a cell will live or die is the proliferating cell nuclear antigen (PCNA) protein (Paunesku et al., 2001). PCNA, the measurement of proliferative activity is very important in assessing tumor grade, time to recurrence, and aggressiveness. Also is one of the nuclear markers used to indicate the proliferative phase of the cell cycle (Akçakavak et al., 2023; Kayaselçuk et al., 2002; Özdemir et al., 2022). The severe PCNA expression observed in tumor cells in this case can be considered as a sign that the tumor has an aggressive character. Furthermore, the fact that less apoptosis occurs despite unusual atypical cell proliferation, as observed in the present case, can be assumed an indication that the oncogenic mutation (mainly p53) may be severe.

The most common clinical manifestations in prostate adenocarcinomas are; constipation, pros-

tatomegaly, pain and hind leg paresis, stranguria, painful abdominal palpation, dysuria, hematuria, tenesmus, anorexia, weight loss. Due to metastasis of the tumor to the lower lumbar vertebrae, pelvis bones and long bones, weakening and hind leg movement disorders can be seen in animals. (Lévy et al., 2014; Maxie, 2015; Smith, 2008). In the current case, while clinical findings were compatible with prostate cancer, it was thought that cross-walking disturbances might have resulted from metastasis. But unfortunately, the necropsy of the dog could not be performed due to the reluctance of the animal owner.

Prostate adenocarcinomas are aggressive, and it has been found that prostate adenocarcinomas frequently metastasize to various organs such as the pelvic and sublumbar lymph nodes, bones and brain. It has been reported that mortality is high in prostate adenocarcinoma (Maxie, 2015). In this case, the formation of a large number of mitosis, severe PCNA expression and less apoptosis in tumor cells causes excessive proliferation of tumor cells and it is thought that metastasis may occur as a result of spreading in various ways. It was also learned that the patient, in this case, died one week after the operation. Since it is known that prostate adenocarcinoma metastasizes to various organs, it is important to follow the diagnosed patient from the point of metastasis in terms of the prognosis of the disease.

Prostate adenocarcinomas are mostly asymptomatic or show symptoms only in the last stages of the tumor and are seen in older animals. For this reason, periodic prostate inspections and cytological examinations, when necessary, especially in advancing ages, are recommended for early diagnosis.

Author Contributions

ATC and MBA performed histopathology and immunohistochemical staining. MO and MT made the final check of the manuscript. All authors read and approved the final version.

Conflict Of Interest

None declared by the authors.

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