Canine Prostate Carcinoma: Four Clinical Cases in Sexually Intact and Neutered Dogs

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ABSTRACT
Prostate cancer is one of the most important malignancies in men. In old men the frequency of prostate cancer at necropsy has been reported to exceed 40%. Dogs are the only large mammals other than humans with a significant incidence of spontaneous prostate cancer. Adenocarcinoma, transitional cell carcinoma and undifferentiated carcinoma are the most common histological type but the precise cell of origin in dog is not known. The incidence of prostatic carcinoma in dogs is low (0.2% - 0.6%). Prostatic carcinomas occur in sexually intact and neutered dogs and the risk increase in castrated dogs associated to pulmonary and bone metastases. The castration does not initiate the development of prostatic carcinoma in dog but does favour tumour progression. In men the early stage detection of prostate cancer can offer various therapies as radical prostatectomy, radial therapy, thermal ablation, anti-androgen therapy, chemotherapy. In dogs the diagnosis is often in advanced stage of the cancer and the survival time for dogs with prostate cancer is poor. The median time reported is 30 days after diagnosis. In this study we reported three cases of prostatic carcinoma in intact sexually dogs and one in a neutered dog. The sexually intact subjects were older (mean age = 10.5 years) and they had prostatic adenocarcinoma (PCA). The interval between castration and onset of prostatic problems was 3 years. All the dogs showed dysuria, macroscopic hematuria, dyschezia and ataxia. All dogs have been euthanized in order to relieve pain and suffering.

Keywords: Prostate; Carcinoma; Neutered Dog

1. Introduction
In human, dog and cat the prostate is a bilobed retroperitoneal gland, encircling the neck of the urinary bladder and the proximal urethra. The normal prostate is an exocrine gland with a tubuloalveolar structure, composed of a glandular component surrounded by a smooth muscle and connective tissue stroma. Regarding the vascular anatomy of the canine prostate gland, each prostatic lobe has an independent vascularization. The blood supply to each lobe is from the homolateral prostatic artery. Three small vessels arise from the prostatic artery (cranial, middle, and caudal) through the prostate gland. The prostatic artery is small, with a wall structure similar to muscular arteries. The prostatic vein is a small-size valved vein. The canine prostate gland has capsular, parenchymal and urethral vascular zones. The surface vessels of the capsule are predominantly veins and the diameter of the arterial vessels is larger than in veins. Trabecular vessels can be of two types: direct and branched. The prostatic parenchyma is supplied by trabecular vessel branches. Periacinar capillaries are fenestrated and form a circular net. The processes of myoepithelial cells embrace both the acinar and periacinar capillaries. The prostatic part of the urethra is supplied by an independent branch of the prostatic artery. The prostatic urethral part is drained by the prostatic vein, the vein of the urethral bulb and the ventral prostate veins. Urethralis muscles begin in the urethral prostatic part [1,2].

Prostate cancer is one of the most important malignancies in men. In old men the frequency of prostate cancer at autopsy has been reported to exceed 40% [3]. Dogs are the only large mammals other than humans with a significant incidence of spontaneous prostate cancer [4]. Adenocarcinoma, transitional cell carcinoma and undifferentiated carcinoma are the most common histological type [5], but the precise cell of origin in dog is not know. The incidence of prostatic carcinoma (PCA) in dogs is low (0.2% - 0.6%) in necropsy studies [6], but it shares several of the features of the disease in humans [7]. Tumour growth outside the prostate is common in dog and frequently there are pulmonary a bone metastases [6]. The prostate is an androgen-dependent gland. Or-
chiectomía resultó en regresión de volumen prostático en el perro con hipertrofia prostática (BPH) y administración de andrógeno a los perros castrados causa hipertrofia del gland [8]. Por lo tanto, es sorprendente encontrar un alto porcentaje de carcinoma prostático en perros castrados [6]. En el cáncer prostático en el perro es un tumour que lleva un mal pronóstico.

En este estudio se reportaron cuatro casos de cáncer prostático en perros intactos (3) y neuterados (1) perros.

2. Materials and Methods

Tres perros de raza y un Border Collie adulto masculino fueron admitidos en el Hospital Veterinario de la Escuela de Medicina Veterinaria de la Universidad de Parma con síntomas clínicos de enfermedad prostática. La edad varió entre 6 y 12 años (media de edad 9.25 años). El peso varió entre 22 kg y 35 kg (media 26 kg) (Table 1). Las dimensiones y la consistencia del gland prostático se medieron usando ultrasonografía convencional. La enfermedad fue diagnosticada usando biopsias de próstata guiadas por ecografía. El diagnóstico se hizo mediante citología. La ecografía fue realizada usando un transductor de fase-array de 3.5 a 7.5 MHz. Para la ecografía Doppler, la muestra volumétrica se dibujó alrededor del gland prostático sin incluir tejido adyacente. Tres mediciones se tomaron.

Table 1. Age and weight of dogs.

<table>
<thead>
<tr>
<th>Dog</th>
<th>Weight</th>
<th>Age</th>
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<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>12</td>
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<tr>
<td>Mean</td>
<td>26</td>
<td>9.25</td>
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4. Discussion and Conclusions

Prostatic carcinoma is a definition with different meanings and mostly the neoplasia is adenocarcinoma (prostate glandular tissue) as in human. In dogs we found adenocarcinoma, transitional cell carcinoma, mixed carcinoma and squamous cell carcinoma. Prostatic carcinomas occur in sexually intact and neutered dogs and pulmonary and bone metastases are common [6]. Some Authors reported that the risk to be associated to pulmonary
and bone metastases increase in castrated dogs [4]. The frequency of prostatic carcinoma in dog is low and the prevalence reported from necroscopy studies ranges between 0.2% and 0.6% [6]. The prevalence of PCA in neutered dogs is not well cleared. The castration does not initiate the development of prostatic carcinoma in dog but does favour Tumour progression [3]. Human and canine prostate cancer had important difference: human prostate neoplasia is highly dependent upon androgen (growth factor), in fact in the men androgen deprivation is a good therapy for prostate cancer. In human males there are pre-malignant marker lesions with risk factors such as familial, diet, inflammation disease, in dog the pre-malignant lesions are uncommon and castration is a risk factor for prostate cancer development. In men most prostate cancer are latent; in dog the aggressiveness of prostate cancer is high. The early stage of human prostate cancer is an intra-epithelial neoplasia (PIN) in dog the relationship between PIN and prostate carcinoma is unknown. Canine prostate neoplasia does not express androgen receptor and the castration may be associated with an increased risk of prostate adenocarcinoma [4,10]. Castration modified the stromal component of the gland from primarily actin-positive smooth muscle cells to vimentin-positive mesenchymal cells. This condition could play a role in the development of prostate cancer in neutered dogs [11]. Human prostatic carcinoma arise in the peripheral zone, in dog is unclear but there is evidence that the neoplasia may stem from ductal epithelium adjacent to the periurethral zone [4]. Human carcinoma is graded using the Gleason system that is a highly accurate predictor of disease progression [4]. Much less is known regarding the pathogenesis and definitive origin of canine prostatic neoplasia. Neoplastic canine prostate frequently contain foci of benign hyperplasia (BPH), cyst (Border Collie) and inflammation. Survival time for dogs with prostate cancer is poor. The median time reported is 21 days [12] and 30 days [4] and most of patients were euthanized at the time of diagnosis. In our cases Border Collie were euthanized two month after cytological diagnosis of carcinoma. In men the early stage detection of prostate cancer can offer various therapies as radical prostatectomy, radical therapy, thermal ablation, anti-androgen therapy, chemotherapy. In dogs the diagnosis is often in advanced stage of the cancer. At this time is not universally accepted the prostatectomy because the prostate cancer is associated with a high rate to metastasis and the surgical procedure has a significant postoperative morbidity and is not clear that this procedure will improve survival [4]. Complication of radiation therapy as chronic colitis, gastrointestinal perforation, necrotic ulceration and chronic cystitis have been reported [13]. It is evident that prostate cancer in dog is aggressive with poor prognosis. We think that when the dogs have advanced stage of benign prostatic hyperplasia before castration could useful performed prostatic biopsies to confirm the absence of cancer because the orchietomy can favour cancer progression.

REFERENCES


Figure 7. Dog lung metastatic neoplastic cells arranged in irregular tubules and solid cords (white arrow H&E 10×).


