Non-inflammatory diseases of the canine prostate gland

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INTRODUCTION
Prostatic diseases occur more frequently in dogs than cats or any other domestic species. This may relate to the continued expansion of the gland throughout life in the dog that enables development of prostatic hyperplasia in this species. Such disorders are more common in older intact male dogs and include squamous metaplasia, hyperplasia, inflammation, neoplasia and cysts. The canine prostate gland is located predominantly in the retroperitoneal space, usually at the pelvic inlet within the pelvic canal, and completely encircles the urethra. The small feline prostate gland, however, is located more distal, does not entirely surround the urethra, and is rarely associated with clinical disease.

This article, the first in a two-part series on prostatic disease in dogs, reviews the non-inflammatory conditions of the gland.

SQUAMOUS METAPLASIA
Squamous metaplasia of prostatic epithelial cells (Fig. 1) results from excessive oestrogenic stimulation. The most common endogenous cause of this is a functional Sertoli cell tumour. Exogenous administration of oestrogenic compounds is another cause. Squamous metaplasia can lead to ductal obstruction and cyst or abscess formation.

Oestrogens can produce prostatic atrophy due to testosterone inhibition, although mild prostatomegaly may result with chronic exposure. Secondary development of cysts or abscesses may further enlarge the gland. Sertoli cell tumour will produce a palpably abnormal testicle with atrophy of the contralateral testicle. Unilateral or bilateral cryptorchidism may be present. Bilateral testicular atrophy occurs with exogenous hyperoestrogenism. Additional signs of hyperoestrogenism include alopecia, hyperpigmentation and gynaecomastia.

Haemogram findings may be consistent with oestrogen toxicity and include a non-regenerative anaemia, thrombocytopenia, granulocytosis or granulocytopenia. Radiography and ultrasonography may demonstrate prostatomegaly. Hypoechoic fluid-filled cavities may also be seen ultrasonographically if cyst or abscess formation has resulted. Increased numbers of squamous cells will be seen in prostatic fluid, with or without inflammatory cells.

Fig. 1: Microscopic features of prostatic epithelial squamous metaplasia: islands of squamous epithelial cells (arrows) replace normal cuboidal prostatic alveolar epithelial cells.
This lesion is reversible and treatment involves removing the oestrogenic source, either by castration if Sertoli cell tumour is causative, or cessation of exogenous oestrogen therapy.

**BENIGN PROSTATIC HYPERPLASIA**

Benign Prostatic Hyperplasia (BPH) (Fig. 2), the most common canine prostatic disorder, is present either grossly or microscopically in almost 100% of sexually intact adult male dogs over the age of seven years, as well as in animals treated with androgenic hormones. It arises spontaneously in the gland as a consequence of ageing and endocrine influence, and may begin as early as 2-3 years of age, becoming cystic after 4 years of age. Whilst its pathogenesis remains unresolved, dihydrotestosterone (DHT) is considered important in promoting hyperplasia predominantly of the glandular component, especially acinar basal cells. Testosterone produced by the testes is converted to DHT by 5-α-reductase in prostatic epithelial cells, and DHT interacts with gland receptors to regulate prostate growth. Since BPH regresses following castration, androgens are also considered essential for its maintenance. Androgen action alone, however, cannot explain BPH, and oestradiol and various mitogenic growth factors are also implicated in its pathophysiology. Chronic inflammation may additionally play a role in disease progression.

 Although most dogs develop BPH, many show no clinical signs. Clinical signs when present may be intermittent and include constipation, blood stained urethral discharge, and blood in the urine or semen. Affected dogs are not sick, and clinical examination (including haemogram and serum biochemistry) is otherwise normal except for prostatomegaly which is usually symmetric and painless. Dysuria is less common as the gland expands uniformly and away from the urethra, in contrast to BPH in man.

On cytological examination, prostatic massage or ejaculate specimens may be haemorrhagic with mild inflammation without evidence of sepsis or neoplasia. Urinalysis may be normal, but some erythrocytes and slightly increased numbers of squamous epithelial cells may be present. A urine culture obtained by cystocentesis should be negative, (if positive, consider concurrent prostatitis). Prostatomegaly is evident on radiography, and ultrasonography demonstrates a normoechoic to slightly hyperechoic, symmetrically enlarged gland with a relatively smooth contour, with or without small fluid-filled cysts.

A biopsy is required for definitive diagnosis. Two microscopic forms of BPH occur: Glandular hyperplasia mostly occurs in dogs below four years of age and is believed to progress to complex hyperplasia in older dogs, with increased stromal tissue and occasionally cystic change. Diagnosis, however, is usually based on physical examination if history and signs are suggestive, and cytological examination, culture and biopsy are rarely indicated.

**Treatment**

BPH responds well to treatment. In cases where clinical signs are present, castration is the most effective and recommended treatment for most dogs, with prostatic size decreasing by 50-70% and clinical signs alleviated within three weeks of surgery. Conversely, medical treatment is often considered in cases where the risk of anaesthesia and surgery is unacceptable, if the affected dog is required for breeding, or if owners do not wish their dog to be castrated.

Finasteride, a 5-α reductase inhibitor, is a compound that has been a focus of medical treatment for BPH in humans. Although not specifically licensed for veterinary use, this drug is used to reduce prostate size in affected dogs. It has been shown to have teratogenic potential in humans, however, and is present in semen of treated patients, so its use may not be advisable for breeding males.

The progestogen delmadinone acetate (Tardak®) is also commonly used, and one of its adverse effects is to induce prostatic squamous metaplasia.

Although oestrogenic compounds such as diethylstilboestrol can effectively treat BPH, they are not valuable long-term treatments and their use cannot be recommended due to severe toxic effects on the bone marrow (anaemia, thrombocytopenia, and pancytopenia) as well as causing prostatic squamous metaplasia and decreased spermatogenesis.

For dogs with clinically silent BPH, or those that are being managed medically, regular evaluation at 4-6 monthly intervals is recommended to monitor for disease progression or complications. Due to the deleterious effects of many drugs used for medical treatment of BPH, castration of breeding dogs is advised once breeding life ends.

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**Fig. 2:** Gross appearance of BPH: urinary bladder (asterisk) and bilaterally symmetrically enlarged prostate gland (arrow).
NEOPLASIA

Of the domestic species, primary prostatic neoplasia occurs most frequently in dogs, with few cases reported in cats. Primary neoplasia is rare accounting for about 5% of all prostatic diseases.

Prostatic adenocarcinoma (PAC) (Fig. 3) is most common and considered to arise from ductal epithelium, although others including transitional cell carcinoma, leiomyosarcoma, and haemangiosarcoma have been reported. PAC occurs most frequently in older animals over ten years of age, and occurs in intact and castrated males. Studies suggest that the risk of PAC may be increased in neutered, compared to intact, male dogs. Although castration does not seem to initiate development of this neoplasm, it may favour its progression. High grade prostatic intraepithelial neoplasia (HGPIN) also occurs in many older dogs with and without prostatic adenocarcinoma, and is suggested to be a precursor to adenocarcinoma in the dog, as in man.

Neoplastic prostate glands are often markedly, asymmetrically enlarged and may impinge on abdominal organs causing faecal tenesmus or dysuria. Haematuria, anorexia and weight loss may also occur. In some cases dogs may initially present to a veterinarian with signs of myelopathy or lameness that are manifestations of skeletal metastases. Radiography may demonstrate prostatomegaly with or without mineralisation, and sublumbar lymphadenomegaly. Metastatic disease may also be evident in the lungs, axial skeleton or appendicular skeleton. Ultrasonography will similarly demonstrate prostatomegaly with an irregular contour and hyperechoic parenchymal foci. Neoplastic epithelial cells may be seen cytologically on evaluation of urine or prostatic fluid. Although biopsy is required for definitive diagnosis (Fig. 4), studies suggest that many cases of neoplasia are missed with this procedure alone, and biopsy of the medial iliac lymph nodes and thoracic radiographs may also be advisable. Haemogram and serum biochemistry are usually normal.

Unfortunately treatment of PAC is usually unrewarding and does not usually respond to androgen deprivation. The lack of markers for prostatic carcinoma makes early diagnosis difficult, and extraprostatic spread (prevalence may be as high as 80%), especially to regional lymph nodes and bone (most frequently the lumbar vertebrae and pelvis), is common. Dogs with skeletal metastases may also be younger at the time of diagnosis than dogs without bone metastases. Surgical prostatectomy is rarely recommended as PAC is not usually diagnosed at an early stage, and this technique often results in urinary incontinence. The prognosis is therefore grave.

PROSTATIC CYSTS

Cystic lesions in the prostate gland are variable. Although intraprostatic cystic change associated with BPH comprises numerous small cysts within the gland parenchyma, true cysts are generally larger, centrally cavitated and fluid-filled with a distinct wall. Such cysts may arise within the parenchyma (retention cysts) or outside the gland (paraprostatic cysts) (Fig. 5). Their pathogenesis is unclear, but while some are considered to be of prostatic origin, some are thought to arise as remnants of the uterus masculinus. Some cysts may develop due to ductal obstruction with glandular accumulation of prostatic secretion.
Cystic prostate glands may be asymmetrically enlarged on rectal examination, and although many cases may show no clinical signs, larger cysts can impinge on abdominal organs causing faecal tenesmus or dysuria. Complications due to local or systemic bacterial infection can also produce signs of haematuria, pain, pyrexia, sepsis, and shock. Cysts or irregular prostatic contour may be evident on radiographic and ultrasonographic examination. Radiography may also demonstrate mineralized foci in some cysts, and ultrasonographically, cysts may be hypoechoic to anechoic with smooth internal margins. Haemogram and serum biochemistry are usually normal, although a neutrophilic leucocytosis with or without a left shift, and toxic neutrophil changes may be present. Urinalysis is usually normal, but increased red blood cells or inflammatory cells may be seen if the cyst communicates with the urethra and is haemorrhagic or has associated inflammation. If aspirated, cyst fluid is usually yellow to red-brown with low numbers of inflammatory cells and a higher protein content than the patient’s urine.

Current treatment recommendations are similar to those for prostatic abscesses and include surgical procedures such as debridement and omentisation, drain insertion, marsupialisation or subtotal prostatectomy.

The second article in this series, to be published in the next issue, will consider inflammatory disorders of the prostate gland in dogs.

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FURTHER READING


1. The most common disorder of the canine prostate gland is:
   a. Prostatic cyst
   b. Prostatic abscess
   c. Squamous metaplasia
   d. Prostatic adenocarcinoma
   e. Benign prostatic hyperplasia

2. The most common endogenous cause of squamous metaplasia of the prostate gland is:
   a. Lymphoma
   b. Sertoli cell tumour
   c. Leydig cell tumour
   d. Squamous cell carcinoma
   e. Prostatic adenocarcinoma

3. Squamous metaplasia in the prostate gland can be associated with all except:
   a. Regenerative anaemia
   b. Thrombocytopenia
   c. Hyperoestrogenism
   d. Cryptorchidism
   e. Granulocytosis

Readers are invited to answer the questions as part of the RCVS CPD remote learning program. Answers appear on page 99.