Diagnostic possibilities in the management of canine prostatic disorders

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ABSTRACT: Various prostatic disorders are described in older intact dogs. Progression of disease commences quite often in dogs aged 5.5 years or older. Clinical symptoms are transient in the beginning, and are difficult to recognize. In fact, patient feels very little, if any, discomfort as troubles develop subsequently. As an exception to the rule there is acute inflammation, symptoms of which are severe, sometimes even life threatening. Diagnosis not meticulously established, when procedure is not met properly, (e.g. recognition of prostatitis without identification of infectious agent) this may result in development of chronic disease, which is often hard to manage. Rectal palpation should be part of routine examination in all older dogs, while correct diagnostic protocol should follow. By means of precise diagnostic protocol, we are able to identify the problem early, often in the curable stage of disease; therefore we are able to maintain fertility of the patient, as well. So far, described prostatic disorders are benign hyperplasia (BPH), squamous metaplasia, prostatic inflammation, both acute and chronic, prostatic cysts and abscesses and neoplasia.

Keywords: dog; prostate gland; urology

Contents

1. Prostatic disorders

Older intact male dogs of all breeds are preferably affected. According to some authors, middle and big size breeds are prone to development prostatic disease, with Doberman pinscher and German shepherd appear being affected more frequently than other breeds (Krawiec and Heflin, 1992). Prostatic disorders include benign prostatic hyperplasia, squamous metaplasia, prostatic inflam-

mation, prostatic abscesses and cysts, as well as neoplasia. Table 1 describes clinical symptoms associated with prostatic disorders in dogs.

1.1. Benign prostatic hyperplasia (BPH)

BPH is a spontaneous, age-dependent change in the structure of the gland of humans, dogs and chimpanzees (Berry et al., 1986; Johnston et al., 2000). In dogs, hyperplasia affects mostly epithelial cells, while in humans the process takes place more frequently within the stroma of the gland (Isaacs, 1984; Heible and Caine, 1986). Although the term hyperplasia is widely used, changes in both the number (hyperplasia) and the size (hypertrophy) of cells always happen. Anyway, in the dog, hyperplasia of the cells is supposed the dominant event (Zirkin and Strandberg, 1984). Prostatic growth, as well as its secretion is controlled by 5-alpha dihydrotestosterone (DHT), originating from testosterone (T) after cleavage by 5-alpha reductase (Berry et al., 1986). In older dogs, the oestrogen/androgen ratio is rapidly changing, when oestrogene predominates. Some authors suggest that the main reason of this change is in decreasing of androgen level, while concentration of oestrogen is rather stable (O'Shea, 1962). However, some other studies confirm that in dogs suffering from BPH, level of oestrogenes, in both serum and prostatic fluid, is significantly elevated compare to young animals (Cochran et al., 1981).

1.2. Squamous metaplasia of the prostate

The term squamous metaplasia describes pathophysiological, as well as pathomorphological entity. It may be part of a more complex prostatic disease, with some other disorder dominating. Mucous membrane and submucosal layer of prostatic urethra, stroma of the gland and periurethral ductal epithelium, are all carriers of oestrogen receptors (Schulze and Barack, 1987). Squamous metaplasia develops after exposure of these receptors to oestrogen stimulation. According to literature, after treatment by estradiol-cyclopentylpropionate, squamous metaplasia has been diagnosed in about 67% of exposed patients (Leeds and Leav, 1969). The same situation can be observed in patients suffering from oestrogen-producing Sertoli cells tumor of testicles (Leeds and Leav, 1969; Lipowitz et al., 1973; Merk et al., 1986). Short-term administration of oestrogen results in metaplasia of region around prostatic urethra and periurethral ductal tissue, while long-term exposure makes whole gland metaplastic. Metaplastic cells are subsequently becoming inactive and may lead to stasis of prostatic fluid within the gland, the situation likely responsible for creating cysts and/or abscesses (Johnston, 1985; Jacobs et al., 1988; Barsanti and Finco, 1989).

1.3. Prostatic cysts

Prostatic cysts are most often observed as a result of benign prostatic hyperplasia. Multiple retention cysts frequently occur (Dorfman and Barsanti, 1995a). As quite a different problem, paraprostatic cysts sometimes develop, while, in fact, there have very little to do directly with the prostate gland (Johnston et al., 2000). Etiopathogenesis of retention cysts has not been recognized exactly, but there is no doubt, various factors, such as hyperestrogenisation, either endogenous or exogenous, play a role. Hyperestrogenisation, for example, causes stasis of prostatic fluid within excretory ducts and is triggering factor of squamous metaplasia. Both these factors put the patient into risk of developing prostatic retention cysts (Olson et al., 1987b; Barsanti and Finco, 1989). Retention cysts as a consequence of sertoli cells tumor has been described, too (Spackman and Roth, 1988). Retention cysts are present within the glandular tissue; they are encapsulated, containing either clear or cloudy fluid (White et al., 1987).

Paraprostatic cysts are single or multiple structures often invading the space in between prostate gland and urinary bladder. They are big, sometimes obstructing pelvic inlet (Olson et al., 1987b). They can compress the descending colon and rectum, as well as other pelvic organs and structures. They can be even factor in developing perineal herniation (Head and Francis, 2002). Paraprostatic cysts probably originate from persistent uterus masculinus (Barsanti, 1995). Sometimes they undergo mineralization (Girard and Despots, 1995), so we can occasionally find segments of cartilagineous or osseous metaplasia within these cystic structures (Girard and Despots, 1995; Wright et al., 1996).

1.4. Prostatic inflammation

The inflammatory process of the prostate gland is not an uncommon urologic disorder in older intact

male dogs (Krawiec, 1994), as lower urinary tract infection generally comes together with prostatic infection. On experimental animal models, it is almost impossible to produce urinary tract infection, while avoiding the prostate gland and vice-versa (Ling et al., 1991). In healthy dogs, prostatic tissue discharges so called prostatic antibacterial factor (PAF) (Barsanti and Finco, 1989). PAF is a low-molecular peptide, containing zinc, responding to bacterial infestation. It is thermo-stable water-solubile substance. The most frequent etiological factor of prostatitis is ascending infection of an aerobic microflora from the urethra.

Hematogenous route of infection from testitis and epididimitis is also possible, as well as in case of septic disease (Dorfman and Barsanti, 1995b). *Escherichia coli* has been the most frequently found pathogen so far, but *Staphylococcus aureus, Klebsiella* spp., *Proteus mirabilis, Mycoplasma canis, Pseudomonas aeruginosa, Enterobacter* spp., *Streptococcus* spp., *Pasteurella* spp., and/or *Haemophillus* spp. can also be found. Even *Brucella canis* can spread into prostate gland, but as a main target, remains in the testicles and epididimis (Ling et al., 1983; Krawiec and Heflin, 1992; Dorfman and Barsanti, 1995b).

In mycoses, *Blastomyces dermatitidis, Cryptococcus neoformans* and *Coccidoides* immitis play a dominant role. Prostatic abscesses develop either after fusion of small areas of infection within the gland, or after infection of prostatic cysts (Baker and Lumsden, 1999).

1.5. Prostatic abscesses

Abscesses develop due to chronic infection, if the infection is not treated or if it is out of control. Infection of prostatic cysts or early stages of neoplasia are factors, as well (Christie, 1983; Barsanti and Finco, 1989). Spheric lesions subsequently filled with purulent exudate occur, enclosed by thick capsula. They are variable in size and number, containing *Escherichia coli* in about 70% of cases, while anaerobic microorganisms can be found in 19% and *Mycoplasma* in 1% of patients (Mullen et al., 1990).

1.6. Prostatic neoplasia

Of all patients suffering from prostatic disorders, only 5% do have malignant tumors (Barsanti and Finco, 1989). The most frequent type of neoplasia observed in dogs as well as humans is malignant adenocarcinoma (PCA) (Obradovich et al., 1987; Barsanti and Finco, 1989). Incidence of PCA varies from 0.28% to 0.6% (Weaver, 1981).

As in humans, prostatic cancer in dogs can cause problems of older animals. Average age of affected dogs is about 9 years (Bell et al., 1991; Krawiec and Heflin, 1992). PCA is prone to metastasis to lumbar lymph-nodes, both inner and outer, to the vertebral body and to the lungs (Durham and Dietze, 1985). The other targets for metastasis are the bladder neck, ureters, colon and pelvic muscle (Barsanti and Finco, 1989).

Some clinical studies dealt with incidence of prostatic cancer in consequence with previous orchidectomy (Obradovich et al., 1987; Bell et al., 1991). One of them actually proved that in castrated dogs the risk factor of developing PCA is 2.38 fold higher than in intact ones (Bell et al., 1991). On the other hand – unlike in humans – malignant prostatic tumour growth in dogs is not involved by decrease of androgen level in serum (anti-androgen therapy, castration). As a result, low level of andro-

Table 1. Clinical symptoms associated with prostatic disorders (modified from Barsanti and Finco, 1986)

Fecal tenesmus	Dysuria	Urethral discharge	Systemic symptoms*	UTI
BPH		BPH		
cysts	cysts	cysts	cysts	
abscesses	abscesses	abscesses	abscesses	
neoplasia	neoplasia	neoplasia		
		bacterial prostatitis	bacterial prostatitis	bacterial prostatitis

UTI = urinary tract infection

*symptoms = including depression, lethargy, fever, anorhexia, pain

gen receptors expression in canine prostatic tumors has been suggested (Bell et al., 1991; Johnston et al., 2000; Leav et al., 2001).

Orchidectomy in dogs is associated with massive reduction of androgen-dependent epithelial cells, while basal cells proliferation often follows (Mahapokai et al., 2000). Therefore, it is highly likely that prostatic carcinoma of the dog originates from these basal cells (Leav et al., 2001). Moreover, in human androgen-independent prosatic carcinoma, the gene expression reflecting presence of basal cells is frequently observed (Bui and Reiter, 1999).

Ductal basal cells reportingly differ from basal cells present within glandular tissue, reacting differently to neoplastic proliferation. Glandular basal cells play a role in BPH, accelerating their growth with age, while from ductal basal cells prostatic cancer can develop (Leav et al., 2001). Castration itself cannot be a real trigger of prostatic cancer. According to some authors, however, it can facilitate development of malignancy by stimulation of androgen-independent basal cell proliferation (Teske et al., 2002).

In other tumors, transitional cell carcinoma of ductal epithelium (Barsanti and Finco, 1989), squamous cell carcinoma (Leib et al., 1986), leiomyosarcoma and lymphoma (Mainwaring, 1990) can develop.

2. Diagnostic possibilities and their usefulness

2.1. Physical examination

Examination is based on general health evaluation by means of trias, hydratation scoring and cardiovascular and respiratory status. After that we proceed with specialized urological examination. We start with rectal palpation with assisted caudodorsal abdominal pressure, shifting the gland to the pelvic inlet. This is easiest to achieve on a standing patient. On the medium-sized dog, the prostate is physiologically the size of a walnut, with a smooth surface, solid consistency, free, isothermic and does not cause pain to the animal during examination (Dorfman and Barsanti, 1995b).

Symetry is evaluated after the central sulcus is identified on the dorsal surface of the gland. From this sulcus, both right and left lobes of the same size originate (Rogers et al., 1988). In giant breed dogs the prostate is often barely palpable and diagnostic ultrasound may be the only dependable method of evaluation of size and inner structure of the gland. Anyway, prostatic rectal palpation is considered the basic non-invasive method and should be utilized as a screening method whenever possible (pre-vaccination e.t.c.). In case of any doubt during rectal palpation, further more specific examination should follow. Table 2 shows the usual laboratory findings in prostatic disorders of the dog.

2.2. Examination of blood and urine

Blood sampling and blood biochemistry is important mainly for patients with systemic symptoms. The screening parameters are those preformed widely during routine blood examination, and are often readily available. On the other hand, urinalysis (the same as rectal palpation) is a must, whenever prostatic disorder is suspected. Leucocytosis with the left-shift and neutrophilia is symptomatic for *acute inflammation*, while in *chronic prostatitis,* the blood count may be within these limits (Dorfman and Barsanti, 1995a). Biochemical parameters are not so specific in patients without systemic alteration, but in one study, alcalic phosphatase levels have been elevated in 35% of animals with experimentally-induced chronic bacterial prostatitis (White and Williams, 1995).

Urinalysis reveals haematuria, leucocyturia and bacteriura in both acute and chronic inflammation (Dorfman and Barsanti, 1995a). Some interesting results may be observed in patients with *squamous metaplasia*. Haematology reveals symptoms of oestrogen toxicity, while biochemical parameters are often without significant alterations (Isaacs, 1984). In prostatic cysts, a haemorrhagic or yellowish discharge from urethra, independent to urination and cytologically different from urine can be observed. The biochemical properties of this fluid are different from those of urine as well. Usually, it is rich in proteins (Barsanti and Finco, 1989). In *prostatic abscesses*, the blood count with white cell elevation is often observed.

The blood count reveals leucocytosis with the left-shift and neutrophilia in up to 75% of patients (Dorfman and Barsanti, 1995a), while the changes are far more profound with septic peritonitis developing following rupture of the abscess. We can also find proteinuria, haematuria, leucocyturia and bacteriuria, while in well-encapsulated abscesses we observe no such changes.

Out of the biochemical parameters, alcalic phosphatase elevation (the same as in chronic inflammation) is frequently found (Hardie et al., 1984; Mullen et al., 1990), while in one study, 40% of patients had hypoglycemia and in 10% azotemia were observed (Mullen et al., 1990).

In *prostatic neoplasia*, no specific laboratory findings are to be expected. However, blood biochemistry reveals uraemia after obstruction of ureters or urethra by the tumor. Blood count is usually within the limits, in case of concomitant infection, leucocytosis and neutrophilia with the left-shift is observed (Barsanti and Finco, 1989; Bell et al., 1991). Of less-specific parameters, decrease in level of calcium (though the reason has not been clearly established as of yet) is occasionally found and elevation of serum alcalic phosphatase can be seen in about 50% of patients (Bell et al., 1991).

Various findings, such as haematuria and leucocyturia are revealed during urinalysis, while some atypical cells are found during microscopy in 17% of cases (Bell et al., 1991).

2.3. Examination of prostatic fluid and semen

Prostatic fluid is expelled during ejaculation, or it can be obtained by prostatic massage. In the case of bacterial infection, where cystitis is suspected, cultivation of semen and prostatic fluid along with cytology is strongly recommended (Barsanti and Finco, 1984, 1989).

The changes in semen quality with the respect to infection depend basically on the infectious agent involved. After experimental infection with *E. coli,* there were no changes in sperm concentration, motility, or morphology for 5 weeks (Barsanti et al., 1986). However, chronic infection affects motility, as well as concentration of defect spermatocytes and fertility of the individual.

During cytology, finding of neutrophyles, macrophages, erytrocytes or free bacteria is not uncommon (Peter et al., 1995). In semen or prostatic fluid in healthy dogs, the concentration of bacteria should not exceed 10 000 in 1 ml. In quality, cultivation of prostatic fluid reveals same results as direct cultivation of prostatic tissue in 80–100% (Ling et al., 1990). In squamous metaplasia, flat epithelial cells are found in prostatic fluid in high numbers (Thrall et al., 1985); in case of hyperplasia, prostatic fluid is haemorrhagic.

Abscedation makes prostatic fluid purulent and/or haemorrhagic and cultivation reveals both aerobic and anaerobic bacterial infection. On the contrary, during neoplasia, prostatic fluid contains abnormal epithelial cells. These abnormal cells are usually big, some with anisocytosis and anisocaryosis. The cytoblasts are irregular, sometimes mitoses can be found.

Cytological finding is, however, only supportive for the final diagnosis. There is a substantial variability in shape and structure of epithelial cells (Thrall et al., 1985). In human medicine, various prostatic markers are used in establishment of final diagnosis. Among the criteria of interest, pH changes and specific gravity of prostatic fluid, as well as cholesterol, zinc, copper, iron, calcium or magnesium prostatic fluid concentration are accepted as significant factors. Even though there were attempts to discover such factors playing role in canine prostatic inflammation, there were no parameters significantly involved while infection was induced experimentally (Branam et al., 1984).

Table 2. Usual laboratory findings in prostatic disorders of the dog (modified from Barsanti and Finco, 1986)

Disorder	Leukocytosis	Hematuria	Pyuria	Bacteriuria	HPF	PPF	PF bacteria
BPH	–	+	–	–	+	–	–
Prostatic cysts	–	–	–	–	–	–	–
Acute prostatitis	+	+	+	+	–	–	–
Chronic prostatitis	–	+	+	+	–	+	+
Prostatic Abscesses	+	+	+	+	–	+	+
Neoplasia	–	+	+	–	+	+	–

BPH = benign prostatic hyperplasia; HPF = haemorrhagic prostatic fluid; PPT = purulent prostatic fluid; PF bacteria = prostatic fluid infection

2.4. Diagnostic imaging

2.4.1. Radiology

Radiology is the first-choice method in evaluation of position, size and outer surface of the prostate gland (Barsanti and Finco, 1989). X-rays usually do not visualize juvenile or reduced gland sufficiently, however, physiologically developed prostate in healthy dogs possess soft tissue density, oval shape with smooth demarcation. The gland usually lies just behind the bladder in or close to pelvic inlet.

Typical is homogenous consistency (Stone et al., 1978). The prostate is considered enlarged when the prostatic diameter, as visualized on the lateral radiographic view, is greater than 70% of the pubic-sacral promontory distance (Feeney et al., 1987). The more prostate gland grows; it subsequently obturates pelvic inlet compromising distal colon and rectum, often clearly visible on the x-rays. Extraprostatic structures in the vicinity, such as paraprostatic cysts are also detectable by radiology.

Paraprostatic cysts are often content of perineal hernias (Head and Francis, 2002). In latero-lateral view there is a triangle of fatty tissue in between cranioventral limitation of prostate and bottom of the bladder (Barsanti and Finco, 1989). Misinterpretation of radiology happens mostly due to malpositioning of the patient during examination, after superposition of more organs or structures (e.g. faeces, muscle, bones of pelvis) (Johnston et al., 1991). On the other hand, x-rays are helpful in detection of metastasis in bony structures and lungs, while for direct examination of prostate gland it is considered supplementary. For better visualization of bladder and urethra, contrast cystourethrography is frequently applied (Johnston et al., 1991).

2.4.2. Ultrasonography

The first diagnostic ultrasonography on the human prostate was performed as early as 1967 (Watanabe et al., 1975). Ever since, many clinical trials focused on prostatic ultrasonography of both humans and dogs have taken place. Ultrasonography is widely recognized as more precise diagnostic tool than x-rays, especially in examination of inner structure of the gland (Johnston et al., 1991). This technique is also more accurate, whenever peritoneal fluid or reduction of intraabdominal fatty tissue causes loss of detail on x-rays. Among essential methods belong transrectal, transurethral and transabdominal ultrasonography. Transrectal and transurethral method are commonly used in human urology (Peeling and Griffith, 1984; Hamper et al., 1986). Prostate gland of humans looks structurarly the same as the gland of the dog. When detailed structural examination is required, probes of frequency 10- or 7.5 MHz are recommended, while for basics, 5- or 3- MHz probes should be satisfactory (Cartee and Rowles, 1983).

Evaluation of sublumbar lymph nodes and diameter of prostatic urethra should be an essential part of prostate gland ultrasonography. Non-enlarged lymph nodes are mainly undetectable, while big and reactive ones are elliptical and hypoechogenic (Johnston et al., 1989). Prostatic urethra is characteristic hypoechogenic zone, passing through hyperechogenic glandular structure (Cartee and Rowles, 1983). Examination of the dog is undergone after positioning to lateral or dorsal recumbency. It mostly does not require sedation or anesthesia. After basic dimensions are obtained, the actual size of prostate gland can be calculated from an

equation volume (cm^3) = [(L + W + D)/2.6] + 1.8

where:

L (length) = cranio-caudal diameter

W (width) = transversal latero-lateral diameter

D (depth) = dorso-ventral diameter (Kamolpatana et al., 1999)

Increase in echogenicity can be observed in most every prostatic disorder. Inflammation or neoplasia can result in hyperechogenic foci, while cyst or abscesses are typically detected as hypo- or anechogenic nodules (Feeney et al., 1987). Paraprostatic cysts are easy to distinguish from other masses in hypogastrium using diagnostic ultrasound (Feeney et al., 1985; Feeney and Johnston, 1986). In one study, effect of hydroxyflutamide on subsequent changes in echogenicity of glandular tissue of the prostate was observed. Along with reduction of glandular cells and overgrowth of interstitial tissue, the overall echogenicity was eventually reduced (Cartee et al., 1990).

Diagnostic ultrasound has been successfully used as a guide in obtaining biopsy samples, as well as in establishing preliminary diagnosis. Using ultrasound in routine biopsy of prostate and other parenchymatous organs significantly reduces morbidity and mortalty of the patient after procedure,

while it facilitates final diagnosis establishment (Smith, 1985).

In human medicine, more sophisticated methods such as a 3D-ultrasound (three-dimensional contrast-enhanced power Doppler ultrasonography) has been recently introduced. However, even these high-tech methods are limited in dependability, and always should be used in combination with other diagnostic tools (Sedelaar et al., 2002).

2.5. Prostatic markers

In semen, some specific chemical substances (so called markers), useful in the diagnosis of prostatic and some other disorders are present. These substances are released by perididymis and prostate gland. Among others, alcalic phosphatase, carnitin, acid phosphatase and canine prostate-specific arginin esterase (CPSE) are well-described (Gobello et al., 2002). In dogs and rabbits, the *alcalic phosphatase* is released by spermatic cord (Muller, 1983; Frenette et al., 1986; Lewis-Jones et al., 1992), while in humans it is mostly released by prostate gland and testicles (Lewis-Jones et al., 1992).

Carnitine is produced by spermatic cord. It is used, along with alcalic phosphatase, for screening of peridimidal ductal system function in azoospermatic dogs (Olson et al., 1987a; Gelmina et al., 1999). *Acid phosphatase* serum level does not differ between sick and healthy dogs (Bell et al., 1995). The most important and significant marker of prostatic secretion in dogs is arginin esterase (CPSE) (Chapdelaine et al., 1984). It is released by prostatic epithelial cells, androgen controlled, and the reason why is that it can be affected by antiandrogen therapy or by castration (Juniewitz et al., 1990). However, validity of screening prostatic markers in dogs appears to be rather limited. CPSE concentration is mostly elevated in dogs with BPH, but there has been identified no difference comparing dogs suffering from BPH, inflammation and/or neoplasia (Bell et al., 1995). Usefullness of some other markers has been, so far, the same story.

2.6. Prostatic biopsy

2.6.1. Fine needle aspiration biopsy (FNAB)

It is inexpensive, easy to perform the minimally-invasive method feasible for a consciouss or slightly sedated patient (Anderson et al., 1994). Sample obtained by FNAB can be used for bacterial cultivation and/or for cytology. The method is useful in a wide range of patients with various prostatic disorders. It is on the borderline between invasive and non-invasive methods.

Perineal or caudal abdominal approach to the gland can be utilized, but lately, abdominal approach has become the dominant method. The results obtained via FNAB reportingly reveal better accuracy compared to prostatic lavage (Thrall et al., 1985). Ultrasonography also enhances the effect of FNAB by better targeting the tissue in question (Zinkl, 1999). In case of acute inflammation, the use of FNAB is in question, since acute peritonitis as a consequence may develop (Dorfman and Barsanti, 1995a). A very effective method to avoid this situation from developing is maintaining of continual negative pressure within syringe during the procedure (Baker and Lumsden, 1999).

Reliability of FNAB in prostatic malignancy is 79 to 80%, but when percutaneous Vim-Tru-Cut biopsy is simultaneously applied, reliability can reach 89% (Nickel and Teske, 1992). Compared to other methods of direct sample obtaining, FNAB has many advantages: Squamous cells in aspirate, for instance, reveal squamous metaplasia, while in prostatic fluid after lavage, the same cells are considered normal (Thrall et al., 1985). In one study, when results after FNAB, US-FNAB (ultrasound-guided FNAB), prostatic lavage and plain massage were compared, after plain FNAB, there were 20 correct diagnoses out of 25 (80%), while after using US-FNAB, the sensitivity was 75% (Powe et al., 2004).

2.6.2. Excisional biopsy, Vim-tru-cut needle biopsy

Histopathological biopsy is the only method offering final diagnosis. In the prostate gland we always recommend biopsy during surgery; while without surgery, whenever less invasive methods fail or in case of poor response to therapy. We should always carry out a biopsy when neoplasia is in question. The samples obtained can be used for cultivation, and evaluated both cytologically and histopathologically. There are two basic methods to perform prostatic biopsy – percutaneous and excisional.

Percutaneous biopsy can be approached from the perineum or transabdominally, with the pa-

tient being sedated or anesthetized (Barsanti and Finco, 1989). The needle introduction is either guided by ultrasonography or performed blindly, with the gland fixed manually to the abdominal wall (Smith, 1985). After the biopsy, mild haematuria sometimes occur, while more serious bleeding or scrotal edema along with orchitis is uncommon (Barsanti and Finco, 1989).

Contraindications of prostatic biopsy include acute inflammation and prostatic abscesses, as acute septic peritonitis may develop. Urethral catheter should be introduced during prostatic biopsy to facilitate visualization of prosatic urethra. Excisional biopsy is performed during surgery, so the tissue can be directly inspected and the sample can be obtained sophistically. Cyst and obscesses should be sucked out just before biopsy (Stone and Barsanti, 1992).

2.7. Prostatic cytology

Normal epithelial cells of the prostate gland are well-defined as cubic or cylindric, containing oval nuclei with small nucleoli. The cytoplasm reveals basic granuli (Thrall et al., 1985). The cells are usually attached to each other, forming a honeycomb shape. Since the shape of the tissue differs throughout the gland (McNeal, 1988), there have been frequent misinterpretations regarding precise description of samples obtained both by biopsy and fine needle aspiration. According to Egawad (2003), the cells of central zone are elongated containing crowded nucleus, with well-visible nucleoli. They have been often mistakenly described as PIN (Prostatic Intraepithelial Neoplasia), sometimes even as either metaplastic, or neoplastic cells. This knowledge (Egawad, 2003) means quite a progress in prostate cytology, making it much more useful. We are able to perform prostatic cytology from samples obtained either by fine needle aspiration, or by excisional biopsy.

2.8. Prostatic intraepithelial neoplasia (PIN) as a predictor of prostatic disease

In human urology, PIN is understood as a quite significant factor in diagnosis of prostatic cancer (Graham et al., 1992; Bostwick, 1995). Identification of morphological and physiological abnormalities, such as basal cell layer disruption (Bostwick and Brawer, 1987), increase in both proliferation index and microvessel density (Montironi et al., 1993), they are all pictures of somehow transitional status in between regular epithelial cells and cancer cells of the gland.

High-grade PIN foci are observed in 85% of men suffering from prostatic cancer (McNeal and Bostwick, 1986). A typical observation in PIN in men reveals mostly abnormal proliferation of ductal epithelium, as well as epithelium of ductuli and acini, with microscopically evident malignant malformations. The same picture has been described in some animals, too. In dogs, it has been observed that histopathological picture of PIN is similar to that in humans, being observed in 66% of male dogs with the final diagnosis of a prostatic malignant tumor (Waters et al., 1997). Former assumptions connecting prostatic cancer in dogs to previous benign prostatic hyperplasia (BPH) failed after study by Madwell et al. (2004), in which 135 samples of prostatic tissue was evaluated histopathologically. The results revealed no finding of PIN neither in 20 samples of healthy gland, nor in 95 samples of gland with BPH. Only in 7 cases of prostatic cancer out of total 20 (37%), PIN had been identified.

Another study (Waters et al., 1998) observed PIN in 55% of old intact dogs, while in less than 10% of old dogs castrated or young intact individuals.The only species in which spontaneous prostatic malignances can be seen beside humans is dog (Waters et al., 1996, 1998). In search for an ideal animal model of prostatic cancer, transgenic mice were found not to be sufficient enough, while at Lobund-Wistar laboratory, rats seem to be prone to developing of prostatic cancer (hormonally influencable) with all the consequences including metastases (Bostwick et al., 2000). However, to date, PIN detection for screening of prostatic cancer of the dog is not dependable enough. There are various factors affecting the results either directly, or indirectly, such as genetics, diet, work and/or exercise (Aquilina et al., 1998; Waters et al., 1996).

3. Discussion

Our review has been focused on the evaluation of basic diagnostic tests and procedures with regard to their usefulness within current small animal practice. This includes owner acceptability of the procedure, too. Among others, rectal palpation of the prostate gland, along with urinalysis belongs

to the basics in diagnostic plans, while palpation should be performed during routine examination (pre-vaccination, for example) of the animal patient. In case of any irregularity, more focused diagnostic protocol should be applied. The common practice is using less invasive methods first, and more invasive ones in the end.

Diagnosis of prostatic cancer based on cytology of prostatic fluid is of rather limited value, because of variability of epithelial cells found (Thrall et al., 1985). According to Ling et al. (1990), results of a quantitative cultivation of prostatic fluid obtained during ejaculation when compared with direct cultivation of prostatic tissue were corresponding in 80 to 90% of patients. Whenever complimentary urinary tract infection is present (most cases), the diagnosis should be confirmed by another method available, because the infectious agent coming from urinary tract usually overgrows prostatic infection (Kivisto et al., 1977). In humans, detection of prostatic intraepithelial neopasia (PIN) has been successfully applied as a marker of prostatic cancer. Waters et al. (1997) identified PIN in 66% of dogs suffering from prostatic cancer, being histopathologically similar to that of humans. On the other hand, Madwell et al. (2004) detected PIN in 37% (7 cases out of 20) of patients with prostatic cancer, while he did not find PIN in 20 samples of healthy glands, nor did he find any PIN in 95 samples of BPH.

The conclusion of this study suggests that in dogs there is no relationship between BPH and prostatic cancer. At present there is no clinical application for PIN detection in dogs. There are more markers known from human urology. Some of them have been tested for their diagnostic value in dogs. Among others, alcalic phosphatase, carnitine, acid phosphatase and canine prostate-specific arginin esterase (CPSE) are the most important ones (Gobello et al., 2002). CPSE is major marker of prostatic secretory function in dogs (Chapdelaine et al., 1984). Its concentration increases in dogs with BPH, but there is no significant difference in concentration between BPH and prostatic inflammation, as well as between BPH and neoplasia (Bell et al., 1995).

Human prostate specific antigen (PSA) is irregularly present in serum and prostatic fluid of both healthy dogs and dogs suffering from various prostatic disorders, so it does not possess any diagnostic value (Bell et al., 1995). Screening of some basic parameters, such as pH, specific gravity, concentration of cholesterol, zinc, copper, iron, calcium or magnesium in prostatic fluid did not reveal any significant diagnostic value. Even in dogs with experimentally-induced bacterial prostatitis the comparison with healthy individuals did not detect any biochemical changes of prostatic fluid (Branam et al., 1984).

Radiology plays a role in the basic evaluation of position and general size of the gland. Because of some limitations, such as inadequate contrast in case of peritoneal fluid accumulation or loss of abdominal fat, exact inspection of prostatic capsula and establishing the size of the gland from x-rays exclusively may sometimes be impossible. However, an important role of radiology is in detection of metastases in bones, lungs and lymph-nodes.

Ultrasonography represented a big break-through in diagnosis of all prostatic disorders. Ultrasonographic appearance of human and dog prostate gland is almost identical. Ultrasonography represents much more sensitive imaging of prostate than radiology, facilitating very fine inspection of inner structure and morphology of the gland (Johnston et al., 1989). Moreover, ultrasonic guidance is useful in the aiming of prostatic biopsy. It significantly decreases morbidity of the patients undergoing biopsy, making prostatic biopsy safer and therefore more acceptable for the owner: the fact facilitating quick final diagnosis (Smith, 1985).

Our favorite method of biopsy is fine needle aspiration (FNAB), as it does not mean big intervention and its reproducibility is quite high. In one study, detection of prostatic cancer via FNAB was as high as 80%, and while it has been in combination with Vim-tru-cut needle biopsy, the sensitivity was 89% (Nickel and Teske, 1992). In another study the correlation between cytology and histopathology was up to as much as 80% (20 samples out of 25). The fact that in this study the ultrasound-guided FNAB was correct in only 75% of cases was explained by some errors during procedure of obtaining and further processing samples (Powe et al., 2004). Evaluation of ultrasound-guided fine needle aspiration is in the scope of our further study, and it may be reported separately later on.

4. Conclusion

There are many ways to evaluate prostate gland: As a golden standard we suggest to proceed from less-invasive diagnostic methods to the more-invasive

ones, keeping the owner informed during each and every step of the protocol, both money-wise, and regarding safety of each procedure. Disadvantages of the so-called "less invasive" methods are rather low specificity, as well as limited diagnostic value. Even the fact of relative safety and low price cannot balance this clear disadvantage.

To find the agreement in acceptable risk and reasonable price, and to be able to establish reliable diagnosis and to overcome some other aspects, such as another disease or multiorgan failure (geriatric patients), or refusing of anesthesia during diagnosis by the owner, the semi-invasive diagnostic procedures have been recently advocated. The most favorable method, in our opinion, is fine needle aspiration biopsy (FNAB) or ultrasound-guided FNAB, followed by cytology, bacterial cultivation or both. This method (with or without ultrasonographic guidance) is quick, cheap, easy to perform, causing minimal pain (anesthesia or sedation is not mandatory), and providing a relatively high reliability.

Risk of developing complications is relatively low, even though there might develope haematuria or peritonitis after peritoneal contamination by aspirate, or iatrogenous urethral damage. Diagnostic misinterpretation may happen after missing of local lesion (especially in procedures without ultrasonic guidance).

Our aim is to advocate FNAB, especially under ultrasonic guidance, the method which can obtain samples directly from affected lesion. Some consider FNAB as too complicated and not sensitive enough, which, in our opinion, is clearly not true. The big advantages of this method are low invasiveness, easy technique, and availability of cytology in most veterinary clinics, as well as quick results and relatively high dependability. Localization of samples obtained by usltrasonography (available in most veterinary clinics, too) means further improvement in result interpretation. We can evacuate cysts and abscesses and proceed with local drug administration (e.g. antibiotics). Moreover, by means of usltrasonographic control, we are able to follow up the treatment process quite effectively.

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