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CLINICAL APPROACH TO PROSTATIC DISEASES IN THE DOG

Running Title: Prostatic disorders in dogs

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Abstract

In small animal practice, prostatic diseases are increasingly encountered. All dogs may experience prostatic disease, but particular care should be addressed to breeding dogs, in which prostatic affection may lead to decrease in semen quality and fertility. The most common prostatic disease is the benign prostatic hyperplasia (BPH) followed by prostatitis, prostatic neoplasia and prostate squamous metaplasia. These diseases do not have pathognomonic symptoms, therefore, making a correct diagnosis may not be easy. An accurate clinical examination and a correct diagnostic protocol are essential in order to begin the most appropriate treatment, and also to do a good prophylaxis where it is possible.

BPH therapy is usually recommended when mild-severe signs are present or if symptoms disturb the patient. New therapeutic approaches, both medical and surgical, allow to maintain fertility in most animals with prostatic disorders. Prostate cancer is relatively infrequent. Elective therapy is the surgical one, but it is considered palliative and can result in important post-operative complications.

The aim of these paper is to lay down the most appropriate diagnostic process describing the aetiologies of prostatic disease, their symptoms, the right investigative tools and therapy.

Keywords: prostate, dog, prostatic diseases, diagnosis, therapy.

INTRODUCTION

Prostatic diseases are very common in male dogs and are the main pathologies affecting the reproductive system; these animals are much more frequently presented for such reasons (Davidson, 2014). Benign prostatic hyperplasia is the most common benign neoplastic disease in both the aging dog and man and therefore the dog has been increasingly used as an experimental animal model for the study of this important human disease. Frequently the clinical approach to prostatic diseases is not easy: these pathologies can occur concomitantly, can be asymptomatic and are often underestimated because many of the major symptoms of prostatic diseases are non-specific. Systemic signs, lower urinary signs, abnormalities of defecation and locomotion disorders are symptoms that occur in prostatic diseases, but are also observed in low urinary tract, intestinal tract and orthopedic pathologies. For a correct management it is essential to know the history and perform a correct physical examination. Development in the diagnostic and therapeutic approaches over the last decade has permitted to maintain fertility in many dogs with prostatic pathologies. (Read and Bryden, 1995; Krawiec and Heflink, 1992).

Anatomy and physiology

The prostate gland is the only accessory sex gland in the male dog and provides, with its secretions, the transport of sperm outwards and an ideal environment for the development and survival of sperm (Branam et al. 1984). It is a bilobed and mobile organ that encircles the urethra and the neck of the urinary bladder. Its anatomic topography is variable and depends on the age and the bladder distension, while only its craniodorsal and cranioventral sides are covered by peritoneum. Prominent medial septum and other minor septa rich of connective tissue and smooth muscular fibers originate from the external thick fibromuscular capsule and split the organ in two major lobes and then in lobules. The glands are tubuloalveolar with a tall columnar secretive epithelium and sporadic basal cells. The openings of prostatic glandular ducts are located in urethra near deferent ducts around the colliculus seminalis.

Prostatic artery from the pudendal internal artery and hypogastric nerve provide the vascular and nervous supply (Evans et al, 2013). Theoretically, the canine prostate passes from three stages of development that usually are not clearly distinguishable. O'Shea (1962) divided prostatic development into three phases: the first, of normal growth, in the young dog; the second, of hyperplasia, during the middle and adult age; the last of senile involution (O'Shea, 1962).

The development and maintenance of prostatic secretory activity are guaranteed by hormone production. Testosterone penetrates prostate cells by diffusion and is metabolized into other steroids by enzymes. More than 95% of the testosterone is converted into DHT by 5α-reductase in the prostate. DHT binds and activates cytoplasmic receptors for androgens with greater affinity than testosterone. Another hormone involved in prostate development is 17β-estradiol, which is synthesized by aromatase. This estrogen works in synergy with androgens (Frick and Aulitzky, 1991).

More recent studies show that 17β-estradiol increases the expression of nuclear receptors for DHT, thus increasing the sensitivity of the prostate to androgens (Gobello and Corrada, 2002).

Moreover, canine prostate-specific arginine esterase (CPSE), the major secretory product of the canine prostate, is the most abundant protein in the dog's prostate fluid and represents more than 90% of the seminal plasma proteins in this species. It could be a useful diagnostic marker to identify prostatic disorders (Chapdelaine et al., 1984).

Prostatic diseases

The prostatic pathologies should be classified into endocrine, inflammatory (septic and non-septic), neoplastic and traumatic (Ballotta and Cunto, 2018). Benign prostatic hyperplasia and squamous metaplasia belong to the first category while acute or chronic prostatitis and prostatic abscess belong to the second one. Cysts frequently occur secondary to other prostatic diseases. It is important to remember that more prostatic diseases can be present simultaneously (Barsanti and Finco, 1986).

Benign prostatic hyperplasia

BPH is a benign neoplastic disease that occurs only in man, dog, chimpanzee and, despite some differences, the natural course of BPH is similar in these species. BPH is the most common prostatic disease diagnosed in the dog and affects about 80% of intact male dogs over 5 years old (Sirinarumitr et al., 2001) and more than 95% of intact male dogs over 9 years old (Gobello and Corrada, 2002). Large breeds such as Doberman, German Shepherd, Rhodesian Ridgeback and Labrador Retriever appear to be predisposed to BPH (Wolf et al., 2012; Polisca et al., 2016; Das et al., 2017;). Several theories have been proposed to explain the etiology but only three facts have proven to be implied in both species:

1. the incidence of BPH increases with advanced age;
2. the presence of functioning testes is required;
3. dihydrotestosterone (DHT), the active metabolite of testosterone, is more concentrated in hyperplastic prostatic tissue compared to normal tissue.

With aging, when the estrogen/testosterone ratio increases, the prostate becomes more responsive to androgen action. The key role in this pathology is probably played by a metabolic shift that promotes the production of DHT due to increase of 5α-reductase activity (Brendler et al., 1983; Gobello and Corrada, 2002). Intraparenchymal cysts are frequently associated to BPH and are formed when hyperplastic glandular ducts become obstructed causing accumulation of prostatic fluid (Barsanti and Finco, 1986) or urine when a communication with the urethra is present (Bokemeyer et al., 2011). Frequently the dogs with BPH are asymptomatic, but when clinical signs are present, the most common is a serous to sanguineous urethral discharge, produced by hyperplastic tissue with increased vascularity. Sometimes sanguineous discharge enters in urinary bladder and so hematuria may be present. Rectal tenesmus, constipation, dischezia and rarely dysuria, strangury and incontinence can occur because of an enlarged prostate or large cysts associated with BPH. Caudal abdominal pain and infertility can be observed, while systemic signs are rarely reported (Krawiec and Heflink, 1992; Read and Bryden, 1995).

A presumptive diagnosis can be made by history, physical examination, laboratory findings and prostatic imaging. Biopsy permits a definitive diagnosis but is rarely recommended (Smith, 2008). Enlargment of the prostate can be detected by rectal palpation during physical examination. The prostate is usually not painful, symmetrically enlarged and with normal consistency. Sometimes the organ is not symmetric because of large intraparenchymal cysts or the cobblestone-like appearance of its surface (Lopate, 2013). Hematologic findings and urinalysis are usually normal even if hematuria may be present (Das et al., 2017) and the prostatic fraction of seminal plasma too is frequently hemorrhagic. Aerobic and anaerobic cultures of seminal plasma and urine are negative (Read and Bryden, 1995) while cytology and bacterial culture of prostate secretions may be useful to exclude or to confirm the concomitance of multiple prostatic disorders, even if do not provide definitive diagnosis of BPH (Greer, 2014). Samples can be obtained by ejaculation, prostatic massage, fine needle aspiration or urethral brushing (Gobello et al., 2002; Lopate et al., 2013). Radiographically it is possible to evaluate prostatic size and position. It is usually enlarged and located in the abdomen. The colon is dorsally displaced and the urinary bladder cranially displaced (Feeney et al., 1987). The normal prostate size should not exceed 70% of the distance between the pubic cranial margin and the sacral promontory, measured in lateral projection; over this value the prostate is enlarged (Atalan et al., 1999). On ultrasonography the prostate appears frequently enlarged and symmetric, with homogeneous parenchyma or with nodular aspect. Nodules are poorly defined and are isoechoic or slightly different from normal parenchyma echogenicity. Frequently one or more cysts are present, which appear like intraparenchymal cavity with variable size and shape and with well-defined margins (Nyland and Mattoon, 2015). Advanced ultrasound techniques, such as colour-coded and pulsed Doppler sonography, contrast-enhanced ultrasound and elastography, can be used for a more complete evaluation of the prostate gland (Günzel-Apel et al., 2001; Vignoli et al., 2011; Feliciano et al., 2015). Doppler evaluation is a non-invasive diagnostic tool easily applicable in clinical practice and, in dogs with BHP, shows a significant increase of blood flow velocity in prostatic artery (Zelli et al., 2013). Although few studies on contrast-enhanced ultrasound are

published, this method, giving detailed information on the prostate gland vascularization, can be useful in detecting early prostate disease, in differentiate between malignant and benign lesions and in staging already diagnosed diseases (Vignoli et al., 2011; Bigliardi and Ferrari, 2011). Elastography evaluates the presence of deformities and tissue stiffness and, despite the few experimental studies about it, seems to be a useful diagnostic tool allowing to discriminate between a normal prostate and a pathological one (Feliciano et al., 2015; Domoslawska et al., 2018).

Serum evaluation of CPSE, considered as the most representative marker of prostate secretion activity, may be helpful for diagnosis because it increases in the course of BHP (Lévy et al., 2009; Wolf et al., 2012; Lévy et al., 2014; Holst et al., 2017; Pinhero et al., 2017). The results obtained by Holst et al. (2017) revealed that dogs with an increase of prostate volume higher than 2,5 times of normal expected volume showed serum CPSE levels more than 90 ng/mL (Holst et al. 2017). The serum evaluation of the CPSE seems to be a new frontier in clinical practice such as screening tests for prostate disease prevention or as routine tests for possible follow-ups (Alonge et al., 2017; Lévy et al. 2017).

It is important to remember that BPH evolution is individual and difficult to predict. The symptoms can be graded according to their severity, frequency and duration thanks to a symptom index validated for BPH (Zambelli et al., 2012). Considering this classification and that the clinical signs may be the same during many years, we can choose the best therapy for the single case and, so, no therapy is usually recommended when mild signs are present or if symptoms do not disturb the patient. In this case the patient is monitored every 3 to 6 months, on the basis of an approach called “watchful waiting” frequently used in human beings (McVary et al., 2011). Therefore, we have different therapeutic options: “watchful waiting”, pharmacological treatment, surgical treatment (orchiectomy, cysts omentalization) (Barsanti and Finco, 1986) and cysts alcoholization (Zambelli et al., 2003). To choose the best treatment, after physical examination and tests, it is possible to divide symptomatic subjects in animal with mild, moderate or severe symptoms. In the first case or if moderate symptoms don’t affect dog and/or owner life, watchful waiting is the best treatment. In every other case, when

symptoms affect dog and/or owner life, pharmacological or surgical treatment should be recommended (Zambelli et al., 2012). In particular situations, when BPH is associated with incontinence caused by bladder hyperdistention, severe dyschezia, presence of perineal hernias, severe recurrent hematuria or urethral discharge, presence of big retention cysts, dysuria/acute urinary retention, castration is the treatment of choice following which prostatic volume decreases within 7-14 days after surgery. The drugs more frequently used for the pharmacological treatment recommended in literature are: 5α-reductase inhibitors (such as Finasteride), antiandrogens (such as Flutamide and Osaterone acetate), GnRH analogs (deslorelin acetate) and progestogens (Smith, 2008). Finasteride is the drug of choice when surgical treatment is not recommended or possible (Sirinarumitr et al., 2001); it prevents the conversion of testosterone to DHT and, like Flutamide, has not been demonstrated to reduce libido and sperm production. Several dosages of Finasteride are reported in the literature (Sirinarumitr et al., 2001; Iguer-Ouada and Verstegen, 1997; Lange et al., 2001) but the most effective protocol that allows the lowest possible doses involves the administration of 1.25 mg Finasteride (regardless of the dog's size and the severity of the disease) PO every 24 hours for 195 days. Osaterone acetate is an anti-androgen agent; the administration of 0,2-0,5 mg/kg/day PO for 7 days leads to a significant decrease in prostate volume, already evident at the end of the treatment (Tsutsui et al., 2001). GnRH agonists have an action similar to endogenous GnRH. The mechanism of action involves the constant release of the active ingredient from the implant that overlaps the physiological one, leading to a supersaturation and down-regulation of the pituitary receptors. The consequent decrease in FSH and LH leads to a drastic reduction of testosterone synthesis (up to 90%) and, in the case of deslorelin acetate (4.7 mg implants), causes an evident decrease in prostate volume (> 50% after 6 weeks) (Trigg et al., 2001). Progestogens (megestrol acetate and medroxyprogesterone acetate) can be used but are not recommended because of the several side effects (Smith, 2008). The employ of an anti-estrogenic compound, tamoxifen citrate, is also reported in the literature; it gives a competitive block on estrogen receptors with a mixed agonist-antagonist mechanism (Corrada et al., 2004). Moreover, some authors suggest the use of plants extract

to treat BPH (Odenthal, 1996), while others demonstrated the efficacy of pulsed electromagnetic field therapy on BHP in dogs with no apparent side effects (Leoci et al., 2014). When large cysts are present, the surgical treatments proposed in literature are: drainage, resection of the cyst with or without drainage placement, omentalization, marsupialization and partial or total prostatectomy (Smith, 2008). Among these, omentalization is the authors' preferred technique, also used to treat prostatic abscesses and described in the relevant chapter. A less invasive technique, not requiring surgery, consists of ultrasound-assisted cysts drainage and alcoholization. However, this medical procedure is not as effective on cysts as it is on abscesses, probably due to the different nature of the cyst's inner surface which seems to resist the alcohol's effect (Zambelli et al., 2003).

Acute and chronic prostatitis and prostatic abscesses

Acute prostatitis (AP) and chronic prostatitis (CP) are defined as an inflammation of the prostate gland. Septic prostatitis is the most common type of prostatic inflammatory disease, even if non-septic prostatitis is possible; sometimes chronic non-septic prostatitis is associated with BPH (Nizanski et al., 2014). In healthy dogs there are some non-specific defense mechanisms to reduce the risk of infections such as urinary flow during micturition, urethral pressure, local production of IgA and prostatic production of antibacterial factor (Shimizu et al., 1995). Conditions that alter these mechanisms or alterations of prostatic tissue such as BPH, squamous metaplasia and neoplasia can predispose to prostatic infections (Smith, 2008). Only one-third of prostatitis is caused by a single bacterial, the other two-third show a mixed growth of several infectious agents or are non-septic (Lévy et al., 2006). The most common responsible pathogens are aerobic organisms such as *E. coli*, *Staphylococcus sp.*, *Streptococcus sp.*, *Proteus sp.*, *Pseudomonas spp.*, *Brucella canis*, *Klebsiella sp.*; other reported pathogens are anaerobic organisms and *Distemper virus* while fungal conditions such as blastomycosis and cryptococcosis are infrequent in the dog (Barsanti and Finco, 1986; Krawiec and Heflink, 1992). Infections are often caused by bacteria ascending the urethra but local dissemination from urogenital organs or hematogenous spread is possible (Barsanti and Finco, 1986).

Sometimes prostatitis may develop into prostatic abscesses (PA). The symptoms vary with the progression of the disease and from acute to chronic prostatitis to prostatic abscess. Dogs with AP frequently present fever, anorexia, lethargy, caudal abdominal pain, constant or intermittent urethral discharge. CP can be present without evident signs and is often associated to recurrent urinary tract infection; sometimes anorexia, lethargy, urethral discharge and poor semen quality are present. Symptoms related to PA vary from signs similar to AP to signs of peritonitis or septic shock if abscess rupture occurs. If present, urethral discharge is hematic or purulent (Wallace, 2001).

Presumptive diagnosis is based on history, physical examination, laboratory findings, urine culture and prostatic imaging. This diagnosis can be confirmed with prostatic fluid culture. Prostatic fluid can be obtained by ejaculation, even if sometimes this is not possible because it is painful, or by prostatic massage (Johnston et al., 2000). On physical examination for AP and PA prostate can be painful when the organ is palpated or during the defecation. Prostatic size can be increased and shape changed if underlying prostatic diseases or PA are present. Usually the prostatic consistency is fibrous for CP while in course of AP and PA the prostate may present an increased firmness and fluctuant areas may be palpated in the case of PA. The hemogram is normal for CP, a neutrophilic leukocytosis with or without left shift is present during AP and PA and elevation of alkaline phosphatase is frequently reported in PA. Pyuria, hematuria and bacteriuria are often observed in PA (Kutzler and Yeager, 2005; Smith, 2008). Cytology from prostatic fluid or tissue is useful for diagnosis. In 80% of case there is a correlation between prostatic fluid cytology and histologic evidence of inflammation (Barsanti et al., 1983). Samples for cytology can be obtained by prostatic massage or in some cases by ejaculation. A fine-needle aspiration and ultrasound-guided biopsy are reliable techniques too and successful diagnosis has been reported in 70% of case, but these techniques must be use with caution because of the potential of creating a septic needle tract (Smith, 2008; Lévy et al., 2014). In particular they are contraindicated in presence of prostatic abscessation (Smith, 2008). In smear of acute prostatitis and prostatic abscess, we observe many granulocytes, red blood cells and bacteria; if present, prostatic cells may be normal or damaged. Radiographically, prostatic abscess occurs

sometimes as a prostatic enlargement, with colon and urinary bladder respectively dorsally and cranially displaced and, in some cases, mineralization is detected. In case of cystouretrography, if the cavitary lesion communicates with the urethra, a reflux of contrast medium into the prostatic parenchyma is observed (Feeney et al., 1987).

Ultrasonography is very useful for diagnosis: prostate is enlarged in size and asymmetric for PA while the parenchyma appears focally or diffusely hypoechoic for AP and PA and hyperechoic for CP. The tissues around the prostate are normal or hypoechoic for AP and PA and normal for CP. Abscesses may be single or multiple, with size varying from small to large, globose or multiloculated shape, hypoechoic or anechoic internal aspect and irregular internal surface.

Elective therapy for prostatitis is based on antibiotic administration for long period, about 4 to 6 weeks (Sirinarumitr, 2009) and, in case of PA, should be associated with other treatment described in the relevant section. Once AP or PA are diagnosed a broad-spectrum antibiotic should be administered but as soon as the antibiogram is available, if necessary, antibiotic therapy should be modified. In dogs with AP or PA the blood-prostate barrier is damaged and so antibiotic can easily pass into the parenchyma (Dorfman and Barsanti, 1995). Different is in dogs affected by CP, for which antibiotic should be chosen between drugs with a good prostatic penetration, because blood-prostate barrier is intact (Dorfman and Barsanti, 1995). Antibiotics that allow good penetration of the prostate barrier are those with high lipid solubility, pKa allowing diffusion of the non-ionised form of the drug across the lipid membrane and low protein binding, such as trimethoprim, chloramphenicol, and the fluoroquinolones such as enrofloxacin, ciprofloxacin and marbofloxacin (Dorfman and Barsanti, 1995; Sirinarumitr, 2009). In all cases of prostatitis, treatment for hormone deprivation (finasteride, osaterone, delsorelin) should be useful to increase the success of the therapy, especially when other conditions, as BPH, are present. In dogs affected by PA, antibiotic therapy should be associated with techniques able to drain the purulent material, such as omentalization (White and Williams, 1995). This is the authors' preferred technique, recommended for abscesses or cysts treatment. During surgery abscess' content is partially aspirated with a syringe in order to

decrease internal pressure. The abscess is opened, the pus removed by suction and internal septa broken-down by digital exploration. After cleaning the cavity with iodine tincture and irrigation with warm saline, the omentum is distended, inserted in the cavity in order to fill it and then suturated with few anchorage stitches. Follow up includes ultrasonographic evaluation, where the omentum appears hyperechoic in comparison with the prostatic parenchyma and it fills the whole cavity. An omentalization with modified technique allows to better safeguard the integrity of the vasa deferentia in breeding animals (Zambelli and Bralia, 2000).

Squamous Metaplasia

Squamous metaplasia (SM) of prostatic cells is a condition secondary to exogenous or more frequently endogenous hyperestrogenism, frequently due to functional Sertoli-cell tumour. SM predisposes the prostate to prostatitis and abscesses (Lévy et al., 2014).

The main clinical signs are correlated to hyperestrogenism: alopecia, hyperpigmentation, gynecomastia, and signs of prostatitis. Other symptoms are non-regenerative anemia, thrombocytopenia, granulocytosis or granulocytopenia. When Sertoli-cell tumour is present, it could be palpated in one or both the testis~~,~~ and sometimes the dog may also be cryptorchid (Lévy et al., 2014).

Presumptive diagnosis of prostatic SM is based on history, physical examination, preputial cytology, testicular and prostatic imaging and testicular histology or cytology. Hyperestrogenism induces modifications in both prostatic and preputial cells: prostatic fine-needle aspiration usually permits to obtain a sample rich in large cells with a small nucleus and granulocytes; preputial swab permits to obtain many superficial cells with more than 30% of keratinization (Gobello and Corrada, 2002). On ultrasonography the prostate aspect is similar to that reported for acute or chronic prostatitis and frequently cysts are present. For a definitive diagnosis, prostatic biopsy or cytology are required (Leeds, 1969).

Metaplasia is reversible after removal of source of estrogens: orchiectomy is the elective treatment in cases of Sertoli-cells tumors while interruption of estrogens administration is recommended when hyperestrogenism is exogenous (Lipowitz et al., 1973).

Prostatic Neoplasia (PN)

Prostatic neoplasia is a rare disease (incidence of 0,43%) both in intact and neutered dogs (Axiak and Bigio, 2012), with Shetland sheepdogs and Scottish terriers having an increased risk (Bryan et al., 2007). The mean age of diagnosis is 10 years. The lack of markers for prostatic cancer in dogs makes early diagnosis difficult and therefore the true incidence of prostate cancer may be higher than currently believed (Teske et al., 2002). A higher prevalence of PN is seen in castrated dogs; however, both castrated and intact animals develop this pathology at the same age. This aspect suggests that castration is not an initiator of cancer, but that it favours tumor progression (Teske et al., 2002; Bryan et al., 2007). PN is considered hormonally independent and tends to metastasize rapidly in about 70-80% of cases through external or internal iliac nodes to vertebral bodies and lungs or may invade urethra, urinary bladder, ureters, colon and pelvic musculature (Hall et al., 1976; Leroy and Northrup, 2009). Adenocarcinoma, transitional cell carcinoma and undifferentiated carcinoma are the most common prostatic neoplasia reported (Cornell et al., 2000; Teske et al., 2002; Smith, 2008; Leroy and Northrup, 2009).

The presenting history is similar to that of other prostatic diseases, but frequently the symptoms are related to increased prostatic size that induces rectal tenesmus, constipation as well as diarrhea, dyschezia, hematuria, dysuria and stranguria. Lameness, pain and paresis of the hind limb (caused by nerve compression and vertebral metastasis), weight loss and caudal abdominal pain are also reported (Leroy and Northrup, 2009; Axiak and Bigio, 2012; Lévy et al., 2014). Secondary infection is reported in 36% of affected dogs and can exacerbate lower urinary tract signs (Leroy and Northrup, 2009).

History, physical examination, laboratory findings and prostatic imaging can lead to a presumptive

diagnosis but definitive diagnosis requires the collection of neoplastic prostatic cells by prostatic fine needle aspiration or biopsy (Axiak and Bigio, 2012). On transrectal examination the prostate is usually painful, asymmetrically enlarged, and with increased firmness. Hematuria is frequently present, non-regenerative anemia, leukocytosis (mature neutrophilia) and increase of the alkaline phosphatase may be reported (Bell et al., 1991; Axiak and Bigio, 2012). As already mentioned, there are not markers for PN as in humans, therefore a serum screening test is not useful as a screening tool (Leroy and Northrup, 2009). Ultrasound is the first choice examination: typically, prostate appears enlarged, asymmetric, with an irregular and poorly defined outline. Focal or diffuse, hyperechoic or mixed lesions can be found throughout the parenchyma. Hyperechoic foci with acoustic shadowing representing mineralization as well as cavitary, cyst-like lesions varying in size, shape, and number may also be present. Extension of pathologic changes to the urethra or neck of the urinary bladder, regional lymphnode enlargement, and disruption of the capsule are ominous ultrasound signs indicating neoplasia. (Smith, 2008; Mattoon and Nyland, 2015). A recent study shows that elastography can be a very helpful diagnostic tool to diagnose prostate neoplasia in dogs, so that some authors recommend including it among the first additional surveys in routine prostate examination (Domoslawska et al., 2018). Prostatic fine-needle aspiration is useful for the diagnosis of PN (Lévy et al., 2014): usually neoplastic prostatic cells are large pleomorphic cells with some characteristics as large vesicular multiple nuclei, multiple prominent nucleoli, eosinophilic intracytoplasmic inclusions or vacuolizations. Cellularity is usually abundant, with single cells rarely organized in clusters and dirty smear background with cellular debris or red blood cells (Leeds, 1969). Radiographic findings in dogs with PN can include prostatomegaly, focal mineralization (representing calcification of the gland parenchyma), irregular and poorly defined gland outlines, colon's dorsal displacement and evidence of metastasis to the lungs and skeleton (Smith, 2008; Leroy and Northrup, 2009; Lévy et al., 2014). If the urethra is involved in the neoplastic process, retrograde cystourethrography can show mural discontinuity or compression. TC, MRI and scintigraphy are also very informative but are rarely performed because of the cost, poor prognosis and lack of efficient

treatment (Leroy and Northrup, 2009; Lévy et al., 2014).

Usually the treatment is not curative and PN is associated with poor prognosis. Castration does not affect the prognosis because neoplasia does not respond to the hormonal ablation strategies used in humans and cytotoxic drugs do not allow to improve the prognosis. Results of radiation therapy for prostate carcinoma have been disappointing and severe adverse effects have developed, so it seems effective only to palliate clinical signs associated with the tumor and to relieve pain associated with skeletal metastasis (Leroy and Northrup, 2009). The use of chemotherapeutic agents is still under evaluation, but it appears that the anti-cancer effect of non-steroidal anti-inflammatory drugs increase the survival times of dogs with prostate carcinoma (Sorenmo et al., 2004). However, because of a high rate of metastasis at the time of patient presentation, the prognosis is too poor to recommend aggressive local therapies; therefore, total prostatectomy is recommended only in few cases where metastasis are not detected (Leroy and Northrup, 2009). Dogs that undergo complete excision of the prostate are at risk of becoming incontinent while other possible complications are colonic necrosis and urinary tract infection (Axiak and Bigio, 2012). The technique for total prostatectomy can be described in some steps. A urethral catheter is placed to aid identification of the prostatic urethra during the surgery. After laparotomy the periprostatic fat is carefully removed from prostatic ventral surface to improve visualization of the prostate. The prostatic vascular supplies are identified in the dorsolateral aspect of the gland. All blood vessels are ligated and the vasa deferentia as well. The urinary catheter is pulled back and the urethra is transacted at the caudal and cranial margins of the prostate. The prostate is removed and the catheter is reinserted in the urinary bladder to facilitate approximation of the urethra. An end-to-end anastomosis of the bladder neck to the membranous urethra is performed using simple interrupted sutures of 4/0 monofilament absorbable material.

CONCLUSIONS

Prostatic diseases are not as infrequent as believed, since many dogs seem to be asymptomatic. Every dog, in particular from 6 years of age (Smith, 2008), may be affected and, in stud dogs, a pathological

condition of this gland can also lead to a worsening of sperm's quality and animal's fertility (Polisca et al., 2016).

Make a diagnosis is not always easy due to the non-specific clinical signs and the possible overlap of different pathologies.

In order to obtain a correct diagnosis, it is necessary to perform an accurate clinical examination and an ultrasound evaluation, the last of which is, to date, the most accurate and least invasive survey available to us. The bacteriological examination of prostate fluids and urine, the cytology of the prostate and/or its fluids and the blood test are also useful, even if a definitive diagnosis can only be obtained by histological examination.

Transrectal palpation of the organ during general medical examination and andrological check-up is important. In addition to this, the evaluation of serum CPSE can be performed because it seems to be very useful in clinical practice not only as a screening test for the prevention of BHP, but also as a test to evaluate the effectiveness of a possible set therapy. Instead, we need further studies in order to identify a prostate tumor marker, which would represent an interesting development for the early diagnosis of the disease.

Regarding the therapy, several protocols have been proposed, even recently, especially for the most widespread conditions (BHP and prostatitis), not neglecting, when possible, the preservation of the treated subjects'reproductive performances. The best results in course of BHP seem to be obtained with the use of 5α-reductase inhibitors, antiandrogens or GnRH analogs associated, in case of concomitant prostatitis, to a targeted antibiotic therapy.

Also when a surgical approach for the treatment of the prostatic cavitary lesions (cysts and abscesses) is needed, the reproductive aspect is increasingly taken into consideration and, therefore, techniques such as omentalization (White and Williams, 1995; Zambelli and Bralia, 2000) are proposed or modified while castration is performed always in less cases and mainly only when necessary.

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