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Total prostatectomy combined with urethral anastomosis in a dog: a case report

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Abstract: Prostate cancer is the most common prostate disease diagnosed in castrated dogs. However, prostate cancer is considered to be quite rare in dog population. The presence of prostate tumours can lead to urethral obstruction. Other clinical signs include asymmetric, painful, hard growths on rectal examination, neurological deficit or lameness of the pelvic limbs and general symptoms such as anorexia, weight loss or difficult urination. The neoplastic process may spread to the neighbouring organs and give metastases to the lymph nodes, lungs and skeletal system. Patient with histopathologically confirmed prostate cancer should be examined for metastases. The prognosis is usually unfavourable because of late diagnosis and the presence of metastases. Therapeutic options include surgery, chemotherapy and radiotherapy. Complete prostatectomy carries with it many complications and often requires osteotomy of pelvic fusions. For that reason, total prostatectomy is not commonly performed in companion animals; however, it should be considered in cases of early detection with the absence of metastases. This report presents the procedure of a complete prostatectomy in a dog with a pre-pubic anastomosis of the urethra, without osteotomy of the pelvic septum. The anastomosis of the urinary tract was placed outside the abdominal cavity, caudally from the laparotomy wound. The presented technique seems to be appropriate for the treatment of malignant tumours of the prostate gland in dogs.

Keywords: prostatectomy; prostate cancer; veterinary surgery; oncology

According to available literature reports, prostate cancer is considered to be quite rare in the dog population and accounts for only 0.2–0.6% of all cases (Durham et al. 1986; Bacon et al. 2016). Lack of accurate data allows for the suspicion that there is much larger number of affected animals (L'Eplattenier et al. 2006). Prostate tumours are a common cause of urethral obstruction (Liptak et al. 2004). In the case of sick animals, there is a rapid growth of the tumour associated with metastases to the lymph nodes, lungs and skeletal system, mainly in the lumbar vertebrae (L'Eplattenier et al. 2006). Despite its rarity, prostate cancer is the most common prostate disease diagnosed in castrated dogs (Bell et al. 1991). Among predisposed animals, medium and large breeds as well as middle-ages and elderly dogs are particularly at risk (Bell et al. 1991; Teske et al. 2002). Prostate cancer

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often results in symptoms similar to other diseases of this gland. Asymmetric, hard, nodular and painful prostatitis in combination with lameness or neurological deficit of pelvic limbs can strongly suggest neoplastic lesions, especially in castrated individuals (Leav and Ling 1968; Hornbuckle et al. 1978). At the same time, clinical symptoms such as anorexia, weight loss or difficult urination are observed (Leav and Ling 1968; Durham and Dietze 1986). The most common prostate tumours are adenocarcinomas and low-grade carcinomas (Bell et al. 1991; Cornell et al. 2000). Not all carcinomas of the prostate develop from glandular epithelium. Many reported cases of adenocarinoma arise not from the secretory prostatic epithelium but from urothelium of the prostatic urethra or the periurethral ducts and are urothelial (transitional cell) carcinomas. The most common histological pattern of canine prostatic adenocarcinoma is intraalveolar. Neoplastic cells form large alveoli filled with papillary projections of glandular epithelium. The tumour cells are round or cuboidal; some are vacuolated and produce mucus. A second pattern is acinar adenocarcinoma in which neoplastic cells are cuboidal and arranged in acini. In some cases, the acini may be filled with solid masses of neoplastic cells (Lai et al. 2008; Agnew and Machlan 2017). In the ultrasound image, single or multiple hyperechoic lesions are observed with asymmetrically enlarged, uneven margins of the gland (Mattoon and Nyland 2002). The presence of mineralisation during the ultrasound examination significantly increases the chances of prostate cancer diagnosis in subsequent diagnostic tests. The neoplastic process may spread to neighbouring organs such as the urethra, bladder or regional lymph nodes (Nyland et al. 2002; Freitag et al. 2007).

The final diagnosis should be confirmed by histopathological examination of the material obtained during biopsy (Nyland et al. 2002). In patients with histopathologically confirmed prostate cancer, additional examinations should be performed to detect the presence of metastases, which are detected even in 89% of diagnosed cases. For this purpose, apart from lymph node biopsy (medial iliac lymph nodes), X-rays of the chest, pelvis, lumbar vertebrae and femurs should be taken (Bell et al. 1991; Cornell et al. 2000). Usually the prognosis is unfavourable. This is the result of the late diagnosis, made most often in advanced stages of the neoplastic process, and often accompanied by metastases. Individuals who are not treated usually die or undergo euthanasia within a month of diagnosis (L'Eplattenier et al. 2006). In the treatment of prostate tumours, various therapeutic combinations are currently used, such as surgery, chemotherapy or radiotherapy (Bacon et al. 2016).

Complete removal of the prostate tumour by complete prostatectomy is burdened with many complications, i.e. urinary incontinence, necrosis of the bladder neck or urethral stricture. The removal of the prostate and the precise fusion of the urethra and the bladder neck often requires a partial or complete osteotomy of the pelvic fusion. However, this procedure is not commonly performed in companion animals due to the abovementioned complications; further, the invasiveness of the surgery combined with the lack of significant improvement in the standard of living of the operated animals mean that there is a lack of acceptance from their caregivers (White 2000). Therefore, partial prostatectomy or other palliative procedures are more often recommended. These include urethral stenting, transurethral resection, cystostomy, chemotherapy, radiotherapy or NSAIDs (nonsteroidal anti-inflammatory drugs) (Goldsmid and Bellenger 1991; Weisse et al. 2006; Freitag et al. 2007). Nevertheless, total prostatectomy should be considered in cases of early detection of prostate cancer with the absence of localised and distant metastases.

This paper presents the procedure of a complete prostatectomy in a dog with a pre-pubic anastomosis of the urethra. The operation was performed without previous osteotomy of the pelvic septum and the anastomosis of the urinary tract was placed outside the abdominal cavity.

CASE REPORT

Anamnesis and diagnostics. An 11-year-old mixed breed dog (castrated at the age of three) was referred to the Wrocław University Cathedral and Clinic of Reproduction with a very difficult history of urination of about three weeks. In the last few days before admission, the patient had a catheter in another medical facility due to the lack of micturition. The patient underwent a thorough clinical examination and additional tests to detect the cause of urethral obstruction. In the ultrasound examination, a prostate of 4 cm × 5.5 cm × 5 cm and an irregular contour was revealed. The structure of the

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organ was heteroechogenic with numerous echogenic fields suggestive of neoplastic lesions. Apart from the changed image of the prostate gland, there were no changes in the remaining abdominal organs, which may be evidence of metastatic processes. Under ultrasound guidance, a fine needle biopsy of the observed changes in the prostate was performed.

In the collected material, apart from numerous erythrocytes and amorphous, slightly acid-consuming masses, the presence of atypical epithelial cells with large, hyperchromatic and pronounced nuclei and small cytoplasmic hem was observed. These features confirmed the suspicion of prostatic adenocarcinoma.

The patient with the diagnosis was referred to the Cathedral and Clinic of Surgery University of Environmental and Life Sciences in Wrocław for further treatment. There, chest and lumbosacral X-rays and CT exams were taken to exclude metastatic changes and complete prostatectomy was performed.

Anaesthesia. After performing control blood tests, it was decided that the patient was eligible for general anaesthesia and surgery. A catheter was introduced into the irradiated vein. The patient underwent intramuscular premedication with a mixture of dexmedetomidine (Orion Farma Dexdomitor 0.5 mg/ml) at a dose of 5 μg/kg with midazolam (Polfa Warszawa, Midanium 5 mg/ml) at a dose of 0.1 mg/kg. After sedating the animal, the operating field was prepared and metamizol (Vet-Agro Pyralgivet 500 mg/ml) was administered intravenously at a dose of 50 mg/kg. General anaesthesia was induced intravenously with propofol (ScanVet, Scanofol 10 mg/ml) at a dose of 2 mg/kg. Then, a tracheotubus with a cuff was introduced and oxygen supplementation started. Painlessness was obtained by local epidural anaesthesia – a mixture of morphine (Polfa Warszawa, Morphini Sulfas WZF 0.1% Spinal, 1 mg/ml) at a dose of 0.1 mg/kg with lignocaine (Polfa Warszawa, Lignocainum Hydrochloricum WZF 2%, 20 mg/ml) was introduced in a sterile manner by puncturing the epidural space between L7/S1 in a 1 : 1 ratio. After placing the patient in position and assessing the effectiveness of local anaesthesia (evaluation of anal sphincter muscle tone, assessment of pain response), tracheotubus was sealed and connected to the Datex Ohmeda S5 semi-closed inhalation apparatus, and the isoflurane vaporiser (IsoVet) was set to 1.5 vol%. During the procedure, intravenous Ringer's solution was administered at a dose of 5 ml/kg/h and the vital parameters were constantly monitored.

Operating technique. Before the beginning of the procedure, a sterile catheter with a diameter of 3 mm was introduced into the bladder. The procedure was started with a midline laparotomy. The skin incision was performed laterally from the foreskin in the caudal direction, reaching further to about 5 cm below the anus. Then, by dissecting the tissues lying deeper and successively binding or coagulating blood vessels of the foreskin, a white line was exposed and then sectioned up to the edge of the pelvic junction.

After opening the abdominal cavity, the urinary bladder was pulled cranially. The found vas deferens were ligated and cut. Then, the peritoneal and retroperitoneal tissues surrounding the prostate were delicately dissected with the supply of blood vessels as close to the prostate gland as possible. After the release of the prostate from the surrounding tissues, the catheter was withdrawn. In the later part of the operation, the urethra between the bladder and the prostate was transversely cut; care was taken that the incision was as close as possible to the prostate. Two stay sutures were placed on the stump of the urethra from the side of the urinary bladder. The pelvic urethra and the crotch side of the penis were then dissected according to the technique presented by Bacon et al. (2016). For this purpose, the bulbospongiosus and ischiocavernosus muscles were dissected and cut.

During dissection, special attention was paid to the artery and deep vein of the penis to maintain their continuity. Through dissection, the pelvic part of the urethra was released from the surrounding tissues up to the prostate and the penis to the level of the penile bone, while maintaining its attachment at the height of the foreskin. In the latter part of the procedure, gonorrhoeal arteries and veins of the penis were delicately dissected. Later, the penis was cut transversely at the level of the sciatic arch with preservation of dissected arteries and veins. This allowed for the removal of the prostate and the pelvic segment of the urethra connected to it as well as part of the severed penis through the wound in the abdominal cavity. The final part of the procedure consisted in reconstructing the continuity of the urethra. For this purpose, the penis released from the surrounding tissues was moved to the caudal

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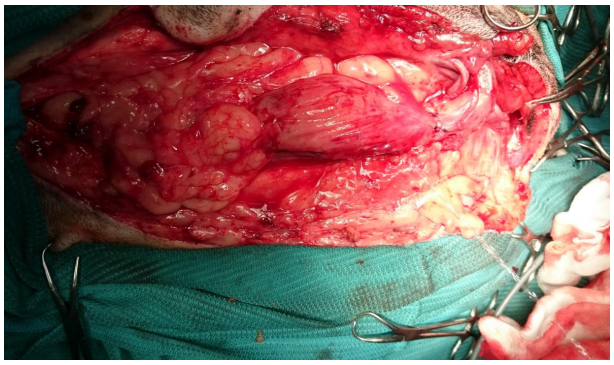

Figure 1. View of the pre-pubic anastomosis of the urethra during the surgical procedure.

White arrow = bladder; black arrow = anastomosis of urethra; blue arrow = penis

edge of the abdominal wound (close to the pubic symphysis) where the urethra was also moved from the bladder side. A catheter with a diameter of 3 mm was inserted into both ends of the urethra. Then, three stay sutures were stitched on the cut ends of the urethra from the bladder side and a dissected section of the penis urethra (Monosyn 3/0, Braun). The ends of the urethra were then joined with a continuous suture (Monosyn 4/0, Braun), which was interrupted during knitting in three places at equal distances to avoid narrowing the urethral lumen (Figure 1). Finally, the laparotomy wound was joined, leaving a small section of the unstitched wound in the caudal part in which the urethra ran, with the anastomosis of the urethra itself left outside the abdominal cavity. This facilitated subsequent control of a possible leak in the anastomosis. Subcutaneous tissue (Monosyn 0, Braun) and skin (Dafilon 0, Braun) were joined in a routine manner. Skin sutures were removed on the 10th day after the procedure. The removed gland was fixed in 10% buffered formalin and submitted for histopathological examination. The results of the study confirmed the cytological diagnosis of prostate adenocarcinoma (Figure 2).

In order to determine the origin of the tumour, immunohistochemistry was performed with an anti-keratin antibody. This antibody (clone MNF116) recognises cytokeratin with molecular weights of 40–58 kDa (cytokeratins 5, 6, 8, 17 and 19). The MNF116 clone exhibited a strong positive reaction with atypical epithelial cells that infiltrated stroma of connective tissue (Figure 3). Such a strongly positive reaction with epithelial cells allowed us to conclude that this prostate cancer originated from the transitional epithelium.

Post-operative treatment. The patient was provided with constant intensive medical care after the procedure, which included fluid therapy, antibiotic therapy with ceftriaxone (Biotrakson 75 mg/kg once a day) and analgesics; for the first 48 hours the patient received buprenorphine (Orion Pharma, Bupaq multidose 0.3 mg/ml) at a dose of 0.02 mg/kg

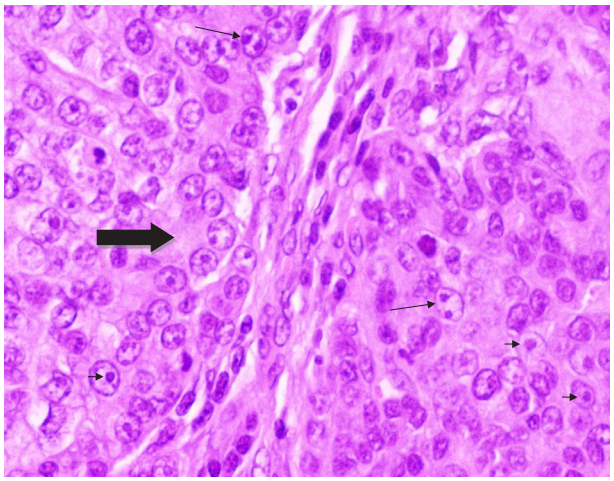

Figure 2. Poorly-differentiated adenocarcinoma. Only one suspected acinar structure (thick arrow) is present in the figure. A single large nucleolus (short thin arrow) or two large nucleoli (long thin arrows) are present in numerous nuclei. The nuclei are large, predominantly vesicular with parachromatin clearing. Staining with haematoxylin and eosin. Magn. 400 ×

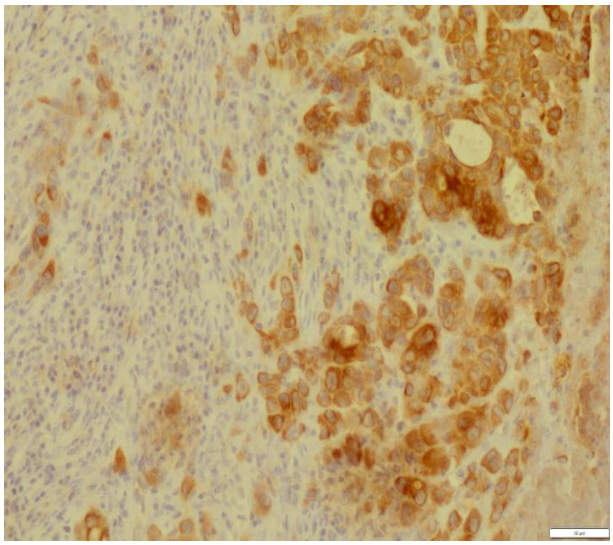

Figure 3. Positive immunohistochemistry reaction of epithelial cells infiltrating the stroma of connective tissue. Immunohistochemical staining with antibody directed against cytokeratin (DAKO, clone MNF 116, Cat. No. M0821) Magn. 100 ×

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Figure 4. Radiological control (uretrography) performed seven days after the operation. The red arrow indicates the enlarged area of the anastomosis

every 6 h and metamizole (Vet-Agro, Pyralgivet 500 mg/ml) at a dose of 50 mg/kg every eight hours. Over the next four days the animal received tramadol (Stada, Tramal 100 mg) at a dose of 5 mg/kg. In addition, once a day the patient was administered meloxicam (Boehringer Ingelheim, Metacam 5 mg/ml), initially at a dose of 0.2 mg/kg. Later, the dose was lowered to 0.1 mg/kg. Seven days after the procedure, a control urethrography was performed (Figure 4) and the catheter was removed from the bladder. However, due to the lack of urination for the next three days, the patient was catheterised twice a day. In the following days, after the postoperative pain ceased, the patient was able to empty its bladder through massage of the abdominal wall. This allowed the owners to take full care of the animal at home without constant medical supervision. About six weeks after the surgery, the owners of the operated dog informed the clinic about the death of the animal and did not give their consent for the post-mortem examinations. For that reason, it was impossible to discover the cause of death.

DISCUSSION

Making the distinction between tumours of urothelial and prostatic origin can be difficult in some cases on the basis only of histological examination. Urothelial tumours are positive for uroplakin III and cytokeratin 7 (Lai et al. 2008; Agnew and Machlan 2017;). According to Agnew and MacLachlan (2017), unequivocal determination of the origin of a tumour is very difficult even with using immunohistochemistry. Lai et al. (2008) proved that most cancers originate from prostate cells (but not all of them) and react positively with the cytokeratin 7 antibody. Using an antibody that detects more than one cytokeratin and observing a strong to very strong reaction in the majority of epithelial cells, allowed us to conclude that the examined tumour was derived from urothelium of the prostatic urethra. Conservative treatment of such malignant prostate tumours allows only a slight extension of the life of sick dogs. The vast majority of them die or undergo euthanasia due to rapid disease progression, causing urethral obstruction and/or metastasis (Liptak et al. 2004; L'Eplattenier et al. 2006; Bacon et al. 2016).

The treatment presented in this report is, according to the best of our knowledge, the first case of prostatectomy using of pre-joint anastomosis. There are reports in the literature in which similar anastomoses were performed in cases of severe pelvic damage to parts of the urinary outflow routes (Bjorling 1984). The surgical technique presented in this paper avoids pelvic osteotomy, often necessary during prostatectomy (Freitag et al. 2007). This makes it possible to reduce the invasiveness of the procedure and its duration. In addition, the lack of osteotomy reduces postoperative pain, hospitalisation and postoperative limitation of the patient's physical activity, which was also confirmed by Bacon et al. (2016).

In the presented case, the patient regained mobility within three days after the procedure without the need for subsequent long-term physical limitation, which occurs in the case of a similar pelvic osteotomy surgery, where approximately six weeks of mobility limitation is recommended (Davies et al. 1990). Performing total prostatectomy allows, in contrast to conservative methods of prostate cancer treatment, for complete removal of the affected prostate, removal of the source of pain and inflammation caused by the presence of the tumour and reduction of the risk of postoperative recurrence. The advantages of such a procedure were also described by Bacon et al. (2016). At the same time, in contrast to the cases operated

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on by Bacon et al. (2016), the patient we operated on had no symptoms of urinary incontinence after surgery, which according to the literature is a very common complication after prostatectomy (White 2000; Freitag et al. 2007) and is observed in between 33% and even 100% of operated dogs. Unfortunately, obstructed urination was still observed in the operated dog in the postoperative period. The effects of this complication were mitigated thanks to the cooperation of the owners, who supported the dog's micturition process by massaging his abdominal wall. The reason for this condition could be long-term catheterisation of the patient before the surgery, which may weaken the bladder muscles. Another reason for the lack of spontaneous micturition may be that the urethra anastomosis with the bladder neck remained outside the abdominal cavity, which allowed a clinical assessment of the presence of a possible anastomotic leak. In addition, the patient's death prevented long-term observation. The lack of micturition should certainly be treated as a postoperative complication; however, it is certainly easier to accept by animal caregivers than incontinence, especially since the patient did not require catheterisation.

Another frequently reported complication after prostatectomy is necrosis of the bladder neck and urethra at the anastomosis site. This is the result of high voltages at the site of the continuity of urinary passageways caused by the shortening of the length of the urethra (Kincaide et al. 1996). The implementation of anterior fusion allows reduction of the risk of tissue necrosis in the anastomosis site by applying sutures without tension.

Undoubtedly, such an invasive procedure as removing a prostate should be based only on strict criteria, whereas in the case of prostate cancer it is difficult to meet patients in the early stage of the disease without metastases. It also requires full awareness and acceptance on the part of the caregivers of the operated dog. The presented case with the described technique seems to be an appropriate direction in the treatment of malignant tumours of the prostate gland in dogs. However, obstructed urination, which was observed in this case may be unacceptable for some owners. For that reason, we are optimistic that carrying out more procedures like the one presented here will allow identification and removal of the cause of the described complication.

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