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CASE REPORT

Companion or pet animals

Needle-tract seeding following transabdominal ultrasound-guided fine-needle aspiration biopsy and cystocentesis of a cytologically diagnosed prostatic carcinoma in a dog

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Abstract

A 10-year-old, neutered, male, mixed-breed dog underwent ultrasound-guided fine-needle aspiration biopsies, leading to cytological suspicion of prostatic carcinoma. A whole-body computed tomography and computed tomography retrograde urethrography were performed, confirming a mineralised asymmetric heterogenous prostatomegaly, with an invasion of the prostatic urethra and bladder trigonum and suspected distant metastasis to multiple organs. Prostatectomy was not recommended due to the invasiveness of the prostatic neoplasia. Instead, medical treatment with toceranib was installed, which led to clinical improvement for 7 months. Eight months after the medical treatment was started, the dog presented with a new para-preputial cutaneous mass and regional lymphadenopathy. Fine-needle aspiration biopsies of the cutaneous mass and right superficial inguinal lymph node were taken. Cytology of the mass and lymph node revealed tumoral epithelial cells compatible with an undifferentiated adenocarcinoma or carcinoma. Given the fact that previous fine-needle aspiration biopsies of the prostate and a cystocentesis were performed, needle-tract seeding was highly suspected.

KEYWORDS
dog, needle-tract seeding, prostatic adenocarcinoma

BACKGROUND

Prostatic neoplasia is relatively uncommon in dogs.[1] The majority of prostatic carcinomas are derived from the ductal area and are undifferentiated or transitional cell carcinomas. Only a small proportion of canine prostatic tumours are adenocarcinomas.[2–5] Canine prostatic adenocarcinomas are highly invasive and metastatic tumours of surrounding organs.[6] Diagnosis can be made by abdominal ultrasound and/or retrograde urethrography, combined with the collection and cytological and/or histopathological examination of tissue samples. Prostatic tissue can be obtained by various methods, including fine-needle aspiration (FNA) biopsies and prostatic wash. Needle-tract seeding of prostatic adenocarcinoma has been described as a very rare complication in people, and tumour seeding following ultrasound-guided FNA biopsies has been described with bladder urothelial carcinomas in dogs as a rare complication.[7–12] However, no reports describing needle-tract seeding of prostatic carcinoma in dogs have been documented. This case report describes needle-tract implantation following cystocentesis and transabdominal ultrasound-guided FNA biopsies of a cytologically diagnosed prostatic carcinoma in a dog.

CASE PRESENTATION

A 10-year-old, neutered, male, mixed-breed dog with a bodyweight of 17.4 kg was referred to our institution for the management of prostatic gland neoplasia. Lethargy and dysorexia were noticed 5 months before the presentation. One month before presentation, the dog was seen by its primary care veterinarian, where a physical examination revealed pale mucosal membranes. Bloodwork demonstrated a microcytic hypochromic regenerative anaemia (haematocrit 24%). An abdominal ultrasound was performed, revealing jejunal lymphadenopathy and suspicion of prostatic neoplasia. Ultrasound-guided FNA biopsies of the prostate, liver and jejunal lymph node were taken by the referring veterinarian and analysed by a board-certified veterinary pathologist. The findings indicated that the prostatic biopsies were largely indicative of a prostatic adenocarcinoma. However, the possibility of a urothelial carcinoma could not be entirely ruled out. The remaining biopsies were consistent with multifocal hepatocellular cholestasis and reactive hyperplasia of the jejunal lymph node.

On physical examination at our institution, the dog had pale mucosal membranes, and tachycardia (140 beats per

minute) and was painful on caudal abdominal palpation. An asymmetrical prostatomegaly was palpated on rectal examination.

INVESTIGATIONS

Complete blood count revealed a severe microcytic hypochromic regenerative anaemia (haematocrit 16.7%, reference interval [RI]: 37%–55%), neutrophilic leukocytosis (white blood cells 21.30 × 10^9 cells/L, RI: 6–15 × 10^9 cells/L; neutrophils 17.04 × 10^9 cells/L, RI: 3.0–11.4 × 10^9 cells/L) and eosinophilia (2.77 × 10^9 cells/L, RI: 0.12–1.5 × 10^9 cells/L).

A whole-body computed tomography (CT) scan was performed under general anaesthesia, demonstrating a small intestinal intussusception surrounded by focal steatite. An asymmetric mineralised prostatomegaly (4 × 3.5 × 2.5 cm), with the right lobe more enlarged than the left lobe, was observed with a heterogenous aspect after intravenous contrast injection. A small prostatic cyst was observed in the left prostatic lobe. Lymphadenopathy of the right medial iliac and sacral iliac lymph nodes, consistent with most likely metastatic disease, was noticed. Multiple pulmonary (right and left caudal lung lobes) nodules, and cerebral and vertebral lesions were visible (Figures 1 and 2). CT retrograde urethrography revealed irregular borders of the prostatic urethra with dorsal displacement of the prostatic urethra (Figures 3 and 4). The bladder trigone was invaded by the prostatic neoplasia, without involvement of the ureteral papillae.

DIFFERENTIAL DIAGNOSIS

Multiple abnormalities were detected on further work-up, including a severe microcytic hypochromic regenerative anaemia, intestinal intussusception, asymmetric prostatomegaly with mineralisations, and lymphadenopathy of the right medial lilac and sacral iliac lymph nodes. Additionally, multiple cerebral, pulmonary and vertebral nodules were detected. Regarding the severe microcytic hypochromic regenerative anaemia, the main differential diagnosis was chronic blood loss (haematuria and/or gastro-intestinal blood loss). The differential diagnosis for the intestinal intussusception included intestinal neoplasia, foreign body ingestion, inflammation/infection or parasites. The main differential diagnosis for asymmetric prostatomegaly, with irregular borders of the prostatic urethra and involvement of the bladder trigone, was neoplasia. As prostatic carcinoma was suspected by previous FNA and cytology at the referring veterinarian, the right medial iliac and sacral iliac lymphadenopathy as well as multiple pulmonary, cerebral and vertebral nodules were suggestive of metastases from the prostatic neoplasia. The right medial iliac and sacral iliac lymphadenopathy can also be reactive lymphadenopathy. The differential diagnosis for the pulmonary nodules included granulomas, abscesses and haematomas. For the cerebral lesion, the differential diagnoses are granuloma and lacunar haemorrhagic infarct, and for the vertebral lesion, fat inclusion or cysts.

LEARNING POINTS/TAKE-HOME MESSAGES

- Needle-tract implantation is possible after transabdominal ultrasound-guided fine-needle aspirations of canine prostatic neoplasia.
- Cystocentesis should be avoided in dogs with prostatic neoplasia.
- Toceranib treatment in a cytologically suspected canine carcinoma may offer a viable option for disease management and can result in prolonged survival in advanced disease.

TREATMENT

Given the presence of a small intestinal intussusception, an explorative coeliotomy was elected. Before anaesthesia, multiple intravenous lactated Ringer's solution boluses of 10 mL/kg per bolus over 15 minutes (Hartmann's solution; B. Braun Vet Care; 30 mL/kg in total) were administered. The dog was premedicated with butorphanol (0.2 mg/kg intravenously [IV]; Dolorex, MSD Animal Health) and midazolam (0.2 mg/kg IV; Midazolam, Mylan), induced with propofol (dose on effect;

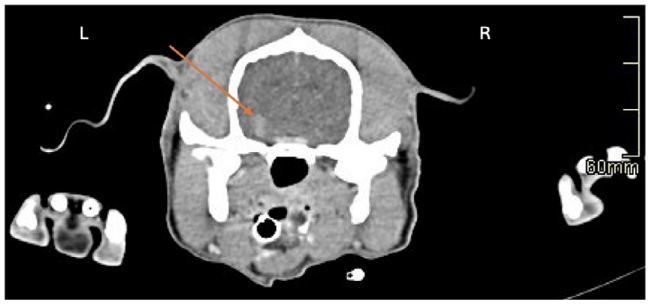

FIGURE 1 Post-intravenous contrast transverse computed tomography (soft tissue window) of the skull. A hyperattenuating nodule is indicated by the orange arrow in the left temporal lobe at the grey–white matter interface. L = left; R = right.

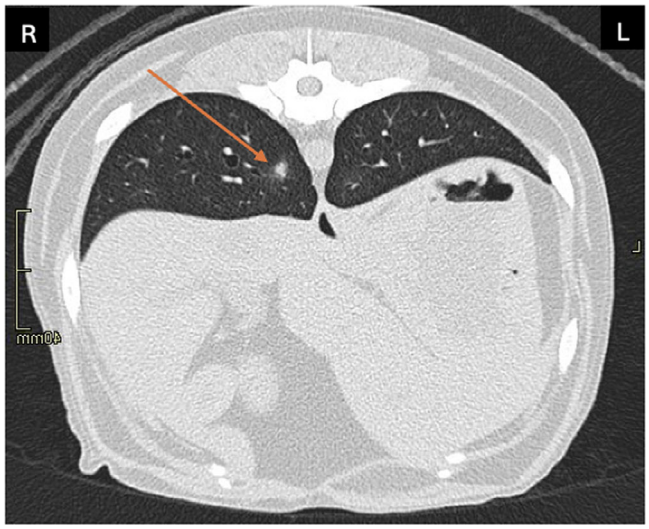

FIGURE 2 Transverse computed tomography (lung window) of the caudal part of the thoracic cavity. A pulmonary nodule is indicated by the orange arrow in the right caudal lung lobe. L = left; R = right.

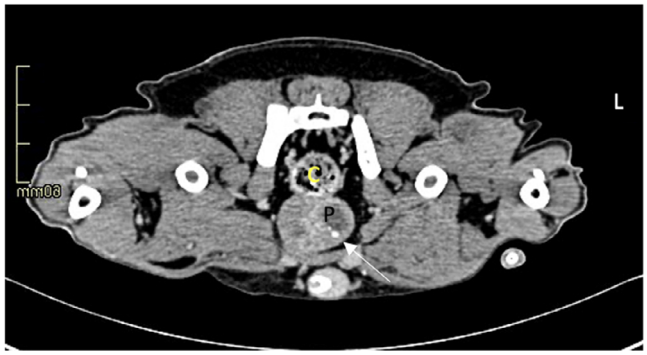

FIGURE 3 Post-intravenous contrast transverse computed tomography (soft tissue window) of the pelvic region. Presence of an asymmetric mineralised (white arrow) prostatomegaly with a heterogenous aspect of the prostatic gland. P = prostatic gland; C = colon; L = left.

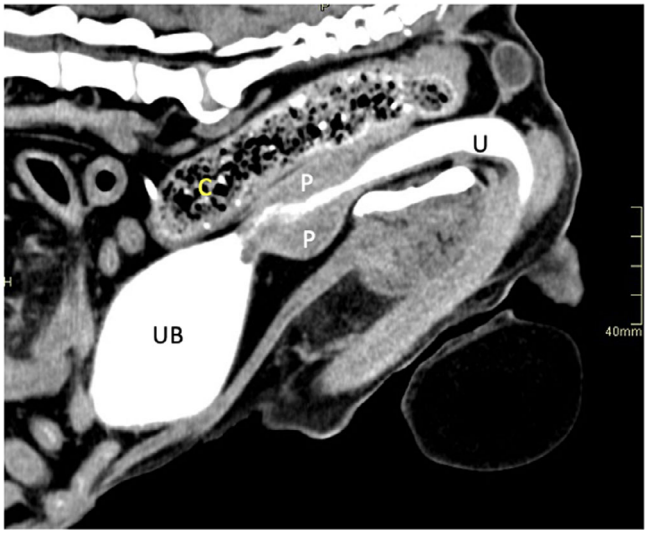

FIGURE 4 Post-contrast sagittal computed tomography retrograde urethrography reconstruction (soft tissue window) of the caudal abdomen and pelvic region. Presence of irregular borders of the prostatic urethra with dorsal displacement of the prostatic urethra. Invasion of the bladder trigonum by the prostate. UB = urinary bladder; C = colon; P = prostatic gland; U = urethra.

Propovet, AST Farma) and was intubated and maintained with inhalant anaesthesia via isoflurane with 100% oxygen and a continuous rate infusion of fentanyl (10 μg/kg/h; Fentadon, Dechra). Cefazoline (20 mg/kg IV; Cefazoline, Sandoz) and isotonic crystalloid fluids were administered perioperatively. Given the present severe anaemia and persistent tachycardia during anaesthesia, a packed-red blood cell transfusion (15 mL/kg over 6 hours) was initiated intraoperatively and continued postoperatively. A jejunal intussusception was confirmed with the presence of a jejunal mass in the middle of the intussusception. An end-to-end jejuno-jejunal anastomosis with 8 cm margins was performed and liver and jejunal lymph node biopsies were taken. No biopsies were taken from the prostate and enlarged iliac lymph nodes to limit the surgical and anaesthesia time. Histopathological examination revealed a jejunal leiomyoma without regional lymph node metastasis and lymphoplasmacytic cholangitis. Afterwards, the dog recovered uneventfully and was discharged after 48 hours of hospitalisation. Fifteen days postoperatively, the dog was clinically doing well. Due to the extent and invasiveness of the prostatic neoplasia, a total prostatectomy was not recommended in this dog. A conservative treatment was opted, consisting of the administration of toceranib (2.87 mg/kg orally every other day; Palladia, Zoetis). Following the initiation of treatment and before the first follow-up visit, a urine-specific gravity test and a urine protein creatinine ratio test were conducted by the referring veterinarian, both of which yielded results within normal limits.

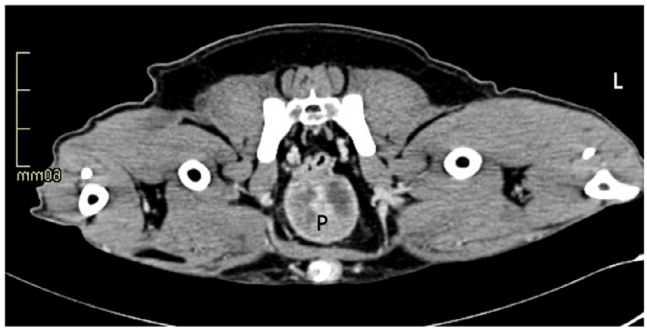

FIGURE 5 Post-intravenous contrast transverse computed tomography (soft tissue window) of the pelvic region 5 months after treatment initiation. Presence of stable prostatic gland disease with enlarged prostatic gland with a heterogenous aspect. P = prostatic gland; L = left.

OUTCOME AND FOLLOW-UP

One month after the start of the medical treatment, the dog was clinically doing fine. A control whole-body (pre- and post-contrast) CT and CT retrograde urethrography scans were performed, and no significant changes in the prostatic lesions were noticed. The prostatic urethra was subtly less compressed than before the start of the treatment.

The dog developed diarrhoea 2 months after the start of the toceranib treatment. A blood examination (complete blood count and biochemistry) was performed, which showed no abnormalities. A cystocentesis and urinary culture led to the diagnosis of bacterial cystitis. The urine-specific gravity was tested and measured at 1.028. Subsequently, urine cytology was conducted, revealing no evidence of cylindruria. *Streptococcus canis* was found in the urine, which is sensitive to multiple antimicrobials, including potentiated amoxicillin. The frequency of toceranib administration was reduced to every 3 days, and antimicrobial treatment with potentiated amoxicillin (20 mg/kg orally twice a day; Synulox, Pfizer) was added for 4 weeks, which resolved the bacterial cystitis. Blood examinations were repeated at every control visit and were within normal limits.

Five months after the start of the treatment, a control whole-body CT and CT retrograde urethrography scan were performed, showing stable disease (Figures 5 and 6).

Eight months after the treatment was initiated, the dog presented with a deterioration of its general condition. A large painful cutaneous para-preputial mass had appeared 1 month before the presentation. On clinical examination, tachycardia (130 beats per minute), tachypnoea (52 respirations per minute), hyperthermia (39°C) and lymphadenopathy of both superficial inguinal and popliteal lymph nodes were noticed. A cutaneous, firm and painful mass (10 × 4 cm) next to the left side of the base of the prepuce was palpated. FNA biopsies of the para-preputial mass and right superficial

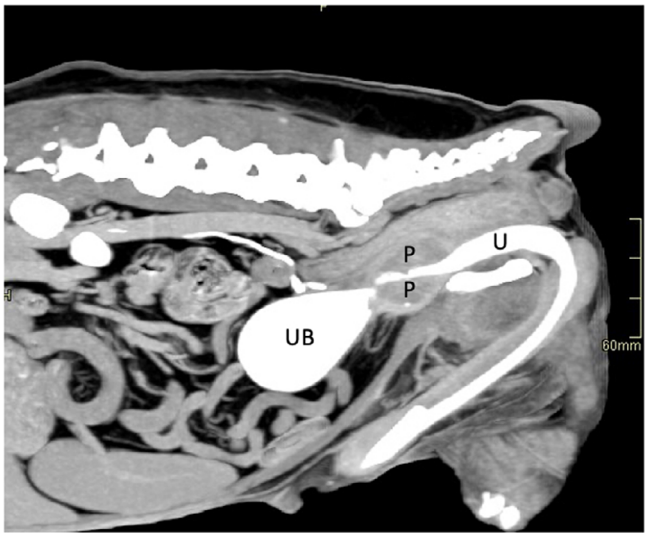

FIGURE 6 Sagittal computed tomography retrograde urethrography reconstruction (soft tissue window) of the caudal abdomen and pelvic region 5 months after initiating treatment, reveals the presence of stable prostatic disease with irregular borders of the prostatic urethra and invasion of the bladder trigonum. UB = urinary bladder; P = prostatic gland; U = urethra.

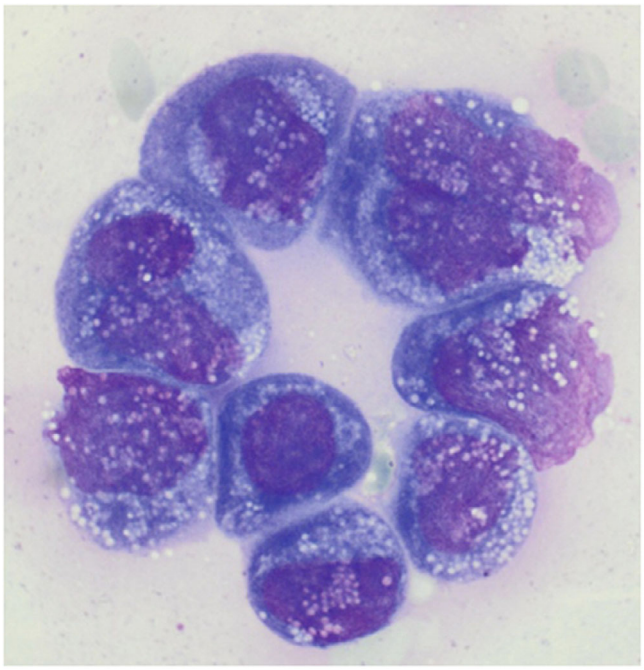

FIGURE 7 Fine-needle aspiration biopsy of the para-preputial cutaneous mass shown with Diff-Quik stain. The presence of round to polyhedral epithelial cells with round to irregular nuclei and single to multiple nucleoli. The cytoplasm is intensively basophilic and contains numerous microvacuoles. Anisocytosis and anisokaryosis are present.

inguinal lymph node were performed. Microscopic evaluation of the para-preputial mass cytology revealed a population of cohesive round-to-polyhedral epithelial cells, with round to irregular nuclei and prominent single to multiple nucleoli. The cytoplasm of these cells was intensively basophilic and contained numerous microvacuoles. Also, anisocytosis and anisokaryosis were present (Figure 7). The same cells were found in the cytology of the lymph node (Figure 8). Cytological findings were suggestive of carcinoma or undifferentiated adenocarcinoma and were most likely metastasis from the prostatic neoplasia. Treatment with toceranib was

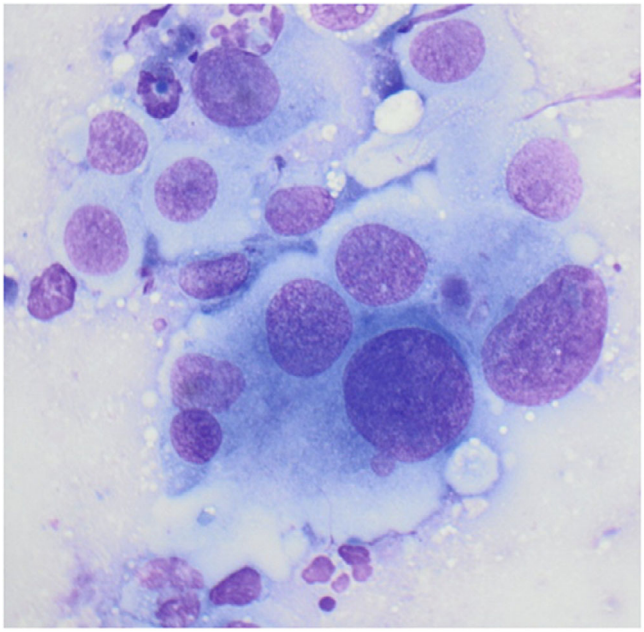

FIGURE 8 Fine-needle aspiration biopsy of superficial inguinal lymph node shown with Diff-Quik stain. The presence of multiple epithelial cells with round to irregular nuclei and single to multiple nucleoli and a basophilic cytoplasm containing numerous microvacuoles. Anisocytosis and anisokaryosis are present.

stopped and replaced by palliative treatment with piroxicam (0.3 mg/kg orally once a day; Feldene, Pfizer).

DISCUSSION

Canine prostatic tumours are relatively uncommon and are often highly aggressive and malignant.[10,13] The majority of prostatic tumours are carcinomas, including urothelial carcinoma, adenocarcinoma, squamous cell carcinoma and undifferentiated carcinoma.[14] Although very rare (less than 1%), mesenchymal tumours of the prostate have also been described.[15] Only a small proportion of the canine prostatic tumours are real adenocarcinomas.[2–5] The dog in the current case report had a prostatic neoplasia with invasion of the prostatic urethra and bladder trigonum, and CT examination showed the presence of pulmonary nodules and cerebral as well as vertebral lesions, highly suspected to be metastases given the clinical context. Based on the cytology of the prostatic FNAs, there was a suspicion of prostatic adenocarcinoma. However, as no histopathology was performed and based on the CT characteristics of the prostatic lesion, this conclusion could not be reached. Therefore, another type of prostatic carcinoma could not be ruled out. As no FNAs or biopsies were taken from the multiple pulmonary nodules, and cerebral and vertebral lesions, metastatic disease could not be confirmed.

In contrast to men, canine prostatic tumours do not respond to anti-androgen therapy, and it has been proven in several different studies that early castration increases the risk of prostatic carcinoma in dogs.[16–20] In our case report, the dog had been castrated at an earlier age. Treatment options for canine prostatic gland tumours include surgery (partial or total prostatectomy), radio- and/or chemotherapy and prostatic artery embolisation. Prostatectomy was in

the past not often performed in dogs due to the tumour extent, the presence of metastases and the high risk of post-operative complications.[20–22] More recent studies showed that total prostatectomy is a viable option, with lower rates of urinary incontinence and longer survival times than previously reported in dogs.[23–26] In these studies, only dogs with tumours confined to the prostate or prostatic urethra without evidence of metastatic disease were considered surgical candidates.[23–26] Radiotherapy can result in local tumour control. However, the effect is only temporary and complications, including urethritis, colitis, urethral or colonic stricture and bladder fibrosis, are reported.[27,28] Recently, the effectiveness of toceranib for the treatment of canine (prostatic) adenocarcinomas and urothelial carcinomas has been described.[29–31] Another recently emerged therapeutic option is cyclo-oxygenase-2 (COX-2) inhibitors, as COX-2 is only expressed by neoplastic epithelial prostatic cells.[32] Additionally, prostatic artery embolisation has recently been described in 20 dogs, resulting in decreased prostatic volume and improved clinical signs 30 days after the embolisation.[33] Due to the extent of the prostatic tumour and the probable metastatic disease (multiple cerebral, pulmonary and vertebral nodules), a total prostatectomy was not recommended, nor was radiotherapy due to financial restrictions. Therefore, conservative treatment with toceranib was initiated, which resulted in stable disease for 7 months. Two months after the start of the toceranib treatment, the dog developed diarrhoea. Gastro-intestinal adverse events during toceranib administration are also reported in previous studies and were resolved most of the time after dose reduction.[29–31] The dog in the present case report survived at least 8 months after toceranib treatment was initiated. Unfortunately, clear information regarding the survival and outcome in dogs with prostatic carcinoma treated with toceranib is lacking.

Transabdominal FNAs are preferred over prostatic wash to obtain prostatic tissue samples, as there is a higher chance to obtain diagnostic samples with a reported diagnostic accuracy of 80%.[29,34] But there is the potential risk of needle-tract implantation, which has been described in urothelial carcinomas of the bladder and/or prostate in dogs.[10–12] However, needle-tract seeding has not yet been reported after transabdominal FNAs of prostatic adenocarcinoma in dogs. To determine the exact cell origin of the cutaneous mass and lymph node, histopathology should have been ideally performed, which was not the case in the current report. However, using FNAs to diagnose primary prostatic adenocarcinomas with multifocal skin, muscle and lymph nodal metastasis has been described, and cytology was considered a sensitive staging tool in detecting metastatic disease of prostatic adenocarcinoma.[35] Given the fact that prostatic gland FNAs were taken by the referring veterinarian, that a cystocentesis was performed at our institution and that the cutaneous mass was located at the level where the FNAs and/or cystocentesis were performed, needle-tract seeding was highly suspected. In people, needle-tract seeding following prostatic biopsy has been reported. However, the incidence is low in men, and therefore, this rare complication does not outweigh the benefit of having an appropriate cancer diagnosis.[7–9,20] Besides, FNA is a minimally invasive sampling procedure, leading to a feasible diagnosis and a suitable tool for cytological and molecular diagnostic purposes.[11,36] Therefore, transabdominal FNAs should be considered for obtaining diagnostic samples. Even in dogs, the risk of tumour seeding is low (1.6%), and seeding is more commonly observed after a laparotomy.[12] Therefore, the attainment of a diagnosis and the possibility of early treatment do not outweigh the rare occurrence of needle-tract seeding.[10–12,29,34] However, in dogs where surgery (prostatectomy) can be beneficial, surgical excision of the needle-tract should be considered.

Although skin metastases in our case report appeared most likely as a result of needle-tract seeding after FNAs of the prostatic gland were performed, spontaneous metastases are also reported. A recent study mentioned the occurrence of cutaneous metastasis of prostatic neoplasia without a history of abdominal surgery or FNA.[35]

In conclusion, toceranib treatment led to relatively long clinical improvement in this dog diagnosed with prostatic carcinoma. However, further studies are indicated to evaluate the prognosis of dogs with prostatic carcinoma treated with toceranib. Clinicians should be aware of the possibility of needle-tract implantation after cystocentesis or transabdominal ultrasound-guided FNAs in dogs suspected of prostatic carcinomas. However, FNAs for the diagnosis of prostatic gland neoplasia should still be considered to obtain feasible diagnostic samples, as the incidence in veterinary medicine is reported as low.

AUTHOR CONTRIBUTIONS

Annick Hamaide, **Stéphanie Noël** and **Géraldine Bolen** were involved in the clinical case management. **Emily Vrijsen** was responsible for the data collection and original draft of the manuscript. **Annick Hamaide**, **Stéphanie Noël** and **Géraldine Bolen** supervised the project and reviewed the manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

FUNDING INFORMATION

The authors have not declared a specific grant for this case report from any funding agency in the public, commercial or not-for-profit sectors.

ETHICS STATEMENT

This manuscript involves the use of non-experimental animals. Ethical approval was not required, as this was a retrospective case report of a client-owned animal. Informed owner consent was obtained for all investigations and treatments related to this patient.

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IMAGE QUIZ

Figure 7 Fine-needle aspiration biopsy of a para-preputial cutaneous mass shown with Diff-Quik stain in a dog that was suspected of having a prostatic adenocarcinoma via fine-needle aspiration of the prostatic mass earlier.

MULTIPLE-CHOICE QUESTION

What is the likely diagnosis?

POSSIBLE ANSWERS TO MULTIPLE-CHOICE QUESTION

A. Cutaneous high-grade/grade III mast cell tumour
B. Benign cutaneous peripheral nerve sheath tumour
C. Cutaneous amelanotic melanoma
D. Cutaneous metastasis from a prostatic carcinoma

CORRECT ANSWER

D. Cutaneous metastasis from a prostatic carcinoma.

There is the presence of round to polyhedral epithelial cells, with round to irregular nuclei and single to multiple nucleoli. The cytoplasm is intensively basophilic and contains numerous microvacuoles. Additionally, anisocytosis and anisokaryosis are present. These cytological findings suggest a carcinoma or undifferentiated adenocarcinoma and are most likely metastasis from the prostatic adenocarcinoma suspected by cytology in this dog.