Transitional Cell Carcinoma in the Distal Urethra of a Female Golden Retriever

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ABSTRACT

Background: Urinary tract tumours represent only 0.5-1% of neoplasms in dogs, and transitional cell carcinoma (TCC) is the most common. It is most common to find TCCs in the trigone region. Diagnosis can be made with image analysis, cytology or histology. With non-infiltrative lesions in the early stages, it is possible to obtain a biopsy by endoscopy. Surgical resection is the treatment option of choice for this tumour. Dogs with poor response to chemotherapy or at an advanced stage of the disease are candidates for palliative treatment. This paper reports an special case of TCC located in the distal urethra of a female dog, obtaining the diagnosis through endoscopy, cytology and immunohistochemistry.

Case: A nine-year old, female, neutered Golden Retriever was referred for examination after suffering vaginal bleeding. Vaginal palpation revealed an apparent mass on the vaginal floor. Cytology by imprinting the mass revealed a carcinoma. A vaginoscopy was performed on the patient. An endoscopic examination showed normal vaginal mucosa, but, through the urethra, a mass was observed in the urethral lumen, with thickening and dilatation of the urinary meatus. A tissue biopsy was obtained. Episiotomy was performed to remove the tumour. Histopathological studies diagnosed the mass as transitional cell carcinoma with incomplete surgical margins. An immunohistochemistry analysis of the tumour was performed.

Discussion: The location of the tumour in the distal urethra makes this case unusual, as this rarely occurs. There are few reports of this location in bitch dogs and they are usually diagnosed at necropsy. This shows the great advantages of endoscopy for the diagnosis of tumours in the urinary tract. There are few cases of this type of tumour being described at this site, and they are usually diagnosed at necropsy. This report shows the great advantages of urethroscopy for the diagnosis of neoplasias of the urinary tract. In this report, owing to the location of the tumour, cytologic diagnosis (carcinoma) could be made quickly by an impression smear. However, we were unable to determine the precise tumour type, because there were no cells with vacuolated basophilic cytoplasm or signet-ring-shaped cells. Distinguishing TCC from other malignant tumours by cytology is complicated, as they are caused by immaturity and there is a lack of differentiation; so, biopsy is suggested. Endoscopy is the most effective method to obtain biopsies of TCC in the urinary tract. An endoscopic examination can be performed with a rigid or flexible endoscope. In the present case, a videoendoscope with a diameter of 9.2 mm was used, owing to the large dilatation of the urinary meatus. The majority of vesical tumours are diagnosed by contrast and negative double-contrast cystography; however, in this case, they did not reveal the presence of a tumour in the bladder. Immunohistochemistry was positive for monoclonal antibodies for TAG-72 in the present case; this is a common finding in 53% of reported cases. Conventional surgery was performed to resect the tumour, because electrosurgical transurethral resection of TCCs in females can cause some surgical complications. This animal had a favourable response after administering NSAIDs (piroxicam). Treatment was still challenging, owing to the difficulties in surgical resection and the poor response to conventional chemotherapy.

Keywords: transitional cell carcinoma, veterinary oncology, small animals, urethroscopy.
INTRODUCTION

Urinary bladder and urethral tumours represent only 0.5-1% of neoplasms in dogs [13]. Transitional cell carcinoma (TCC) is the most common, affecting the lower urinary tract [12]. TCC is a locally invasive tumour that may cause metastasis [19,21]; it usually affects middle-aged-to-old dogs with an average age of 10 years. A racial predisposition for Shelties, Scottish Terriers and West Highland White Terriers has also been described. It is more common to find TCC in the bladder trigone region, and in males it is common for the prostate to be involved [6]. Diagnosis can be made based on clinical symptoms and the results of image analysis, cytology or histology. With non-infiltrative lesions in the early stages, it is possible to obtain a biopsy by endoscopy.

Surgical resection is the treatment option of choice for tumours in the bladder or urethra [13]. Owing to difficulties in tumour removal and the poor response to chemotherapy, patients with local, advanced and/or systemic TCC are candidates for palliative treatment [11].

CASE

A female, nine-year old, spayed Golden Retriever of 40 kg was presented with severe acute bleeding from the vagina. The patient had previously undergone spaying and a radical mastectomy for a mammary gland carcinoma. Upon physical examination, all constants presented between ranks. But, upon palpation of the vagina, a hard, pedunculated and mobile mass, apparently on the floor of the vagina, was found right at the urinary meatus. A vaginal cytology showed evidence of a carcinoma (Figure 1). Chest radiographs discarded metastasis. Nothing abnormal was detected in routine abdomen-positive and -negative radiographs or a double medium-contrast cystogram (Figure 2). Laboratory tests only showed a slight increase in ALT (75 IU/L ranging from 12-55 IU/L) and AST (85 IU/L range of 4-70 IU/L).

The animal was referred for a vaginoscopy using a flexible videoendoscope with a diameter of 9.2 mm (Olympus GIF-Q150). The vaginal mucosa was of normal aspect and the tumour was located at the exit of the urinary meatus (Figure 3). The edges of the meatus were thickened and dilated, permitting the introduction of the endoscope.

It was decided, in this case, to perform an open surgery. After episiotomy, a urinary meatus was located. The expansion and thickness of the wall of the urethra (ca. 3 to 4 mm) were checked and the tumour was located. A urethrotomy was performed; the tumour was base-resected and the urethrotomy closed one layer with 4-0 polypropylene. To avoid urethral stricture, a silicone Foley catheter was fitted (14 French).

The animal pathology laboratory confirmed TCC. Additionally, immunohistochemistry analysis for monoclonal antibodies of TAG-72 was positive (Figure 4). Currently, the patient is under PO treatment with firocoxib (Previcox - 227 mg/24 h) and has not relapsed; at this time, there has been no recurrence of the tumour or of vaginal bleeding.
Figure 2. Right lateral view double contrast cystogram, in which neoplasia is not seen at the level of the urinary bladder.

Figure 3. Urethroscopy showed the tumour located at the urinary meatus. The tumour was located at the distal urethra portion.

Figure 4. A) Note the papillary structures formed by epithelial cells with moderated cytoplasm exhibiting an abundant granular appearance and a round-to-oval nucleus, with one or two vesiculated and prominent nucleoli and some signet-ring cells (H&E 1000×). B) Detail of fibrosis demonstrated with Masson’s trichrome 400×. C) Immunohistochemistry showed positivity to TAG-72 monoclonal antibodies.
**DISCUSSION**

The location of the tumour in the distal urethra makes this case unusual, as this rarely occurs [20]. In one report, this tumour was in the pelvic portion of a female Samoyed, but a urethroscopy was not performed, and it was only observed at necropsy [16]. This shows the great advantages of endoscopy for the diagnosis of tumours in the urinary tract.

Actually, there is no statistical evidence of a gender preference of TCC [12,13]. Nevertheless, TCC is more common in older dogs and in those weighing over 10 kg [12], that is, similar to this case.

It has also been reported that ovariohysterectomy predisposes TCC [15,18]. In this case, it is believed that this fact does not have any influence, because the dog was spayed just one month before diagnosis.

Urine sedimentation analysis successfully identifies 30-50% of affected dogs [12]. Traumatic catheterisation and puncture also have good diagnostic effectiveness [10], but, in this case, owing to the location of the tumour, rapid cytological diagnosis by impression smear was performed. In this case, it was not possible to determine the exact tumour type, because there were no cells with vacuolated basophilic cytoplasm or that were signet-ring-shaped cells. In addition, the features that distinguish TCC from other malignant tumours were difficult to recognise by cytology, because they are caused by immaturity and lack of differentiation; so, biopsy is recommended [22]. Cystoscopy is the most effective method to obtain a biopsy of TCC in the urinary tract [1]. Endoscopic examination of the urethra can be performed with a rigid or flexible endoscope in females, and because of the size of the urethra, a slightly larger diameter can be employed. In the present case, a urethroscopy biopsy was obtained using a videoendoscope with a diameter of 9.2 mm, and this was possible because of the great dilatation of the distal urethra and urinary meatus.

Contrast and negative double-contrast cystography did not reveal the presence of a tumour in the bladder; however, 96% of dogs with a filling defect or a mass in the lower urinary tract can be diagnosed by this technique [12].

Additionally, 53% of dogs with TCC were positive for TAG-72 [2]. In the present report, the immunohistochemistry was positive to monoclonal antibodies for TAG-72.

Surgical resection is the treatment of choice for any solid tumour located in the bladder or urethra. Owing to the difficulty in the removal of the tumour and the poor response to chemotherapy [11], typical patients with local, advanced and/or systemic disease are candidates for palliative techniques [13]. Treatment of urethral TCC consists of resection of the mass combined with chemotherapy. Conventional surgery was chosen to remove the tumour instead of electrosurgery with polipectomy, so as to eliminate the possibility of leaving the tumour in situ. In addition, electrosurgical transurethral resection of TCC cannot be recommended in females, because of a high intra- and postoperative complication rate [8].

Treatment is still challenging, owing to difficulties in the surgical resection and the poor response to conventional chemotherapy [4]. A favourable response after administering NSAIDs (piroxicam) was observed. The exact mechanisms by which these responses are achieved are still poorly understood. However, attention has focused on this drug’s ability to inhibit cyclooxygenase (COX)-1 and -2 and, consequently, the roles that these enzymes play in malignant transformation [14,17]; both COX-1 and -2 are present in TCC tumour cells [7].

In this case, treatment with firocoxib was performed, owing to its prior success in the treatment of TCC as a monotherapy, according to a previously published report [3], and the ease of administration compared with piroxicam [9]. Nevertheless, a greater effectiveness had been demonstrated by combining NSAIDs with mitoxantrone therapy [6]; to date, the owners have discussed the possibility of adding this drug to the treatment.

Although the survival of animals with this type of tumour is short, in this case, the survival period could be a bit longer, as it has been shown that dogs with solitary bladder or urethral tumours have significantly longer median survival times than dogs with tumours located in both the bladder and the urethra [12]. Moreover, it has also been reported that spayed females have a longer survival period, which is attributed to them possessing a shorter and wider urethra with less chance of a blockage; as they do not have a prostate, the cancer is also less likely to develop metastases [15].

The bitch presented in this paper developed the tumour in the distal portion of the urethra, which is rare. Finally, this case emphasises the importance
of urethroscopy for the location of lower urinary tract tumours and in the taking of biopsies. Possibly with the routine use of this diagnostic technique, veterinarians will begin to identify this tumour more frequently in the distal urethra of female patients.

MANUFACTURER

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REFERENCES


