



## CASE REPORT

### Primary Prostatic Adenocarcinoma in a Domestic Short-Haired Cat

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#### ABSTRACT

An 8-years-old, domestic short-haired cat was presented for constipation and symptoms referable to the lower urinary tract. A solid mass located in the caudal area of the abdomen was palpated. Abdominal ultrasonography, positive-contrast retrograde urethrocytography and total body computed tomography showed the presence of a prostatic neof ormation occupying almost completely the pelvic cavity. The neof ormation displaced dorsolaterally the descending colon and completely englobed the prostatic urethra, without apparent involvement of the urethral lumen. Histopathologic examination revealed a prostatic carcinoma. Neoplastic cells showed a moderate to intense cytoplasmatic expression of AE1/AE3, while no expression of cytokeratin 7 and Uroplakin III was observed. Topographical, histological and immunohistochemical findings were consistent with a diagnosis of primary adenocarcinoma of the prostate body.

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#### INTRODUCTION

Prostatic disorders are rare findings in cats. However, their real prevalence is unknown, mostly due to the common veterinary practice of neutering peripubertal animals. Few cases of adenocarcinoma of the prostatic body have been reported in cats (Hubbard *et al.*, 1990; Caney *et al.*, 1998; LeRoy and Lech, 2004) and, recently, an adenocarcinoma of the prostatic disseminated portion has been described (Tursi *et al.*, 2008). In dogs, most prostatic carcinomas are of ductal/urothelial origin and have a high incidence in castrated males. Furthermore, in the canine species, age is a well-known risk factor for prostatic carcinoma and the average age at diagnosis is 10 years (Christensen *et al.*, 2018). Similarly, in cats, prostate carcinoma seems to develop in old age while orchietomy does not show to affect the incidence of the disease (Caney *et al.*, 1998; LeRoy and Lech 2004; Tursi *et al.*, 2008). This report describes a primary prostatic adenocarcinoma in a male cat resulting in constipation and urethral obstruction.

#### CASE HISTORY

An 8-years-old, domestic short-haired cat was presented to the referring veterinarian with a history of

tenesmus and constipation. The cat tested positive for feline immunodeficiency virus and was neutered only two weeks before the onset of symptoms. After a first unsuccessful attempt of medical treatment lasted one month, the referring veterinarian performed a colotomy to remove a fecaloma that in the meantime had formed.

Six months after the colotomy, the cat was referred to the veterinary teaching hospital of the University of Pisa for a relapse of the initial symptomatology, tenesmus and constipation, and the onset of symptoms referable to the lower urinary tract: pollakiuria, stranguria and hematuria. On clinical examination, abdominal palpation revealed the presence of a solid mass located in the caudal area of the abdomen. A complete blood count and a biochemical profile revealed microcytosis (MCV 34.4 fL, range 41.3-52.0 fL), dysproteinemia (A/G ratio 0.71, range 1.0-1.4) hyperglobulinemia (Glob 4.9 g/dL; range 2.6-3.2 g/dl) and hypercholesterolemia (Chol 408 mg/dL, range 65-230 mg/dL). Urine was collected via cystocentesis. A mild hematuria and proteinuria were found, no bacteria were isolated on culture.

The transabdominal ultrasound examination was performed using a Toshiba Aplio 400 equipped with a 5–13 MHz linear array transducer and a 6.6–8.0 MHz microconvex transducer. Longitudinal and transverse scans of the mass were evaluated, revealing a round-

shaped neof ormation with the maximum diameter of about 3 cm, irregular margins and a heterogeneous echotexture. The neof ormation was close to the distal portion of the descending colon, caudal to bladder neck (Fig. 1A). After placement of a urethral catheter, the lesion showed to encircle asymmetrically the urethra.

No other anomalies were observed by abdominal ultrasonography, although the prostate was not detected. The perineal ultrasound scan did not allow to further characterize the mass.

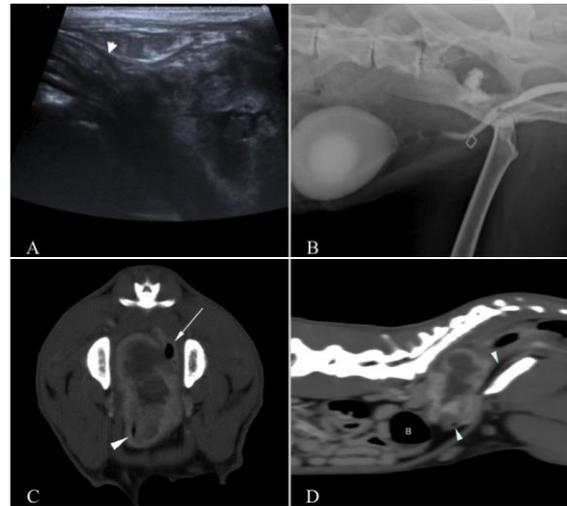
After the ultrasound examination, the cat was anaesthetized for contrast urethral radiography and total body computed tomography (CT). Positive-contrast retrograde urethrocytography showed a slight reduction of the urethral lumen at its prostatic portion. However, the urethral inner surface appeared smooth and regular (Fig. 1B).

The CT revealed the presence of a mass, 5 cm x 3 cm x 2.5 cm, occupying almost completely the pelvic cavity. The mass showed a ring enhancement with hypoattenuation of the center; margins were lobulated and defined. The descending colon was displaced dorsolaterally and a ventral displacement of the urethra, which was completely englobed in the lesion, was observed (Fig. 1C, 1D). Medial iliac and hypogastric iliac lymph nodes were enlarged in size, with homogeneous enhancement.

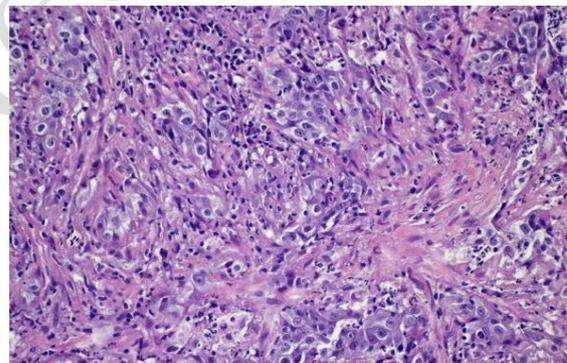
Biopsy samples were obtained by using a TRU-CUT needle. Tissue samples were fixed in 10% neutral buffered formalin, embedded in paraffin and sectioned at 4  $\mu$ m. Hematoxylin and eosin (HE) stain was used for histopathological examination. The sampled tissue was part of a highly infiltrative and not encapsulated epithelial neoplasia composed of irregular nests and cords infiltrating the preexisting stroma and smooth muscle fascicles. Neoplastic cells had a pale, abundant cytoplasm and contained round to ovoid large nuclei with a prominent centrally located nucleolus or small multiple nucleoli (Fig. 2). Anisokaryosis and anisocytosis were present and atypical mitotic figures were frequently observed, ranging from 2 to 4 per high-power field (400 x). Nests and cords were separated by a poorly cellular fibrous stroma infiltrated by numerous neutrophils. Normal prostatic parenchyma was not present. Immunohistochemistry using monoclonal mouse anti-human cytokeratin 7 (CK7; DAKO, clone OV-TL 12/30, dilution 1:75), monoclonal mouse anti-human cytokeratin clones AE1/AE3 (CK AE1/AE3;) and polyclonal rabbit anti human uroplakin III (UIII;) was performed. Normal urinary bladder epithelium was included as CK7 and UIII positive control, while a sample of haired skin was used as control for CK AE1/AE3.

Neoplastic cells showed a moderate to intense cytoplasmatic expression of AE1/AE3, while no expression of CK7 or UIII was observed (Fig. 3). Topographical, histological and immunohistochemical findings were consistent with a diagnosis of primary adenocarcinoma of the prostate body.

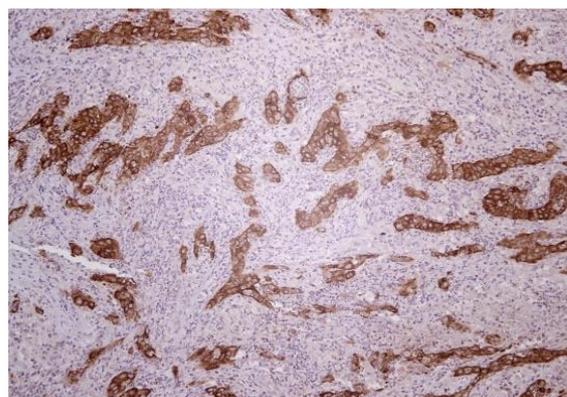
Because of the poor prognosis, the owner decided to undertake only symptomatic and supportive therapy. A specific dietary management (increasing food fiber content), addition of vaseline with meals, a medical treatment using meloxoral 0.1 ml/kg/die and enrofloxacin 5 mg/kg/die were administered. For few months, the



**Fig. 1:** A: Ultrasonographic sagittal scans revealed a round-shaped pelvic mass with irregular margins and heterogeneous echotexture. The neof ormation was close and caudal to bladder neck (arrowhead). B: Positive-contrast retrograde urethrocytography revealed a slight reduction of the prostatic urethral lumen, although the urethral inner surface was smooth and regular. It is possible to see the extravasation of contrast medium into the prostatic ducts (\*). C-D: Transversal (C) and sagittal (D) multiplanar reconstruction CT images revealed the presence of a mass occupying most of the pelvic cavity. The mass had defined margins and a ring-enhancing appearance with a hypoattenuated center surrounded by a bright rim. The descending colon was displaced dorsolaterally, on the left (arrow), and the urethra displaced ventrally, on the right. The urethra was completely englobed in the lesion (arrowhead). (B) Bladder.



**Fig. 2:** The cells are round to oval, with poorly defined border enclosing moderate amounts of pale eosinophilic, finely granular cytoplasm. The nuclei are round to ovoid with coarsely clumped chromatin and one or two prominent nucleoli. HE, 400x.



**Fig. 3:** Immunohistochemistry demonstrates intense cytoplasmic expression of cytokeratin (clone AE1/AE3) in the cytoplasm of neoplastic cells. IHC, Monoclonal Mouse Anti-Human Cytokeratin Clones AE1/AE3, DAKO Avidin-biotin complex (ABC) method, 200x.

owner has reported the partial remission of clinical signs and a significant improvement of patient's quality of life. Eight months later, the cat was presented in emergency for lethargy, anorexia and anuria. At physical examination, the bladder was overdone, harsh and painful. A urinary catheter was placed and the bladder drained of urine but, within 24 hours, the urethral obstruction relapsed and the owner elected for euthanasia. The authorization for the necropsy was not granted.

## DISCUSSION

The incidence rate of prostate cancer is very low in cats and this makes it difficult to identify risk factors involved in the development of the disease, such as age and castration.

In literature, the prostate cancer occurs in cats with a median age of 8 years (from 6 to 12 years old), the same age of the cat described in the present case report (Hubbard *et al.*, 1990; Caney *et al.*, 1998; LeRoy and Lech 2004; Tursi *et al.*, 2008). Although an extremely small number of cases is described, age seems to represent an important risk factor for the onset of prostate carcinoma, the same as in dogs. Castrated dogs are at increased risk of prostate tumor (with an OR of 3.9 in castrated versus intact dogs) and this is because sex hormones seem to exert a protective action on prostatic tissue (Christensen *et al.*, 2018). In cat population, where the majority of subjects are neutered, castrated males do not seem more predisposed to prostate tumor than intact ones and this may suggest that different pathogenic mechanisms are involved compared to those hypothesized in dogs. Interestingly, the cat of the present study was castrated only two weeks before the onset of symptoms and thus likely the neof ormation was already present at time of the surgery.

The observed clinical presentation, with constipation and symptoms referable to the lower urinary tract, has remarkable similarities with what reported by other authors (Caney *et al.*, 1998; LeRoy and Lech, 2004).

Identifying a neoplastic lesion as a primary prostatic adenocarcinoma is complex on the basis of anatomical location and morphology alone (Oh *et al.*, 2016). Urothelial carcinomas can have a prostatic location, although, they do not originate from the prostatic parenchyma. Carcinomas that originate from the transitional epithelium of the prostatic urethra or of the periurethral ducts, often invade the prostatic parenchyma and this can occur from intraductal extension or from direct infiltration of the neoplastic tissue (Bates and Baithun 2000). An accurate histological evaluation supported by immunohistochemistry, as well as a precise topographical localization of the neof ormation, could be helpful to properly define the origin of a prostatic neoplasia. However, the heterogenous histologic appearance of prostate carcinomas, coupled with the lack of a prostate-specific immunohistochemical marker suitable for feline tissues, makes the accurate

classification of prostate carcinomas difficult with traditional light microscopic evaluation. The uroplakins are apical membranes proteins that play an important role in regulating membrane permeability of transitional epithelium. In human urogenital cancer, CK7 and UIII have been used to identify the urothelial origin of tumor cells (Mai *et al.*, 2001).

If in dogs with a normal prostate UIII and CK7 staining is restricted to the urethra and periurethral ductal cells, a high percentage of the canine prostate carcinoma expresses UIII and CK7 (Lai *et al.*, 2008) supporting a ductal origin of this tumor, while the origin from peripheral acini or dedifferentiation of neoplastic prostatic epithelium to a less differentiated, urothelium-like tissue, are less likely (LeRoy *et al.*, 2004).

Even though few phenotypical studies have been conducted on feline prostate carcinoma and few information is available about their immunoreactivity, positive staining for AE1/AE3 and negative staining for UIII and CK7, combined with topographical findings, support the diagnosis of primary adenocarcinoma of the prostate body. Except that a fine needle biopsy could be not properly representative of the totality of the tumor and sampled from a less differentiated area, since solid prostatic tumors with increasing invasiveness lose their expression of CK7 and UIII (Ramos-Vara *et al.*, 2003).

**Authors contribution:** MT and MS followed the clinical course of the case and collected clinical data. TM and SC performed the diagnostic imaging procedures. VB performed the histological and immunohistochemical analysis. MT and AR arranged the figures and drafted the manuscript. All authors read and approved the final article.

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