

In-Situ Transitional Cell Carcinoma of Urinary Bladder in a Cat

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Abstract

Urinary bladder tumors in cats, unlike in dogs, usually appear outside of the trigonal region as localization. These tumors are confused with urinary tract infections associated with hematuria in a clinical sense. Cytological examination and ultrasound (USG) imaging techniques are very valuable, but histopathological approach is the golden key. In this case neutered male, mixed, 17-year-old cat was brought to the clinic with non-obstructive hematuria attacks. A superficial hypoechoic mass located at the apex of the urinary bladder was detected in the USG imaging technique. No discernible findings were found by cytological examination. After removal of the suspected area, the biopsy specimen was presented to the pathology department for histopathological examination. Histopathological examination revealed transitional cells covering entire surface of the mucosal epithelium and showing growth into the lumen, and they were characterized by mild anisocytosis and anisokaryosis. The patient was diagnosed as in-situ non-papillary, non-infiltrating type of transitional cell carcinoma (in-situ carcinoma). These tumors are quite rare and have better prognosis. The condition of the patient was completely resolved without medical treatment in the postoperative period. When this case report was prepared, 6 months after the operation, there was no recurrence in the patient. Contrary to infiltrative urinary bladder tumors, in-situ carcinoma could be completely cured by surgically, therefore the case was found worthy to be presented.

Keywords: In-situ carcinoma, bladder tumor, cytology, histopathology

INTRODUCTION

Tumors of the urinary bladder is commonly seen in dogs, cats and cattle. Bovine tumors are generally found in association with enzootic hematuria, and bracken fern (*Pteridium aquilinum*) is generally presented as the one of the main causative carcinogens for the occurrence of these tumors. In dogs, these tumors represent 1% of all canine neoplasms and they are even less frequent in cats (1). Epithelial tumors are most commonly seen in cats and dogs and are composed of papilloma, adenoma and carcinoma, in which transitional cell carcinomas (TCC) are most commonly diagnosed in dogs, and occur less frequently in cats (2). On the other hand, TCC has also been reported in some captive fishing cats (*Prionailurus viverrinus*) (3, 4).

TCC is usually seen in old dogs with the average of age between 9 to 11 years (2). Adult cats are found more frequently affected and the frequency increase with age (5). Although there is no significant differences between female and male TCC, females, especially neutered females, are have high risk than males (6). The reason for that is supposed to be decreased frequency of urination in females which results in longer exposure of the causative carcinogens with the bladder epithelium (2). In a study neutered males cats are presented as more commonly affected, and they are classified as high grade according to canine classification system (7). Other risks factors for developing TCC in dogs are can be multifactorial. Between them exposure to insecticides for flea and tick control, exposure to marshes sprayed with insecticides for mosquito control, obesity, as mentioned above female sex, cyclophosphamide administration (8) and some breeds (such as Scottish, West Highland White, and Fox Terriers, Shetland Sheepdogs, and Beagles) can be mentioned ordered (2).

Almost all cases show clinical problems (9), such as hematuria, pollakiuria, cystitis, or dysuria, but none of them can be seen as a significant feature for bladder tumors (6). In cats TCC tumors are usually missed until the occurrence of lower urinary tract symptoms of geriatric cats (2). Definitive

diagnosis can be done by the cytological, histopathological demonstration of the neoplastic cells from the bladder mass or by imaging techniques using radiography or ultrasonography, or visualization of the mass by contrast cystography or laparotomy (10). Between these methods, contrast cystography is found useful for the visualization of the bladder tumors (6). USG (11) and cytological examination (12) can rapidly lead to detect the primary tumors of the urinary bladder. But grading schemes of the tumor can only be performed by histopathological examination (2). In addition cytological examination may not give reliable results, because TCC is commonly composed of inflammation and it can be not possible to differentiate the neoplastic transitional cells from inflammatory cells (10).

Transitional cell carcinomas in dogs are usually located in the trigone areas of the bladder wall, because urine is pooled in this area that leads to longer exposure of the epithelium with the toxins in urine. However, the localization can be found outside of the trigone (7). Histopathological features of the TCC show various variants, which characterized by various degree of changes in transitional epithelium. Most of the TCCs are found anaplastic, invasive and tend to metastases, thus they can be classified as high grade and are accepted as one of the most malignant tumors (2). Metastasis can be detectable radiographically or by gross examination at necropsy (6, 13). Metastasis have been reported in lungs, lymph nodes, bones (13) and rarely in joints (14) and many organs will have metastasis if they are searched for thorough gross inspection. The features of metastatic potential can be ordered as: nonpapillary (flat, sessile), infiltrating, vascular invasion, desmoplasia, minimal lymphoid inflammation and urethral involvement (15). Tumor grading scheme is depended on growth patterns, cell type, degree of differentiation, depth of invasion, and a strong peri-tumoral lymphocytes infiltration (16). The staging of the bladder carcinoma is performed by TNM system. In a review study, staging of the tumor is considered useful to determine the prognosis and to provide better treatment plan. Median survival time for dogs

with different stages has also been emphasized that for cases with T3 tumors have 118 days median survival, and 218 days for T1 or T2 tumors. N0 tumors have median survival time of 234 days, but N1 tumors have median survival time of 70 days. While dogs with distant metastasis have median survival time of 105 day, it is 203 days for dogs without distant metastasis (10). On the other hand in-situ carcinomas do not metastases, they represent the most well-differentiated variant. The tumor cells proliferate in basal membrane and remain there, do not tend to breach the basal membrane. Therefore, in-situ carcinomas can be found as an incidental lesion at autopsy (2).

In this report, the case was classified according to the World Health Organization (15) system of canine transitional cell carcinomas that are classified into four groups: a. Papillary and infiltrative, b. Papillary and non-infiltrative, c. Non-papillary and infiltrative, d. Non-papillary and non-infiltrative (in-situ carcinoma).

MATERIALS AND METHODS

A neutered male, mixed, 17-year-old cat with the complaints of hematuria and a recurrent chronic cystitis was brought to the clinic for examination. Ultrasonographic (USG) examination was performed to observe if there is any obstruction in this region. A mass suspected of neoplasia was detected. Regarding to the findings of USG examination, a smear was prepared from the urine and stained with May Grünwald-Giemsa to distinguish the lesion from neoplasia. Afterwards, the suspicious mass on the wall of urinary bladder of the patient was totally extirpated and sent to the pathology department for histopathological examination. After the 24h fixation, the specimen was routinely processed, embedded into paraffin blocks. Sections of 4 µm thickness were cut from the blocks, stained by Hematoxylin-Eosin (H&E) and examined by light microscopy.

RESULT AND DISCUSSION

Clinical findings

The patient had already prolonged cystitis problems. In the detailed clinical examination, the cat was found to be slightly tense on abdominal palpation, with a moderately sized, hard bladder and had moderate to severe, intermittent and painless hematuria, dysuria and mild constipation. Besides these findings the patient had loss of appetite.

After histopathological evaluations, cat was re-examined for the clinic staging and revealed neither lymph node involvement (N:0) nor distant metastasis (M:0).

Ultrasonographic Findings

The patient was examined by USG and revealed no obstructive mass at the entrance of the urethra; however a superficial mass of 1.22 x 2.60 cm was detected on the wall of the urinary bladder far from the trigonal region. The mass was characterized by increased echogenicity located in the distal portion of the urinary bladder (Fig. 1, 2).

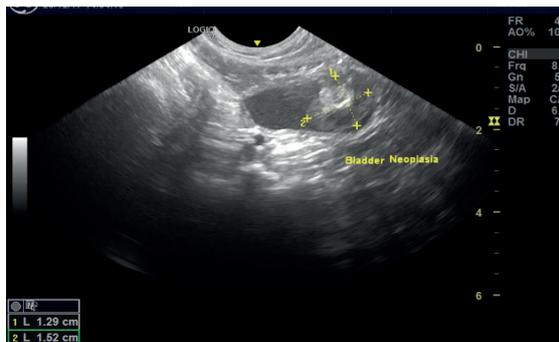


Fig. 1. Urinary -bladder, cat, a superficial mass on the bladder wall.

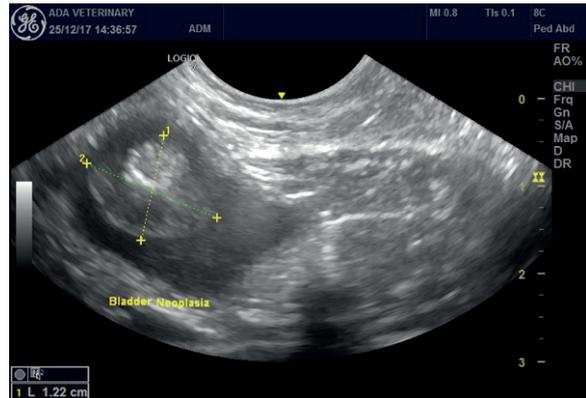


Fig. 2. Urinary -bladder, cat, a superficial mass on the bladder wall.

Cytological Findings

Cytological examination of the urine smear revealed dense erythrocytes (Fig. 3, 4), moderate number of neutrophils (Fig. 4) and very small numbers of desquamative transitional cells (Fig. 3) and debris. But transitional cells showed no significant atypia.

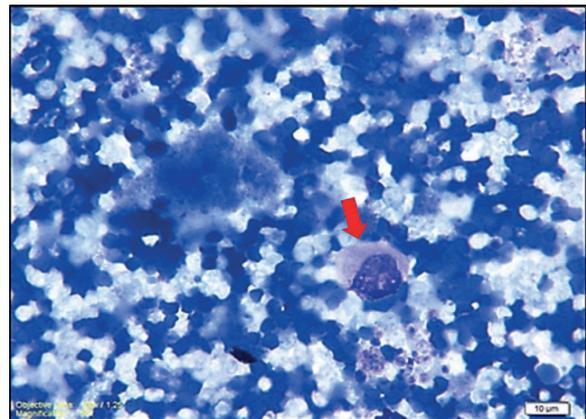


Fig. 3. Urinary Bladder, cat, background compose of dense erythrocytes, debris material and a transitional epithelium (arrow).

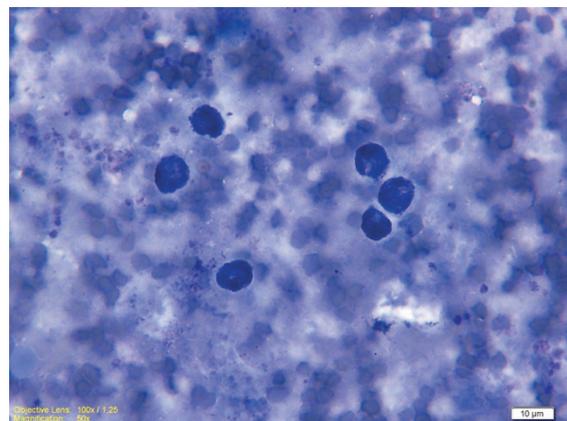


Fig. 4. Urinary Bladder, cat, background compose of dense erythrocytes, a few numbers degenerated inflammatory cells and debris material.

Histopathological Findings

The tissue specimen of the urinary bladder showed prominent proliferation in transitional cells (Fig. 5) through the lumen. Neoplastic transitional cells covered the entire mucosal surface, but remained only in the lamina propria and did not breach the basement membrane. Neoplastic cells were found in ovoid morphology and had eosinophilic cytoplasm. There was mild anisokaryosis and a small amount of mitosis (Fig. 6, 7). No vascular or lymphatic invasion was found. There were multiple foci of hemorrhages in mucosa. Multiple hematomas, lymphocytic and neutrophilic infiltration, large necrotic areas (Fig. 5, star) and calcification foci (Fig. 5, arrow) were observed in submucosa and muscular layers.

According to clinical, USG and histopathological findings, the case was diagnosed as non-infiltrative transitional cell carcinoma (in-situ carcinoma).

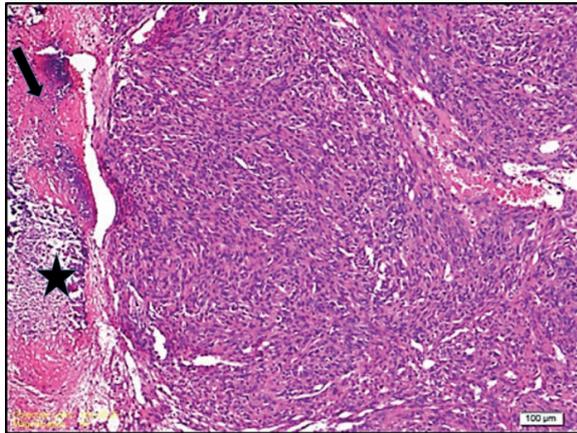


Fig. 5. Urinary bladder, cat, in-situ carcinoma representing thickened of the transitional epithelium. Necrotic areas (arrow) and foci of calcification (star) are seen in the submucosal and muscular layer. H&E.

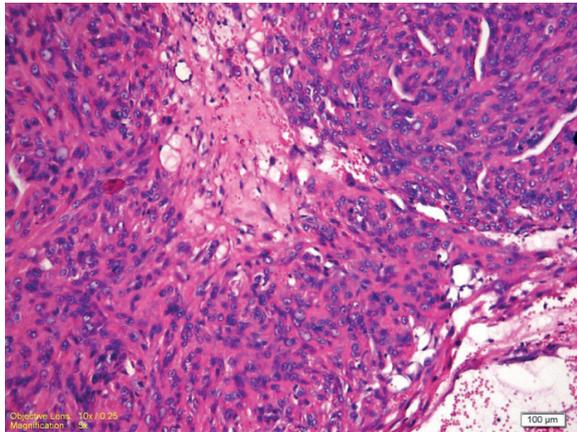


Fig. 6. Urinary bladder, cat, neoplastic cells show mild anisokaryosis and mitosis. H&E.

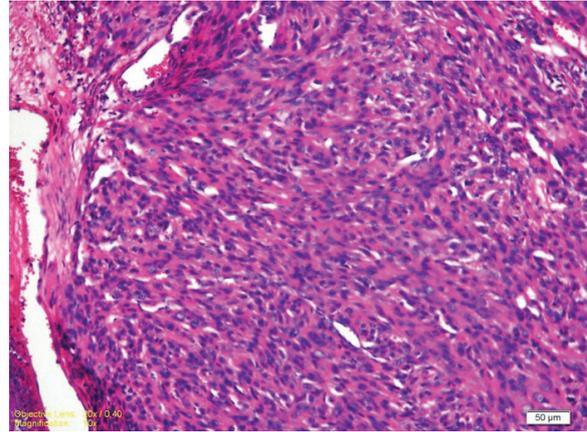


Fig. 7. Urinary bladder, cat, neoplastic cells show mild anisokaryosis and mitosis. H&E.

Transitional cell carcinoma has previously been reported in geriatric cats (5) with symptoms of chronic lower urinary tract disease (7). With old age and prolonged clinic, this condition resembled to the patient observed in this case.

In this case report, the neoplastic mass was also found outside the trigonal region. It has already been reported that in contrast to the dogs, bladder tumors can also be located outside of the trigonal region in cats (7), because of their anatomical features (17).

As a diagnosis methods, several imaging techniques, such as radiography, USG or cystography have been used in other studies (6, 16, 7). In the present case report, the mass was detected by USG, and then cytological examination from the urine sample was performed to detect the neoplastic cells. Unfortunately, the cytological examination failed to detect the neoplastic cells. It has already been mentioned that cytological examination can be effective only in %20 -%30 cases, in case the tumor cells are found in the urine sample. However, negative results cannot be interpreted as the absence of neoplasia, if there is no neoplastic cells in the smear (2). Therefore, in this case the confirmation of the diagnosis was performed by further histopathological examination. Our histopathological findings revealed that the tumor had severe proliferation of the neoplastic transitional cells within the surface of the epithelium. No deep infiltration or vascular or lymphatic invasion was determined. According to WHO classification system the case, based on these histopathological findings, was diagnosed as non-infiltrative transitional cell carcinoma (in-situ carcinoma), which one of the rarest variant of the TCC in cats and likely attributed as an early neoplastic transformation of the bladder epithelium (2). In contrast to this case, other variants of TCC are more anaplastic (15). Between the other variants of TCC, the most common type of the bladder tumors is assumed as papillary and infiltrating TCC in domestic animals. They are very aggressive and have poor prognosis. Indeed, the classification system of WHO is available for dogs, but there was no validated system for cats in use, therefore, we also applied the canine classification system to this case report as in another study by WILSON et al. (7). Using the classification system described above, the prognosis of the was better interpreted. After the operation the patient showed very good prognosis. Although no medical treatment has been used for the patient in the post-operative period and no recurrence was observed during the period from operation until today.

CONCLUSION

In conclusion, the case showed that the clinic symptoms of lower urinary tract in geriatric cats should be reconsider for the possibility of bladder tumors. USG, cytology and histopathology have been performed as diagnostic tools in this case report and revealed that one should also give more attention that negative results revealed by cytological examination always does not mean the absence of tumor, so in this condition the case should be confirmed by histopathology. Moreover histopathology is required to determine the classification of the tumor to interpret the prognosis of the patient.

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