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CASE REPORT

Unusual Cutaneous Metastasis of Urethral Transitional Cell Carcinoma in a Dog

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ABSTRACT

A 12-year-old spayed female Maltese dog was presented due to 4 months history of hematuria and pollakiuria. Based on the cytology, radiology, urethral transitional cell carcinoma (TCC) was diagnosed. No metastasis and invasion to adjacent organ was revealed at the first presentation and the dog was treated with piroxicam. Erosion and plaque-like mass were noted at right inner thigh (256 days after first presentation) and confirmed as unusual cutaneous metastasis of urethral TCC by post-mortem and histopathological findings.

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INTRODUCTION

Primary urethral neoplasia is rare in both dogs and cats, and transitional cell carcinoma (TCC) and squamous cell carcinoma (SCC) is most common tumors (Davies and Read, 1990; Chung *et al*., 2014). TCC represents 90% of all bladder tumors and often detected in the trigone area of the bladder (Henry, 2003). Usually, bladder TCC may extend into the urethra; however, some cases of TCC originated from the urethral epithelium (Santos *et al*., 2007). Cutaneous metastasis of TCC is rare in humans (less than 1%) and not-recognized as a metastasis site in canine TCC (Mueller *et al*., 2004). The clinical features of cutaneous metastasis could be similar with other skin diseases and it's easy to overlook or misdiagnose due to skin is not-recognized as metastasis site in canine TCC. This report described the cytology, imaging features of CT scan, and histopathological findings from unusual cutaneous metastasis of urethral TCC in a dog.

CASE PRESENTATION

History and clinical examination: A 12-year-old spayed female Maltese dog was referred due to hematuria and pollakiuria for 4 months. Empirical antibiotics were given to the dog by the referring veterinarian, but hemauria was recurred. There were no abnormalities except vulvar swelling on physical examination. Complete blood counts and serum biochemistry profiles were within normal. Abdominal radiographs showed increased soft tissue density behind the urinary bladder. Calcification was also noted within the soft tissue opacity in cranial and middle part of pelvic cavity (Fig. 1A). Ultrasonograph showed no other abnormalities in urinary bladder and upper urinary tract except a round tubular mass with central calcification behind the urinary bladder (Fig. 1A). Urinalysis revealed abundant red blood cells, neutrophils, cocci form bacteria and few transitional epithelial cells. Excretory and retrograde urography was used to define the extent of the mass in the kidney, bladder and lower urinary tract. There were no structural abnormalities of the kidney and urinary bladder in excretory urography. But leakage of contrast medium through the urethra was noted in retrograde urography (Fig. 1C). Vaginal cytology and find needle aspiration of the mass revealed, anisocytosis, anisokaryosis, and high nuclear to cytoplasm ratio which are consistent with malignant neoplasias. The cytoplasm contained small pale vacuoles and the nucleoi was prominent (Fig. 1D and E). Computed tomography (CT; Asteion 4®, Toshiba, Japan) revealed a round tubular mass (17 mm X 53 mm) without meatastasis and invasion to adjacent organ within a pelvic cavity (Fig. 2). Based on the results obtained here, this case was definitely diagnosed urethral transitional cell carcinoma. Because of the impossibility of complete excision and the poor prognosis for long-term survival, the owner declined to further treatments including chemotherapy and surgical resection. Thus palliative treatment with piroxicam and antibiotics were initiated.

Treatment and prognosis: Piroxicam (Crown Pharm, Seoul, Korea) was once daily given with dose of 0.3 mg/kg (PO). For treatment of urinary tract infection, ciprofloxacin (10 mg/kg, once daily PO; New Gen Pharm, Seoul, Korea) was also administered based on the culture and sensitivity

test. Despite tumor size was not decreased after medication, there was improved clinical signs including pain during urination, hematuria and pollikiuria. The urethral mass was then re-evaluated one to three months interval and round, well-marginated plaque-like mass lesion was newly observed in right inner thigh 256 days after the first presentation (Fig. 3A). Multiple metastatic nodules in the bilateral lung were also noted on the thoracic radiography. Fine needle aspiration of the skin mass showed that the malignant epithelial cells which had the same features with the urethral mass in this case (Fig. 3B). Clinical signs of the dog were deteriorated, and the skin mass and multiple metastatic lung nodules were enlarged during 3 months. Urethral mass was invaded into urinary bladder and lung metastasis was worsened. The dog had 1-year life expectancy.

On histopathologic examination, the mass had polyhedral neoplastic cells with pleomorphic nuclei, eosinophilic cytoplasm, and distinct cell outline. The packed neoplastic cells were infiltrated to the lamina propria and muscularis interna layer (Fig. 3C&D). Based on histopathology results, this case was diagnosed as a transitional cell carcinoma of urethra which metastasized to other parts of the body including the skin. The dog was in stable disease states during 256 days and survived 356 days only with piroxicam treatment.

DISCUSSION

According to a literature described previously (Davies and Read, 1990), primary urethral neoplasia is often invasive and metastasis to local lymph nodes, pelvic organs, lungs and vertebrae occurs approximately 30% in dogs. It was commonly reported that bladder TCC to the several adjacent organs is metastasized. Approximately 50% of the dogs had distant metastases at death and 14% of the dogs were died due to metastatic disease (Mutsaers *et al*., 2003). Most common metastatic sites include lung, regional lymph nodes, and liver. Recently, one study reported cutaneous metastasis of canine TCC during the 7-year study, 104 cases were confirmed as TCC and cutaneous metastasis was detected in 10 (9.6%) cases, mean of 123 days (median, 38 days) after diagnosis of the primary TCC (Reed *et al*., 2013). However, in case reports and literature review, skin was not included both common and miscellaneous metastatic sites and cutaneous metastasis of canine TCC was recognized quite unusual (Henry, 2003; Mutsaers *et al*., 2003).

In the present dog, the primary mass was positioned at the proximal urethra and metastasis to the skin was quite unusual and atypical. Urinary bladder involvement was occurred 3 months after the skin metastasis and the dog lived 356 days after definite diagnosis was made.

In general, due to the invasiveness and metastasis of urethral TCC, complete surgical resection is often not feasible (Caswell, 2011). Single-agent chemotherapy using cisplatin, carboplatin, mitoxantrone and vinblastine were evaluated and median survival time of them was around 130 days (Mutsaers *et al*., 2003). More favorable median survival time was reported when using combination agents and it could be up to 358 days (Henry *et al*., 2003; Mutsaers *et al*., 2003). Non-steroidal anti-inflammatory drug (NSAID) therapy with piroxicam alone or

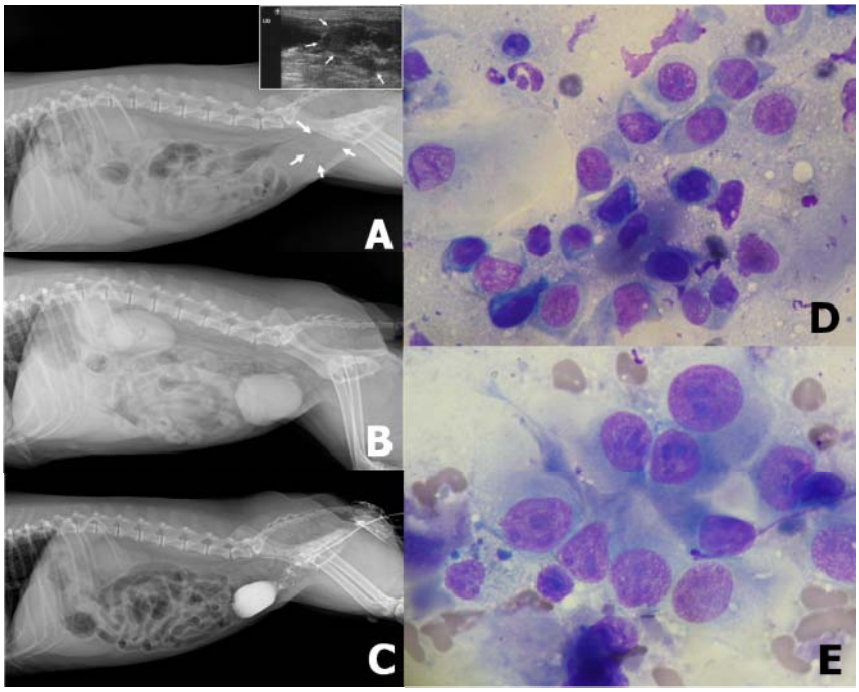

Fig. 1: Radiographs and cytologic evaluation of a dog with urethral carcinoma. **(A)** Abdominal radiographs (plain) revealed abnormal soft tissue opacity behind the urinary bladder and a round tubular mass with central calcification lesions were obtained through ultrasonogram (inset). Excretory urography **(B)** revealed structurally and functionally normal kidney, ureter and urinary bladder and retrograde urography **(C)** showed leakage of contrast medium through the urethra. Vaginal cytology **(D)** exhibited epithelial cells with anisocytosis, anisokaryosis, basophilic cytoplasm, and increased nuclear to cytoplasm (N/C) ratio (Diff-Quik stain, X 400). **(E)** Fine needle aspiration of the mass also reveled anisocytosis, anisokaryosis, high N/C ratio, and the prominent nucleoi (Diff-Quik stain, X 1000).

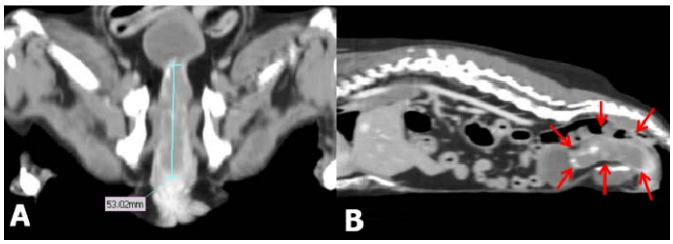

Fig. 2: CT image of a dog with urethral carcinoma. A round tubular mass (17 mm X 53 mm) was observed within a pelvic cavity on dorsal (A) and sagittal (B) view (arrow). No metastasis and invasion to adjacent organ including urinary bladder was noticed.

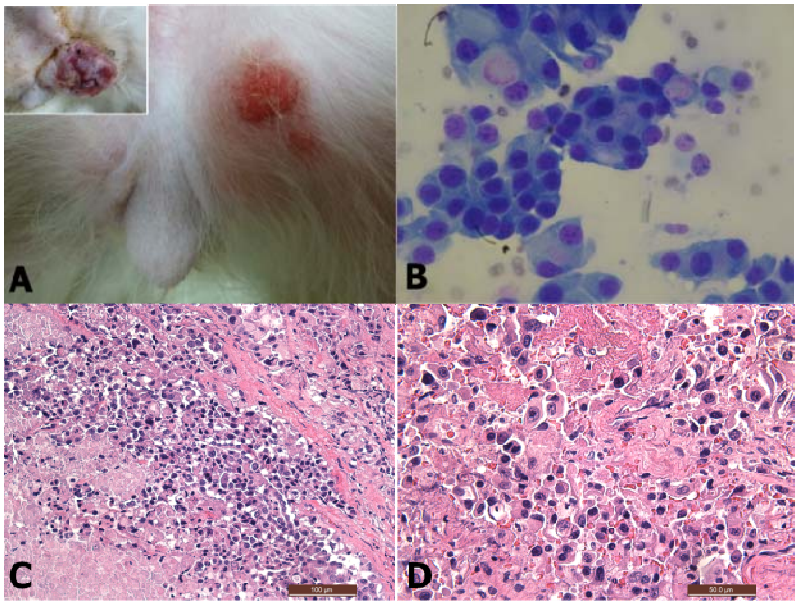

Fig. 3: Gross and cytologic evaluation of skin lesions and histopathology of the urethral mass. **(A)** Round, well-marginated, plaque-like firm mass was observed right inner thigh skin 256 days after the first presentation. The skin mass was enlarged and ulcerated at 350 days after the first presentation (inset). **(B)** A cytology of the skin mass exhibited anisocytosis, anisokaryosis, and high N/C ratio, and prominent nucleoi which were the same patterns with the urethral mass (Diff-Quik stain, X 400). **(C)** Diffuse infiltration of neoplastic transitional cells to lamina propria and muscularis interna layer was marked (Haematoxyllin & eosin). **(D)** Neoplastic cells were polyhedral with eosinophilc cytoplasm and pleomorphic one or two nuclei were prominent. Most cells had distinct boundaries and nucleoli were visible (haematoxyllin & eosin).

combination with other chemotherapy agents is commonly used in dogs with TCC (Knapp *et al*., 1994). Other treatment options such as, radiation and photodynamic therapy has been evaluated. However further investigation is necessary (Henry, 2003).

The dog well tolerated to piroxicam administration and adverse effects were not noticed throughout treatment period. Although complete or partial remissions were not achieved, primary tumor was relatively controlled with piroxicam and the dog has been in stable for 256 days. Complete urinary tract obstruction in most cases was common cause of death in dogs with TCC. But this did not occur in this dog until died.

Conclusion: This report highlighted a case of urethral TCC with unusual cutaneous metastasis in a dog. Due to cutaneous metastasis is relatively rare in dogs, it is important to recognize a plaque-like mass could be an extensive metastasis of urethral TCC. This dog was managed with piroxicam alone for a long-time, however the prognosis is generally guarded after the cutaneous metastasis.

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