Haemangiosarcoma of the urinary bladder in a dog

JM LIPTAK[a], WS DERNELL and SJ WITHROW
Animal Cancer Center, Colorado State University, 300 West Drake Road, Fort Collins, CO 80523, United States of America.

Haemangiosarcoma of the urinary bladder is reported in a dog. The bladder mass was detected incidentally during physical examination. Partial cystectomy with unilateral ureteroneocystostomy were performed to remove the tumour en bloc. Necrosis of the urinary bladder was diagnosed 10 days postoperatively and the dog was euthanased.
Aust Vet J 2004;82:213-215

BUN	Blood urea nitrogen
hpf	High power field
HSA	Haemangiosarcoma
PCV	Packed cell volume
RR	Reference range
WCC	White cell count

Case report

A 7-year-old, male castrated Golden Retriever was referred for assessment of multiple subcutaneous masses. The masses were soft and fluctuant, approximately 2 cm in diameter, and distributed along the ventral abdomen and thorax. These masses were confirmed as lipomas on cytological examination of fine-needle aspirates. An incidental finding during physical examination was a large, non-painful, mid-abdominal mass. Lateral and ventrodorsal radiographs of the abdomen revealed a large mass, 11 by 14 cm, occupying the right caudal abdomen (Figure 1). No further diagnostic tests were permitted at this time as the dog was asymptomatic.

The dog presented again 22 days after initial examination with a 7-day history of decreased appetite and activity level. On physical examination, mucous membranes were pale and the abdominal mass was palpable and unchanged from the previous examination. Ultrasound examination of the abdomen revealed a large mass of mixed echogenicity which encompassed and displaced the urinary bladder. The origin of the mass could not be determined. Furthermore, there was moderate hydronephrosis of the right kidney and right-sided mega-ureter to the level of the abdominal mass. Cytological examination of an ultrasound-guided fine-needle aspirate of the mass was consistent with a mesenchymal tumour, possibly HSA given the highly vascular nature of the sample. There was no evidence of pulmonary metastasis on left lateral, right lateral, and ventrodorsal thoracic radiographs. Venous blood was submitted for haematological and serum biochemical examination, coagulation profile, and blood typing. Haematological abnormalities included a regenerative anaemia (PCV 26%, RR 40 to 55%; 3.3% reticulocytes) and mild neutrophilic leukocytosis (WCC 17.9 x 10^3/µL, RR 4.5 to 15.0 x 10^3/µL; segmented neutrophils 13.8 x 10^3/µL, RR 2.6 to 11.0 x 10^3/µL). Serum biochemical analysis was within the reference limits, including creatinine (1.2 mg/dL, RR 0.7 to 1.8 mg/dL) and BUN (20 mg/dL, RR 7 to 32 mg/dL). Coagulation profile was normal and blood type was A-positive.

[a]Current address is Department of Clinical Studies, Ontario Veterinary College, University of Guelph, Ontario N1G 2W1, Canada.

The dog was anaesthetised and a ventral midline exploratory celiotomy was performed. A large mass, approximately 20 cm diameter, was present in the right caudal abdomen arising from the dorsal surface of the urinary bladder (Figure 2). The right kidney was enlarged and firm, the right ureter was dilated to the level of the mass, and a single nodule was present in the left lateral liver lobe. The hepatic mass was removed, fixed in 10% formalin, and submitted for histological examination. Stay sutures were placed in the apex of the bladder and paramedian along the ventral aspect to the level of the bladder neck and proximal urethra. The urinary bladder could not be isolated from the remainder of the abdominal cavity with laparotomy sponges due to the size and location of the mass.

A ventral cystotomy was performed to examine the bladder mucosa. The left ureter was catheterised with a 3F red feeding tube. Isolation of the left ureter from the mass was attempted but it was found to course beneath the capsule and then into the body of the mass. When the left ureter was dissected from the tumour capsule, neoplastic infiltration of the ureteral wall was observed at the level of ureteral penetration into the body of the mass. The left ureter was ligated cranial to the origin of its subcapsular course and transected. The mass was excised with 1 cm margins of grossly normal urinary bladder and preservation of the caudal vesicular vessels. Due to concerns regarding renal function following ureteral re-implantation,[1] the right kidney and ureter were also preserved. Following removal of the urinary bladder mass, the transected left ureter was followed cranially and found to originate from the right kidney. The right ureterovesical junction was identified and catheterised. This ureter was followed

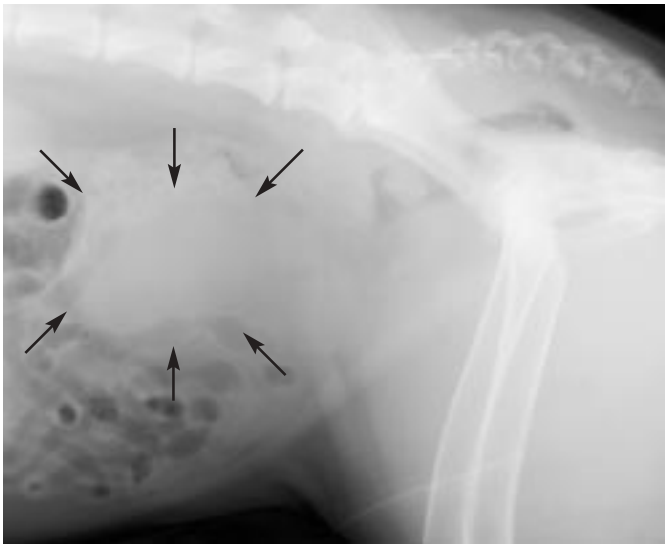

Figure 1. A lateral abdominal radiograph of a 7-year-old Golden Retriever showing a large mass in the mid-to-caudal abdomen displacing the colon dorsally, bladder caudoventrally, and the intestines cranially (arrows).

cranially from the urinary bladder and found to originate from the left kidney. Hence, the left ureter crossed midline and entered the right ureterovesical junction, while the right ureter, previously believed to be the left ureter, coursed the mirror image of the left ureter and entered the left ureterovesical junction. A 4 mm full-thickness stab incision was performed with a #15 scalpel blade into the apex of the urinary bladder. The transected ureter was pulled through the stab incision into the lumen of the bladder. The caudal end of the ureter was excised and submitted for histological examination. The ureter was then spatulated and sutured to the bladder mucosa with simple interrupted 5-0 polyglyconate suture material (Figure 3). The dorsal partial cystectomy and ventral cystotomy were closed in two layers. The mucosal layer of both incisions was closed with 5-0 polyglyconate in a simple continuous pattern. The serosal layer was closed with 4-0 polyglyconate, the dorsal incision in a simple continuous pattern and the ventral incision in a Cushing's pattern. The abdominal cavity was lavaged with 2 litres of warm isotonic saline, the celiotomy incision was closed routinely, and an indwelling urethral catheter inserted.

The dog recovered uneventfully. The following day, urine production was 3 mL/kg/d, and serum creatinine and BUN levels were within the normal reference range. The dog was discharged with instructions to observe urination and administer sustained-release morphine (15 mg by mouth every 8 h), carprofen (75 mg by mouth every 12 h), and amoxicillin-clavulanate (500 mg by mouth every 12 h). The dog became listless, inappetent, anuric, and began vomiting approximately 36 hours postoperatively.

Uroperitoneum was suspected due to leakage from one of three separate surgery sites in the urinary bladder. However, despite compelling evidence of uroperitoneum on the basis of abdominal fluid analysis [peritoneal fluid creatinine (4.8 mg/dL) and potassium (5.8 mEq/L) were greater than serum levels],[2] there was no loss of serosal detail on survey abdominal radiographs and no evidence of urine leakage following contrast studies of the urinary system with excretory urography and retrograde urethrocystography. As a result, the dog was managed conservatively with intravenous fluids, continuous rate infusion of fentanyl (2 µg/kg/h), nil by mouth, and an indwelling urinary catheter. After 24 hours of no food or water, the dog was fed a commercially available, bland diet and began vomiting approximately 3 hours after eating. Traumatic pancreatitis was suspected on the basis of increased amylase level (1398 IU/L, RR 50 to 1200 IU/L). The dog was managed as previously described with nil by mouth for a further 24 hours and the addition of a continuous rate infusion of metoclopramide (1 to 2 mg/kg/d). Water and food were re-introduced after 12 and 24 hours, respectively, without vomiting and creatinine (1.3 mg/dL) and amylase (1114 IU/L) levels returned to normal while BUN remained within the normal RR (12 mg/dL).

Urinary incontinence was observed following removal of the urinary catheter. A large, turgid, and moderately painful bladder was palpated, despite urinary incontinence. Detrusor muscle instability was suspected as a result of damage from the dorsal partial cystectomy and ventral cystotomy. Treatment included bethanecol (2.5 mg by mouth every 6 h), cisapride (10 mg by mouth every 12 h), phenoxybenzamine (5 mg by mouth every 24 h), diazepam (5 mg by mouth every 8 h), and intermittent urinary catheterisation.[3] However, the dog did not respond to treatment, with no resolution of urinary incontinence or retention after 4 days.

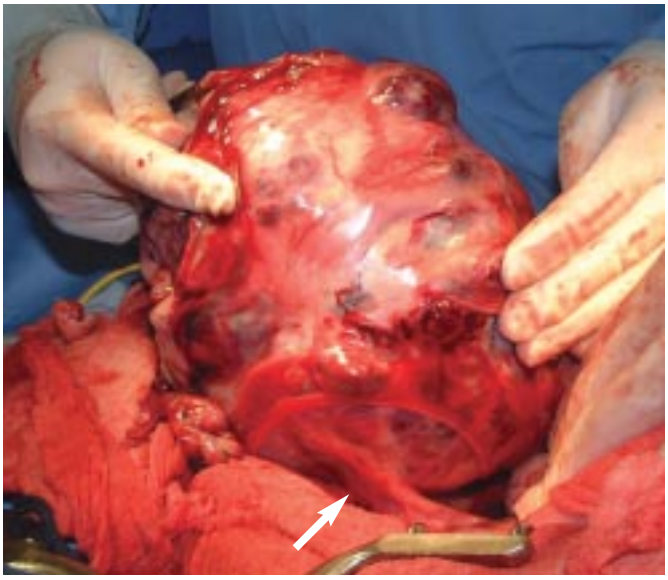

Figure 2. An intra-operative view of a 20 cm diameter mass arising from the dorsal wall of the urinary bladder. The right ureter, which had crossed the midline and entered the bladder at the left ureterovesical junction, can be seen entering the mass (arrow).

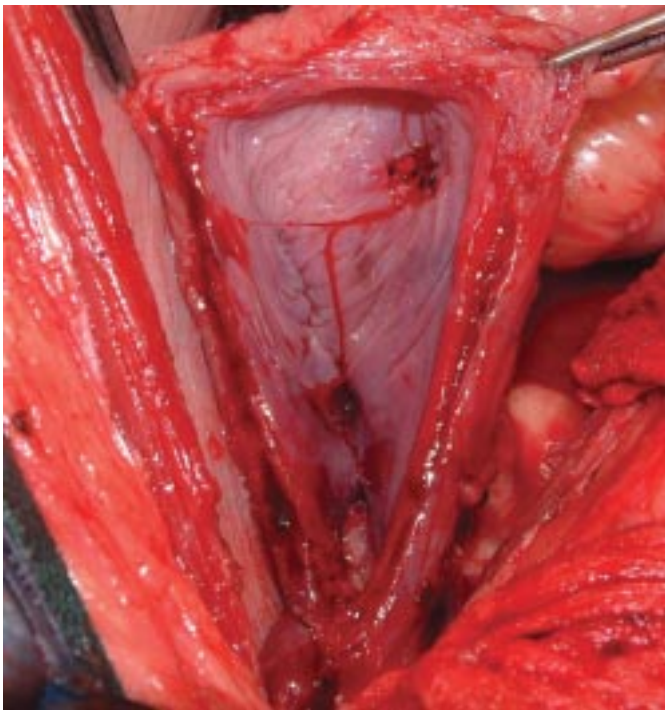

Figure 3. An intra-operative view of the urinary bladder through the ventral cystotomy following partial cystectomy of the dorsal bladder wall. The mass (above) has been removed and ureteroneocystostomy of the right ureter into the apex of the bladder has been performed.

The dog was anaesthetised for a flank laparotomy and placement of a cystostomy tube, with the aim of decompressing the bladder and allowing the detrusor muscle sufficient time to recover normal function. At surgery, the urinary bladder appeared yellow, transparent and necrotic. The dog was immediately transferred to a surgery theatre for a complete exploratory celiotomy. The urinary bladder was necrotic to the level of the proximal urethra.

The bladder was filled with urine and both the left and right ureters appeared patent. Proliferative tissue surrounded the re-implanted right ureterovesical junction, although the ureter remained patent and functional. The owners declined further treatment and the dog was euthanased.

Histological and immunohistochemical examination of the urinary bladder mass revealed a completely resected, grade II HSA. There was no evidence of neoplastic tissue in the distal right ureter and the hepatic mass was diagnosed as a hepatocellular adenoma.

Discussion

Bladder tumours account for approximately 1% of all canine cancers.[4] The majority of bladder tumors are epithelial, with transitional cell carcinoma the most common, although sarcomas are occasionally reported.[4] Primary HSA of the bladder is rare in dogs with only three cases published in the veterinary literature.[5-7] Comparatively, urinary bladder HSA is also very rare in humans with fewer than 15 cases reported.[8]

HSA is a malignant tumour originating from vascular endothelial cells and can originate from any site in the body.[9] In dogs, HSA most frequently involves the spleen, right atrium, and cutaneous and subcutaneous tissue.[9] Visceral HSA has an aggressive biological behaviour with a high metastatic rate and poor survival time.[9] However, due to the paucity of cases of urinary bladder HSA in dogs and the unfortunate outcome in the present case, the biological behaviour of this form of visceral HSA in dogs is unknown. In the present case, the HSA was very large and the dog was asymptomatic, which is suggestive of a more benign course of disease than normally associated with visceral HSA. In humans, urinary bladder HSA behaves in a similarly aggressive manner to other forms of HSA.[8]

The cause of urinary bladder necrosis in the present case is unknown. Bladder necrosis has been reported following partial cystectomy for a rhabdomyosarcoma in a dog, although this became apparent within 48 hours of surgery.[10] In the present case, necrosis of the bladder was identified 10 days postoperatively, suggesting that necrosis was caused by a postoperative rather than an intra-operative event. However, an indwelling urinary catheter was used for most of the postoperative period to manage presumed uroperitoneum and then urinary retention. Urinary diversion may have masked the clinical signs associated with acute bladder necrosis. The caudal vesicular vessels appeared to be maintained during partial cystectomy of the dorsal bladder wall. These vessels may have thrombosed secondary to manipulation of the urinary bladder during resection and closure. Alternatively, thrombosis of the caudal vesical or parent arteries may have been associated with direct endothelial damage or a localised coagulopathy, both of which can occur in dogs with HSA.[11,12] The dog was euthanased when bladder necrosis was diagnosed.

Segments of the gastrointestinal tract can be used to reconstruct an orthotopic bladder as a urinary reservoir.[13] Total cystectomy with urinary diversion was discussed, but declined on the basis of potential significant postoperative complications, such as urinary tract infection, pyelonephritis, and metabolic complications including hypochloraemic acidosis.[14]

In conclusion, the present dog was diagnosed with HSA of the urinary bladder and this is a rare location for this type of tumour. There is a paucity of reports on the aetiology and pathophysiology of urinary bladder necrosis and the cause remains unknown in the present case. However, such a complication should be considered when extensive dissection and resection of the urinary bladder is planned.

Acknowledgements

The authors thank the students, staff, and veterinarians involved in the management and care of this dog.

References

1. Gregory CR, Lirtzman RA, Kochin EJ et al. A mucosal apposition technique for ureteroneocystostomy after renal transplantation in cats. *Vet Surg* 1996;25:13-17.
2. Schmiedt C, Tobias KM, Otto CM. Evaluation of abdominal fluid: peripheral blood creatinine and potassium ratios for diagnosis of uroperitoneum in dogs. *J Vet Emerg Crit Care* 2001;11:275-280.
3. Lane IF. Diagnosis and management of urinary retention. *Vet Clin N Am Small Anim Pract* 2000;30:25-57.
4. Phillips BS. Bladder tumors in dogs and cats. *Compend Contin Educ Pract Vet* 1999;21:540-547, 564.
5. Brown NO, Patnaik AK, MacEwen EG. Canine hemangiosarcoma: retrospective analysis of 104 cases. *J Am Vet Med Assoc* 1985;186:56-58.
6. Martinez SA, Schulman AJ. Hemangiosarcoma of the urinary bladder in a dog. *J Am Vet Med Assoc* 1988;192:655-656.
7. Srebernik N, Appleby EC. Breed prevalence and sites of haemangioma and haemangiosarcoma in dogs. *Vet Rec* 1991;129:408-409.
8. Engel JD, Kuzel TM, Moceanu MC, Oefelein MG, Schaeffer AJ. Angiosarcoma of the bladder: a review. *Urology* 1998;52:778-784.
9. Clifford CA, Mackin AJ, Henry CJ. Treatment of canine hemangiosarcoma: 2000 and beyond. *J Vet Intern Med* 2000;14:479-485.
10. Davies JV, Read HM. Urethral tumours in dogs. *J Small Anim Pract* 1990;31:131-136.
11. Brooks M. Coagulopathies and thrombosis. In: Ettinger SJ, Feldman EC, editors. *Textbook of veterinary internal medicine*. 5th edn. Saunders, Philadelphia, 2000:1839-1840.
12. Boswood A, Lamb CR, White RN. Aortic and iliac thrombosis in six dogs. *J Small Anim Pract* 2000;41:109-114.
13. Smith JJ, Swierzewski SJ. Augmentation cystoplasty. *Urol Clin N Am* 1997;24:745-779.
14. Stampfer DS, McDougal WS, McGovern FJ. Metabolic and nutritional complications. *Urol Clin N Am* 1997;24:715-722.

(Accepted for publication 13 August 2003)

The effect of GnRH analogs on urinary incontinence after ablation of the ovaries in dogs

Urinary incontinence occurs in approximately 20% of dogs following removal of the ovaries. Loss of the gonads results in oestrogen deficiency and a chronic increase in the production of FSH and LH, which may adversely affect the sphincter function of the urethra. Oestrogen replacement therapy and sympathomimetics, such as ephedrine and phenylpropanolamine (PPA), are effective in some of the affected dogs, but many of these subsequently relapse. To investigate the role of elevated gonadotrophins, depot preparations of GnRH analogues were used to reduce the gonadotrophin levels. Treatment, using leuprolide, deslorin, buselerin or triptorelin, was given once or twice to 13 ovariectomised, incontinent dogs which were either refractory to α-adrenergics or in which α-adrenergics were contraindicated. In seven dogs treatments with GnRH analogues alone (n=11) resulted in continence for 50 to 738 days (mean 247). Where treatments with GnRH did not resolve incontinence completely, additional treatment with PPA was successful in all but one dog. Additional treatment with PPA restored complete continence for 21 to 367 days (mean 159). All treatments caused long-term reduction of circulating FSH and LH concentrations to very low or undetectable levels, with no observed adverse effects.

Reichler IM et al. *Theriogenology* 2003;7:1207-1216.