Case Report Rapport de cas

Management of bilateral idiopathic renal hematuria in a dog with silver nitrate

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Abstract — Renal hematuria has limited treatment options. This report describes management of bilateral idiopathic renal hematuria in a dog with surgically assisted installation of 0.5% silver nitrate solution. Initial treatment resulted in freedom from clinical signs or recurrent anemia for 10 months; however, recurrence of bleeding following a nephrectomy resulted in euthanasia.

Résumé — Gestion de l’hématurie rénale idiopathique bilatérale chez un chien à l’aide du nitrate d’argent. L’hématurie rénale offre des options de traitement limitées. Ce rapport décrit la gestion de l’hématurie rénale idiopathique bilatérale chez un chien à l’aide de l’installation assistée par chirurgie d’une solution de nitrate d’argent de 0,5 %. Le traitement initial a produit une disparition des signes cliniques ou de l’anémie récurrente pendant 10 mois. Cependant, la récurrence des saignements après une néphrectomie se sont traduits par l’euthanasie.

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contained layered hyperechoic material consistent with blood clots. Both kidneys contained small cortical cysts, and had normal vasculature and flow; kidney sizes were within the reference range (RR: 3.2 cm to 6.4 cm for dogs weighing 5 to 14 kg). Three-view thoracic radiographs were normal. The dog received a packed red blood cell (pRBC) transfusion (10 mL/kg BW over 3 h) without complication. Twelve hours after transfusion the packed cell volume (PCV) and total solids (TS) were 30% (RR: 39% to 53%) and 60 g/L (RR: 60 to 80 g/dL), respectively.

The following day cystoscopy [using a 2.1 mm rigid Karl Storz cystoscope (Karl Storz GmbH & Co. KG, Tuttingen, Baden-Württemberg, Germany)] was performed while the dog was anesthetized pre-anesthetic medication included hydromorphone (Hydromorphone HCl; Baxter Healthcare, Deerfield, Illinois, USA), 0.1 mg/kg body weight (BW), IM; induction with propofol (Propofol; Abbott Laboratories, North Chicago, Illinois, USA), 6 mg/kg BW, IV; general anesthesia was maintained with inhaled isoflurane (Isoflurane; Piramal Healthcare, Piramal Critical Care, Bethlehem, Pennsylvania, USA) and oxygen.

The ureteral orifices were normal in appearance and clear to yellow jets were visualized from each. The portion of the bladder mucosa that was visualized appeared normal and there was no evidence of overt bleeding, although complete visualization of the entire bladder mucosa was precluded due to the presence of large consolidated blood clots. Because a cause of the severe hemorrhage had not been identified and the large blood clots that were preventing complete visualization of the bladder wall could not be removed during cystoscopy, a second cystotomy was done (9). Several large blood clots were extracted from the urinary bladder and clear urine was visualized from both ureters. The urinary bladder and ureters were grossly normal. A bladder wall biopsy was collected prior to closing in a simple continuous and Cushing’s pattern using 3-0 PDS (PDS-II: 3-0; Ethicon, Somerville, New Jersey, USA). The linea alba was closed in an interrupted horizontal mattress pattern with 3-0 PDS, and the skin was apposed with adhesive tissue glue (Vetbond Tissue Adhesive; 3M Health Care, St. Paul, Minnesota, USA). Bladder wall histopathology revealed mild chronic multifocal mucosal hyperplasia.

Post-operative care included 0.45% NaCl (0.45% NaCl; Abbott Laboratories), 60 mL/kg BW/day, supplemented with potassium chloride (Potassium chloride; Hospira, Lake Forest, Illinois, USA), 0.05 mEq KCl/kg BW/h, fentanyl (Fentanyl; Hospira) continuous rate infusion (CRI), 3 μg/kg BW/h, and amoxicillin-clavulanic acid (Clavamox; Pfizer Animal Health, New York, New York, USA), 13.75 mg/kg BW, PO, q12h.

The following day the dog was bright, alert, and responsive. A repeat CBC disclosed a regenerative anemia (HCT 23.3%, 262 000 reticulocytes), thrombocytosis (469 × 10^3/UL, RR: 190 to 468 × 10^3/UL), leukocytosis (14.49 × 10^3/UL, RR 4.39 to 11.61 × 10^3/UL), mature neutrophilia (13.62 × 10^3/UL, RR: 2.84 to 9.11 × 10^3/UL), and lymphopenia (0.580 × 10^3/UL, RR: 0.59 to 3.30 × 10^3/UL). A transdermal fentanyl patch (Fentanyl Transdermal System; Corium International, Grand Rapids, Michigan, USA), (50 μg) was placed and iron dextran (Iron Dextran; Phoenix Pharmaceuticals, St. Joseph, Missouri, USA), 10 mg/kg BW, IM, was administered. Prior to discharge the next day the dog was noted to have 1 episode of passage of discolored, red urine. The dog was discharged from the hospital with a presumptive diagnosis of idiopathic renal hematuria and instructions to be given tramadol (Tramadol HCl; Amneal Pharmaceuticals, Glasgow, Kentucky, USA), 2 mg/kg BW, PO, q8h, ferrous sulfate (Ferrous sulfate; Plus Pharma, Commack, New York, New York, USA), 8 mg/kg BW, PO, q24h, amoxicillin-clavulanic acid, a transdermal fentanyl patch (50 μg/h) and famotidine (Famotidine; Baxter Healthcare), 1 mg/kg BW, PO, q12h.

The dog was taken to the referring veterinarian 2 d after discharge for malaise, pollakuria, and stranguria with passage of large blood clots. Focal urinary bladder ultrasound revealed multiple blood clots and a worsening anemia with PCV and TS of 20% and 65 g/L, respectively.

On return to VHC NCSU the dog’s physical examination was unchanged from previous assessments. On initial assessment the PCV and TS were 19% and 64 g/L, respectively. A major cross match was completed prior to a transfusion of packed RBC (10 mL/kg BW over 3 h). Twelve hours later PCV and TS were 27% and 50 g/L, respectively.

A cystoscopy was repeated under general anesthesia (premedication, induction, and general anesthesia as previously described) revealing large organized blood clots and discolored urine jets from the right ureteral orifice. The dog was transferred to surgery for an exploratory laparotomy and cystotomy. Intraoperatively the ureters were catheterized towards the kidneys with a 3 French red rubber catheter (3 French red rubber catheter; Kendall Sovereign Feeding Tube + Urethral Catheter, Tyco Healthcare, Mansfield, Massachusetts, USA). The left ureter revealed gross hematuria. Urine from the right catheter was grossly normal and was collected for urinalysis which revealed microscopic hematuria (> 50 RBC/hpf). A 0.5% silver nitrate solution (0.5% silver nitrate solution; Teva Pharmaceuticals, Sellerville, Pennsylvania, USA) was filtered with a 0.2 μm nylon membrane filter prior to injecting 1.5 mL into the left renal pelvis via the ureteral catheter. The left ureter was manually occluded for approximately 15 min. The left renal pelvis was flushed with 10 to 15 mL of sterile 0.9% NaCl (Hospira). The bladder and body wall closure and post-operative care were as previously described.

The following day a transdermal fentanyl patch (50 μg/h) was placed and maintenance fluids (0.45% NaCl) were halved (30 mL/kg BW/day). A limited biochemical panel disclosed a decreased BUN (1.1 mmol/L), decreased creatinine (44.2 μmol/l), hypocalcemia (2.2 mmol/L, RR: 2.3 o 2.9 mmol/L), hypoalbuminemia (25 g/L), hyperchloremia (124 mmol/L, RR: 108 to 122 mmol/L), and decreased bicarbonate (17 mmol/L, RR: 18 to 25.8 mmol/L). The PCV and TS remained stable at 34% and 64 g/L, respectively. The dog had one episode of passage of light pink-colored urine. A second limited biochemical panel disclosed hypoalbuminemia (29 g/L), and mild hyperkalemia (5.7 mmol/L, RR: 4 to 5.3 mmol/L). At the time of discharge, the urine was grossly normal and medica-
tions were as previously described.

The dog was re-evaluated 1 wk after surgery by the referring veterinarian. The PCV and TS were 37% and 72 g/L,
respectively. A focal urinary bladder ultrasound revealed a ven-
trally thickened bladder wall with minimal luminal debris. Urine
via cystocentesis was cloudy with a pH of 5.0 (RR: 5.5 to 7.0),
and hematuria (RBC > 50, RR: 0 to 3 RBC/hpf).

One month after surgery, the owner reported no evidence of
gross hematuria or other clinical abnormalities and the
PCV and TS were normal at 44% and 70 g/L. Urinalysis via
cystocentesis disclosed grossly cloudy urine, and hematuria
(21 to 50 RBC/hpf). The dog was administered yunnan baiyao
(Yunnan baiyao; Activeherb Technology, San Diego, California,
USA), 0.25 g, PO, q12h for persistent microscopic hematuria
by the referring veterinarian.

Six months after surgery, a focal urinary ultrasound, uri-
analysio, biochemistry panel, and PCV/TS were repeated. Both
kidneys were unchanged in size and vascular flow; the urinary
bladder was thickened at the apex with small amount of luminal
debris. Renal function appeared to be normal as assessed by
results of a serum biochemistry panel (BUN 19 mmol/L, and
creatinine 0.7 mmol/L). Urinalysis via cystocentesis disclosed
light red urine and hematuria (RBC 50, RR: 0 to 3 RBC/hpf).
The PCV and TS were 48% and 80 g/L, respectively.

Ten months post-procedure the patient was presented with
acute onset lethargy and with gross hematuria. The dog’s
physical examination was unchanged from previous assess-
ments. Diagnostics included a CBC, limited biochemistry
panel, and focal urinary tract ultrasound. Abnormal results
included a regenerative anemia (HCT 29.1%; 165 000 reticulo-
cytes), increased neutrophils with a left shift (17.16
103/mg, L; 1.54
103/µL; 1.54
103/band neutrophils)
and decreased albumin (29 g/L). Ultrasound revealed a urinary
bladder clot and mild left renal pelvic dilation with luminal
hyperechoic debris. A laparotomy and cystotomy were repeated
under general anesthesia (premedication, induction, and general
anesthesia as previously described) revealing large organized
blood clots in the bladder lumen. Both ureters were catheter-
ized as previously described. A blood clot was palpated in the
left renal pelvis. External digital manipulation and sterile saline
flushes were repeated but did not dislodge the clot. The 0.5% silver nitrate solution was injected into the left renal pelvis via
the ureteral catheter as previously described. The bladder,
body wall closure, and post-operative care were as previously
prescribed and the patient was discharged from the hospital 2 d
after surgery. At discharge the urine was grossly normal with
intermittent organized blood clots being passed.

One week following discharge the patient was taken to the refe-
ring veterinarian for recurrent gross hematuria and dysuria. A CBC
disclosed a regenerative anemia (HCT 12.2%; 222 000 reticulo-
cytes) and a mature neutrophilia (19.15
103/µL). Urinary
bladder ultrasound confirmed large blood clots within the bladder
lumen. The dog received a pRBC transfusion (10 mL/kg BW over
4 h) without complication prior to an exploratory laparotomy,
selective arterial ligation (10) of the left renal artery and cystotomy.
Active hemorrhage from either kidney was not present precluding
arterial ligation. A left nephrectomy was performed as described
elsewhere (11). The post-operative PCV was 22%. The kidney and
renal pelvis were grossly normal in appearance. Histopathology of
the left kidney revealed mild to moderate subacute neutrophilic
and lymphocytic pyelonephritis and ureteritis with nodular glo-
merular amyloidosis.

Two days after surgery, the dog required urinary catheteriza-
tion due to urethral obstruction secondary to large blood clots.
The PCV and TS were 16% and 50 g/L, respectively. A pRBC
transfusion (10 mL/kg BW over 4 h) was repeated and 12 h
post-transfusion the PCV and TS were 22% and 50 g/L, respec-
tively. The dog was administered yunnan baiyao (frequency
increased to 0.25 g PO, q6h) and methenamine (Urex; Vatring
Pharmaceuticals, Wytheville Virginia, USA) (10 mg/kg BW, PO,
q6h). Gross hematuria, urethral obstruction, and blood
loss anemia persisted for the next 24 h. The creatinine was
increased (309 mmol/L) suspected secondary to a right ureteral
obstruction evident on repeat urinary tract ultrasound. The dog
was humanely euthanized with pentobarbital (Fatal Plus; Vertex
Pharmaceutical, Cambridge, Massachusetts, USA), 1 mL/5 kg
BW, IV, due to right renal hemorrhage that resulted in ureteral
obstruction and subsequent azotemia. The right kidney was not
obtained for histopathology.

Discussion

This report describes surgically assisted instillation of aseptically
filtered 0.5% silver nitrate solution into a renal pelvis with gross
hemorrhage via a catheterized ureter. Following instillation,
the ureter was manually occluded to ensure contact time and
subsequent eschar formation. This procedure is different from
protocols reported in the human literature which describe
installation of a 0.25% to 1.0% solution through a ureteral
catheter placed with cystoscopic guidance. The catheter remains
in situ up to 3 d to allow for repeated instillations (12–14).
Fluoroscopic-guided renal pelvic installation of silver nitrate has
been performed in veterinary medicine with reported success
and minimal complications (15).

Silver nitrate is a cauterizing agent that coagulates cellular
protein resulting in an eschar (12) and cessation of hemor-
rhage. Installation of silver nitrate into the urogenital tract has
been reported in the human literature for treatment of renal
hematuria, bladder hemorrhage, and chyluria (12,13). Reported
complications include flank pain, nausea, vomiting, hematuria,
acute renal and hepatic failure, and necrotizing ureteritis but are
uncommon (12–14).

The dog in this case exhibited intermittent bleeding with its
severity resulting in a clinical anemia requiring multiple transfu-
sions. Two cystoscopic procedures and a third cystotomy were
initially required to confirm the kidneys as the source of the
hemorrhage. The left kidney was determined to be the primary
source of hemorrhage, urinary blood clots, and clinical anemia
on the initial and subsequent evaluations; however, gross hem-
orrhage was visualized from the right ureter during cystoscopy
prior to the patient’s first treatment but was not repeatable at
that time or on multiple gross examinations. An intra-operative
urinalysis at the first treatment time revealed microscopic
hematuria. The combination of these findings is indicative of
intermittent hemorrhage from the right kidney. The possibil-
ity of catheter-induced trauma accounting for the microscopic
hematuria exists but is thought to be less likely given the previ-
nous cystoscopic finding of gross hemorrhage. Given the bilateral
involvement on initial evaluation and concern for preservation of renal function, nephrectomy was not considered a viable treatment option. Both kidneys were not treated with silver nitrate simultaneously because there was concern that the silver nitrate could induce acute renal injury. Instead, the left kidney was chosen for treatment because that is the side that had gross hematuria during surgical exploration.

Ten months following the procedure, gross hematuria and blood loss anemia recurrent. The left renal pelvic hematoma was suggestive that the left kidney was again the primary source of hemorrhage, and instillation of a 0.5% silver nitrate solution was repeated on the left side only. A urinalysis was not obtained from the right kidney to monitor for microscopic hematuria and the urine was grossly normal in appearance.

The transient response to the second instillation of silver nitrate could be a result of inadequate contact time and lack of eschar formation due to the large blood clot in the renal pelvis that could not be removed. Alternatively the presumed left-sided persistent bleeding could have resulted from the histologically confirmed subacute pyelonephritis rather than a recurrence of the idiopathic hemorrhage. The pyelonephritis was either bacterial, secondary to contamination during the recent surgical procedure, or an expected sterile inflammatory reaction to the silver nitrate solution. Urine was not cultured prior to instillation and it is possible that bacteria smaller than the size restriction of the nylon membrane present in the silver nitrate solution could have been introduced during the procedure.

Gross examination of urine exiting the ureteral catheter at the time of second silver nitrate instillation and left-sided nephrectomy failed to reveal gross hemorrhage from either kidney. Given the known bilateral involvement as evident by gross hemorrhage visualized on cystoscopy prior to the first treatment and documented on urinalysis, it is plausible that the source of the continued bleeding was actually the right kidney that was not treated at any time with the silver nitrate solution. Due to the lack of knowledge regarding the long-term effects and safety of the silver nitrate solution and previous cessation of hemorrhage with unilateral treatment, bilateral simultaneous instillation was not considered to be a safe treatment option.

The dog was administered a urinary antiseptic agent, metenamidine, prior to euthanasia. This compound is hydrolyzed to formaldehyde in the urine which may have pro-coagulation properties. The dog received the medication for less than 24 h prior to euthanasia and its efficacy could not be evaluated.

This case report demonstrates the importance of alternative treatment options for cases of idiopathic renal hematuria. As in this report, previous cases of bilateral renal bleeding resulted in death or euthanasia due to the lack of treatment options once a nephrectomy has been performed. The initial response to the chemical cauterization with silver nitrate was favorable and resulted in 10 mo without clinical signs or anemia.

The authors believe that the yunnan baiyao administered did not contribute to the dog’s 10-month interval without gross hematuria. Following the initial treatment the dog was free of gross hematuria for 1 month before the yunnan baiyao was started by the referring veterinarian. The medication was administered for persistent microscopic hematuria, which was documented to be occurring from the untreated right kidney and did not resolve on subsequent urinalyses. Additionally this medication at increased frequency failed to resolve right-sided gross hemorrhage following the dogs left nephrectomy. The efficacy of this agent in the treatment of idiopathic renal hematuria is unknown. Its contribution to controlling or preventing recurrence of gross hemorrhage after the initial treatment cannot be determined in this case.

The recurrence of blood loss anemia and documented blood clots in bladder and ureters bolsters the possibility that the right kidney was the source of the hemorrhage following the second silver nitrate treatment. Given the intermittent nature of the hemorrhage from either kidney and lack of grossly visualization at the time of the nephrectomy, it cannot be definitively stated that second silver nitrate treatment was unsuccessful.

Chemical cauterization with silver nitrate solution should be considered a viable option for treatment of severe idiopathic renal hematuria. This case report demonstrates resolution of clinical signs and anemia for 10 months following instillation of a 0.5% silver nitrate solution into a grossly hemorrhaging renal pelvis. The efficacy of subsequent silver nitrate treatments cannot be fully evaluated given the known bilateral involvement. Additional studies exploring the efficacy, safety, and long-term effects of renal pelvic silver nitrate instillation are warranted.  

References