Hematuria and transitional cell papilloma of the renal pelvis treated via unilateral nephrectomy in an alpaca

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Case Description—An 11-year-old 72-kg (158-lb) sexually intact female alpaca was examined for diagnosis and treatment of hematuria of 4 months’ duration.

Clinical Findings—Pigmenturia was detected by the owner when the alpaca was 8 months pregnant. Radiographic, ultrasonographic, vaginal speculum, and cystoscopic evaluation of the urinary tract revealed normal vaginal and urethral epithelia and increased bladder vessel tortuosity, with pulses of hemorrhage from the left ureter. Regenerative anemia and mild leukopenia were detected and serum urea nitrogen and creatinine concentrations were within reference ranges.

Treatment and Outcome—Chronic hematuria resolved after unilateral nephrectomy of the left kidney, and no dysfunction was detected in the remaining kidney. Histologic evaluation of the kidney revealed a transitional cell tumor in the renal pelvis.

Clinical Relevance—Although anemia is common in South American camelids, hematuria is an uncommon sign of this condition. Chronic urinary tract infection, toxin ingestion, and neoplasia causing hematuria or hemoglobinuria should be considered in South American camelids with pigmenturia. Thorough and systematic evaluation of the urinary tract should be performed to locate the site of hemorrhage to treat hematuria appropriately. (J Am Vet Med Assoc 2008;232:1206–1209)

A 11-year-old female alpaca was evaluated at the Veterinary Teaching Hospital of The Ohio State University with a history of hematuria of 4 months’ duration. There was no history of stranguria. The referring veterinarian diagnosed bacterial cystitis (bacteriologic culture of urine yielded Escherichia coli, Streptococcus spp, and Enterococcus spp) and initiated intravesicular antimicrobial treatments (ticarcillin and amikacin) periodically. The referring veterinarian also initiated twice weekly injections of vitamin K (1.42 mg/kg [0.65 mg/lb]) to provide cofactors necessary for production of coagulation factors.

On physical examination, the alpaca was bright, alert and responsive, weighed 72 kg (158 lb), and had a body condition score of 4/10. On admission, heart rate was 100 beats/min (reference range, 60 to 90 beats/min), respiratory rate was 30 breaths/min (reference range, 10 to 30 breaths/min), and rectal temperature was 37.8°C (99.5°F; reference range, 37.5° to 38.9°C [99.5° to 101.0°F]).1 The mucous membranes were slightly pale. There were no abnormal sounds heard via auscultation of the thorax.

When placed in a stall, the alpaca urinated red fluid without clots or evidence of stranguria. The pigmenturia occurred throughout urination. Urine dipstick analysis revealed 3+ blood, 2+ protein, and pH of 9.0; specific gravity was 1.022. After centrifugation, the urine was clear yellow with red sediment. Evaluation of the urine revealed 3+ blood, 2+ protein, and pH of 9.0; specific gravity was 1.022. After centrifugation, the urine was clear yellow with red sediment. Evaluation of the urine was performed on urine collected via a bladder catheter.

Complete blood count revealed PCV of 17% (reference range, 24% to 35%). Thrombocyte count was 360,000 X 103 (reference range, 206 to 1.1 X 105 X 109 X 1012). There were 2.5 X 109 segmented neutrophils/L (reference range, 0 to 2 X 109 X 1012). Mean corpuscular volume was 35 fl (reference range, 21 to 30 fl) and mean corpuscular hemoglobin concentration was 37.9 g/dL (reference range, 39.2 to 46.1 g/dL). There were 2.5 X 109 band neutrophils/L (reference range, 0 X 109 X 1012). 2.5 X 109 segmented neutrophils/L (reference range, 2.1 to 9.5 X 109 X 1012). 1.1 X 109 lymphocytes/L (reference range, 0.9 to 4.4 X 109 X 1012). 0.1 X 109 monocytes/L (reference range, 0 to 0.6 X 109 X 1012). There was 0 X 109 eosinophils/L (reference range, 0 to 3.3 X 109 X 1012). The thrombocyte count was within reference range (251 X 109 X 1012). There were 2.6 X 109 X 1012 thrombocytes/L.

MRI = Magnetic resonance imaging

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plasma protein concentration was 4.9 g/dL (reference range, 5.3 to 7.6 g/dL). Values of the serum biochemical profile were within reference ranges, including BUN concentration of 12 mg/dL (reference range, 12 to 33 mg/dL) and creatinine concentration of 2.1 mg/dL (reference range, 1.3 to 2.7 mg/dL). To rule out the possibility of hemorrhage from the vaginal canal or uterus, a vaginal speculum examination was performed. The vaginal vault and closed cervix were normal without evidence of hemorrhage.

On the basis of the history, clinical signs, laboratory findings, and absence of visible trauma to the reproductive tract, chronic blood loss from the urinary tract was presumed to be a likely cause of the hematuria. Differential diagnoses included inflammation, urolithiasis, trauma, vascular anomaly or varicosities, and neoplasia of the urinary tract.

To further identify the source of blood loss, transabdominal and transrectal ultrasonography was performed. Transrectal ultrasonography (5 MHz, linear array) revealed that the uterus was involuted and considered normal for an alpaca at 1 month after parturition. However, the urinary bladder contained a large volume of hyperechoic, nonshadowing echogenicities suggestive of cystitis or hemorrhage. The bladder wall appeared normal and lacked hyperechoic foci with acoustic shadowing observed in cystolithiasis. Transabdominal ultrasonography with a variable wavelength sector probe (frequency range, 3 to 9 MHz) was performed on both kidneys. The renal pelvices appeared normal and had prominent echogenicity associated with renal pelvic fat. Abdominal radiography and positive and double-contrast cystography were performed after placement of a flexible rubber urinary catheter by first instilling 30 mL of iodinated contrast material and removal of the contrast material and replacement with air. No radiographic abnormalities were detected in the bladder.

These findings decreased the likelihood that urinary bladder neoplasia, urolithiasis, or cystitis was a cause of hematuria. Results of urinalysis and serum biochemical analyses did not support renal dysfunction severe enough to suggest renal failure. Furthermore, although the ultrasonographic appearance of both kidneys did not reveal mass lesions in either kidney, the technique may not have been appropriate to detect tumor tissue with density similar to or less than that of intrapelvic fat.

To directly evaluate the lower portion of the urinary tract, including the mucosal surfaces of the urethra, urinary bladder, and ureteral openings, cystoscopy was performed. There were no grossly visible abnormalities in the urethral mucosa. Small abnormalities were seen in the urinary bladder mucosa, including focal cystitis and increased vessel tortuosity of the cranial aspect of the bladder wall. Most importantly, cystoscopy revealed macroscopically normal urine flowing from the right ureteral opening into the bladder, whereas pulses of red urine were observed originating from the left ureteral opening (Figure 1). Following cystoscopy, the list of differential diagnoses was further revised to include lesions of the upper portion of the urinary tract (renal and ureteral), including neoplasia and pyelonephritis.

Intravenous pyelography, renal scintigraphy, and MRI were not performed to limit costs and risks associated with additional anesthetic protocols. Unilateral nephrectomy of the left kidney and ureter was considered the method most likely to determine the source of hemorrhage.

The nephrectomy was carried out through a left paralumbar laparotomy incision. The approach was chosen on the basis of the presence of the left kidney in the retroperitoneal space, adjacent to the spleen on the left side, and the reduced need to manipulate the intestines with this approach.

Because the alpaca’s presurgical PCV was 14% and the total plasma protein concentration was 4.0 g/dL, the alpaca received a blood transfusion of 500 mL of fresh whole blood at a rate of < 20 mL/kg/h (9.1 mL/lb/h) immediately prior to surgery. Anesthesia was then induced with 90 mL of a mixture of guaifenesin (5%) and ketamine (0.1%), followed by intubation and maintenance with 2.5% isoflurane in oxygen. During surgery, the alpaca also received 500 mL of lactated Ringer’s solution and 250 mL of hetastarch. The alpaca was positioned in right lateral recumbency, and the left paralumbar approach to the abdomen and retroperitoneal space exposed the left kidney. The abdomen was explored manually, the ureters were palpably normal, and there were no additional abnormalities. A unilateral nephrectomy was performed after gross examination in situ did not reveal abnormalities. This procedure was conducted by bluntly dissecting the tissue surrounding the renal hilus, and the renal artery, vein, and ureter were isolated and ligated with size 3 chromic gut en mass. The retroperitoneal space, peritoneum, and transversus muscles were closed with size 0 chromic gut. The internal and external abdominal oblique muscles were closed together with size 3 chromic gut in a simple continuous pattern. The skin was closed with nonabsorbable braided polyamide suture. The left kidney was bisected in the sagittal plane (Figure 2) prior to placement in neutral-buffered 10% formalin for histologic examination.

Gross examination of the resected, formalin-fixed left kidney revealed a raised, irregular, papillary, exophytic mass 1.0 to 1.5 cm in diameter filling the renal pelvis and extending outward toward the renal medulla (Figure 2). The mass was connected to the renal pelvic...
epithelium but did not invade the adjacent parenchyma. On microscopic examination, the mass consisted of numerous papillary projections of atypical proliferative renal transitional epithelium supported by delicate fibrovascular connective tissues (Figure 3). Atypical transitional epithelial cells were cuboidal to columnar, typically in layers of 3 to 10 cells, with lightly eosinophilic granular cytoplasm supported by an intact basement membrane. Mitoses were uncommon (approx one/four 400X fields). Occasional foci of coagulation necrosis and RBCs were seen. There was no evidence of suppurrative or granulomatous inflammation compatible with pyelonephritis. These findings were considered consistent with a well-differentiated renal transitional cell papilloma. The cause of hematuria appeared to be papillary projections undergoing infarction and necrosis with hemorrhage into the pelvic spaces.

The alpaca recovered well after surgery, and serum biochemical analyses performed 2 days after surgery revealed BUN and creatinine values within reference ranges. One day after surgery, the urine was yellow, clear, and voided without difficulty. One week later, the alpaca and its cria were discharged. The owner reported normal urination without evidence of blood, leukocytes, or protein (urine dipstick analysis) in the urine and normal appetite and weight gain 2 months after discharge. Serum biochemical analyses at that time revealed BUN concentration of 34 mg/dL and creatinine concentration of 1.9 mg/dL. The PCV had increased to 23%, and the total plasma protein concentration was 6.0 g/dL.

**Discussion**

Anemia, although a common finding in South American camelids, is not typically associated with hematuria. To our knowledge, although renal neoplasia has been reported, renal transitional cell papilloma as a cause of hematuria has only been reported in a llama at postmortem examination.

The clinical history reported by the owners of the alpaca reported here was not consistent with severe anemia; for example, there was no evidence of lethargy; however, a mild increase in respiratory and heart rates on admission may have been associated with low PCV. The mucous membranes had mild pallor, but there was no evidence of petechiae or icterus suggestive of coagulopathy or hemolysis, respectively. Hematuria was the main clinical sign.

Ultrasoundographic and contrast urographic evaluation of the bladder excluded lesions such as cystic calculi, cystitis, and urinary bladder neoplasia. Surprisingly, ultrasonographic evaluation of both kidneys revealed normal findings; thus, ultrasonography was not sufficiently sensitive to differentiate between the papilloma and normal renal pelvic fat. Perhaps the use of other imaging techniques or modalities such as computed tomography, MRI, renal scintigraphy, or IV pyelography would have revealed the tumor and determined whether unilateral or bilateral renal involvement was present.

Causes of hemorrhage from the proximal portion of the urinary tract may include infection, trauma, toxicosis, nephrolithiasis, neoplasia, and vascular anomalies. Medical management of hematuria should involve supportive care, including administration of blood transfusions and antimicrobials for bacterial infections. In other species, hematuria associated with chronic bacterial infection (eg, renal abscess and pyelonephritis), mycotic infection, urolithiasis, and renal neoplasia have been reported. Other treatments, including administration of α-amino caproic acid and formalin (IV) have not been reported in camelids. The use of plasma to supplement coagulation factors or orally administered hematinsics was not attempted in the alpaca reported here, although they may have temporarily reduced hemorrhage and provided iron for RBC production. The alpaca did receive vitamin K; however, this was not effective in reducing the frequency or severity of hematuria. Medical management of hematuria is not always successful. In most reports, nephrectomy is thought to be required to completely resolve blood loss. Reports of renal neoplasia also suggest that early recognition of renal involvement, which permits appropriate surgical intervention, is critical. Our decision to remove the left kidney rather than biopsy the kidney
or manage the alpaca medically was based on evidence of unilateral disease. Results of transabdominal renal biopsy may have been informative if renal pelvic tissues were obtained, but the potential for renal hemorrhage after biopsy was also considered prior to surgery.

Previous reports4 describe the use of a ventral midline approach to the right kidney in a llama with an ectopic ureter. The left flank approach is slightly more complicated than the ventral midline approach in that the number of layers which must be incised and closed is greater than with the ventral midline approach; however, it is not necessary to position the animal with the head lowered, providing improved visualization of the renal hilus. Both procedures apparently have limitations with respect to isolation and resection of the terminal portion of the ureter in camelids.3

Primary renal neoplasia is rare in domestic animals and accounts for < 1% of all neoplasms.10,17 A variety of primary renal neoplasms have been described, including epithelial tumors (renal cortical adenoma, renal carcinoma, oncocytoma, transitional cell carcinoma, transitional cell papilloma, and squamous cell carcinoma), primary mesenchymal tumors (fibroma, fibrosarcoma, and hemangiosarcoma), and a tumor derived from embryologic components (nephroblastoma).18–21 Few cases of spontaneous renal papillomas or renal transitional cell papillary hyperplasia in animals have been published and are primarily reported in nonhuman primates and laboratory rats.19,20 Most renal pelvic papillomas, however, have been studied in experimental carcinogenesis models in rats.21–23

Other renal neoplasms have been reported in camels, such as renal teratoma in a llama,24 renal lymphosarcoma,8,25 and nephroblastoma in a guanaco.26 In those case reports, pigmentation was not a major clinical sign, and hematuria was only reported in 1 case.7 Multicentric urinary papilloma involving both kidneys and a ureter was described in a llama with anemia, weakness, and hematuria.7 Although detected at a more advanced stage, with marked anaplasia and metaplasia, the tumor was of similar origin to that described in the present report. In that llama, an association between suspected bracken fern ingestion and bovine papilloma virus infection was suggested.7 In the alpaca reported here, the tumor appeared to be limited to the kidney without grossly evident involvement of the ureter.

The alpaca had hematuria and mild regenerative anemia associated with blood loss, as in enzootic hematuria. Hemolytic disease was ruled out by lack of hemoglobinuria and icterus. The initial WBC count was less than the lower limit of the reference range, which was also compatible with enzootic hematuria. However, return of WBC counts to reference range and higher PCV 2 months after surgery suggested the hemorrhage was unilateral. Approximately 1 year after this female’s last hospital visit, this female gave birth to a healthy cria. Unfortunately, we have not been successful in determining whether bovine papilloma virus was in renal tissues preserved for histologic examination, as described.7

References