

DIAGNOSIS AND TREATMENT OF A UNILATERAL RENAL CYSTADENOMA IN AN AFRICAN LION (*PANTHERA LEO*)

Author(s): Ronan Eustace, D.V.M., Jacob Rubin, D.V.M., Dipl. A.C.V.S.,
Kimberly A. Thompson, D.V.M., M.P.V.M., Dipl. A.C.V.P.M., Kyle Snowdon,
D.V.M., James G. Sikarskie, D.V.M., M.S., Dipl. A.C.Z.M., Colleen Monahan,
D.V.M., and Rebecca C. Smedley, D.V.M., MS., Dipl. A.C.V.P.

Source: Journal of Zoo and Wildlife Medicine, 48(3):906-909.

Published By: American Association of Zoo Veterinarians

<https://doi.org/10.1638/2016-0242.1>

URL: <http://www.bioone.org/doi/full/10.1638/2016-0242.1>

BioOne (www.bioone.org) is a nonprofit, online aggregation of core research in the biological, ecological, and environmental sciences. BioOne provides a sustainable online platform for over 170 journals and books published by nonprofit societies, associations, museums, institutions, and presses.

Your use of this PDF, the BioOne Web site, and all posted and associated content indicates your acceptance of BioOne's Terms of Use, available at www.bioone.org/page/terms_of_use.

Usage of BioOne content is strictly limited to personal, educational, and non-commercial use. Commercial inquiries or rights and permissions requests should be directed to the individual publisher as copyright holder.

DIAGNOSIS AND TREATMENT OF A UNILATERAL RENAL CYSTADENOMA IN AN AFRICAN LION (*PANTHERA LEO*)

Ronan Eustace, D.V.M., Jacob Rubin, D.V.M., Dipl. A.C.V.S., Kimberly A. Thompson, D.V.M., M.P.V.M., Dipl. A.C.V.P.M., Kyle Snowden, D.V.M., James G. Sikarskie, D.V.M., M.S., Dipl. A.C.Z.M., Colleen Monahan, D.V.M., and Rebecca C. Smedley, D.V.M., MS., Dipl. A.C.V.P.

Abstract: A renal tubular cystadenoma was diagnosed in a 14-yr-old male African lion (*Panthera leo*). During a routine health evaluation, a left renal mass was identified via physical examination, radiographs, and abdominal ultrasonography. The mass was 30 × 15 cm in size and had a thin capsule with central hypoechoic fluid, suggestive of a perirenal cyst. An exploratory celiotomy with partial nephrectomy was performed without complications. Histologically, the tumor was characterized by a thick fibrous capsule surrounding multiple, variable-sized cysts that markedly compressed the adjacent fibrotic and atrophied renal cortex. Immunohistochemical labeling for Aquaporin-1 and Tamm-Horsfall protein was consistent with a renal tubular cystadenoma of proximal tubule origin. Renal cystadenomas are an uncommon benign epithelial neoplasm. There are only two documented case reports in domestic cats. This report represents the first documentation, to the authors' knowledge, of a renal cystadenoma in a lion.

Key words: African lion, kidney, neoplasia, *Panthera leo*, renal cystadenoma.

BRIEF COMMUNICATION

A routine health examination was performed on a 14-yr-old male intact African lion (*Panthera leo*) at the Potawatomi Zoo. The animal was hand-injected intramuscularly with midazolam (Midazolam 50 mg/ml, ZooPharm, Fort Collins, Colorado 80522, USA; 0.1 mg/kg), medetomidine (Medetomidine 20 mg/ml, ZooPharm; 0.03 mg/kg), and ketamine (Ketamine 200 mg/ml, ZooPharm; 2.8 mg/kg), then intubated with a 22-mm cuffed endotracheal tube (Jorvet™, Jorgensen Laboratories, Loveland, Colorado 80538, USA) and maintained on isoflurane (Isothesia™, Butler Animal Health Supply, Dublin, Ohio 43017, USA) for the duration of the procedure. An 18-ga, 1-1/2-inch intravenous catheter (BD Angiocath™, Becton Dickinson Infusion Therapy Systems, Sandy, Utah 84070, USA) was placed in the right medial saphenous vein, and lactated ringer's

solution (LRS, Hospira Lake Forest, Illinois 60045, USA) was administered intravenously for the entire procedure at 10 ml/kg/hr.

A midabdominal mass was identified during abdominal palpation. Transabdominal ultrasonography revealed an approximately 30 × 15-cm cystic mass adjacent to the left kidney extending to the lateral abdominal wall. The cystic structure had a thick capsule and contained hypoechoic fluid between the capsule and renal parenchyma. The renal tissue adjacent to the mass appeared compressed. The right kidney, liver, gallbladder, adrenal glands, representative loops of small intestines, and urinary bladder appeared grossly normal. An ultrasound-guided fine needle aspirate of the mass yielded 60 ml of clear yellow fluid. Samples were submitted for aerobic microbial culture, electrolyte analysis, and cytologic analysis. On lateral abdominal radiographs, the mass displaced the intestines and compressed the descending colon. Anesthesia was reversed with atipamezole (Antisedan®, Pfizer Animal Health, New York, New York 10017, USA; 0.2 mg/kg im).

Cytologic evaluation of the aspirated fluid revealed a modified transudate with a low number of macrophages, a large amount of intracellular hemosiderin, and a small amount of blood. No atypical cells were noted. These findings were consistent with a resolving hematoma or a poorly cellular cyst with hemorrhage. The ratio of fluid to peripheral serum creatinine was 1:6, and the ratio of fluid to peripheral serum potassium was

From the Potawatomi Zoo, 500 S. Greenlawn Avenue, South Bend, Indiana 46615, USA (Eustace); the Michigan State University College of Veterinary Medicine, 784 Wilson Road, East Lansing, Michigan 48910, USA (Rubin, Thompson, Snowden, Sikarskie); and the Diagnostic Center for Population and Animal Health, Michigan State University, Lansing, MI 48823, USA (Monahan, Smedley). Present addresses: (Thompson) Binder Park Zoo, 7400 Division Drive, Battle Creek, Michigan 49014, USA; (Snowdon) University of Tennessee College of Veterinary Medicine, 2407 River Drive, Knoxville, Tennessee 37996. Correspondence should be directed to Dr. Eustace (reustace@potawatomizoo.org).

1 : 0, which is inconsistent with published reports of uroabdomen in domestic cats. Creatinine and potassium in abdominal fluid from cats with uroabdomen were 2 times and 1.9 times the serum creatinine and potassium levels, respectively, in one report.¹³ Aerobic culture of the fluid revealed no growth. Hematologic and serum biochemistry values were within normal limits; however, the creatinine was slightly elevated when compared to reported reference ranges in free-ranging lions (creatinine 3.3 mg/dl [reference range, 0.6–4.00 mg/dl]; free-ranging lion reference range 0.89–3.23 mg/dl).^{4,6} Further, creatinine values for this lion had progressively increased as this animal aged and suggested possible underlying subclinical kidney disease. The coagulation profile was within normal limits for a domestic cat. Urinalysis obtained from cystocentesis showed proteinuria (+3) and hematuria (+3) and the urine sp gr was 1.039.

Based on the ultrasound appearance of the mass and cytologic evaluation, the primary differential diagnosis for the left cystic kidney mass was a perirenal cyst or pseudocyst, but other possible differentials included polycystic kidney disease, abscess, hematoma, granuloma, echinococcosis, and renal neoplasia. The blood work changes were suggestive of early possible chronic renal disease.

To further evaluate this mass, the lion was immobilized with the previously described protocol 2 wk later for an abdominal celiotomy. During surgical preparation, the patient received meloxicam (Metacam®, Boehringer Ingelheim, Vetmedica Inc., Saint Joseph, Missouri 64506, USA; 0.1 mg/kg sc), penicillin G procaine (PenOne Pro, Norbrook Laboratories Limited, Newry, Northern Ireland; 22,000 IU/kg im), sodium cefazolin (Cefazolin, West-Ward Pharmaceutical Corp., Eatontown, New Jersey 07724, USA; 22 mg/kg iv every 90 min during surgery), famotidine (Famotidine, West-Ward Pharmaceutical Corp.; 0.5 mg/kg sc), and lactated ringers solution (LRS, Hospira Inc.; 3,000 ml iv and 2,000 ml sc during surgery). An arterial catheter was placed in the right dorsal pedal vessel to monitor direct blood pressure and a dopamine HCL continuous rate infusion (Dopamine, 40 mg/ml, Hospira Inc.; 2.5 mcg/kg/min iv) was administered intraoperatively during the surgery after the lion exhibited a brief period of hypotension associated with manipulation of the renal mass (mean arterial blood pressure 32 mmHg).

During celiotomy, the left kidney was found to be grossly enlarged compared to the contralateral

kidney, measuring 30 × 15 cm, with prominent capsular vasculature, a thickened capsule, and multiple fibrous omental adhesions. The other abdominal organs were grossly normal. Intraoperative ultrasound showed no evidence of communication of the cyst and renal pelvis and, based on gross observation at the time of surgery, the mass appeared to be well demarcated, expansive, and within the renal cortex. Due to the possibility of underlying renal disease, a kidney-sparing surgery technique was elected. A small incision was made into the cyst and approximately 2 L of yellow fluid were removed. A partial nephrectomy to remove the abnormal tissue, which was three times the size of the remaining kidney, was then performed and the renal capsule was closed with 2-0 PDS II (PDS®, Ethicon Inc., Somerville, New Jersey 08876, USA) in a simple continuous pattern. After ensuring there was adequate hemostasis, the abdomen was lavaged with saline and closed in a routine, 3-layer closure.

Postoperative medications included tramadol (Pfizer; 3 mg/kg po bid for 14 days) and meloxicam (Metacam®, Boehringer Ingelheim, Vetmedica Inc.; 0.05 mg/kg, po sid for 5 days). The lion developed an 8 × 4-cm seroma overlying the ventral abdominal incision which intermittently produced small amounts of serosanguinous fluid for the next 10 days. The lion was prescribed cephalexin for 14 days to minimize the risk of infection (Cephalexin Capsules, USP, Ascend Laboratories, LLC Montvale, New Jersey 07645, USA; 25 mg/kg po bid). The seroma resolved in 14 days and the lion recovered with no further complications. One, 6, and 9 mo postsurgery, blood was collected under operant conditioning from the lateral tail vein for serum biochemistry and a complete blood count. The values remained unchanged from previous blood work.

Histopathologic evaluation of the portion of the removed kidney identified a cystadenoma (Fig. 1A–C). The cystadenoma consisted of variable-sized cysts surrounded by a thick fibrous capsule that markedly compressed the adjacent fibrotic and atrophied renal cortex. The cysts were generally lined by a single layer of attenuated to cuboidal neoplastic epithelium. Within some of the cysts there were short tubulopapillary proliferations of neoplastic epithelial cells. The neoplastic cells had indistinct cell borders, moderate amounts of eosinophilic foamy cytoplasm, round, finely-stippled nuclei with a prominent nucleolus, mild anisokaryosis, and there were 2 mitotic figures in 10 high-power fields. In the adjacent compressed and atrophied kidney parenchyma,

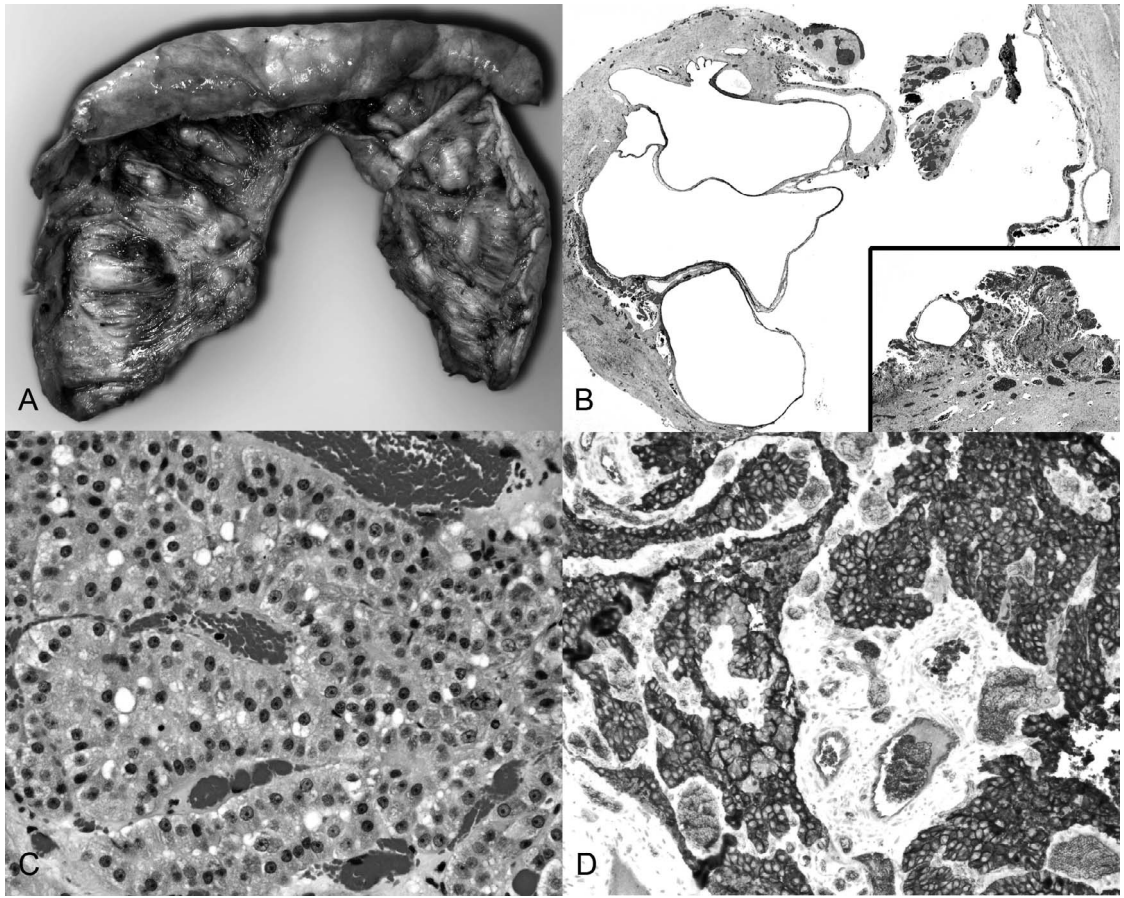


Figure 1. (A–D) Renal tubular cystadenoma, 14-yr-old male African lion (*Panthera leo*). **A.** Incised renal tubular cystadenoma. Histologically, the mass was composed of multiple, variable-sized cysts that markedly compressed the adjacent outer atrophied and fibrotic renal cortex. **B.** Inset shows more solid papillary proliferation of neoplastic cells; in these areas **C.** neoplastic cuboidal to columnar epithelial cells were arranged in tubules and showed mild anisokaryosis and anisocytosis. Hematoxylin and eosin (H&E) stain. **D.** Immunohistochemically, neoplastic cells showed diffuse perimembranous to cytoplasmic labeling for Aquaporin-1. Diaminobenzidine chromagen.

there was diffuse segmental membranous glomerulopathy. Immunohistochemistry for Aquaporin-1 and Tamm-Horsfall protein was performed to confirm renal tubular origin (Fig. 1D). Aquaporin-1 is expressed by proximal renal tubular epithelium and the thin descending limbs of Henle's loops while Tamm-Horsfall protein is expressed by the thick ascending limbs of Henle's loops.² Neoplastic cells had diffuse perimembranous to cytoplasmic labeling for Aquaporin-1 and were nonimmunoreactive for Tamm-Horsfall protein, indicating the cystadenoma was most likely of proximal renal tubular origin.

Though chronic renal disease is an important cause of mortality and morbidity in captive felids, reports of renal neoplasia are scarce.^{5,8,10,14} Prima-

ry renal neoplasms are also uncommon in domestic cats.⁹ Lymphoma is the most-common renal neoplasm reported in domestic cats, either unilaterally or bilaterally.^{3,9} Other primary renal neoplasms reported in domestic cats include carcinomas, nephroblastomas, hemangiosarcomas, and adenomas, all of which are usually unilateral.⁹ Renal cystadenoma is a rare benign epithelial neoplasm that has only been characterized in two case reports in domestic felines but has not been described in an exotic felid.^{7,12} Renal cystadenomas are more common in domestic dog populations and can be associated with canine nodular dermatofibrosis.¹ A genetic basis or paraneoplastic syndrome has been proposed for the association between this skin disease and

renal cystadenomas in dogs.¹ This lion had no evidence of nodular dermatofibrosis or other skin lesions. Similar to the reports in domestic cats, the tumor was present in one kidney and the contralateral kidney appeared unaffected based on gross and ultrasonographic evaluation.

Additional testing that is commonly performed for similar cases in domestic animals, such as glomerular filtration rate measurement or a computerized tomography scan, were not pursued due to limited availability of nearby facilities capable of handling a lion. Ultrasound, radiography, cytologic evaluation, microbial cultures, and routine blood work did not result in a diagnosis in this case and were suggestive of a perirenal pseudocyst; therefore, surgical exploration was needed to obtain representative biopsies. Perirenal pseudocysts are nonepithelial lined, fluid-filled fibrous sacs that surround the kidney.¹¹ They can be unilateral or bilateral. Chronic renal disease has been implicated in their pathogenesis.¹¹

If diagnosis and treatment of a renal cystadenoma is initiated early in the course of the disease, surgical excision may be palliative and possibly curative.⁵ However, other conditions such as malignant renal neoplasia, perirenal pseudocysts, polycystic kidney disease, abscesses, hematomas, or granulomas must be excluded. The cystadenoma in this case was an incidental finding and was not associated with any clinical signs, which is consistent with the previous reported cases in domestic felines. However, due to the large size of the neoplasm in this lion, clinical signs resulting from a mass effect likely would have occurred in the near future.

Acknowledgments: The authors would like to thank the staff at the Potawatomi Zoo and Drs. Kirk Munoz and Drew Armstrong for their efforts and help in this case.

LITERATURE CITED

1. Bønsdorff TB, Jansen JH, Thomassen RF, Lin-gaas F. Loss of heterozygosity at the FLCN locus in early renal cystic lesions in dogs with renal cystadenoma and nodular dermatofibrosis. *Mamm Genome*. 2009;20(5):315–320.
2. Brandt L, Bohn A, Charles J, Ehrhart E. Localization of canine, feline, and mouse renal membrane proteins. *Vet Pathol*. 2012;49(4):693–703.
3. Henry CJ, Turnquist SE, Smith A, Graham JC, Thamm DH, O'Brien M, Clifford C. Primary renal tumours in cats: 19 cases (1992–1998). *J Feline Med Surg*. 1999;1(1999):165–170.
4. International Species Information System, Physiological data reference values. [CD-ROM] Apple Valley (MN): International Species Information System. c2002.
5. Junginger J, Hansmann F, Herder V, Lehmbecker A, Peters M, Beyerbach M, Wohlsein P, Baumgärtner W. Pathology in captive wild felids at German zoological gardens. *PLoS ONE*. 2015;10(6):1–30.
6. Mass M, Keet D, Nielen M. Hematologic and serum chemistry reference intervals for free-ranging lions (*Panthera leo*). *Res Vet Sci*. 2013;95:266–268.
7. Mosenco AS, Culp WTN, Johnson V, French A, Mehler SJ. Renal cystadenoma in a domestic shorthair. *J Feline Med Surg*. 2008;10(1):102–105.
8. Newkirk KM, Newman SJ, White LA, Rohrbach BW, Ramsay EC. Renal lesions of nondomestic felids. *Vet Pathol*. 2011;48(3):698–705.
9. North SM, Banks TA. Tumors of the urinary system. In: *Small animal oncology*. Edinburgh, Scotland: Elsevier, Saunders Ltd.; 2009. p. 151–171.
10. Owston MA, Ramsay EC, Rotstein DS. Neoplasia in felids at the Knoxville Zoological Gardens, 1979–2003. *J Zoo Wildl Med*. 2008;39(4):608–613.
11. Raffan E, Kipar A, Barber PJ, Freeman AI. Transitional cell carcinoma forming a perirenal cyst in a cat. *J Small Anim Pract*. 2008;49(3):144–147.
12. Report C, Baloi P, Chicca F Del, Ruetten M, Gerber B. The human Bosniak model applied to a cat with renal cystadenoma. *Tierartliche Prax Kleintiere*. 2015;1(17):45–49.
13. Stafford JR, Bartges JW. A clinical review of pathophysiology, diagnosis, and treatment of uroabdomen in the dog and cat. *J Vet Emerg Crit Care*. 2013;23(2):216–229.
14. Wack R. Treatment of chronic renal failure in nondomestic felids. In: Miller RE and Fowler ME eds.; *Zoo and wild animal medicine*, 6th Edition. St. Louis (MO): Elsevier Inc.; 2008. p. 462–465.

Accepted for publication 13 March 2017