Adrenal gland function in a dog following unilateral complete adrenalectomy and contralateral partial adrenalectomy

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Case Description—A 40.3-kg (88.7-lb) 6-year-old spayed female Labrador Retriever was evaluated because of acute unilateral epistaxis.

Clinical Findings—During the initial evaluation of the dog, systemic hypertension and a left adrenal gland mass were detected. The left adrenal gland mass was surgically removed; results of histologic examination of the mass indicated it was a pheochromocytoma. Ten months later, the dog was evaluated because of persistent systemic hypertension and development of polyuria, polydipsia, and excessive panting. Abdominal ultrasonography revealed a mass in the cranial aspect of the right adrenal gland; results of MRI suggested the mass was a malignant tumor.

Treatment and Outcome—Epistaxis resolved after treatment and resolution of severe systemic hypertension. A partial right adrenalectomy was performed to remove the right adrenal gland mass. Results of histologic examination of the mass indicated it was a well-differentiated carcinoma of the cortex of the adrenal gland. Results of ACTH stimulation tests after surgery indicated the dog had adequate adrenal gland function.

Clinical Relevance—Partial adrenalectomy may be a safe and feasible treatment option to preserve adrenal gland function in dogs with small eccentrically located adrenal gland masses, particularly for dogs that have undergone removal of the contralateral adrenal gland. (*J Am Vet Med Assoc* 2013;242:1398–1404)

A 40.3-kg (88.7-lb) 6-year-old spayed female Labrador Retriever was brought by its owner to the University of Georgia Veterinary Teaching Hospital because of acute left unilateral epistaxis. Three months prior, pituitary-dependent hyperadrenocorticism had been diagnosed on the basis of results of a low-dose dexamethasone suppression test (serum cortisol concentrations at the baseline time and 4 and 8 hours after dexamethasone administration were 5.6, 1.2, and 2.8 µg/dL, respectively; baseline reference interval, 1.0 to 6.0 µg/dL). The dog also had a history of hypothyroidism, elbow joint osteoarthritis, suspected atopy, obesity, and resolved heartworm infection.

At the time of examination at the hospital, the dog was receiving hydroxyzine (0.25 mg/kg [0.11 mg/lb], PO, q 12 h), firocoxib (0.5 mg/kg [0.23 mg/lb], PO, q 24 h), trilostane (6.25 mg/kg [2.84 mg/lb], PO, q 24 h), and levothyroxine sodium (0.017 mg/kg [0.008 mg/lb], PO, q 12 h). Physical examination findings included left unilateral epistaxis, tachycardia (200 beats/min), obesity (body condition score, 9/9), and 2 subcutaneous masses located on the right lateral aspect of the abdominal region (maximum length, 1.5 cm [0.6 inches]) and right prescapular region (maximum length, 3.5 cm [1.4 inches]). Other physical examination findings were unremarkable. Results of a CBC indicated nonregenerative anemia (HCT, 25.5%; reference interval, 36.6% to 59.6%), presumably attributable to acute blood loss because of epistaxis. Results of Doppler blood pressure measurement were consistent with severe hypertension (systolic blood pressure, > 200 mm Hg). Results of coagulation tests were within reference intervals. Results of cytologic examination of fine-needle aspirates of the subcutaneous masses of the right lateral aspect of the abdominal region and the right prescapular region were consistent with mast cell tumor and lipoma, respectively. Results of serum biochemical analyses indicated high alkaline phosphatase activity (187 U/L; reference interval, 10 to 119 U/L), hyperglycemia (333 mg/dL; reference interval, 66 to 109 mg/dL), and hyperphosphatemia (8.3 mg/dL; reference interval, 2.9 to 5.1 mg/dL). Results of urinalysis indicated minimally concentrated urine (urine specific gravity, 1.015) and mild proteinuria (dipstick protein value, 1+ [scale, 0 to 3+]). Serum thyroxine concentration was high (4.3 µg/dL; reference interval, 0.9 to 3.9 µg/dL).

Packed canine RBCs (12 mL/kg [5.5 mL/lb]) and fresh-frozen plasma (6 mL/kg [2.7 mL/lb]) were administered IV to the dog. Nitroprusside (0.5 µg/kg/min), hydralazine (0.25 mg/kg, PO, q 12 h), and phenoxybenzamine (1.5 mg/kg [0.68 mg/lb], PO, q 12 h) were administered to the dog for the treatment of hypertension. Treatment with trilostane and firocoxib was discontinued until resolution of hypertension because those drugs can cause serum electrolyte concentrations higher or lower than the reference intervals and renal damage, respectively. After treatment with nitroprus-

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side and hydralazine, blood pressure decreased and epistaxis resolved. Tramadol (2.5 mg/kg [1.1 mg/lb], PO, q 12 h) was administered, and the levothyroxine sodium dosage was decreased (0.01 mg/kg [0.0045 mg/lb], PO, q 12 h) because high serum thyroxine concentrations may have been contributing to hypertension in the dog.

Thoracic radiographic findings for the dog were unremarkable. Abdominal radiography revealed a rounded appearance of the ventral aspect of the spleen and flattening of the craniolateral aspect of the left kidney. Retroperitoneal structures were obscured in abdominal radiographic images. A mass of the caudal aspect of the left adrenal gland was identified via abdominal ultrasonography. Abdominal CT indicated a left adrenal gland mass (diameter, 5.2 cm [2.0 inches]) with possible invasion of the left phrenicoabdominal vein. Ultrasonography indicated the cranial and middle aspects of the right adrenal gland were diffusely enlarged (maximum adrenal gland diameter, 1.2 cm [0.5 inches]). No distinct nodules were identified in ultrasonographic or CT images.

The next day, left adrenalectomy and excision of the mast cell tumor on the right lateral aspect of the abdominal region were performed; no complications occurred during surgery. The right adrenal gland appeared enlarged, but no distinct mass was observed. Because of the potential for complications after removal of both adrenal glands during the surgery and the lack of definitively identifiable right adrenal gland nodules or masses, the right adrenal gland was not removed. Enlargement of the right adrenal gland was potentially attributable to long-term trilostane treatment.[1] Results of histologic examination of the tissues removed during surgery indicated a left adrenal pheochromocytoma and complete excision of a grade II mast cell tumor.

Two weeks following surgery, results of an ACTH stimulation test were unremarkable (baseline serum cortisol concentration, 4.8 µg/dL [reference interval, 2 to 6 µg/dL]; serum cortisol concentration 1 hour after ACTH administration, 10.9 µg/dL [reference interval, 6 to 18 µg/dL]); therefore, trilostane administration was not reinstituted. Subsequently, multiple ACTH stimulation tests were performed; results were not consistent with hyperadrenocorticism (baseline serum cortisol concentration range, 4.8 to 5.9 µg/dL; range of serum cortisol concentrations 1 hour after administration of ACTH, 10.9 to 15.2 µg/dL).

During a 10-month period after surgery, systemic hypertension in the dog persisted (systolic blood pressure range, 160 to 260 mm Hg). Hypertension was treated with various medications administered alone or in combination, including phenoxybenzamine (0.25 to 1.5 mg/kg, PO, q 12 h), hydralazine (0.25 to 0.5 mg/kg, PO, q 12 h), amlodipine (0.2 to 0.26 mg/kg [0.09 to 0.12 mg/lb], PO, q 12 h), and enalapril (0.25 mg/kg, PO, q 12 h). Results of CBCs performed during this period were unremarkable. Results of serum biochemical analyses indicated mild hyperglycemia (123 mg/dL) and hypermagnesemia (2.4 mg/dL; reference interval, 1.4 to 2.2 mg/dL). Serum alkaline phosphatase activities for the dog increased during the 10-month period from 187 U/L (at the time of the initial examination) to 575 U/L. Results of retinal examinations performed during that period were unremarkable, and no evidence of hypertensive retinopathy was detected.

Because of persistent and poorly controlled systemic hypertension and the development of polyuria, polydipsia, and excessive panting, the dog was reevaluated at the hospital 10 months after left adrenalectomy. Results of a CBC performed at that time were unremarkable. Results of serum biochemical analyses indicated high BUN concentration (31 mg/dL; reference interval, 8.5 to 28.5 mg/dL) and alkaline phosphatase activity (785 U/L), mild hyperglycemia (135 mg/dL), and a creatinine concentration within the reference interval (1.0 mg/dL; reference interval, 0.2 to 1.2 mg/dL). Serum aldosterone concentrations were determined to detect hyperaldosteronism as a potential cause for hypertension. The serum aldosterone concentration was low (4.0 pmol/L; reference interval, 12 to 957 pmol/L); therefore, hyperaldosteronism was ruled out as a cause of hypertension. Results of urinalysis indicated isosthenuria (urine specific gravity, 1.012) and proteinuria (dipstick protein value, 3+). The urine protein-to-creatinine ratio was not determined. Results of an ACTH stimulation test performed at that time were unremarkable (baseline serum cortisol concentration, 5.9 µg/dL; serum cortisol concentration 1 hour after administration of ACTH, 15.2 µg/dL).

Thoracic radiographic findings for the dog at that time were unremarkable; no evidence of intrathoracic metastatic disease was detected. Abdominal radiography revealed generalized hepatomegaly. Abdominal ultrasonography indicated absence of the left adrenal gland and right adrenal gland enlargement (diameter, 1.2 cm [0.47 inches]) with a 1.3 × 0.9 × 0.9-cm (0.51 × 0.35 × 0.35-inch; length × height × width) well-demarcated hyperechoic nodule in the cranial aspect of the gland (**Figure 1**). Abdominal MRI was performed; pulse sequences were selected to discriminate between benign and malignant tumors, as is performed during MRI of adrenal glands of humans.[2–4] Magnetic resonance images of the abdomen of the dog were acquired in multiple planes via T2-weighted steady-state fast spin echo, short tau inversion recovery, and pre- and postcontrast-enhanced T1-weighted liver acquisition and volume acceleration sequences. Chemical shift MRI was performed with a double-echo fast low-angle shot sequence to discriminate between benign and malignant tumors. A 3-D time-of-flight MRI angiography sequence was performed to detect vascular invasion of tumors. The MRI revealed 2 right adrenal gland nodules. Both nodules were in the cranial aspect of the right adrenal gland; the nodules measured 0.6 × 0.7 × 1.4 cm (0.2 × 0.3 × 0.6 inches) and 0.4 × 0.3 × 0.5 cm (0.2 × 0.1 × 0.2 inches). The largest nodule was eccentrically positioned and may have been located in the cortex of the adrenal gland; this nodule had chemical shift MRI features consistent with a malignant tumor (**Figure 2**).[2–4] No macroscopic evidence of vascular invasion of the phrenicoabdominal vein or the caudal vena cava was detected in MRI angiogram images.

Because of persistent poorly controlled hypertension, imaging findings suggestive of a metastatic or primary mass in the right adrenal gland, and results of other tests that ruled out other common causes of hyperten-

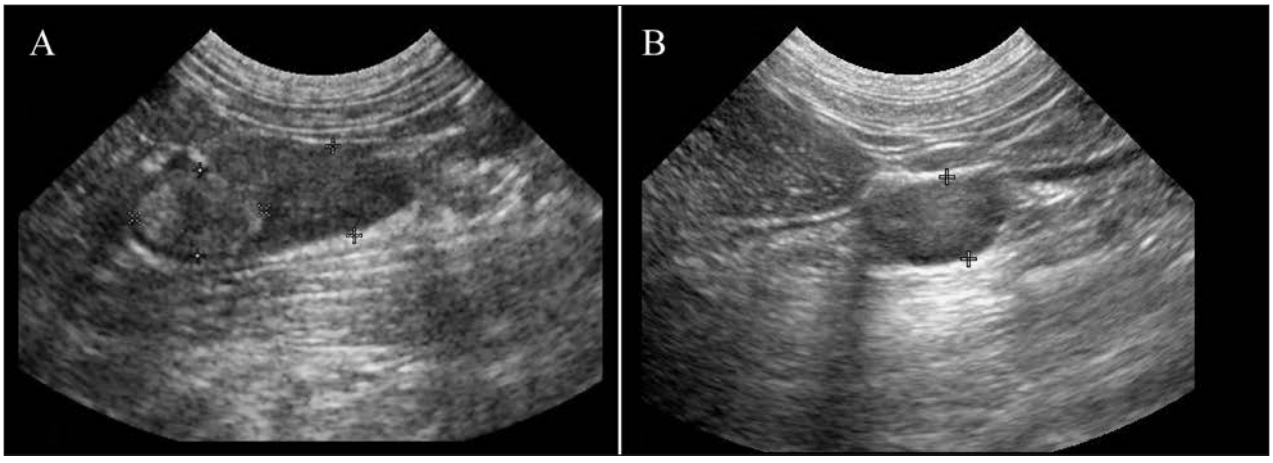

Figure 1—Representative sagittal plane ultrasonographic images of the right adrenal gland of a 6-year-old spayed female Labrador Retriever. A—Image obtained before partial right adrenalectomy. Notice the nodule (1.33 cm × 0.88 cm [0.52 × 0.35 inches]) of mixed echogenicity in the cranial aspect of the right adrenal gland. A suspected poorly defined isoechoic nodule was identified between the cranial and caudal aspects of the gland. The caudal aspect of the right adrenal gland had a maximum diameter of 0.94 cm (0.37 inches). B—Image obtained 6 months after partial right adrenalectomy. The maximum diameter of the right adrenal gland is 0.84 cm (0.33 inches). Notice the margins of the right adrenal gland are smooth; no abnormalities are observed in the surrounding retroperitoneal fat. Digital measurement tools are shown in each ultrasonographic image.

sion, partial adrenalectomy was performed for the dog. Prior to surgery, the owner was counseled regarding the risks of incomplete tumor excision (for which additional surgery would be required) or nonfunctional adrenal gland tissue remnants. The owner agreed to performance of the surgery and accepted the potential risks of the surgery because the owner did not want to administer medications for treatment of iatrogenic hypoadrenocorticism for the duration of the dog's life.

Prednisone (0.2 mg/kg, PO, q 24 h) and fludrocortisone acetate (0.00625 mg/kg [0.00284 mg/lb], PO, q 12 h) administration was started before surgery as prophylactic treatments for possible inadequate adrenal gland reserve function in the dog. Blood crossmatching was performed before surgery. The dog was premedicated with oxymorphone (0.2 mg/kg, IM) and midazolam (0.2 mg/kg, IM), and anesthesia was induced with etomidate (1 mg/kg [0.45 mg/lb]), IV) and midazolam (0.1 mg/kg [0.045 mg/lb], IV). Sevoflurane was administered in oxygen via a circle anesthesia circuit and endotracheal tube to effect. Cefazolin (22 mg/kg [10 mg/lb], IV, q 90 min) was administered to the dog during surgery. An exploratory laparotomy was performed via a ventral midline approach. The appearance of the left adrenalectomy site was unremarkable. The cranial aspect of the right adrenal gland had a prominent swelling; the middle and caudal aspects of the right adrenal gland appeared grossly normal. The cranial aspect of the right adrenal gland was dissected free from the caudal vena cava and associated retroperitoneal fat. No tumor invasion of the caudal vena cava was detected.

The phrenicoabdominal vein was ligated on either side of the adrenal gland, and a guillotine technique was performed to remove the cranial aspect of the right adrenal gland. The mass and a grossly normal adrenal gland tissue margin of approximately 2 mm were removed. The caudal aspect of the adrenal gland was left intact and not dissected free from retroperitoneal tissues.

After the cranial aspect of the right adrenal gland of the dog was removed, a transverse section from the caudal margin of the removed tissue was submitted for intraoperative histologic examination of frozen tissue sections to ensure complete excision of the mass; the remainder of the tissue was fixed in neutral-buffered 10% formalin and submitted for routine histologic examination. Grossly, the adrenal gland tissue submitted for evaluation of frozen sections contained a portion of a well-circumscribed mass that did not extend to the surgical margin. Frozen tissue sections were evaluated by a board-certified veterinary pathologist (EWH). Histologic examination of frozen sections of the surgical margin of the tissue sample stained with H&E indicated histologically normal medullary and cortical adrenal gland architecture and no neoplastic cells. On the basis of the gross and microscopic appearance of the tissue removed during surgery, the lesion was determined to have been completely excised. However, to ensure an adequate surgical margin, additional right adrenal gland tissue (5.0 × 3.0 × 2.0 mm [2.3 × 1.4 × 0.9 inches]) was removed by use of a guillotine technique; this tissue was fixed in neutral-buffered 10% formalin and submitted for routine histologic examination. A sublumbar lymph node was removed, and multiple liver biopsy samples were obtained. The duration of surgery was 165 minutes, and recovery of the dog occurred uneventfully. After surgery, the systolic blood pressure of the dog ranged from 150 to 160 mm Hg; the day after surgery, the systolic blood pressure ranged from 180 to 260 mm Hg.

Results of histologic examination of formalin-fixed tissues obtained during surgery were consistent with a well-circumscribed, nonencapsulated adrenal gland cortical carcinoma that compressed the medulla and focally obliterated the cortex. Results of immunohistochemical evaluation of tissues stained for synaptophysin and chromogranin were negative; therefore, pheochromocytoma of the right adrenal gland was ruled out. However, the additional right adrenal gland tissue obtained during surgery (from the area just caudal to the initially excised cranial aspect of the gland) had tumor

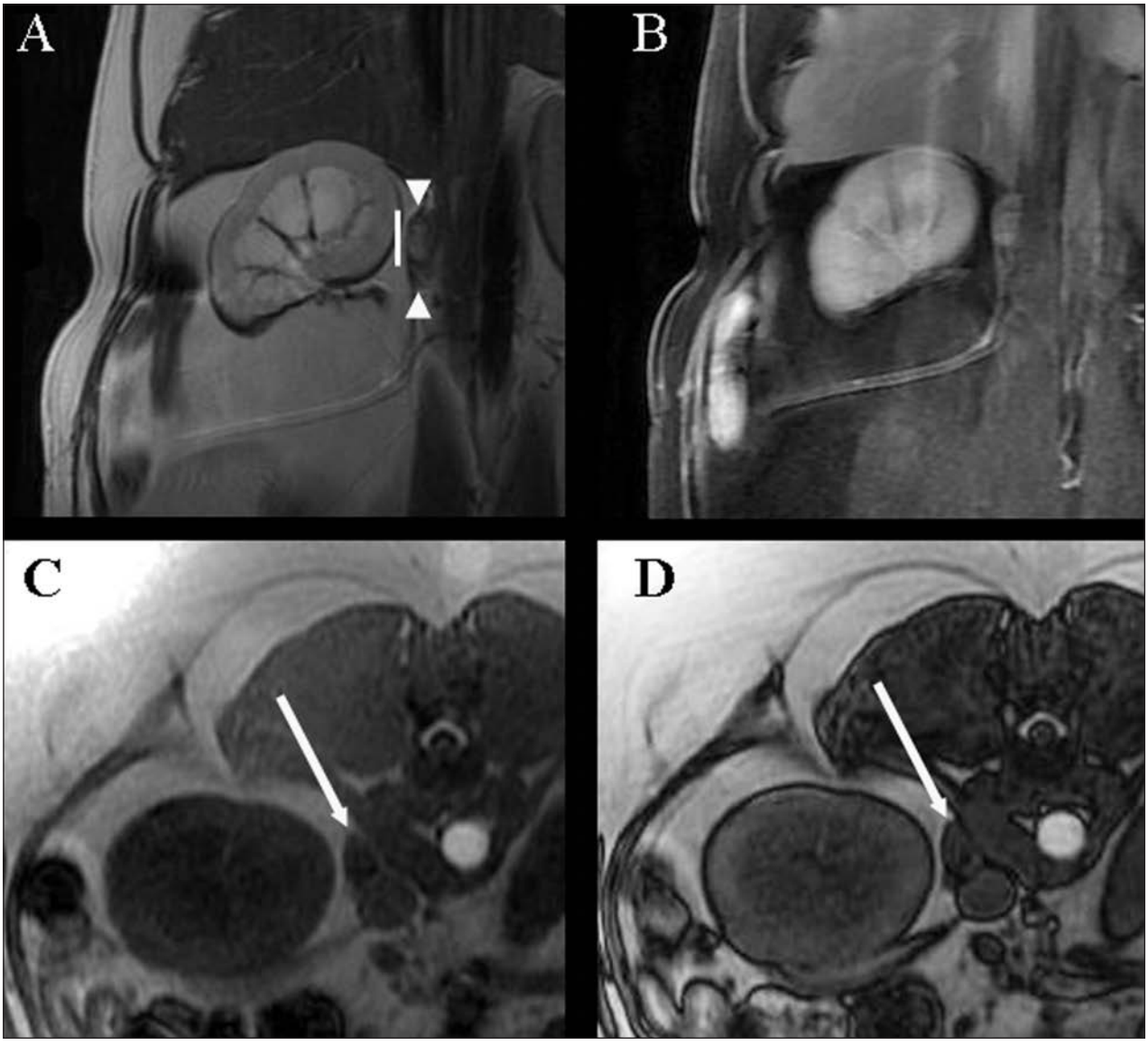

Figure 2—Representative magnetic resonance images of the right adrenal gland of the dog in Figure 1 obtained before partial right adrenalectomy. A—Dorsal plane T2-weighted sequence image. Notice the cranial and caudal aspects of the right adrenal gland (arrowheads) located medial to the right kidney. Notice the cranial pole of the adrenal gland nodule (adjacent to the solid white line). B—Contrast-enhanced T1-weighted liver acquisition and volume acceleration sequence image. C—In-phase chemical shift image. Notice the right adrenal gland nodule (arrow). D—Opposed-phase chemical shift image. Notice the right adrenal gland nodule (arrow). Notice that the signal intensity of the right adrenal gland nodule is not lower in the opposed-phase chemical shift image in panel D than it is in the in-phase chemical shift image in panel C; this signal intensity pattern indicates the nodule is malignant.

cells (characterized by variably vacuolated cortical cells with foci of hematopoiesis); these findings were similar to those for the adrenocortical carcinoma of the cranial aspect of the gland. The lymph node had no evidence of metastasis, and liver biopsy samples had changes consistent with steroid hepatopathy.

During the month after the second surgery, the systolic blood pressure of the dog ranged from 160 to 300 mm Hg, and serum alkaline phosphatase activity was persistently high (708 to 888 U/L). Serum electrolyte concentrations were within reference intervals; therefore, prednisone and fludrocortisone dosages were gradually decreased and then administration was discontinued. Results of ACTH stimulation tests performed during this time indicated adequate adrenal gland function (baseline serum cortisol concentration, 2.7 µg/dL; serum cortisol concentration 1 hour after administration of ACTH, 4.2 µg/dL). Polyuria and polydipsia had resolved, and excessive panting of the dog was subjectively improved. Systolic blood pressure in the dog measured 2 weeks after discontinuation of prednisone administration was clinically normal (140 mm Hg). Results of an ACTH stimulation test performed at that time indicated adequate adrenal gland function (baseline serum cortisol concentration, 3.3 µg/dL; serum cortisol concentration 1 hour after administration of ACTH, 5.2 µg/dL).

Six months after the second surgery, the dog was still obese and had severe systemic hypertension (systolic blood pressure, 280 mm Hg). Results of a CBC,

serum biochemical analyses, and urinalysis were similar to results of previously performed tests. Results of an ACTH stimulation test performed at this time indicated adequate adrenal gland function (baseline serum cortisol concentration, 4.5 µg/dL; serum cortisol concentration 1 hour after administration of ACTH, 5.1 µg/dL). Thoracic radiographic findings were consistent with moderate left atrial enlargement, and no evidence of pulmonary metastasis was detected. Abdominal radiography revealed persistent hepatomegaly and ultrasonographically normal shape and echogenicity of the remaining right adrenal gland tissue with no evidence of tumor recurrence (Figure 1). The remaining portion of the right adrenal gland had a diameter of 0.84 cm (0.33 inches), and regions consistent with infarction were detected in both kidneys. After 9 months, the dog continued to have hypertension, proteinuria (dipstick protein value, 3+), and urine specific gravities (1.012 to 1.020) indicating minimally concentrated urine.

Fourteen months after the second surgery, the dog was receiving tramadol (2.2 mg/kg [1.0 mg/lb], PO, q 12 h), amlodipine (0.28 mg/kg [0.13 mg/lb], PO, q 12 h), enalapril (0.45 mg/kg [0.20 mg/lb], PO, q 12 h), phenoxybenzamine (0.89 mg/kg [0.40 mg/lb], PO, q 12 h), levothyroxine (0.018 mg/kg [0.008 mg/lb], PO, q 12 h), and hydralazine (0.89 mg/kg, PO, q 12 h). Treatment with dirlotapide was started (0.05 mg/kg [0.02 mg/lb], PO, q 24 h for 2 weeks, followed by 0.1 mg/kg, PO, q 24 h for 2 weeks). Results of a blood pressure measurement performed with an oscillometric cuff by the owner at home indicated the dog had a systolic blood pressure of 160 mm Hg. Results of a urinalysis indicated isosthenuric urine (specific gravity, 1.011) and persistent proteinuria (dipstick protein value, 2+). The urine protein-to-creatinine ratio was high (1.77; reference interval, < 0.5). Thoracic and abdominal radiographic findings were similar to those determined 8 months previously; no evidence of pulmonary metastasis was detected. Abdominal ultrasonography revealed no evidence of tumor recurrence at the site of the left adrenal gland but did reveal mildly increased right adrenal gland size (diameter, 1.2 cm [0.5 inches]), compared with previous measurements. The remaining right adrenal gland tissue had ultrasonographically normal echogenicity with no evidence of masses, and no potentially metastatic lesions were detected in the abdomen. Recommendations for the dog included weight loss, continued blood pressure monitoring, ACTH stimulation testing, and restaging of the adrenal gland tumors via thoracic radiography and abdominal ultrasonography.

Because the condition of the dog had not substantially changed during 14 months after the second surgery, the prognosis for the dog regarding adrenal gland tumors was considered good. The prognosis for the dog regarding hypertension was considered guarded; we were hopeful that hypertension would improve with weight loss. At the time of the present report, the differential diagnoses for persistent hypertension in the dog included glomerulosclerosis, atherosclerosis, and arteriosclerosis; idiopathic hypertension; obesity; white-coat hypertension (ie, high blood pressure of a patient in a clinical setting without high blood pressure in other settings); or, less likely, undetected metastasized pheochromocytoma.

Discussion

Concurrent adrenal gland cortical tumors and contralateral pheochromocytoma, as detected in the dog of the present report, have been previously identified in dogs[5–8] and a cat.[9] However, performance of unilateral complete and contralateral partial adrenalectomy followed by detection of adequate adrenal gland function in dogs has not been reported, to the authors' knowledge. Partial adrenalectomy may be performed for select animals in which a small mass is located in 1 pole (ie, cranial or caudal aspect) of an adrenal gland; this technique is especially useful if the contralateral adrenal gland is diseased or has been previously removed. Although iatrogenic hypoadrenocorticism in dogs can be medically treated, surgical treatment that does not require lifelong administration of medication and monitoring of an animal may be preferred by some owners.

Results of intraoperative histologic examination of frozen sections of tissue obtained from the dog of the present report suggested that the right adrenal gland carcinoma had been completely excised; however, tumor cells were detected during histologic examination of an additional tissue sample obtained from the surgical margin of the remaining portion of the right adrenal gland. This tissue may have corresponded with one of the lesions (the smallest mass) identified in MRI images before the second surgery, although repeated abdominal MRI was not performed to confirm that assumption. Despite detection of neoplastic cells in one of the right adrenal gland tissue samples, that adrenal gland seemed to have a clinically normal structure and function 6 and 14 months following the second surgery. If a portion of the tumor was present in the dog after that surgery, the tumorous tissue may have undergone ischemic necrosis or grown slowly and therefore would not have been detected during abdominal ultrasonography. At the time of the present report, the dog was in clinically stable condition.

Partial adrenalectomy can be successfully performed because of extensive collateral blood circulation in the adrenal glands. Humans have up to 60 small arteries in each adrenal gland,[10] and 20 to 30 arterioles that arise from the aorta and renal and phrenicoabdominal arteries enter various aspects of each adrenal gland in dogs.[11] Venous blood from adrenal glands in dogs and humans predominantly enters central adrenal gland veins that terminate in the left renal vein or caudal vena cava (for left and right adrenal glands, respectively). Results of a study[12] of human cadavers indicate numerous veins in the adrenal gland capsule provide additional venous blood outflow, which suggests that the phrenicoabdominal vein can be successfully removed, as was performed for the dog of the present report. Although it is preferable to maintain the central adrenal gland vein, it may be safely ligated and removed. However, excessive mobilization of an adrenal gland remnant should be avoided to prevent disruption of peripheral veins that would cause venous congestion, which can impair adrenal gland function.[13]

Other authors[14] have recommended that > 25% of an adrenal gland should be retained in humans undergoing partial adrenalectomy to avoid hypoadrenocorticism or dependence on administration of exogenous steroid drugs.[14] Human patients are most likely to become dependent on administration of such drugs after undergoing partial adrenalectomy at the same time as complete removal of the contralateral adrenal gland or after removal of an adrenal gland mass ≥ 4 cm in diameter. Between 0% and 29% of humans who undergo partial adrenalectomy have long-term dependence on exogenous corticosteroid drugs.[15,16]

A potential complication of bilateral adrenalectomy is induction of hypoadrenocorticism. Although animals with hypoadrenocorticism have a good prognosis,[17] complications can develop. Although uncommon, animals undergoing treatment for hypoadrenocorticism can develop acute signs of severe adrenal gland insufficiency during acute injury, illness, or stress, which can be life threatening. An additional concern is that the amounts of exogenous glucocorticoids and mineralocorticoids required by an animal may vary during treatment for hypoadrenocorticism,[17] and administration of high doses of such drugs may cause hypertension.[18] Additionally, side effects of exogenous glucocorticoids include polyuria, polydipsia, and polyphagia, which can affect the quality of life for owners and animals. Because obesity may have been a contributing factor for hypertension in the dog of the present report, polyphagia would have been detrimental. Although this dog had a risk of development of hypoadrenocorticism after surgery, the cost and requirement for lifelong administration of medication to the dog were avoided.

Few reports[5,19] have been published regarding the complications, morbidities, and mortality rates of animals after bilateral adrenalectomy; these studies included low numbers of animals that underwent that procedure. Results of those studies differed; 1 of 3 dogs that underwent bilateral adrenalectomy in one of the studies[19] died, and dogs of the other study[5] that underwent the procedure had a mean survival time of approximately 3.5 years.

Persistent hypertension is uncommon in dogs and cats. Few causes of this problem have been identified; therefore, a diagnosis of idiopathic persistent hypertension is commonly made for such animals. Primary hypertension has been identified in dogs[20–22] and affects up to 18% to 20% of cats.[23] However, subclinical kidney disease and hyperaldosteronism were not definitively ruled out for all animals in those studies.

Although a diagnosis of pituitary-dependent hyperadrenocorticism had been made for the dog of the present report, results of ACTH stimulation tests were unremarkable after discontinuation of administration of trilostane and removal of the left adrenal gland pheochromocytoma. Results of the low-dose dexamethasone test may have been falsely positive for pituitary-dependent hyperadrenocorticism because the dog had a pheochromocytoma at the time the test was performed; dogs with concurrent illness have a high risk of false-positive results for that test.[24] Although rare, ectopic ACTH-secreting pheochromocytomas have been detected in humans.[25,26]

Potential causes of persistent hypertension in a dog that does not have glucosuria, a low circulating aldosterone concentration, and serum cortisol concentrations within the reference range after performance of an ACTH stimulation test include glomerulosclerosis, arteriosclerosis, and atherosclerosis; undetected metastasized pheochromocytoma; obesity; white-coat hypertension; and idiopathic hypertension. Although glomerulosclerosis was likely not the initial cause of hypertension in the dog of the present report, chronic hypertension may have caused damage to glomeruli.[27] Severe uncontrolled hypertension in the dog may have caused vascular damage (arteriosclerosis and atherosclerosis), which would have increased vascular total peripheral resistance.[28,29] Minimally concentrated urine and proteinuria in the dog may have been attributable to hypertension or early kidney disease that might have contributed to hypertension. Determination of urine protein-to-creatinine ratios may have been beneficial for monitoring the dog's response to treatment.[30]

Pheochromocytomas in dogs can metastasize to local lymph nodes, liver, lungs, or bones.[8,31,32] In the dog of the present report, no evidence of metastasis was detected in ultrasonographic or MRI images of the abdomen or during the first or second abdominal surgeries. However, microscopically detectable metastatic pheochromocytoma could not be definitively ruled out for the dog.

A relationship between obesity and hypertension in humans has been clearly identified; it seemed reasonable to conclude that there was a relationship between severe obesity and hypertension in the dog of the present report. Few studies have been conducted to identify obesity as a primary cause of hypertension in animals; therefore, a diagnosis of obesity as a cause of hypertension in animals is typically made via exclusion of other causes.[33,34] The dog of the present report may have had severe systemic hypertension secondary to obesity because hypertension persisted despite treatments.

Blood pressure can be affected by many factors including stress or anxiety. A white-coat effect on blood pressure has been identified for Greyhounds[35] and cats.[36] Repeated measurement of blood pressure during several days may reduce this effect[22,37]; however, blood pressure in the dog of the present report was persistently high despite determination of multiple measurements. The persistent severe hypertension in this dog was likely attributable to multiple factors, and long-term monitoring and treatment of the dog were recommended.

Factors considered before performance of partial right adrenalectomy in the dog of the present report included persistent hypertension, increasing size of the right adrenal gland nodule (determined via ultrasonography), and willingness of the owner to manage potential complications in the dog after surgery. Although hypertension in the dog did not resolve, metastatic pheochromocytoma seemed to be unlikely as an underlying cause because a second abdominal exploratory procedure and repeated staging via abdominal ultrasonography and thoracic radiography did not reveal evidence of metastasis. The other adrenal gland tumor (adrenocortical carcinoma) seemed to be controlled via adrenalectomy, prior to local invasion and metastasis.

Partial adrenalectomy for the dog of the present report resulted in functional remaining adrenal gland tissue. For dogs with small eccentrically located adrenal gland masses, partial adrenalectomy may be a safe and feasible treatment option to preserve adrenal gland function. Minimal complications were detected in this dog, although performance of this technique in additional dogs would be needed before further conclusions regarding the technique could be determined.

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