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Retrospective study of aldosterone and progesterone secreting adrenal tumors in 10 cats

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Abstract

Background: Primary hyperaldosteronism caused by adrenal neoplasia has been well described in cats. Multiple corticosteroid abnormalities occur in a subset of affected cats, but characterizations of this syndrome are limited to several case reports.

Objectives: To describe a series of cats with adrenal tumors secreting aldosterone and additional corticosteroids.

Animals: Ten cats with multiple corticosteroid secreting adrenocortical tumors.

Methods: Retrospective case series. Medical records of cats with adrenal tumors secreting both aldosterone and progesterone were identified. Data concerning historical findings, clinicopathologic features, treatments, and outcomes were retrieved from medical records.

Results: All 10 cats had diabetes mellitus in addition to biochemical features of hyperaldosteronism such as hypokalemia. High corticosterone concentrations were observed in all 3 cats in which this corticosteroid was measured. Ultrasound examinations revealed unilateral adrenal tumors in all 10 cases, and the contralateral adrenal gland was either atrophied or not identified in 5 cats. Three of 4 cats developed hypoadrenocorticism after surgical adrenalectomy. Three cats achieved diabetic remission after adrenalectomy. Two cats treated with adrenalectomy survived >1 year, 1 cat survived 6.5 months, and 1 cat was alive 5.5 months after diagnosis. Survival >1 year occurred in 2 of 4 cats treated with medical management alone. Two cats were not treated.

Conclusions and Clinical Importance: The presence of multiple corticosteroid abnormalities should be considered in cats with aldosterone secreting adrenal tumors, especially those with concurrent diabetes mellitus. Both surgical and medical management can result in long-term survival, although diabetic remission was documented only in cats undergoing adrenalectomy.

1 | INTRODUCTION

Primary hyperaldosteronism (PHA) is an endocrine disorder characterized by inappropriate aldosterone secretion, which occurs independent of normal stimuli and feedback mechanisms.[1-3] In health, aldosterone plays a vital role in maintaining normal electrolyte concentrations and acid-base status, and its secretion is primarily regulated by plasma potassium concentrations and the renin-angiotensin-aldosterone system.[2-4] The aldosterone excess in PHA results in abnormal sodium retention and potassium excretion, which lead to hypertension and polymyopathy, respectively.[1,5,6] Primary hyperaldosteronism is a common and increasingly recognized syndrome in middle-aged to older cats, and many cases occur as the result of aldosterone secreting adrenocortical tumors.[5-8]

Adrenal tumors causing PHA have been well characterized in cats, but most reports have not considered the possibility of additional corticosteroid abnormalities.[5-7] An evaluation of feline blood samples submitted to a diagnostic endocrinology laboratory for aldosterone measurements revealed that multiple corticosteroid abnormalities were common in cats with hyperaldosteronism.[9] Nearly one-third of cats with marked increases in aldosterone concentrations, defined as ≥3000 pmol/L, have concurrent progesterone concentrations 5-fold or more above the upper-end of the reference interval (RI).[9] Cats with adrenal tumors secreting aldosterone and additional corticosteroids are described in several case reports.[8,10-13] Some of these cats had concurrent muscle atrophy, alopecia, or a pot-bellied appearance in addition to the classic clinical signs of PHA.[10-12] Diabetes mellitus is also a common comorbidity in cats with progesterone-secreting adrenal tumors, which is hypothesized to be a result of progesterone mediated insulin-resistance.[10,11,14,15] Two cats with aldosterone and progesterone secreting adrenocortical tumors and concurrent diabetes mellitus had a poor outcome and were euthanized or died soon after diagnosis whereas 2 PHA cats with biochemical hyperprogesteronemia that was not accompanied by associated clinical signs survived over 18 months after adrenalectomy.[10-13]

Beyond these few case reports, there is limited information concerning the clinicopathologic features and long-term outcomes of cats with adrenal tumors secreting aldosterone and additional corticosteroids. The limited published information also raises concerns that those cats with clinical manifestations of both hyperaldosteronism and hyperprogesteronism have poor outcomes. In the authors' anecdotal experience, a variety of outcomes are possible in affected cats with both surgical and medical management. The objectives of this study were to describe the clinicopathologic features, treatments, and outcomes of a series of cats with adrenocortical tumors secreting both aldosterone and progesterone.

2 | MATERIALS AND METHODS

2.1 | Cats

Medical records of cats diagnosed with an adrenal tumor causing PHA and concurrent hyperprogesteronism were examined. Cases were identified through a combination of medical records search and external case consultations (Figure 1). The diagnosis sections of medical records at the Michigan State University Veterinary Medical Center were searched from January 2010 through April 2021 for the following terms: aldosterone, aldosterone-secreting, hyperaldosteronism, and aldosteronism. Several additional cases in which the primary veterinarian had consulted with one of the study authors (D.K. Langlois or K.R. Refsal) and shared medical records during that time also were included. Medical records were reviewed to identify cases in which minimum diagnostic testing had been performed and a diagnosis of PHA because of an aldosterone secreting adrenal tumor had been confirmed. Minimum diagnostics tests included serum biochemical analyses, abdominal ultrasound examination, and measurement of serum or plasma aldosterone and progesterone concentrations. The diagnosis of PHA was confirmed on the basis of clinical and laboratory findings that included sonographic identification of an adrenal mass in conjunction with hypokalemia and severely increased plasma aldosterone concentrations (aldosterone >1000 pmol/L; RI, 194-388 pmol/L). Cases meeting the above criteria that also had progesterone concentrations ≥5 nmol/L (RI ≤2.0 nmol/L for spayed and castrated cats) were included in the study. Information collected from medical records included signalment, history, physical examination findings, other diagnostic testing results when applicable, treatment, and both short-term and long-term outcomes. Descriptive statistics were used to summarize the data.

2.2 | Corticosteroid assays

Measurements of adrenal corticosteroids were performed at the Michigan State University Veterinary Diagnostic Laboratory, which is an American Association of Veterinary Laboratory Diagnosticians accredited laboratory. Plasma or serum aldosterone concentrations were measured with a commercially available radioimmunoassay kit (ACTIVE Aldosterone RIA, Beckman Coulter, IMMUNOTECH s.r.o., Prague, Czech) in 9 of the 10 cats. Serum progesterone concentrations were measured in the same 9 cats with a commercially available competitive chemiluminescent immunoassay (Immulite 2000 Progesterone, Siemens Healthcare Diagnostics Ltd, Gwynedd, UK) that has been described by others for use in cats.[16,17] Cortisol concentrations also were determined using a chemiluminescent immunoassay
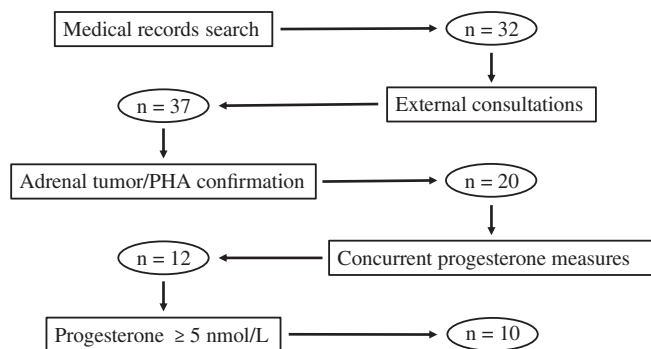
FIGURE 1 Flowchart depicting the approach for identifying the 10 cats with aldosterone and progesterone secreting adrenal tumors that were included in the case series

(Immulite 2000 Cortisol, Siemens Healthcare Diagnostics Ltd) that has been described for use in cats.[18] Detailed descriptions of these assays as well as the assay for corticosterone measurements are available in Supporting Information Appendix 1. Corticosteroid measurements in 1 cat were performed before 2015, and different radioimmunoassay kits were being used in our laboratory (Coat-a-Count, Siemens Medical Solutions Diagnostics, Los Angeles, California) at that time. Descriptions of the assays used for hormones measurements in this cat can be found elsewhere.[9]

FIGURE 2 Image of a 10-year-old castrated male cat with an aldosterone, progesterone, and corticosterone secreting adrenal tumor. Note the pendulous abdomen and pot-bellied appearance. The aldosterone, progesterone, and corticosterone concentrations in this cat were 4065 pmol/L (194-388 pmol/L), 26 nmol/L (RI ≤2 nmol/L), and 205 nmol/L (≤32 nmol/L), respectively. The non-neoplastic adrenal gland was atrophied (1.8 mm in height at cranial and caudal regions) based on ultrasound assessment, and the stimulated cortisol concentration after ACTH administration was abnormal at 68 nmol/L (RI, 97-207 nmol/L). RI, reference interval

3 | RESULTS

3.1 | Cats

Medical records from 10 cats with PHA and concurrent hyperprogesteronism were identified and reviewed. Selected clinical and biochemical characteristics of the individual cats are available online (Table S1). The median age at diagnosis was 10.5 years (range, 8-15 years); 8 cats were castrated males and 2 were spayed females. Historical abnormalities at the time of diagnosis were varied and included lethargy and weakness in 8 cats, with hind limb weakness and cervical ventroflexion specifically noted in 3 cats and 2 cats, respectively. Polyuria, polydipsia, and weight loss were reported in 6 cats each. Additional clinical signs included hyporexia in 4 cats and visual deficits in a single cat. Six cats had been diagnosed previously with diabetes mellitus and were being treated with insulin, 3 of which were recent diagnoses in the past month. The other 3 previously diagnosed diabetic cats had been diabetic for >1 year, and 2 of these cats had experienced recent worsening of clinical signs (polyuria, polydipsia, and weight loss) and glycemic control despite increased insulin doses. Other reported abnormalities included chronic diarrhea in one cat and recent onset of seizures and chronic megacolon in another cat.

Physical examination revealed generalized muscle wasting in 4 cats and generalized weakness in 2 cats. Systolic heart murmurs were auscultated in 5 cats, one of which had a presystolic gallop sound. Dermatological abnormalities were observed in 7 cats, and specific abnormalities included diffuse seborrhea in 6 cats, alopecia in 5 cats, and a dull hair coat

in 2 cats. Two cats, including 1 with diffuse seborrhea and facial alopecia, had a pendulous abdomen (Figure 2). Blood pressure measurements obtained by Doppler sphygmomanometry were available for 8 cats, and 5 of these cats had systolic blood pressures >170 mm Hg. Two cats had evidence of hypertensive retinopathy on fundic examination including dilated vasculature and multifocal areas of tapetal hyporeflectivity.

3.2 | Clinicopathologic findings

Serum biochemical profiles revealed hypokalemia in all 10 cats. The median potassium concentration was 2.8 mmol/L (range, 2.1-3.5 mmol/L). Metabolic alkalosis and increased creatine kinase activity were common. These and other hematologic and biochemical findings are summarized in Table 1. In addition to the 6 cats with known diabetes mellitus, the 4 remaining cats were also diagnosed with diabetes mellitus based on clinical signs, fasting hyperglycemia, and glucosuria.

The median plasma or serum aldosterone concentration was 3668 pmol/L (range, 1461-4577 pmol/L; RI, 194-388 pmol/L), and the median serum or plasma progesterone concentration was 19 nmol/L (range, 7-151 nmol/L; RI ≤2 nmol/L). Baseline cortisol measurements also were available for 8 cats. Baseline cortisol concentrations (RI, 15-97 nmol/L) were abnormally high in 1 cat at 232 nmol/L and abnormally low in 1 cat at 11 nmol/L. Baseline cortisol concentrations were normal in the other 6 cats, but were in the lower half of the RI (range, 18-56 nmol/L). Complete ACTH stimulation testing was performed in 3 of the cats with low-normal baseline cortisol concentrations;

TABLE 1 Hematologic and serum biochemical findings in the 10 cats with aldosterone and progesterone secreting adrenal tumors

Variable	Low	Within RI	High
HCT	6/10	2/10	2/10
Potassium	10/10	0/10	0/10
Sodium	2/10	6/10	2/10
TCO₂	0/8	1/8	7/8
CK	0/7	0/7	7/7
Creatinine	0/10	9/10	1/10
Fructosamine	0/5	0/5	5/5

Note: Data are provided as the number of cats in which the laboratory variable was low, high, or within the laboratory provided reference interval (RI). Most variables were selected because of their potential association with PHA or hyperprogesteronism whereas hematocrit was selected because it was abnormal in most cats.

Abbreviations: CK, creatine kinase; HCT, hematocrit; PHA, primary hyperaldosteronism; RI, reference interval; TCO₂, total carbon dioxide.

cortisol concentrations 1 hour after administration of 5 μg/kg synthetic ACTH (RI, 97-207 nmol/L) were low-normal in 1 cat at 125 nmol/L and abnormally low in 2 cats at 32 and 68 nmol/L. Corticosterone concentrations (RI ≤32 nmol/L) were measured in 3 cats, and the values were abnormally high in those 3 cases at 287, 205, and 279 nmol/L.

3.3 | Abdominal radiographs and ultrasound examinations

Abdominal radiographs were performed in 6 cats, and an abnormal soft tissue opacity was observed near the cranial aspect of the left or right kidney in 5 cats. Faint mineralization was noted within 3 of the lesions. All 10 cats had adrenal masses identified during abdominal ultrasound examination including 4 cats with left adrenal gland masses and 6 cats with right adrenal gland masses. The median tumor diameter at the largest dimension was 21 mm (range, 11-51 mm). Masses were described as having abnormal or heterogeneous echotexture in all cases, and mineralization was present in 1 case. Invasion of the adrenal mass or tumor-associated thrombi were apparent in the caudal vena cava in 2 cases. The contralateral adrenal gland was small (<3.0 mm height at cranial and caudal regions) in 3 cats, not identified in 2 cats, and normal in size in 5 cats.[19,20] The 2 cats with abnormally low cortisol concentrations after ACTH administration and the 1 cat with an abnormally low baseline cortisol concentration were among the 5 cats in which the contralateral adrenal gland was either small or not identified. Hyperechoic hepatic parenchyma and hepatomegaly were present in 8 cats each and speculated to be a result of diabetic hepatopathy.[21] The cat with a mineralized adrenal mass also had evidence of widespread metastases including numerous hypoechoic nodules and masses throughout the liver and a large 4.2 cm hypoechoic mass in the splenic head. Aspiration cytology of the splenic mass was suggestive of neuroendocrine malignancy.

3.4 | Treatment and outcome

Four cats were treated with surgical adrenalectomy (Table S2). All 4 cats received varying duration (range, 1-11 weeks) of medical treatment for PHA and diabetes mellitus before surgery which included combinations of potassium gluconate, spironolactone, amlodipine besylate, and insulin. Surgical adrenalectomy was performed without complication in all 4 cats, and cavotomy and extirpation of a tumor thrombus also was performed in 1 cat in which a preoperative computed tomographic assessment identified a 25 mm tumor thrombus extending from the adrenal mass into the dorsolateral aspect of the caudal vena cava. Histopathologic assessment of adrenal tissue was consistent with an adrenocortical carcinoma in all 4 cats (Figure 3). In the cat with the vena cava tumor thrombus, neoplastic cells were identified in surrounding omental tissue and fat consistent with carcinomatosis. All 4 cats were discharged from the hospital 2 days after surgery. The various combinations of potassium gluconate, amlodipine besylate, and spironolactone that were used for PHA treatment were discontinued in all 4 cats within 2 weeks of surgery.

Three of 4 cats treated with adrenalectomy developed lethargy, hyporexia, and mild hyperkalemia (range, 5.3-6.0 mmol/L) within 2 weeks of surgery. The 3 cats were diagnosed with adrenal insufficiency based on abnormally low baseline aldosterone concentrations (<14 pmol/L) in all 3 cats in conjunction with an abnormally low baseline cortisol concentration (<5.5 nmol/L) in 1 cat and abnormally low cortisol concentrations after ACTH administration in the other 2 cats. These 3 cats were among those in which the non-neoplastic adrenal gland was either small or not identified during abdominal ultrasound examination. Two of the cats were treated with prednisolone PO and desoxycorticosterone pivalate SC; 1 cat was treated for 1 month and 1 cat was treated for 3.5 months. The other cat that developed adrenal insufficiency was treated with prednisolone PO and fludrocortisone PO until the time of its death. Three of the 4 cats that were treated with adrenalectomy achieved a diabetic remission, which occurred 1 month, 2 months, and 8 months after surgery, respectively.

Survival times were variable in the 4 cats treated with adrenalectomy. The cat with histologically identified carcinomatosis, which had persistent adrenal insufficiency and diabetes mellitus, died from complications of pulmonary metastases and pleural effusion 5 months after adrenalectomy, which was 6.5 months after PHA diagnosis. The cat requiring 3.5 months of treatment for adrenal insufficiency did achieve a diabetic remission at 8 months, but redeveloped diabetes mellitus 17 months after adrenalectomy. This cat was euthanized 1.5 months later because of concerns with diabetes mellitus and progression of known chronic kidney disease, which was nearly 21 months after PHA diagnosis. The other cat that developed adrenal insufficiency achieved a diabetic remission 2 months after surgery and was alive and clinically well 4.5 months after adrenalectomy, which was 5.5 months after PHA diagnosis. The 1 cat that did not develop adrenal insufficiency achieved a diabetic remission 1 month after adrenalectomy, and this cat remained normoglycemic and
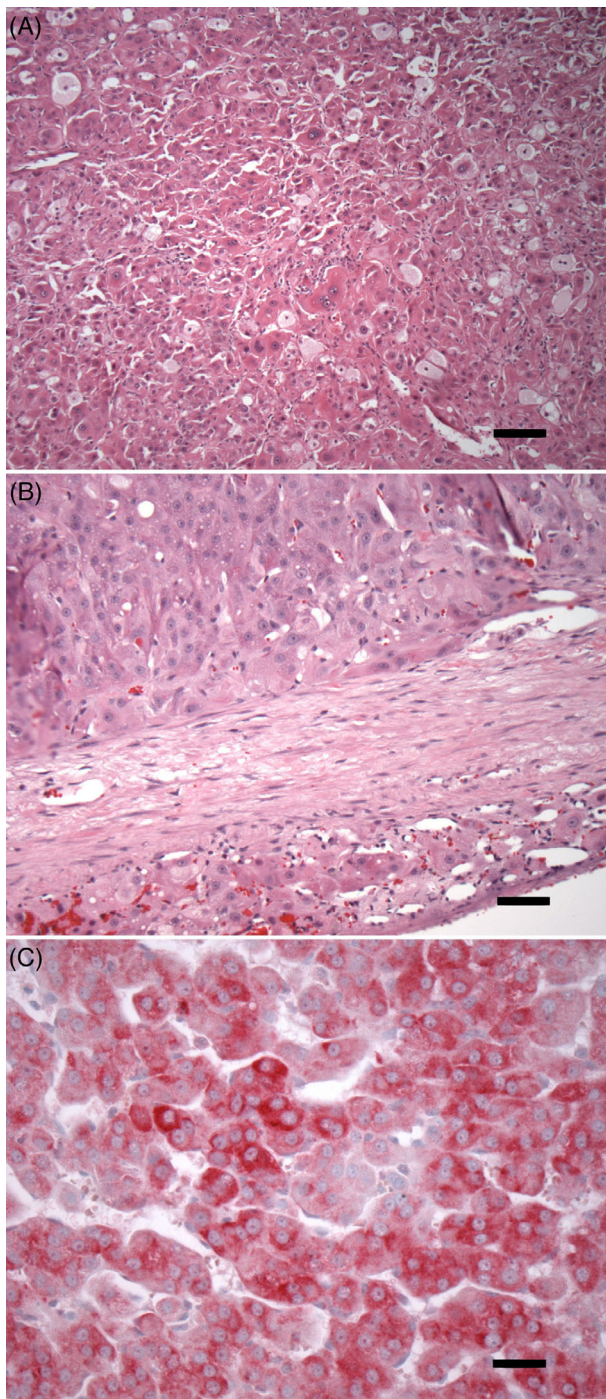
FIGURE 3 Photomicrograph of a stained section of adrenal gland from an 8-year-old castrated male mixed breed cat with an aldosterone (1461 pmol/L), progesterone (13 nmol/L), and corticosterone (287 nmol/L) secreting adrenocortical carcinoma. A, Proliferative neoplastic adrenocortical cells are arranged in sheets and packets separated by fine fibrovascular stroma. Cells display marked anisocytosis and anisokaryosis, and occasional multinucleation (hematoxylin and eosin stain, ×10, scale bar = 140 μm). B, Neoplastic cells multifocally invade into and through the adrenal gland capsule warranting carcinoma designation (hematoxylin and eosin stain, ×20, scale bar = 70 μm). C, Neoplastic cells have strong cytoplasmic immunolabeling for Melan-A (Vector red chromogen, ×40, scale bar = 35 μm) confirming adrenocortical origin

normokalemic for 3 years after adrenalectomy and was euthanized for unrelated reasons.

Medical treatment alone was pursued for 4 cats (Table S3) Surgical treatment was not recommended for one of these cats because of widespread metastases; surgical treatment was recommended but declined for the other 3 cats. Two of the 4 cats survived >1 year. These 2 cats remained clinically well for >1 year while being treated with potassium gluconate, spironolactone, insulin, and a low-carbohydrate prescription diet. One cat developed hypertension 13 months after diagnosis that required initiation of amlodipine besylate. This cat was euthanized 19.5 months after diagnosis because of abdominal discomfort and quality of life concerns that were thought to be the result of progressive tumor enlargement (tumor diameter of 45 mm on repeat ultrasound examination). The other cat was euthanized 16 months after diagnosis because of progressive osteoarthritis and recent development of ascites, which was not investigated further. Two other cats treated with medical management had shorter survival times. One of these cats was treated with amlodipine besylate, insulin, and a low-carbohydrate prescription as well as toceranib phosphate because of known metastatic disease. Continued anorexia and lethargy presumed to be a result of metastatic disease led to euthanasia after 2 months. The other cat was treated with potassium gluconate, spironolactone, insulin, and mirtazapine. This cat was euthanized 20 days after diagnosis because of continued lethargy and hyporexia as well as the recent development of suspected pancreatitis and kidney disease.

Two cats were not treated and were euthanized within 1 day of diagnosis because of owner concerns related to illness severity and comorbidities. One was anorectic, in poor body condition, and had advanced chronic kidney disease, poorly controlled diabetes mellitus, severe periodontal disease, and small intestinal thickening. The other cat had historical chronic constipation and hypertrophic cardiomyopathy and also had a recent onset of seizures and visual deficits.

4 | DISCUSSION

Ten cats with adrenal tumors secreting aldosterone and progesterone were characterized in our study, which despite limited numbers, is the largest reported collection of such cases. Affected cats had clinical and biochemical abnormalities typical of mineralocorticoid excess.[1,2,5] Weakness, lethargy, hypokalemia, metabolic alkalosis, increased creatine kinase activity, and hypertension were common. Clinical features attributable to corticosteroid abnormalities besides aldosterone were also present. Various dermatologic abnormalities were observed in the majority of cats, and 2 cats had a pot-bellied appearance. More importantly, all cats in the case series had diabetes mellitus. In 7 of 10 cases, this was a new or recent diagnosis. In 2 of the remaining 3 cases, longer-standing diabetes mellitus had become poorly regulated in recent months. Both progestogens and glucocorticoids induce insulin resistance, and the authors speculate that diabetes mellitus in these cats was related to sustained increases in these diabetogenic hormones.[22-24] Diabetes mellitus is documented in most cats with

progesterone secreting adrenal tumors.[10,11,14,15] These findings suggest that the presence of diabetes mellitus in cats with PHA should prompt veterinary clinicians to consider the possibility of abnormal concentrations of other adrenal corticosteroids.

Similar cases of multiple corticosteroid-producing adrenal tumors are documented in other species, yet the cellular mechanisms underlying multiple hormone production have not been clearly established and are likely multifactorial.[25-29] A notable finding in our study was the presence of an adrenocortical carcinoma in all 4 cats in which adrenal tissue was available for histopathologic examination. The medically treated cat with widespread metastases presumably had a carcinoma too. Previous case reports of aldosterone and progesterone secreting adrenal tumors in cats have similarly identified underlying adrenal carcinomas when adrenal histopathology was recorded.[11,13] Conversely, approximately 40% of aldosterone secreting adrenal tumors have been identified as adrenal adenomas across several studies.[6-8,30] The possibility that multiple hormone production is suggestive of a carcinoma as opposed to an adenoma is intriguing. Additional studies are needed to substantiate this finding and determine if it is of clinical or prognostic value.

Another finding in this study was the evidence of hypothalamic-pituitary-adrenal (HPA) axis suppression in several cats. The non-neoplastic adrenal gland was either not visualized or atrophied in 5 cases. The 2 cats with abnormally low stimulated cortisol concentrations after ACTH administration and the 1 cat with an abnormally low baseline cortisol concentration were among these 5 cases. Both atrophy of the non-neoplastic adrenal gland and suppressed cortisol concentrations might be predictors of postoperative adrenal insufficiency. All 3 cats that developed hypoadrenocorticism and associated clinical illness after surgery had sonographic evidence of adrenal atrophy, 1 of which was a cat with an abnormally low cortisol concentration after ACTH administration. Cortisol suppression is reported in cats with progesterone secreting adrenal tumors.[11,31,32] Enzymatic abnormalities within neoplastic cells and progesterone-induced displacement of cortisol from peripheral receptors have been speculated to be involved in HPA axis suppression.[13] However, there is a strong correlation between progesterone and corticosterone concentrations in cats with PHA.[9] Unfortunately, corticosterone was only measured in 3 cats in this study, but concentrations were abnormally high in all 3 cases. A more simplistic mechanism for the cortisol suppression could be that excess corticosterone secretion was occurring in some cases. The relative contributions of corticosterone and progesterone to HPA axis suppression require further study, but clinicians should be mindful of this suppression because it can influence postoperative management in some cases.

Medical and surgical treatments of aldosterone secreting adrenal tumors are described in several case series.[5-8,30,33] Median survival times of 196 to 304 days are reported with medical management consisting of potassium supplementation, aldosterone-receptor antagonists, and antihypertensives.[5,33] Surgical adrenalectomy is associated with median survival times ranging from approximately 300 days to greater than 1000 days.[6-8,30] It is not known if these survival times can be extrapolated to cases of multiple corticosteroid secreting adrenal tumors, but

2 previous case reports of combined PHA, hyperprogesteronism, and diabetes mellitus suggested poor long-term outcomes with both cats surviving ≤8 weeks.[10,11] Not surprisingly, the 2 cats in our series with metastatic disease, 1 that was treated surgically and 1 that was treated medically, also had poor long-term outcomes. However, a unique aspect of our case series was the prolonged survival times observed in several cats. Three of the cats treated with surgical adrenalectomy experienced diabetic remission; 2 cats survived >1 year and 1 cat was still alive and clinically well several months after adrenalectomy. Two of the cats that were treated medically also survived >1 year, but both cats remained diabetic. This was not surprising since the administered treatments would not suppress adrenal corticosteroid production. The small numbers of cases do not permit conclusions to be drawn on the efficacy of specific treatments or allow detailed comparisons of surgical vs medical management, but the positive long-term outcomes in some cats were an encouraging finding.

All cats included in the case series had both aldosterone and progesterone concentrations measured, but one limitation of our study is that measurements of additional adrenal corticosteroids were variable. Estradiol and androstenedione were not measured in any cats, likely because there was no clinical evidence consistent with alterations in these hormones. Conversely, corticosterone was only measured in 3 cats, and increased corticosterone secretion might have occurred in additional cats and contributed to clinical abnormalities. Unfortunately, corticosterone measurements are not currently offered by commercial veterinary laboratories. Baseline cortisol concentrations were not measured in 2 cats, and only 3 cats underwent ACTH stimulation testing. More comprehensive cortisol testing would have aided in identifying HPA axis suppression. Another possible limitation is that plasma renin activity was not measured in any of the cats, nor were fludrocortisone suppression tests performed. Aldosterone to renin ratios and fludrocortisone suppression tests might be important to the diagnosis of PHA in some cases, although this has not been definitively established.[5,34-36] Determination of plasma renin activity is seldom available outside of research settings, and the specificity of an increased aldosterone to renin ratio for PHA in cats is questionable.[37] In the largest study of fludrocortisone suppression tests for the diagnosis of PHA, aldosterone concentrations alone were discriminatory between cats with and without PHA.[34] These tests could be useful in some cases with equivocal laboratory and imaging findings, but they would not have added diagnostic value in our series in which hypokalemia, severely increased aldosterone concentrations, and sonographic evidence of a unilateral adrenal mass were apparent in all cases.

In conclusion, the presence of diabetes mellitus in cats with aldosterone secreting adrenal tumors should raise concern for concurrent abnormal progesterone or glucocorticoid concentrations. The higher concentrations of these additional corticosteroids are capable of inducing HPA axis suppression as evidenced in some cases by atrophy of the non-neoplastic adrenal gland, abnormally low cortisol concentrations, and development of adrenal insufficiency after surgical adrenalectomy. Outcomes appear to be variable, but survival times >1 year were observed in some cats, and diabetic remissions are possible after adrenalectomy.

CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

This study was reviewed and approved by representatives of the Michigan State University College of Veterinary Medicine Research Committee.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.