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Multiple corticosteroid abnormalities in cats with hyperaldosteronism

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Abstract

Background: The frequency with which multiple corticosteroid abnormalities occur in cats with aldosterone secreting adrenocortical tumors is unknown.

Objectives: To evaluate adrenal-derived corticosteroids in cats in which blood samples were submitted for measure of aldosterone.

Animals: Two hundred ninety-seven cats.

Methods: Retrospective study. Analysis of a convenience sample of previously submitted serum or plasma. Progesterone, corticosterone, and cortisol were measured in feline serum or plasma samples submitted to an endocrinology laboratory for aldosterone measurements. Demographics and clinical history were retrieved from submittal forms when provided. Statistical testing was performed to investigate associations among the adrenal corticosteroids.

Results: Progesterone and corticosterone concentrations were strongly correlated ($\rho = 0.74$; $P < .001$). Progesterone (median, 5 nmol/L; interquartile range, 3-10 nmol/L) and corticosterone (113 nmol/L, 38-250 nmol/L) in cats with markedly increased aldosterone concentrations (≥3000 pmol/L) were higher than progesterone (1 nmol/L, 1-2 nmol/L) and corticosterone (12 nmol/L, 3-25 nmol/L) in cats with normal aldosterone concentrations ($P < .001$ for both comparisons). Progesterone concentrations ≥10 nmol/L (normal, ≤2 nmol//L) occurred in 24 of 76 (32%) cats with aldosterone concentrations ≥3000 pmol/L. Cortisol was lower in cats with aldosterone concentrations ≥3000 pmol/L as compared to those with aldosterone concentrations <500 pmol/L (59 nmol/L, 27-103 nmol/L vs 103 nmol/L, 49-182 nmol/L; $P = .002$).

Conclusions and Clinical Importance: Multiple corticosteroid abnormalities occur in a subset of cats with hyperaldosteronism. The magnitude of increases in progesterone and corticosterone in some cats with hyperaldosteronism is likely to be clinically relevant.

KEYWORDS
adrenal cancer, corticosterone, cortisol, progesterone

Abbreviation: PHA, primary hyperaldosteronism.

1 | INTRODUCTION

Primary hyperaldosteronism (PHA) is an increasingly recognized disease in older cats that is often caused by functional adrenocortical neoplasia.[1-3] Aldosterone is the main mineralocorticoid produced by the zona glomerulosa cells of the adrenal cortex, and it is involved in critical processes such as regulation of blood pressure, electrolytes, acid-base status, and intravascular fluid volume.[1,2] The consequences of PHA include sodium retention and potassium wasting which commonly manifest as hypertension and polymyopathy, respectively.[1-4] Polymyopathy-induced weakness, lethargy, and cervical ventroflexion and hypertension-induced retinopathy and kidney disease are common in affected cats.[1-6] The exact prevalence of PHA is unknown, but clinical and biochemical similarities with chronic kidney disease likely lead to misdiagnosis and under-recognition in cats.[1,2,4,5]

Most reports of functional adrenal tumors causing PHA have documented moderate to marked increases in circulating aldosterone concentrations, but other hormones are not typically measured.[1,3,5] Various intermediates such as progesterone and corticosterone are produced in the normal mineralocorticoid synthesis pathway, and these hormones might also be affected in cases of adrenocortical neoplasia.[2] Indeed, concurrent increases in other adrenal steroid hormones, namely progesterone, occasionally occur in cats with aldosterone secreting adrenal tumors.[7-11] The increases in these other adrenal corticosteroids are of sufficient magnitude to result in clinical consequences beyond just those of aldosterone excess, which includes insulin resistance, hypothalamic-pituitary-adrenal axis suppression, and various dermatologic abnormalities.[7-11]

The frequency with which hyperprogesteronism and other steroid abnormalities occur in cats with PHA is unknown, but our observations at Michigan State University College of Veterinary Medicine suggest that additional corticosteroid abnormalities occur more frequently in cases of PHA than previously recognized. The objectives of this study were to investigate potential abnormalities and associations of adrenal corticosteroids, including progesterone, corticosterone, and cortisol, in cats undergoing measurement of baseline aldosterone concentrations. We hypothesized that these hormones would be altered in cats with hyperaldosteronism.

2 | MATERIALS AND METHODS

2.1 | Laboratory samples

Serum and plasma samples from cats with clinical or biochemical evidence of PHA are submitted routinely to the endocrinology section of the Michigan State University Veterinary Diagnostic Laboratory for measurement of baseline aldosterone concentrations. Other hormone measurements typically are not requested by submitting clinicians. In the years 2009 and 2011, progesterone, corticosterone, and cortisol concentrations were measured in feline serum or plasma samples in which measurements of baseline aldosterone concentrations had been requested by the submitting veterinarian. These hormones were selected because suppressed cortisol concentrations had been observed in 2 cats with mixed clinical signs of glucocorticoid and mineralocorticoid excess, progesterone and corticosterone are in close proximity in the mineralocorticoid pathway, and all 3 hormones are potentially diabetogenic.[2,7,8] Submitted samples from the years 2009 and 2011 were included in the study provided there was sufficient serum or plasma volume available after the aldosterone assay was performed. There were no inclusion or exclusion criteria related to demographics, history, or clinical data. General demographic information and available clinical information were retrieved from the submittal forms.

2.2 | Corticosteroid assays

All samples for measurement of aldosterone and other adrenal corticosteroid concentrations were analyzed at the Michigan State University Veterinary Diagnostic Laboratory, which is an American

TABLE 1 Characteristics of 297 cats with laboratory submissions for measurement of serum or plasma aldosterone concentration

	Aldosterone concentrations (pmol/L)				
	<500	500–999	1000–2999	≥3000	*P* value
Age in years	13; 9–15 n = 88	13; 10.5-14 n = 57	13; 9.5-16 n = 69	12; 10-14.3 n = 73	.99
Sex (female/male)	42%/58% n = 90	47%/53% n = 55	34%/66% n = 65	48%/52% n = 76	.36
History available	40% 37 of 92	36% 21 of 58	45% 32 of 71	42% 32 of 76	.77
Testing for PHA	89% 33 of 37	90% 19 of 21	94% 30 of 32	97% 31 of 32	.64

Note: Values for age represent the median and IQR whereas values for sex represent the percentage of cats that were female and male, respectively. History available represents the percentage of cases in which any amount of clinical history was provided. Testing for primary hyperaldosteronism (PHA) was the percentage of cases with available clinical history in which the history was consistent with testing for a possible diagnosis of PHA. These historical abnormalities included hypokalemia, hypernatremia, hypertension, generalized weakness, and the presence of an adrenal mass, alone or in combination. Sample size is provided in each cell because the specified clinical information was not provided on all submissions. None of the characteristics were statistically different between groups as assessed by Kruskal-Wallis testing (age) or χ^2 testing (sex, history, and testing for PHA).

Association of Veterinary Laboratory Diagnosticians accredited laboratory. Aldosterone concentrations were measured at the time the submission was received by the laboratory. Any excess serum or plasma was frozen at −20°C, and the additional corticosteroids were measured in batch analyses. Descriptions of the radioimmunoassay kits used for measurements of aldosterone, progesterone, corticosterone, and cortisol (Coat-a-Count, Siemens Medical Solutions Diagnostics, Los Angeles, California) in this study are available in Supplemental Appendix S1.

2.3 | Data and statistical analysis

Descriptive statistics were used to summarize demographics and hormone concentration data. Data were reported as medians and interquartile ranges (IQR) because they were not normally distributed as assessed by Shapiro-Wilk testing and boxplot analysis. For statistical analyses, cases were grouped into 4 categories based on aldosterone concentrations. The first grouping consisted of cats with aldosterone concentrations <500 pmol/L (normal to mild increases) as the upper-end of normal for baseline aldosterone concentrations is reported to be approximately 400-500 pmol/L across multiple studies.[1,3,7,8] The second grouping consisted of cats with aldosterone concentrations of 500-999 pmol/L (moderate increases). This grouping represented cats with increased aldosterone concentrations in the range of what is reported with various disease processes including kidney disease, heart disease, hypovolemia, and PHA.[3,12-15] The third grouping consisted of cats with aldosterone concentrations of 1000-2999 pmol/L (severe increases). This range of values would be most likely to occur in cats with aldosterone secreting adrenal tumors, although other disease processes occasionally are associated with hormone concentrations in this range.[2,3,12,16-19] The final grouping consisted of cats with aldosterone concentrations ≥3000 pmol/L (marked increases). Concentrations of this magnitude are observed in cases of aldosterone secreting adrenal tumors, but would not be expected to occur with most other disease processes.[12-15,19]

Demographics of the cats were compared among the aldosterone groupings using χ^2 testing for categorical data or Kruskal-Wallis testing for continuous data. Progesterone, corticosterone, and cortisol concentrations were compared across the 4 groupings using Kruskal-Wallis testing with Dunn's post hoc testing. Spearman's rank correlation coefficients (ρ) were calculated to further investigate associations among the adrenal corticosteroids. Finally, the proportion of cats with progesterone concentrations exceeding 2 cut-points (≥5 and ≥10 nmol/L) were compared between those cats with normal aldosterone concentrations and those with marked increases in aldosterone concentrations using Fisher exact testing. Concentrations of progesterone that are capable of causing clinically relevant disease are unknown, but a cut-point ≥5 nmol/L is clearly abnormal in neutered cats and cats in anestrus across multiple studies.[20,21] Progesterone concentrations vary during diestrus and several reproductive abnormalities, but are usually ≥10 nmol/L in these conditions.[20-23] Statistical analyses were performed with commercially available software

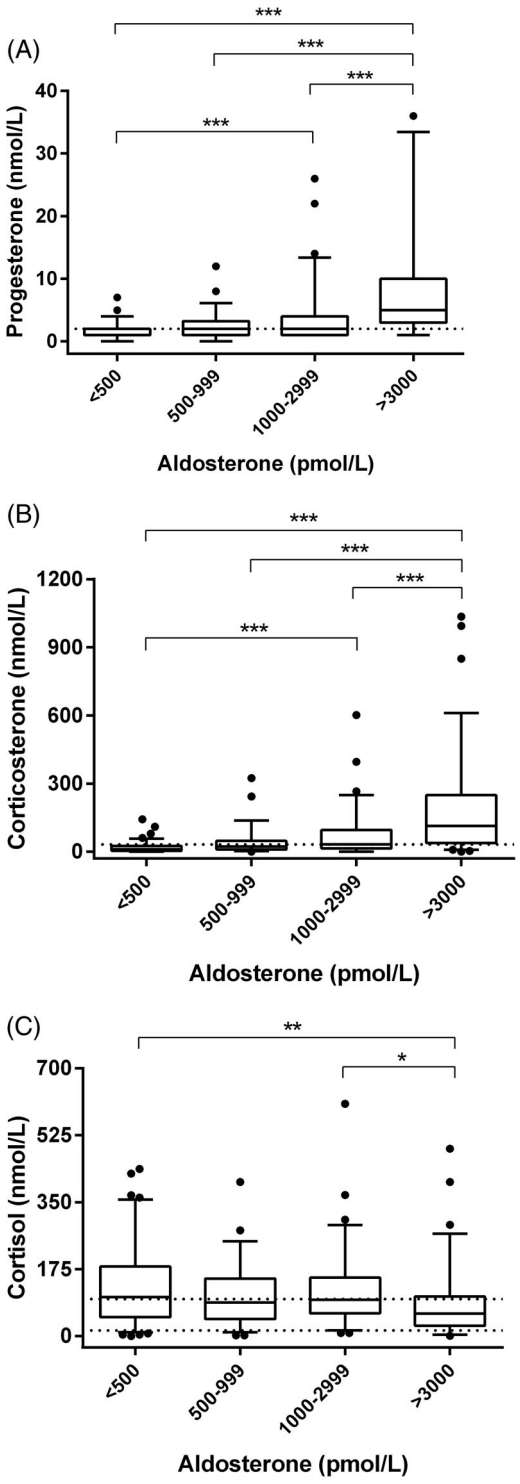

FIGURE 1 Box-and-whisker plots depicting baseline concentrations of (A) progesterone, (B) corticosterone, and (C) cortisol when grouped by baseline aldosterone concentrations of: <500 pmol/L (n = 92), 500-999 pmol/L (n = 58), 1000-2999 pmol/L (n = 71), and ≥3000 pmol/L (n = 76). The horizontal line within each box represents the median, the lower and upper boundaries of each box represent the 1st and 3rd quartiles, and the whiskers represent the 5%-95% range. Dots represent individual values outside of this range. The dashed horizontal lines in each panel represent the reference interval. Kruskal-Wallis testing with Dunn's post hoc testing was used for comparisons of hormone concentrations across groups. *P = .005, **P = .002, ***P ≤ .001

TABLE 2 Corticosteroid concentrations in samples submitted for aldosterone measurements in 297 cats when grouped by aldosterone concentrations

	Aldosterone concentration			
	<500 pmol/L	500–999 pmol/L	1000-2999 pmol/L	≥3000 pmol/L
	n = 92	n = 58	n = 71	n = 76
Progesterone (≤2 nmol/L)	1 (1-2)	2 (1-3)	2 (1-4)	5 (3-10)
Corticosterone (≤32 nmol/L)	12 (3-25)	23 (9-48)	32 (15-96)	113 (38-250)
Cortisol (15-97 nmol/L)	103 (49-182)	88 (45-151)	95 (60-153)	59 (27-103)

Note: The values for progesterone, corticosterone, and cortisol concentrations are expressed as median (IQR). The reference interval is shown in parentheses under each hormone. Statistical comparisons are shown in Figure 1.

(GraphPad Prism Version 6.0; GraphPad Software Inc, La Jolla, California), and values of $P \leq .05$ were considered significant.

3 | RESULTS

3.1 | Cats

Two hundred ninety-seven out of a total of 585 samples submitted for analysis of aldosterone had sufficient serum or plasma available for measurements of the additional corticosteroids and were included in the study. Age information was available for 287 cats, and the median age was 13 years (IQR, 10-15 years). Breed information was available for 269 cats and included domestic shorthair (n = 198), domestic longhair (n = 28), domestic medium hair (n = 21), and various pure breed cats (n = 22). Historical information was inconsistently provided by submitting veterinarians, with varying amounts of information provided for 122 of 297 (41%) cats. Abnormalities consistent with PHA, which were considered to be hypokalemia, hypernatremia, hypertension, generalized weakness, and history of an adrenal mass, alone or in combination, were described in 113 of 121 (93%) cases. Demographic features of the cats with normal to mildly increased (<500 pmol/L, n = 92), moderately increased (500-999 pmol/L, n = 58), severely increased (1000-2999 pmol/L, n = 71), and markedly increased (≥3000 pmol/L, n = 76) aldosterone concentrations are presented in Table 1.

3.2 | Corticosteroids

Plasma or serum progesterone and corticosterone concentrations were higher in the groupings of cats with severely increased and markedly increased aldosterone concentrations as compared to cats with normal to mildly increased aldosterone concentrations ($P < .001$; Figure 1A,B). The hormone concentrations in the various aldosterone groupings are further summarized in Table 2. Plasma or serum progesterone concentrations were significantly and positively correlated with plasma or serum corticosterone concentrations ($P < .001$; Figure 2A). Only 2 of 92 (2%) cats with aldosterone concentrations <500 pmol/L had progesterone concentrations ≥5 nmol/L (reference interval [RI], ≤2 nmol/L) whereas 40 of 76 (53%) cats with aldosterone concentrations ≥3000 pmol/L had progesterone concentrations ≥5 nmol/L ($P < .001$). No cats in the <500 pmol/L aldosterone group had progesterone concentrations ≥10 nmol/L whereas 24 of 76 (32%) cats in the ≥3000 pmol/L aldosterone group had progesterone concentrations exceeding this cut-point ($P < .001$).

Cortisol concentrations were decreased in cats with markedly increased aldosterone concentrations as compared to those with normal to mildly increased aldosterone concentrations ($P < .001$; Figure 1C). When evaluating cats in which progesterone or corticosterone concentrations were above the RI, cortisol was inversely correlated with both of these hormones ($P < .001$; Figure 2B,C). A total of 31 cats had progesterone concentrations ≥10 nmol/L. Eleven of these 31 (36%) cats had concurrent cortisol concentrations that were <15 nmol/L (RI, 15-97 nmol/L), which was a higher proportion than the 12 of 171 (7%) cats with normal progesterone concentrations that had cortisol concentrations <15 nmol/L ($P < .001$).

4 | DISCUSSION

Our study documented that multiple corticosteroid abnormalities are common in cats with hyperaldosteronism. Over 30% of cats with aldosterone concentrations ≥3000 pmol/L had notable increases in progesterone concentrations (≥10 nmol/L; RI, ≤2 nmol/L). Corticosterone concentrations in cats with aldosterone concentrations ≥3000 pmol/L were 10-fold greater than corticosterone concentrations in cats with normal aldosterone concentrations. Indications for aldosterone testing in cats other than PHA screening are rare in the clinical setting. The median age of 13 years and the fact that 93% of available histories revealed abnormalities consistent with aldosterone excess suggest that most cats were being tested for PHA. Aldosterone concentrations are reported to be >1000 pmol/L in approximately 90% of cases of aldosterone-secreting adrenal tumors.[3,16-18] Aldosterone concentrations are increased in some cats with heart disease and kidney disease, but the magnitude of increase is usually less than what is observed in cats with aldosterone secreting adrenal tumors.[12-14] The magnitude of increased aldosterone concentrations in cats with PHA because of bilateral adrenal hyperplasia also is less severe than in cases of adrenal tumors, with concentrations <1000 pmol/L occurring in over 90% of cats with bilateral adrenal hyperplasia.[19] As such, most cats with severe (1000-2999 pmol/L) and marked increases (≥3000 pmol/L) in aldosterone concentrations in our laboratory study

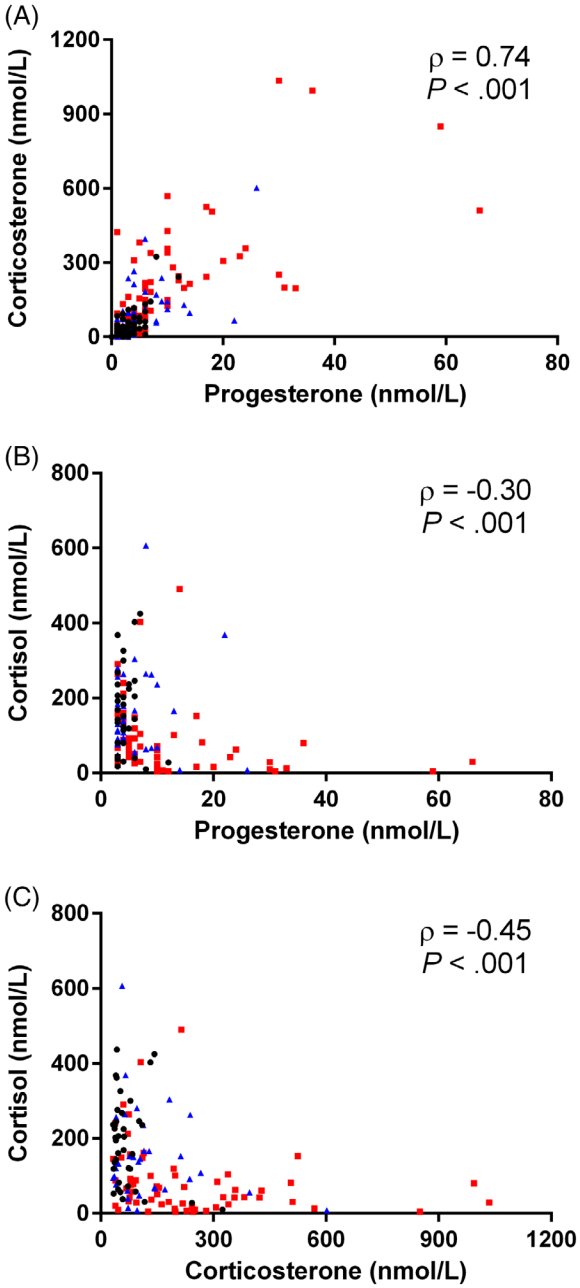

FIGURE 2 Scatterplots depicting (A) progesterone and corticosterone concentrations in the entire study population of 297 cats, (B) progesterone and cortisol concentrations in the 126 cats with progesterone concentrations exceeding the RI, and (C) corticosterone and cortisol concentrations in the 132 cats with corticosterone concentrations exceeding the RI. Cats with normal to moderately increased aldosterone concentrations (<1000 pmol/L) are depicted by black dots. Cats with severely (1000-2999 pmol/L) and markedly increased (>3000 pmol/L) aldosterone concentrations are depicted by blue triangles and red squares, respectively. The Spearman's correlation coefficient (ρ) and associated *P* values are shown in the upper-right of each panel

were likely to have adrenocortical neoplasia. Even though historical and clinical information were unavailable for many cats, it does not detract from overall results. Our findings indicate that the syndrome of multiple corticosteroid secreting adrenal tumors in cats is more common than previously thought.

The reasons why multiple corticosteroid abnormalities occurred are unknown. Multiple corticosteroid secreting adrenal tumors occur in several species including humans, yet the underlying mechanisms have not been studied in detail.[24-29] Both corticosterone and progesterone are in close proximity in the mineralocorticoid steroidogenic pathway.[8,24,30,31] Perhaps accelerated aldosterone production caused increases in these intermediates. However, this is unlikely to be the only explanation because there were many cats with marked increases in aldosterone concentrations in which corticosterone and progesterone remained normal. Alternatively, neoplastic cells might directly secrete multiple hormones in some cases, or subpopulations of the neoplastic cells might secrete separate hormones.[24,32,33]

The magnitude of increases in these additional corticosteroids is likely to be of clinical relevance in some cases. Progesterone concentrations capable of causing clinical hyperprogesteronism are not defined and likely depend on both degree and duration, but values in the range of what is expected during diestrus and gestation were observed in some cats.[20,22] This range of progesterone concentrations is also similar to progesterone concentrations in several cats with progesterone secreting adrenal tumors and concurrent diabetes mellitus.[7,8,10,34,35] The strong correlation between corticosterone and progesterone was another interesting finding in our study, and many cats with hyperaldosteronism had concurrent increases in both of these corticosteroids. Unfortunately, there is a paucity of information about corticosterone effects in dogs and cats. Corticosterone is seldom measured in these species, and most commercial laboratories do not offer assays for this corticosteroid.[27] Still, the 10-fold increase in corticosterone in cats with markedly increased aldosterone concentrations as compared to cats with normal aldosterone concentrations was striking. In addition, cats with more pronounced increases in corticosterone and progesterone concentrations often had suppressed cortisol concentrations (Figure 2B,C). These findings support the possibility of clinically relevant glucocorticoid effects and hypothalamic-pituitary-adrenal axis suppression in some cases. However, additional studies are needed to determine how often clinical abnormalities actually occur as a result of progesterone and corticosterone excess in cats with PHA as well as to determine the relative contributions of each of these hormones to potential clinical signs.

One limitation of the present study is that many of the laboratory submittal forms lacked detailed clinical information. Although we were able to perform meaningful assessments of the data, this additional information would have permitted more in-depth analyses and strengthened our conclusions. Another potential limitation is that there are many other adrenal steroids and intermediates that were not measured in the present study. These additional corticosteroids warrant consideration in future studies, but they were beyond the scope of this investigation. We focused on hormones that were likely to be affected based on pathways of adrenocortical steroid synthesis, previous reports of progesterone and aldosterone secreting adrenal tumors, and our anecdotal observations in the laboratory.[2,7,8]

In summary, both progesterone and corticosterone were increased frequently in cats with hyperaldosteronism. In some of

these cats, the increases in progesterone and corticosterone might be of substantial magnitude to result in clinical signs of progestogen or glucocorticoid excess. Clinicians should consider the possibility of multiple corticosteroid abnormalities when assessing cats for PHA.

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CONFLICT OF INTEREST DECLARATION

The hormone assays were performed at the Michigan State University Veterinary Diagnostic Laboratory, which offers commercial veterinary endocrinology testing. The university was not involved in review of this manuscript. No authors have a 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 exempt from IACUC review. 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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REFERENCES

1. Schulman RL. Feline primary hyperaldosteronism. *Vet Clin North Am Small Anim Pract*. 2010;40:353-359.
2. Harvey AM, Refsal KR. Feline hyperaldosteronism. In: Mooney CT, Peterson ME, eds. *BSAVA Manual of Canine and Feline Endocrinology*. 4th ed. Glouchester, UK: BSAVA; 2012:204-214.
3. Ash RA, Harvey AM, Tasker S. Primary hyperaldosteronism in the cat; a series of 13 cases. *J Feline Med Surg*. 2005;7:173-182.
4. Chiaramonte D, Greco DS. Feline adrenal disorders. *Clin Tech Small Anim Pract*. 2007;22:26-31.
5. Djajadiningrat-Laanen S, Galac S, Kooistra H. Primary hyperaldosteronism: expanding the diagnostic net. *J Feline Med Surg*. 2011; 13:641-650.
6. Djajadiningrat-Laanen SC, Galac S, Boeve MH, et al. Evaluation of the oral fludrocortisone suppression test for diagnosing primary hyperaldosteronism in cats. *J Vet Intern Med*. 2013;27:1493-1499.
7. Briscoe K, Barrs VR, Foster DF, Beatty JA. Hyperaldosteronism and hyperprogesteronism in a cat. *J Feline Med Surg*. 2009;11:758-762.
8. DeClue AE, Breshears LA, Pardo ID, et al. Hyperaldosteronism and hyperprogesteronism in a cat with an adrenal cortical carcinoma. *J Vet Intern Med*. 2005;19:355-358.
9. Guerios SD, Souza HMC, Bacon NJ. Adrenocortical tumor in a cat secreting more than one type of corticosteroid. *JFMS Open Rep*. 2015;1(2):2055116915617970.
10. Quante S, Sieber-Ruckstuhl N, Wilhelm S, Favrot C, Dennler M, Reusch EC. Hyperprogesteronism due to bilateral adrenal carcinomas in a cat with diabetes mellitus. *Schweiz Arch Tierheilkd*. 2009;151: 437-442.
11. Leshinsky J, Beatty JA, Fawcett A, et al. Aldosterone and progesterone-secreting adrenocortical adenocarcinoma in a cat with a concurrent meningioma. *JFMS Open Rep*. 2016;2:1-7.
12. Jensen J, Henik RA, Brownfield M, Armstrong J. Plasma renin activity and angiotensin I and aldosterone concentrations in cats with hypertension associated with chronic renal disease. *Am J Vet Res*. 1997;58:535-540.
13. MacDonald KA, Kittleson MD, Larson RF, et al. The effect of ramipril on left ventricular mass, myocardial fibrosis, diastolic function, and plasma neurohormones in Maine Coon cats with familial hypertrophic cardiomyopathy without heart failure. *J Vet Intern Med*. 2006;20: 1093-1105.
14. Pedersen KM, Pedersen HD, Haggstrom J, Koch J, Ersbøll AK. Increased mean arterial pressure and aldosterone-to-renin ratio in Persian cats with polycystic kidney disease. *J Vet Intern Med*. 2003; 17:21-27.
15. Torrente C, Silvestrini P, Ruiz de Gopegui R. Severe life-threatening hypokalemia in a cat with suspected distal renal tubular acidosis. *J Vet Emerg Crit Care*. 2010;20:250-257.
16. Lo AJ, Holt DE, Brown DC. Treatment of aldosterone-secreting adrenocortical tumors in cats by unilateral adrenalectomy: 10 cases (2002-2012). *J Vet Intern Med*. 2014;28:137-143.
17. Daniel G, Mahony OM, Markovich JE, et al. Clinical findings, diagnostics and outcome in 33 cats with adrenal neoplasia (2002-2013). *J Feline Med Surg*. 2016;18:77-84.
18. Willi B, Kook PH, Quante S, et al. Primary hyperaldosteronism in cats. *Schweiz Arch Tierheilkd*. 2012;154:529-537.
19. Javadi S, Djajadiningrat-Laanen SC, Kooistra HS, et al. Primary hyperaldosteronism, a mediator of progressive renal disease in cats. *Domest Anim Endocrinol*. 2005;28:85-104.
20. Ferré-Dolcet L, Yeste M, Vendrell M, Rigau T, Rodríguez-Gil JE, Del Alamo MMR. Uterine and placental specific localization of AQP2 and AQP8 is related with changes of serum progesterone levels in pregnant queens. *Theriogenology*. 2020;142:149-157.
21. Jursza E, Kowalewski MP, Boos A, Skarzynski DJ, Socha P, Siemieniuch MJ. The role of toll-like receptors 2 and 4 in the pathogenesis of feline pyometra. *Theriogenology*. 2015;83:596-603.
22. Andrews CJ, Thomas DG, Welch MV, Yapura J, Potter MA. Monitoring ovarian function and detecting pregnancy in felids: a review. *Theriogenology*. 2020;157:245-253.
23. Traas AM. Feline reproduction. In: Ettinger SJ, Feldman EC, eds. *Textbook of Veterinary Internal Medicine*. Vol 2. 7th ed. St. Louis, MO: Saunders; 2010:1940-1948.
24. Glaz E, Racz K, Varga I, et al. Mineralocorticoid production of adrenal cortical adenomas. *J Steroid Biochem Mol Biol*. 1993;45: 57-64.
25. Terzolo M, Osella G, Ali A, et al. Subclinical Cushing's syndrome in adrenal incidentaloma. *Clin Endocrinol (Oxf)*. 1998;48:89-97.
26. Tauchmanova L, Rossi R, Biondi B, et al. Patients with subclinical Cushing's syndrome due to adrenal adenoma have increased cardiovascular risk. *J Clin Endocrinol Metab*. 2002;87:4872-4878.
27. Behrend EN, Weigand CM, Whitley EM, Refsal KR, Young DW, Kemppainen RJ. Corticosterone- and aldosterone-secreting adrenocortical tumor in a dog. *J Am Vet Med Assoc*. 2005;226:1662-1666.
28. Reine NJ, Hohenhaus AE, Peterson ME, Patnaik AK. Deoxycorticosterone-secreting adrenocortical carcinoma in a dog. *J Vet Intern Med*. 1999;13:386-390.
29. Syme HM, Scott-Moncrieff JC, Treadwell NG, et al. Hyperadrenocorticism associated with excessive sex hormone production by an adrenocortical tumor in two dogs. *J Am Vet Med Assoc*. 2001; 219:1725-1728.

30. Feldman EC. Hyperadrenocorticism in cats. In: Feldman EC, Nelson RW, Reusch CE, Scott-Moncrieff CR, eds. *Canine and Feline Endocrinology and Reproduction*. 4th ed. St. Louis, MO: WB Saunders; 2015:452-484.
31. Raman PB, Sharma DC, Dorfman RI, Gabrilove JL. Biosynthesis of C-18-oxygenated steroids by an aldosterone-secreting human adrenal tumor. Metabolism of [4-14C]progesterone, [1,2-18H] 11-deoxycorticosterone, and [4-14C]pregnenolone. *Biochemistry*. 1965;4:1376-1385.
32. Peppa M, Pikounis V, Papaxoinis G, et al. Adrenocortical carcinoma secreting cortisol, androgens, and aldosterone: a case report. *Cases J*. 2009;2:8951.
33. Spath M, Korovkin S, Antke C, et al. Aldosterone- and cortisol-co-secreting adrenal tumors: the lost subtype of primary aldosteronism. *Eur J Endocrinol*. 2011;164:447-455.
34. Boord M, Griffin C. Progesterone secreting adrenal mass in a cat with clinical signs of hyperadrenocorticism. *J Am Vet Med Assoc*. 1999;214: 666-669.
35. Rossmeisl JH Jr, Scott-Moncrieff JC, Siems J, et al. Hyperadrenocorticism and hyperprogesteronemia in a cat with an adrenocortical adenocarcinoma. *J Am Anim Hosp Assoc*. 2000;36: 512-517.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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