Primary Hyperaldosteronism in a Cat

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Introduction

This case report describes a nine-year-old male neutered domestic shorthair cat that presented for muscle weakness, a cardiac arrhythmia, and hypokalemia. The cat was diagnosed with primary hyperaldosteronism using systolic blood pressure measurement, abdominal ultrasound, echocardiography and baseline serum aldosterone levels. The patient was medically managed with spironolactone, amolodipine, potassium gluconate and atenolol until a unilateral adrenalectomy was performed. After surgery, serum potassium and blood pressure normalized, and the arrhythmia resolved. The cat made a full recovery and had no recurrence of the disease three years after the initial diagnosis.

Primary hyperaldosteronism (PHA), which is also called Conn's disease in the human literature, was first reported in humans in 1955 and in cats in 1983. [1] PHA is caused by the autonomous secretion of mineralocorticoids, primarily aldosterone, from the adrenal gland. The principal function of aldosterone is regulation of systemic blood pressure and homeostasis of extracellular fluid volume. In humans, PHA is now recognized as the most common cause of endocrine hypertension – it is found in six percent of all human patients with arterial hypertension and up to 11% of people with therapy-resistant hypertension. [2,3] PHA was an under-recognized cause of hypertension in people for many years, and may similarly be an under-recognized cause of systemic hypertension and hypokalemia in cats.

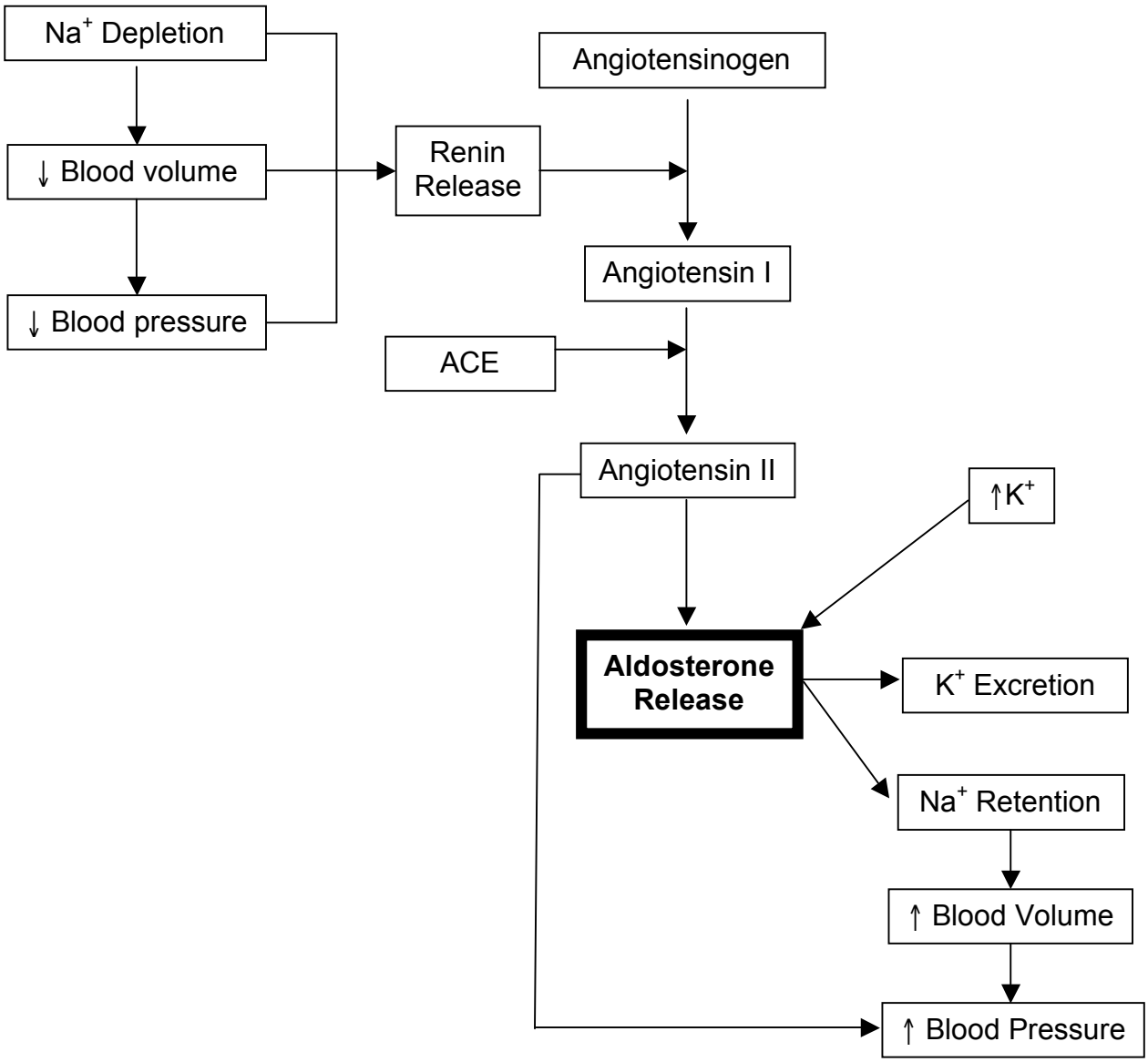
The adrenal glands lie near the cranial pole of the kidneys and are comprised of two distinct parts: the adrenal medulla and the adrenal cortex. The adrenal medulla is the central 20% of the adrenal gland and is functionally related to the sympathetic nervous system, secreting epinephrine and norepinephrine. The adrenal cortex has three distinct layers: the zona glomerulosa, the zona fasiculata, and the zona reticularis. These three layers secrete hormones called corticosteroids that are derived from the steroid cholesterol, and include mineralocorticoids, glucocorticoids and sex hormones. The zona glomerulosa is a thin layer just underneath the adrenal capsule and produces mineralocorticoids, which primarily effect extracellular sodium and potassium homeostasis. Aldosterone is the primary mineralocorticoid produced and accounts for approximately 90% of all mineralocorticoid activity. [4] The zona fasiculata layer, the middle and widest layer of the adrenal cortex, secretes glucocorticoids.

Glucocorticoids are important for blood glucose regulation, and also have effects on protein, fat and carbohydrate metabolism. Finally, the zona reticularis, the deepest layer of the adrenal cortex, secretes glucocorticoids as well as small amounts of sex hormones, especially androgenic hormones, with effects similar to testosterone.

There are four factors that affect the regulation of aldosterone: (i) increased potassium ion concentration in the extracellular fluid increases aldosterone secretion; (ii) increased activity of the renin-angiotensin system (leading to increased levels of angiotensin II) increases aldosterone secretion, (iii) increased sodium ion concentration in the extracellular fluid slightly decreases aldosterone secretion; (iv) adrenocorticotropic hormone (ACTH) release from the anterior pituitary gland is necessary for aldosterone secretion but has little effect on controlling the rate of secretion. [4]

Serum potassium ion concentration and the renin-angiotensin system are the most potent factors regulating secretion of aldosterone (Figure 1). [4] A small increase in potassium ion concentration results in a large increase in aldosterone secretion. Similarly, activation of the renin-angiotensin system in response to decreased blood flow to the kidneys or sodium loss also triggers a sizable increase in aldosterone secretion. The kidneys increase renin secretion in response to a decrease in circulating blood volume or renal blood flow sensed by stretch receptors of the juxtaglomerular apparatus. [4] In addition, decreased delivery of sodium and chloride to the macula densa cells in the proximal renal tubules also stimulates renin secretion. [2,4] Renin cleaves angiotensinogen (produced by the liver) into angiotensin I, which is hydrolyzed to angiotensin II by angiotensin-converting-enzyme (ACE). Angiotensin II stimulates aldosterone secretion, and is also a powerful vasoconstrictor. [2] Aldosterone then acts on the kidneys to excrete excess potassium ions and to increase extracellular fluid volume and arterial pressure via increased sodium retention. Once homeostasis is restored, renin production is reduced and the aldosterone concentration declines. [2,4]

Figure 1 – Regulation of Aldosterone Secretion



Excess production of aldosterone by the adrenal glands may be due to primary or secondary causes. PHA is caused by autonomous secretion of aldosterone from one or both adrenal glands, resulting in clinical signs relating to hypertension, hypokalemia or both. PHA results in suppressed plasma renin activity and is therefore called low-renin hyperaldosteronism. [3] Approximately one-half of cats with PHA have unilateral aldosterone secreting adenomas, and most of the remaining cats have unilateral adrenal carcinomas. [5] Bilateral adrenal nodular hyperplasia of the zona glomerulosa can also cause PHA in cats, although the prevalence of this is not known. [5,6] Secondary hyperaldosteronism is the result of a disease or disorder that results in dehydration, hypotension or reduced renal perfusion that stimulates the renin-angiotensin-aldosterone system (RAAS) to synthesize the hormone aldosterone in excessive quantities. [7,8] Causes of secondary hyperaldosteronism include renal disease, heart disease, and hypoproteinemia of any cause. This response is called high-renin hyperaldosteronism. [3]

Although increased aldosterone results in sodium retention, it has a small effect on plasma sodium concentration. A rise in aldosterone acts on the distal collecting tubules and collecting ducts to promote sodium resorption with concurrent loss of potassium and hydrogen ions. [9] However, the plasma sodium concentration changes minimally, because when sodium is reabsorbed by the tubules, there is simultaneous osmotic resorption of an equivalent amount of water. [4] Additionally, small increases in extracellular fluid sodium concentration stimulate thirst and increase water intake. Sodium retention and the subsequent increase in the extracellular fluid volume results in elevated blood pressure. [3,4] Aldosterone may also increase blood pressure by increasing total peripheral resistance. [3]

Excess aldosterone causes hypokalemia due to the loss of potassium ions into the urine in exchange for sodium retention. [4,9] It also stimulates transport of potassium from the extracellular fluid into cells of the body. [4] Excessive secretion of aldosterone from adrenal tumors can result in profound hypokalemia, and when the potassium ion concentration falls to less than one half of normal, severe muscle weakness can develop due to alteration of electrical excitability of normal nerve and muscle fiber membranes, which prevents transmission of the normal action potentials. [4] Clinical muscle weakness is likely to occur when plasma potassium concentrations fall to less than 3.0 mEq/L. [8] Excess aldosterone production also causes secretion of hydrogen ions in exchange for sodium ions in the cortical collecting tubules, causing decreased hydrogen ion concentrations in the extracellular fluid, which results in mild alkalosis. [2,4,8,10]

Excess aldosterone can affect the cardiovascular system through several processes, including hypokalemia, systemic hypertension, left ventricular hypertrophy, cardiac fibrosis, and aldosterone induced arrhythmias. Hypokalemia can result in cardiac arrhythmias because low potassium causes delays in ventricular depolarization, increases the duration of the action potential, and increases automaticity, resulting in supraventricular and ventricular arrhythmias. [10, 12, 13] Prolonged systemic hypertension due to increased circulating volume can result in myocardial hypertrophy. [2] In human medicine, prolonged elevations in aldosterone have been linked to marked left ventricular hypertrophy, cardiac fibrosis, and arrhythmogenic disorders, including atrial fibrillation and ventricular tachyarrhythmias. [14,15,16]

Cats with PHA are typically middle-aged to geriatric, and there is no breed or sex predilection. [5] Approximately 40 cases have been reported in the veterinary literature, with a median age of 13 years, and a range of five to 20 years. [3,5,8,17,18,19] Clinical signs associated with PHA are due to potassium wasting (leading to muscular weakness) and sodium retention (resulting in hypertension). Thus, presenting complaints can be classified into two groups: hypokalemic polymyopathy and acute onset blindness. Hypokalemic polymyopathy appears more commonly associated with PHA caused by an adenoma or carcinoma, while acute blindness appears to be more common in cats with PHA associated with bilateral adrenal nodular hyperplasia. [5,6]

Muscle weakness is the most common complaint (11 of 13 cats in one study [5]), and can range from episodic forelimb weakness to cervical ventroflexion to acute onset of severe weakness. [5,6,18,19,20,21] Other reported signs include dysphagia, [18] lethargy, and anorexia. [20,21] Polyuria and polydypsia were also reported in 23% of cases in one study (three of 13 cases). [5] Acute onset blindness caused by intraocular hemorrhage and retinal detachment is also commonly reported, ranging from two of 13 cases in one study [5] to seven of 11 cases in a second study. [6]

Physical examination findings in cats with PHA are somewhat non-specific, and may include weakness in forelimbs or hind limbs, ataxia, cervical ventroflexion, abdominal mass, heart murmur, and vision loss with retinal detachment and hemorrhage on fundic exam. [5,6,17,19,20,21,22] Because PHA is a disease originating from the zona glomerulosa of the adrenal gland, affected patients typically do have not abnormalities associated with excessive cortisol production or in cortisol metabolism. [8] However, cats with aldosterone-secreting adrenocortical carcinomas with concurrent hyperprogesteronism have been reported. [9,17] In these cats, signs of hyperprogesteronism typically predominate,

including secondary diabetes mellitus, polyuria, polydipsia, polyphagia, poor coat condition, seborrhea, thin fragile skin and potbellied appearance. [9,17]

Physical exam findings of mild or intermittent muscle weakness are non-specific and can point to orthopedic, neurologic or metabolic problems. Differential diagnoses for cervical ventroflexion or severe muscular weakness include neuromuscular disease (myasthenia gravis, myopathies, muscular dystrophies, congenital or acquired myopathies), metabolic and nutritional encephalopathies (hypokalemia, hypoglycemia, hepatic encephalopathy, thiamine deficiency), intracranial neoplasia (meningioma, pituitary tumors, lymphoma), inflammatory disorders (feline infectious peritonitis, toxoplasmosis), and toxin ingestion. The primary differential diagnosis for acute vision loss with evidence of retinal detachment and hemorrhage on fundic exam is systemic hypertension (blood pressure >160-170 mmHg) and causes include chronic renal failure, primary hypertension, hyperthyroidism, diabetes mellitus, PHA, pheochromocytoma, chronic anemia and hyperadrenocorticism. [22,23]

No specific hematologic abnormalities associated with PHA have been identified. [5,6,9,19,20] The most significant and common biochemical abnormality is hypokalemia, which can range from mild to severe. In one study, all 13 cases reported had hypokalemia at presentation, ranging from 1.9 to 3.2 mmol/L (reference range 4.0 – 5.5). [5] In a second report, six of 11 cases of PHA were hypokalemic at presentation, with potassium levels ranging from 2.3 to 3.3 mmol/L (reference range 3.4 – 5.2). [6] Because there are many causes of hypokalemia (including decreased dietary intake, gastrointestinal loss, urinary loss and intracellular translocation), PHA may be overlooked as a differential diagnosis, especially in cases of mild hypokalemia. In addition, some cats with PHA caused by bilateral adrenal nodular hyperplasia presenting with acute blindness as the primary complaint may have normal serum potassium levels. [6] Serum sodium concentration is typically within the reference range in cats with PHA due to plasma volume expansion. [5,6,16,20] Creatinine kinase is frequently elevated, especially in cats presenting with hypokalemic polymyopathy, but the degree of elevation is variable. [5,16,20] In a case series of 13 cats, 10 had elevated creatinine kinase, and all 10 cats presented with polymyopathy. [5] Creatinine kinase ranged from 209 to 56,240 IU/L, with a mean of 6,837 IU/L (reference range < 120 IU/L). [5]

Serum urea nitrogen and creatinine may also be elevated in cats with PHA, but the degree of elevation is variable. In a series of 13 cats with PHA, seven had elevated serum urea nitrogen, and three had elevated creatinine. [5] The presence of azotemia may hinder the diagnosis of PHA, since hypokalemia and hypertension may be considered elements of renal disease. [3,9] In addition, research suggests that hyperaldosteronism caused by bilateral adrenal nodular hyperplasia may potentiate renal damage. With this form of PHA, aldosterone is not as severely elevated, and renin may be incompletely suppressed. As a result, increases in both angiotensin II and aldosterone may contribute to progression of renal damage by promoting vascular thrombosis and fibrosis, as well as promoting sustained systemic arterial hypertension. [6,9] In addition, chronic hypokalemia may impair responsiveness of the kidneys to anti-diuretic hormone, and may also induce or potentiate nephropathy, leading to a decrease in renal blood flow, defects in urine concentrating ability, and possible induction of tubular nephropathy. [9,10,11,21,24] Urinalysis is non-specific in diagnosing PHA. In nine of 13 cats where urine specific gravity was reported, it ranged from 1.010 to 1.040, with a mean value of 1.029. [5]

Cats with PHA are frequently hypertensive. In a case series study of 13 cats with PHA, 11 cats had systolic blood pressure in excess of 160 mmHg, and reported blood pressures ranged from 160 to 250 mmHg. [5] In another series of 11 cats with PHA from bilateral adrenal nodular hyperplasia, all 11 had systolic blood pressure in excess of 160 mmHg, ranging from 185 to 270 mmHg. [6] Hypertension may be an earlier development in the progression of PHA than hypokalemia, as five of 11 cats with hypertension and confirmed PHA had normal potassium levels at initial presentation. [6] PHA may therefore be an under-recognized cause of idiopathic hypertension in cats. In a 2000 study of 69 cases of ocular lesions associated with systemic hypertension in cats, only one cat had confirmed PHA, while 38 cats had no clearly identified cause for hypertension. [22] The screening criteria for ruling out PHA in this study included finding a normal sodium to potassium ratio – it has since been shown that almost all cats with PHA have normal serum sodium concentration, and that cats with bilateral nodular hyperplasia may not be hypokalemic at initial presentation. [6] It is possible that PHA was overlooked as a cause for hypertension in this study.

Cats with PHA often have evidence of cardiovascular disease, including heart murmurs, radiographic evidence of cardiomegaly, and ventricular hypertrophy noted on echocardiogram. [1,18,19,20] Despite the high frequency of arrhythmias reported in human medical literature for patients with PHA [14,15,16], arrhythmias have not been reported

as a clinical finding in cats presenting with PHA in the veterinary literature. Arrhythmias in cats may result from electrolyte derangements including hypokalemia, generalized systemic disorders such as hypoxemia, systemic hypertension, hyperthyroidism, or severe anemia, or may be purely cardiac in origin. [13,25] In two recent retrospective studies looking at cats presenting with atrial fibrillation and ventricular tachyarrhythmias, almost all cats with arrhythmias on physical exam had evidence of structural heart disease on echocardiogram, including left atrial enlargement, left ventricular hypertrophy, and unclassified cardiomyopathy. [26,27] These results suggest that a comprehensive cardiac evaluation, including an echocardiogram, is warranted in cats presenting with an arrhythmia. [25]

PHA should be suspected in cats with hypokalemia (often refractory to oral potassium supplementation) and hypertension for which another cause cannot be identified. [3] The diagnostic approach to confirming suspected PHA should include diagnostic imaging of the adrenal glands and obtaining a baseline plasma aldosterone concentration. Abdominal ultrasound is the preferred imaging modality, although magnetic resonance imaging and computed tomography may also be utilized. [2,3,7,9] Adrenal masses are rarely visible radiographically. [7,9] Ultrasound findings in cats with PHA usually reveal a unilateral adrenal mass. Reported masses range in size from 10 to 35 mm in diameter, and right-sided masses are reported approximately twice as commonly as left-sided masses. [5,6,9,18,19,20,21] Other findings may include bilateral adrenal enlargement, normal adrenal glands, adrenal calcification, and changes in adrenal echogenicity. [2,5,6,19,20,21] If an adrenal mass is identified, determination of whether there is invasion of the caudal vena cava or distal metastasis should be attempted in preparation for surgery, although failure to identify invasion of the caudal vena cava does not predict an uncomplicated adrenalectomy. [3,9] In addition, the contralateral adrenal gland should be carefully evaluated, as bilateral adrenal enlargement can occur with bilateral nodular hyperplasia, and unilateral adrenalectomy will not be curative in these cases. [5,6] Identification of a visible adrenal mass alone does not necessarily mean that it is a functional neoplasm of the zona glomerulosa and is responsible for the clinical signs. [3] In addition, the absence of adrenal gland abnormalities does not rule out PHA, as cats with PHA due to bilateral adrenal nodular hyperplasia often have no or very minor changes associated with the adrenal glands. [6]

Confirmation of PHA is also based on finding an elevated plasma aldosterone concentration with a concurrently low plasma potassium level. [2,3,5,6,7,9] Serum aldosterone measurement is widely available in most veterinary laboratories and does not require special handling. There is no reported benefit in measuring an ACTH-stimulated aldosterone value. [7,9,17] Because potassium is a major stimulus for aldosterone secretion by the zona glomerulosa, finding aldosterone in the high-normal range in a cat with hypokalemia provides evidence for insufficient suppression of aldosterone secretion and indicates that there may be autonomous secretion of aldosterone. [2,3,5,6,7,9] The highest aldosterone concentrations usually occur with adrenocortical tumors, where the concentration often exceeds 1,000 pmol/L. [9] In a case series report of 13 cats with PHA, the aldosterone level ranged from 877 to 14,653 pmol/L, with a mean of 5,820 (reference range 150 – 430 pmol/L). [5] Cats with bilateral adrenal nodular hyperplasia of the zona glomerulosa may have milder elevations of aldosterone, including values at the upper end of the reference range. [6,7] In one report, only four of 11 cats with confirmed PHA due to adrenal nodular hyperplasia had aldosterone measurements outside of the reference range. [6] Of the seven cats that had aldosterone within the reference range, five had at least one aldosterone level that tested in the upper half of the range. [6]

Ideally, plasma renin concentration would also be measured to help differentiate primary from secondary hyperaldosteronism. With PHA, renin should be decreased, reflecting autonomous secretion of aldosterone and suppression of the renin-antgiotensin system. In contrast, cats with elevated aldosterone due to secondary hyperaldosteronism should have elevated renin values. [2,3,7,9,12] Plasma renin alone cannot be used alone to diagnose PHA, since it may be in a normal range with both adrenocortical tumors and bilateral adrenal nodular hyperplasia, and plasma renin does not appear to be as suppressed in cats with PHA caused by bilateral adrenal nodular hyperplasia. [3,6,7] The ratio of aldosterone to renin is therefore regarded as the most reliable screening test for PHA. An elevated ratio is most consistent with PHA, and provides evidence for excessive aldosterone secretion, even with normal renin levels. [3,6,7] All 11 cats with PHA due to bilateral nodular hyperplasia in one report exceeded the reference range for the aldosterone to renin ratio on at least one occasion. [6] Unfortunately, renin measurements are not widely available from veterinary laboratories. In addition, the test requires a large blood sample (four mL) and careful collection and handling, including very rapid freezing of separated plasma. [2,3,7,9] Some drugs (ACE inhibitors, beta blockers) as well as increased dietary salt intake may affect the renin measurement. [7,9] In addition, there can be day-to-day variation in plasma renin values. [3,5,6,9]

Urinary aldosterone to creatinine ratio (UACR) is a new test that is being explored to diagnose PHA in cats, and has been used in humans to diagnose PHA. [28] The test represents a measurement of urinary aldosterone excretion over time, and does not require special handling. In one study, reference ranges for UACR were established for 42 healthy cats. [28] Twenty-two cats were then administered oral sodium chloride to determine if oral salt loading would suppress UACR; no significant suppression was found in any cat. In contrast, administration of oral fludrocortisone to 15 healthy cats did result in suppression of aldosterone secretion, while a cat with confirmed PHA due to an adrenocortical carcinoma did not experience significant suppression of aldosterone excretion. Measurement of the UACR combined with fludrocortisone-induced suppression may be a useful tool for the diagnosis of PHA in the future. [28]

There is currently no validated test available to confirm PHA. [3] However, in cats with persistent hypokalemia, hypertension or both, finding an adrenal mass combined with a high aldosterone concentration is usually sufficient to diagnose PHA. [5,9,18] PHA caused by bilateral adrenal nodular hyperplasia may present a more difficult diagnostic challenge, since imaging may show normal or only mildly enlarged adrenal glands. [6] However, baseline aldosterone in the high normal range when potassium concentration is low should make PHA a strong consideration. [2,3,6]

Initial treatment of PHA should focus on correcting hypokalemia and hypertension. For mild hypokalemia, potassium gluconate can be administered orally (PO) at a dose of 2 to 6 mEq per day, although more severe cases may require intravenous potassium chloride supplementation. [2,5,7,9] Amlodipine besylate, a calcium channel blocker, is the drug of choice for managing hypertension, and is administered at 0.1 mg/kg PO q24h. [2,3,5,7,9,23] Hypertension associated with PHA usually resolves when cats are administered amlodipine, but may become refractory over time and necessitate increased dosages. [5,9] The addition of spironolactone (1 to 2 mg/kg PO q12h), a synthetic aldosterone antagonist that binds to aldosterone receptors in the distal convoluted tubules, also assists in controlling both hypokalemia and hypertension. [2,3,7,9] A reported side effect of spironolactone in cats is severe facial dermatitis, and anorexia, diarrhea and vomiting are reported at doses in excess of 4 mg/kg. [3,9] A newer generation of aldosterone antagonist, eplerenone, is being examined in humans with PHA. It has a lower affinity for androgen, estrogen and progesterone receptors than spironolactone, but its use has not yet been examined in cats. [2,7]

Treatment of cats presenting with arrhythmias where PHA is suspected should focus initially on correcting potentiating factors such as anemia, hypokalemia, hypertension and hyperthyroidism, and resolving congestive heart failure, if present. [12,25] When serum potassium falls to a concentration of less than 3.5 mEq/L in cats, there is an increased risk of spontaneous depolarizations, especially premature ventricular contractions, and hypokalemia can cause arrhythmias to be refractory to antiarrhythmic therapy. [12,25] Normokalemia should therefore be restored prior considering antiarrhythmic therapy. [12,25] Treatment of ventricular arrhythmias, one of the most common classes of cardiac rhythm abnormalities in cats, is challenging due to the unproven survival benefit of antiarrhythmic therapy, the palliative nature of treatment, and occurrence of medication intolerance. [25] In addition, in human medicine, modulating the RAAS pathway alone has shown to be successful in treating arrhythmias in some patients with PHA. [15] Antiarrhythmic therapy in cats should be considered when the arrhythmia is causing overt clinical signs, treatment of precipitating factors has not reduced the frequency of the arrhythmia, or a sustained tachycardia persists at a rate that effects hemodynamic stability (greater than 260 beats per minute has been suggested). [12,25] Antiarrhythmic therapy for non-life threatening ventricular arrhythmias may consist of sotalol (2.0 mg/kg PO q12h) or atenolol (0.25 to 1.0 mg/kg PO q12h to q24h), both of which are beta-adrenergic blockers. [12] These therapies are anecdotally supported but remain unproven in the cat. [12,25] Cats receiving anti-arrhythmic therapy should be monitored for mental dullness, syncope or onset of presyncope/lethargy. [12,25]

For unilateral adrenal disease, surgical removal of the affected gland is the optimal treatment, and surgery is typically curative for both adenomas and carcinomas. [2,3,5,7,9,19,20] Even cats with evidence of invasion of the caudal vena cava from an adrenal tumor may be considered candidates for surgery. [14] Cats that survive the immediate post-operative period may survive for years (five of five cats that survived the perioperative period were alive between 240 and 1,803 days in one study [5]), and hypokalemia and hypertension typically resolve rapidly after surgery without further medical treatment. [2,3,5,19,20] Plasma aldosterone levels also return to low or normal post-operatively. [5,14] Post-operative adrenal insufficiency has not been reported, and cortisol supplementation is not required, since PHA does not suppress pituitary ACTH secretion. [7,9] The perioperative mortality rate associated with surgery is high, with approximately one-third of cases dying due to peri- or post-operative hemorrhage. [2,5,7,9,17]

If surgery for unilateral disease is not possible (financial limitations, non-resectable tumor) or PHA is due to bilateral adrenal nodular hyperplasia, cats can be medically managed with potassium supplementation, amlodipine and spironolactone, but development of renal disease is a common outcome. [2,3,7,9] In one report, the survival period for two cats with PHA that were medically managed ranged from 304 to 984 days, and both cats succumbed to chronic renal disease. [5] In a second report of 11 cats with PHA due to bilateral nodular hyperplasia, six cats were followed from eight to 20 months after the initial diagnosis, and all cats experienced a gradual rise in plasma values of urea and creatinine, indicating progression of renal insufficiency. [6]

Prognosis for vision recovery in cats with retinal detachment is dependent on the duration of the detachment prior to treatment and the state of the retina at time of detachment. Early recognition of hypertensive retinopathy and rapid anti-hypertensive treatment offers the best prognosis for return of vision. [22] In a study of 69 cases of cats with ocular lesions associated with systemic hypertension, approximately one-half of the cats with early clinical signs (multi-focal retinal edema or hemorrhage) and control of hypertension had either lack of progression or partial resolution of retinal lesions. [22] Effective antihypertensive treatment can lead to retinal reattachment but restoration of vision generally occurs only in a minority of cats. [22,23]

Clinical Report

A nine-year-old male neutered 6.7 kg domestic shorthaired cat presented for a second opinion regarding a nine month history of muscular weakness and hypokalemia that had not fully responded to potassium supplementation, as well as the development of a new cardiac arrhythmia. The owner reported that she had initially observed lameness in the cat's thoracic limbs nine months previously and had taken her cat to a veterinarian for an examination. No pain had been localized by the veterinarian on the cat's physical examination, and the cat had initially been treated by the referring veterinarian with a four day course of meloxicam[(a)] (dosage not available). The cat's lameness appeared to improve on the first day of treatment, but the lameness returned the next day. She returned to her veterinarian for a recheck approximately one week later. On examination, the cat was capable of jumping from the floor to a counter, but the veterinarian observed that the cat had a shortened, hypometric gait. The veterinarian did not note any neurologic or orthopedic abnormalities. The owner reported that laboratory work (not available) showed that the cat had very low potassium. He was hospitalized and treated with intravenous fluids with potassium supplementation for several days and then discharged on oral potassium supplementation (dosage not available). His

veterinarian rechecked him several days after his discharge, and his potassium was still low despite supplementation. His daily oral potassium supplementation was increased, and his owner felt that he appeared to respond well. His gait normalized, and recheck potassium levels at his veterinarian several weeks later (laboratory results not available) were within normal limits. His owner eventually discontinued the potassium supplementation, as she felt that his clinical signs had fully resolved.

The cat's thoracic limb weakness recurred approximately nine months later and his owner returned to her veterinarian for a recheck examination. On examination, an arrhythmia was ausculted with occasional premature beats; no murmur was ausculted. The cat was also observed to have a shortened stride in his thoracic limbs. In-house serum electrolytes [(b)] obtained by the veterinarian (Table 1) showed low potassium (2.9 mmol/L, reference range 3.5 – 5.8), with normal chloride and sodium. Thoracic radiographs obtained by the referring veterinarian showed a normal cardiac silhouette, pulmonary parenchyma and vasculature. The cat was discharged on oral potassium supplementation (potassium gluconate[(c)] 0.3 mEq/kg q12h), and an appointment for a second opinion consult was scheduled three days later.

During the consultation on day one, the owner reported that the only abnormality she had observed was a return of intermittent lameness in the forelimbs, but she wasn't sure which limb. She felt that the cat was otherwise normal, including appetite, energy, thirst and urination. He had been receiving potassium supplementation twice a day since her visit with the referring veterinarian three days previously. On examination, the cat weighed 6.72 kg, was euthermic (38.0° C), bright and alert. He had a heart rate of 220 beats per minute (bpm), with intermittent premature beats ausculted with accompanying femoral pulse deficits. He appeared symmetrically muscled and in good body condition (BCS 6/9). A thyroid slip was not palpated, pupil size was symmetrical, and pupillary light response (both direct and consensual) was present. He was reluctant to walk in the exam room, but no gait abnormalities were observed. No pain was elicited on orthopedic examination of the forelimbs, and no gross neurologic deficits were observed. A review of the referring veterinarian's thoracic radiographs showed a normal cardiac silhouette, pulmonary parenchyma and vasculature.

Table 1 - In House Blood Test Results from Referring Veterinarian

Date	Test	Laboratory Value	Reference Range
Three Days Before Initial Presentation	Na^+	160 mmol/L	150 - 165
	K^+	**2.9 mmol/L (L)**	3.5 – 5.8
	Cl^-	118 mmol/L	112 - 129

Systolic blood pressure was obtained in the exam room via ultrasonic Doppler [(d)]. The blood pressure was obtained with the owner present and prior to obtaining other diagnostics to minimize stress. The patient was placed in right lateral recumbency, and blood pressure was measured using the left radial artery and a two cm cuff. His systolic blood pressure was severely and consistently elevated at 240 mmHg. Minimal restraint was required and the cat appeared calm, so "white coat" hypertension was considered unlikely.

In house laboratory work [(e)] was performed to recheck his electrolyte status (Table 2), and he was hypokalemic (potassium 2.96 mmol/L, reference range 3.4 – 5.6). Renal parameters (blood urea nitrogen and creatinine) were within normal limits.

The initial problem list included intermittent forelimb lameness or weakness, a cardiac arrhythmia, hypertension, and hypokalemia. The differential diagnoses for the forelimb lameness included orthopedic abnormalities (osteoarthritis, soft tissue injury, neoplasia), hypokalemic myopathy, neuromuscular disease (myasthenia gravis, nerve sheath tumor), or cardiovascular accident (thromboembolism in the right subclavian artery). The differential diagnoses for the cardiac arrhythmia included severe hypertension, prolonged hypokalemia, primary heart disease, cardiac thyrotoxicosis, or any systemic disease resulting in inflammation. Differential diagnoses for severe hypertension included secondary hypertension (chronic renal disease, hyperthyroidism, PHA, and pheochromocytoma) and primary idiopathic hypertension, in which no predisposing cause is found. Differential diagnoses for hypokalemia included PHA or renal disease.

Table 2 – In House Blood Test Results

Date	Test	Laboratory Value	Reference Range
Day 1	PCV	42%	27 – 46
	Total Protein	7.4 g/dL	5.5 – 7.8
	Hct	44%	27 – 46
	Hb	14.8 g/dL	8.5 – 16.0
	Na^+	150.2 mmol/L	145.0 – 158.0
	K^+	**2.96 mmol/L (L)**	3.4 – 5.6
	Cl^-	114.4 mmol/L	104.0 – 128.0
	iCa^+	1.13 mmol/L	0.90 – 1.30
	Glucose	100 mg/dL	64 – 118
	BUN	22 mg/dL	20 – 30
	Creatinine	1.4 mg/dL	0.6 – 2.4
	TCO2	21.6 mEq/L	17 – 23
	Anion Gap	15.1 mEq/L	13-27

An abdominal ultrasound [(f)] was performed from a ventral abdominal approach with the cat in supine position using a 4.0-10.0 mHz probe. An approximate 2.0 x 1.5 cm hypoechoic right adrenal mass was observed (Figure 2a and 2b). The mass appeared well encapsulated, with no apparent invasion of the surrounding vessels. The left adrenal gland was visualized and appeared normal in size and shape. The rest of the abdominal ultrasound was unremarkable, with no evidence of metastatic disease. Differential diagnoses for the right adrenal mass included an aldosterone secreting adenoma or carcinoma, a cortisol or progesterone secreting adenoma or carcinoma, a pheochromocytoma, or a non-functional adenoma. Given the cat's hypokalemia, forelimb lameness or weakness, hypertension and lack of physical exam findings consistent with hyperprogesteronism or hypercortisolism, PHA was the primary differential diagnosis considered.

A Lead-II electrocardiogram (ECG) [(g)] was performed with the cat in right lateral recumbency on a nonconductive surface to characterize the arrhythmia (Figure 3). ECG electrodes were placed immediately distal to the right and left elbows, and to the right and left stifles. The paper speed recorded at 25 mm/second. The cat's heart rate was approximately 200 bpm, and the rhythm was primarily sinus, with regular R-R intervals. Motion artifact was present, making it difficult to clearly observe P wave activity between many of the QRS complexes. Wide, bizarre premature complexes were present occurring either singly or as three or four complexes in a row at a rate of greater than 300 bpm. These complexes were much wider and taller than the normal sinus QRS complexes and also had very deep T waves. These complexes were classified as premature ventricular complexes (PVCs) and the rhythm abnormality was classified as paroxysmal ventricular tachycardia. Primary differential diagnoses for paroxysmal ventricular tachycardia included primary myocardial disease (hypertrophic cardiomyopathy, restricted or unclassified heart disease, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy), hypokalemia, systemic hypertension, and thyrotoxic heart disease. Systemic disease due to infection, inflammation or neoplasia was also a differential diagnosis.

Figure 2a - Ultrasound Image of Right Adrenal Mass

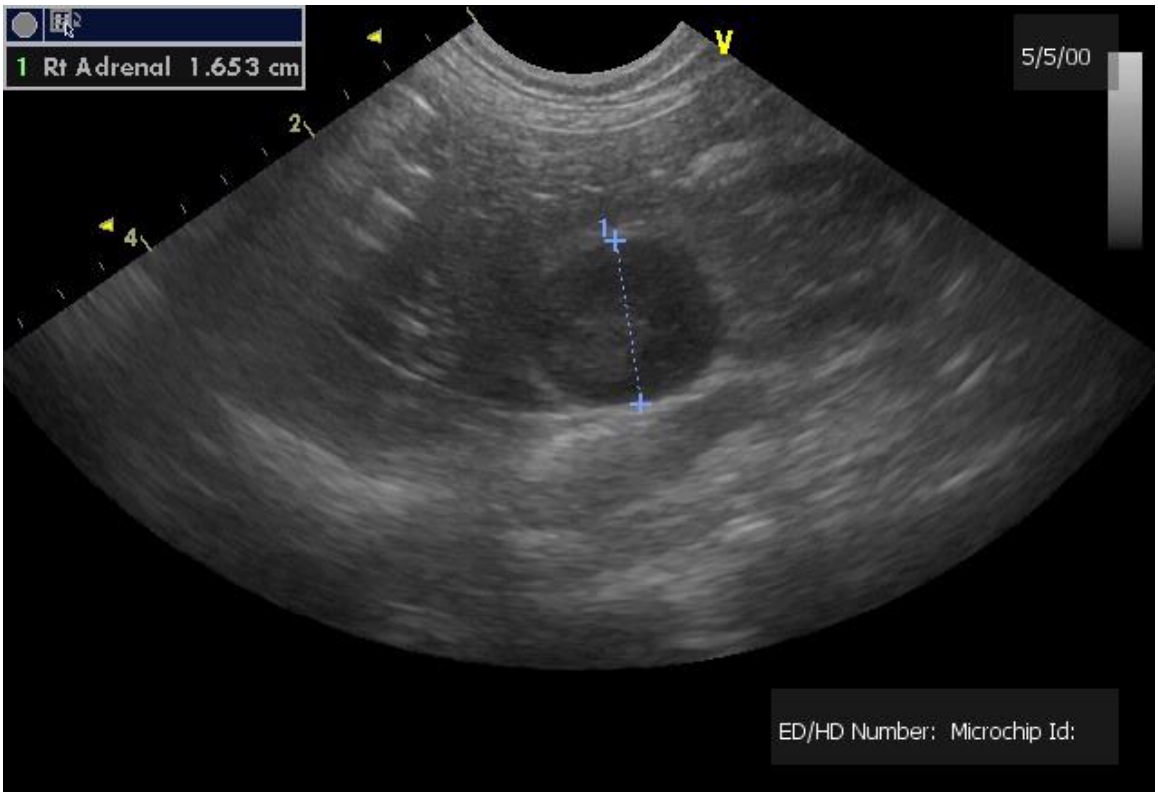


Figure 2b - Ultrasound Image of Right Adrenal Mass (with Doppler)

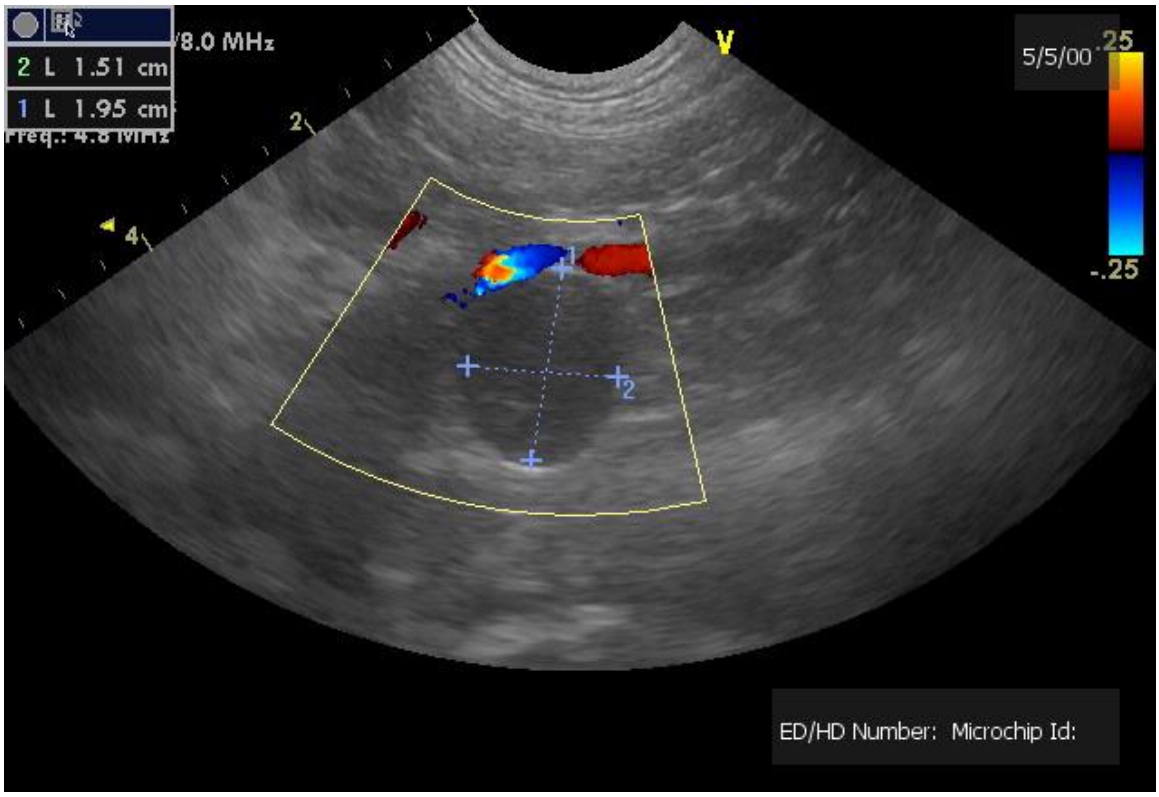
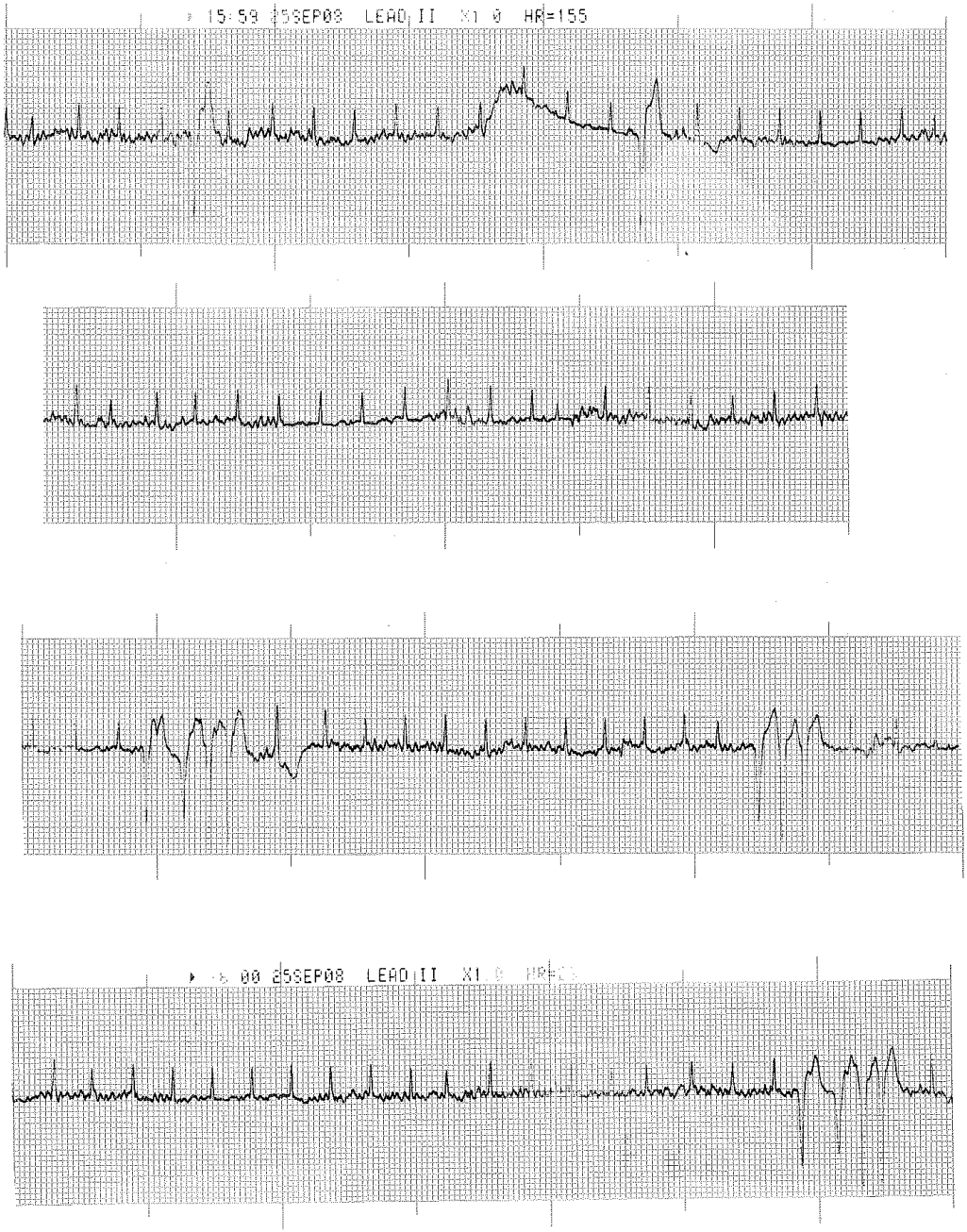


Figure 3 – Lead II Electrocardiogram



Paper speed: 25 mm/s

An echocardiogram [f] was performed to evaluate the cat's heart (Echocardiogram Measurements – Table 3). A 3.0-8.0 mHz phased array transducer was utilized, and two-dimensional measurements were taken from a right parasternal approach while the cat was in right lateral recumbency. Doppler readings were taken from a left parasternal approach while the cat was in left lateral recumbency. The left atrium appeared moderately enlarged, and the left ventricle appeared mildly dilated at end diastole and at end systole; the interventricular septal wall measurements were within normal limits, while the posterior wall appeared slightly thickened at end diastole, but was within normal limits at end systole; this may have reflected mild inaccuracy in measurement. The short axis measurement of aorta also appeared below the reference range; this was also attributed to mild inaccuracy in the measurement rather than evidence of pathology. Systolic function, as determined by fractional shortening, appeared mildly diminished. No valvular abnormalities were identified on color flow Doppler. Pulsed-wave and continuous-wave Doppler were used to assess the left and right ventricular outflow tracts, which were unremarkable. An irregular cardiac rhythm was observed during the examination.

The primary differential diagnosis for mild left atrial and left ventricular enlargement with no mitral valve insufficiency or septal defects was feline restrictive/unclassified cardiomyopathy. However, because PHA was a primary differential diagnosis for the cat's muscular weakness, hypokalemia, hypertension and right adrenal mass, chronic intravascular volume overload due to sodium retention and osmotic resorption of free water was also considered a possibility, perhaps potentiating mild underlying heart disease. The heart disease was not considered significant enough to cause the paroxysmal tachycardia.

Table 3 – Echocardiogram Measurements

2-D	Measurement	Reference Range
IVSd	4.9 mm	4.5 mm ± 0.8
LVIDd	**17.9 mm (H)**	15.4 mm ± 1.6
LVPWd	**5.1 mm (H)**	4.1 mm ± 0.7
IVSs	6.1 mm	7.8 mm ± 1.17
LVIDs	**11.9 mm (H)**	7.5 mm ± 1.7
LVPWs	7.2 mm	7.8 mm ± 1.05
%FS	**33.54% (L)**	53% ± 11
LA SAX	**14.4 mm (H)**	11.3 mm ± 1.7
Ao SAX	**7.4 mm (L)**	9.5mm ± 1.4
LA/Ao SAX	**1.9x (H)**	1.2x ± 0.2
Doppler	Measurement	Reference Range
LVOT Vmax	0.94 m/s	1.1 m/s ± 0.2
RVOT Vmax	0.96 m/s	0.9 m/s ± 0.2

Key:

IVSd = interventricular septum diastole; LVIDd = left ventricular interventricular diameter diastole; LVPWd= left ventricular posterior wall diastole; IVSs = interventricular septum systole; LVIDs = left ventricular interventricular diameter systole; LVPWs = left ventricular posterior wall systole; %FS = % fractional shortening; LA SAX – left atrium short axis; Ao SAX = aorta short axis; LA/Ao SAX = ratio of left atrium to aorta short axis; LVOT Vmax = left ventricular outflow tract maximum velocity; RVOT Vmax = right ventricular outflow tract maximum velocity

A serum chemistry profile, complete blood count, total T4 and urinalysis were sent to a reference laboratory, and results were available at the end of day one [(h)] (Table 4, 5 and 6). Potassium was mildly decreased (3.0 mEq/L, reference range 3.4 – 5.6), consistent with the in-house laboratory work. Creatinine kinase was elevated (9,369 IU/L, reference range 56 – 529 IU/L). The primary differential diagnosis for elevated creatinine kinase was muscle damage secondary to hypokalemic polymyopathy. There were no abnormalities on the complete blood count. The urinalysis showed hyposthenuria (urine specific gravity 1.005, reference range 1.015 – 1.060). The primary differential diagnosis for hyposthenuria was impaired responsiveness of kidneys to anti-diuretic hormone due to prolonged hypokalemia. Mild hematuria was also reported in the urinary analysis (21 – 50 rbc/hpf); the primary differential diagnosis for mild hematuria was traumatic cystocentesis; other causes, such as idiopathic cystitis, cystolith, or bladder wall mass were considered less likely based on the unremarkable appearance of the bladder on ultrasound.

The complete problem list included muscular weakness, hypokalemia refractory to supplementation, elevated creatinine kinase, hyposthenuria, severe systolic hypertension, paroxysmal ventricular tachycardia, mild left atrial and left ventricular enlargement with decreased left ventricular systolic function, and a right adrenal mass. The primary differential diagnosis was PHA, and a baseline aldosterone assay was sent to a university laboratory [(i).]

The cat was discharged to the owner at the end of day one on supplemental potassium gluconate [(c)] (0.6 mEq/kg PO q8h), amlodipine[(j)] (0.09 mg/kg PO q24h), spironolactone (0.93 mg/kg PO q12h) and atenolol (0.93 mg/kg PO q12h). He was scheduled for a recheck and possible surgical exploration five days later, pending results of the aldosterone assay. The aldosterone assay showed a significant elevation in resting aldosterone (1,370 pmol/L, reference range 194 – 388 pmol/L), confirming the diagnosis of PHA (Table 7).

Table 4 – Reference Laboratory Test Results

Serum Chemistries

Date	Test	Laboratory Value	Reference Range
Day 1	AST (SGOT)	98 IU/L	10 – 100
	ALT (SGPT)	94 IU/L	10 – 100
	Total Bilirubin	0.2 mg/dL	0.1 – 0.4
	Alkaline Phosphatase	18 IU/L	6 – 102
	GGT	2 IU/L	1 – 10
	Total Protein	7.5 g/dL	5.2 – 8.8
	Albumin	3.4 g/dL	2.5 – 3.9
	Globulin	4.1 g/dL	2.3 – 5.3
	Cholesterol	117 mg/dL	75 – 220
	BUN	27 mg/dL	14 – 36
	Creatinine	1.5 mg/dL	0.6 – 2.4
	BUN/Creatinine Ratio	18	4 – 33
	Phosphorous	3.1 mg/dL	2.4 – 8.2
	Calcium	9.8 mg/dL	8.2 – 10.8
	Glucose	96 mg/dL	64 – 170
	Amylase	901 IU/L	100 – 1200
	Lipase	117 IU/L	0 – 205
	Sodium	154 mEq/L	145 – 158
	Potassium	**3.0 mEq/L (L)**	3.4 – 5.6
	Chloride	112 mEq/L	104 – 128
	Creatinine Kinase	**9,369 IU/L (H)**	56 – 529
	Triglyceride	75 mg/dL	25 – 160
	Magnesium	1.7 mEq/L	1.5 – 2.5

Table 5 – Reference Laboratory Test Results

Complete Blood Count

Date	Test	Laboratory Value	Reference Range
Day 1	WBC	8.9 10^3/µL	3.5 – 16.0
	RBC	9.8 10^6/µL	5.92 – 9.93
	HGB	14.5 g/dL	9.3 – 15.9
	HCT	47 %	29 – 48
	MCV	48 fL	37 – 61
	MCH	14.9 pg	11 – 21
	MCHC	31 g/dL	30 – 38
	Comment: RBC Morphology normal		
		Absolute %	
	Neutrophils	6,586 /µL 74	2500 – 8500
	Lymphocytes	1,246 /µL 14	1200 – 8000
	Monocytes	178 /µL 2	0 – 600
	Eosinophils	890 /µL 10	0 – 1000
	Basophils	0 /µL 0	0 – 150
	Platelet Estimate	Adequate	
	Platelet Count	301 10^3/µL	200 – 500

Table 6 – Reference Laboratory Test Results

T4 and Urinalysis

Date	Test	Laboratory Value	Reference Range
Day 1	T4 (Total)	2.73 µg/dL	0.8 – 4.0
	Urinalysis (Complete)		
	Color	Yellow	
	Appearance	Clear	
	Specific Gravity	**1.005 (L)**	1.015 – 1.060
	pH	7.0	5.5 – 7.0
	Protein	Negative	Negative
	Glucose – Strip	Negative	Negative
	Ketones	Negative	Negative
	Bilirubin	Negative	Negative
	Occult Blood	2+ **(H)**	Negative
	WBC/HPF	None Observed	0 – 3
	RBC/HPF	**21 – 50 (H)**	0 – 3
	Casts/LPF	None Observed	Hyaline 0 – 3
	Crystals/HPF	None Observed	
	Bacteria	None Observed	None Observed
	Transitional Epithelia/HPF	None Observed	None – Rare
	Squamous Epithelia/HPF	None Observed	None – Few
	Renal Epithelia/HFP	None Observed	None – Rare
	Carbon Dioxide	22 mEq/L	12 – 30

Table 7 - Endocrine Results

Date	Test	Laboratory Value	Reference Range
Day 1	**Aldosterone, Baseline**	**1,370 pmol/L (H)**	194 – 388

On day six, the cat was admitted to the hospital for an exploratory laparotomy performed by a Diplomate of the American College of Veterinary Surgeons. On physical examination, he weighed 6.5 kg and was euthermic (38.3° C); his heart rate was approximately 180 bpm, and intermittent premature beats were ausculted. His systolic blood pressure, taken in a manner identical to that at his initial presentation, was 160 mmHg. In-house laboratory work [(e)] (Table 8) showed normal potassium (3.64 mmol/L, reference range 3.4 – 5.6) and a mildly elevated TCO2 (24 mEq/L, reference range 17 - 23). The mild metabolic alkalosis was attributed to PHA and the resulting urinary excretion of hydrogen ions in exchange for sodium ion retention. A 22-gauge intravenous (IV) cephalic catheter was inserted, and he was placed on an isotonic crystalloid replacement solution [(k)] supplemented with 40 mEq/L potassium chloride at 2.15 mL/kg/hour for six hours prior to surgery. Approximately 45 minutes before anesthetic induction, he was pre-medicated with methadone HCl (0.2 mg/kg subcutaneously).

Anesthesia was induced with propofol [(l)] (3 mg/kg IV) and diazepam (0.15 mg/kg IV), and the cat was maintained on inhalant sevoflurane [(m)]. During surgery, the cat was placed on thermal support [(n)], and blood pressure (systolic, diastolic, and mean arterial), oxygen saturation level, respiratory rate, carbon dioxide level, heart rate and rectal temperature were monitored [(o)] every five minutes. A crystalloid replacement solution [(k)] without supplemental potassium was administered intravenously at a rate of 10 mL/kg/hour. The cat received an injection of cephalexin (22 mg/kg IV) at the commencement of the surgery. A ventral midline surgical approach was used. A right adrenal mass was located dorsal to the vena cava. The mass was intimately associated with the wall of the vena cava and separation was difficult. Blunt and sharp dissection, electrocautery and hemoclips were used to aid in dissecting the mass from the lumbar muscle and the vena cava. The surgical site was lavaged with saline and inspected for hemorrhage. The adrenal mass was submitted to a reference laboratory for histopathology [(h)]. The linea alba was closed with 2-0 polydioxanone suture [(p)], the subcutaneous tissue was closed with 3-0 Poliglecaprone 25 monofilament suture [(q)], and the skin was closed with 3-0 nylon.

Table 8 – In-house Blood Test Results – Pre-operative

Date	Test	Laboratory Value	Reference Range
Day 6 8:32 a.m.	PCV	40%	27 – 46
	Total Protein	7.7 g/dL	5.5 – 7.8
	Hct	41%	27 – 46
	Hb	13.5 g/dL	8.5 – 16.0
	Na^+	153.9 mmol/L	145.0 – 158.0
	K^+	3.64 mmol/L	3.4 – 5.6
	Cl^-	116.2 mmol/L	104.0 – 128.0
	iCa^+	1.20 mmol/L	0.90 – 1.30
	Glucose	85 mg/dL	64 – 118
	BUN	23 mg/dL	20 – 30
	Creatinine	1.4 mg/dL	0.6 – 2.4
	TCO2	**24.5 mEq/L (H)**	17 - 23
	Anion Gap	14.3 mEq/L	13 - 27

There were no complications during the approximate 90-minute surgery. The cat was mildly hypothermic at the end of surgery (36.4° C), and thermal support [(n)] was maintained post-operatively until the cat's rectal temperature was 37.2° C. Post-operative in-house laboratory work [(e)] (Table 9) showed hypokalemia (3.13 mmol/L, reference range 3.4 – 5.6) and mildly elevated TCO2 (24.1 mEq/L, reference range 17 – 23). Total protein had decreased post-operatively from 7.7 g/dL to 6.0 g/dL, while the packed cell volume (PCV) remained stable at 40%. The decrease in total protein was attributed to a combination of blood loss and dilution from IV fluid therapy, while the stable PCV was likely the result of release of red blood cells from the spleen via splenic contraction.

The cat was maintained on an IV crystalloid replacement solution [(k)] at 2.15 mL/kg/hour supplemented with 40 mEq/L potassium chloride. Post-operative analgesia consisted of methadone HCl (0.30 mg/kg subcutaneously q4h) and a single subcutaneous injection of meloxicam [(a)] (0.1 mg/kg).

The cat was monitored overnight by a veterinarian and a registered veterinary technician. A physical examination was performed approximately eight hours after surgery. The cat's heart rate was 170 bpm; no arrhythmia was ausculted. He was euthermic (101.6°), and his respiratory rate was 20 breaths per minute. Systolic blood pressure [(d)] was measured in the same manner as previously and it was 140 mmHg. In-house laboratory work [(e)] was also rechecked eight hours post-operatively (Table 9), which showed mild alkalemia (TCO2 24.8 mEq/L, reference range 17 - 23), mild hyperglycemia (134 mg/dL, reference range 64 - 118), and mildly elevated blood urea nitrogen (BUN) (32 mg/dL, reference range 20 - 30). The creatinine, while in the reference range, had also increased slightly from the results earlier in the afternoon (1.7 mg/dL versus 1.5 mg/dL, reference range 0.6 – 2.4). In addition, the PCV had decreased from 40% to 30%, while the total protein was stable. The primary differential diagnosis for mild hyperglycemia was stress caused by pain, anxiety, or fear. The primary differential diagnosis for increasing BUN and creatinine levels with normal systolic blood pressure was inadequate renal perfusion due to dehydration and blood loss, with resulting hypovolemia. The decrease in the PCV was attributed to blood loss and dilution from IV fluid therapy. Despite increasing renal values, no changes were made to fluid therapy overnight. The cat began to eat small amounts when offered food.

Table 9 – In-house Blood Test Results – Post-operative

Date	Test	Laboratory Value – Immediately Post Operative	Laboratory Value – Eight Hours Post Operative	Reference Range
Day 6	PCV	40%	30%	27 – 46
	Total Protein	6.0 g/dL	6.0 g/dL	5.5 – 7.8
	Hct	39%	32%	27 – 46
	Hb	12.9 g/dL	10.5 g/dL	8.5 – 16.0
	Na^+	152.6 mmol/L	151.7 mmol/L	145.0 – 158.0
	K^+	**3.13 mmol/L (L)**	3.66 mmol/L	3.4 – 5.6
	Cl^-	114.6 mmol/L	115.6 mmol/L	104.0 – 128.0
	iCa^+	1.11 mmol/L	1.17 mmol/L	0.90 – 1.30
	Glucose	116 mg/dL	**134 mg/dL (H)**	64 – 118
	BUN	23 mg/dL	**32 mg/dL (H)**	20 – 30
	Creatinine	1.5 mg/dL	1.7 mg/dL	0.6 – 2.4
	TCO2	**24.1 mEq/L (H)**	**24.8 mEq/L (H)**	17 - 23
	Anion Gap	15 mEq/L	13.0 mEq/L	13 - 27

The next morning (day seven), the cat was euthermic (38.3° C), weighed 6.5 kg, and was bright and alert. His heart rate was 160 bpm; no arrhythmia was ausculted, and systolic blood pressure measured via ultrasonic Doppler [(d)] was 124 mmHg. Morning in-house laboratory work [(e)] (Table 10) showed normal potassium (3.93 mmol/L, reference range 3.4 – 5.6), mild alkalemia (TCO2 24.8 mEq/L, reference range 17 - 23), and increasing renal values (BUN 42 mg/dL, reference range 20 – 30; creatinine 2.1 mg/dL, reference range 0.6 – 2.4). Free catch urine was collected for evaluation of urine specific gravity, and it was 1.034, well concentrated for a cat on IV fluid therapy. The elevated BUN and creatinine combined with concentrated urine was attributed to pre-renal causes, likely decreased glomerular filtration rate due to inadequate hydration, blood loss, and resulting hypovolemia over the previous 24 hours. In addition, the anion gap was slightly decreased (12.7 mEq/L, reference range 13 - 27); laboratory error was thought to be the most likely cause of the decreased anion gap. Total protein had also decreased overnight from 6.0 g/dL to 5.6 g/dL, while the PCV remained stable. Differential diagnoses for this change included mild post-operative hemorrhage with attendant splenic contraction.

The cat's IV fluids were changed to a crystalloid replacement solution [(k)] with no additional potassium supplementation, and the fluid rate was reduced to a rate of 1.08 mL/kg/hour. Analgesia was changed from subcutaneous methadone to sublingual buprenorphine (0.005 mg/kg q8h). No amlodipine [(j)], atenolol, spironolactone or oral potassium gluconate [(c)] was administered.

Serum electrolytes were rechecked in-house [(e)] approximately seven hours later during the afternoon of day seven (Table 10). These results were similar to the values obtained earlier in the morning – potassium remained stable despite withdrawal of all potassium supplementation, and renal values were slightly higher (BUN 46 mg/dL, reference range 20 – 30; creatinine 2.3 mg/dL, reference range 0.6 – 2.4). The IV catheter was removed, and the cat was administered 200 mL of a replacement crystalloid solution [(k)] subcutaneously prior to discharge to provide additional hydration. The cat was discharged to the owner in the afternoon with instructions for the cat to wear an e-collar until sutures were removed in 14 days, to keep the cat indoors, and to limit activity. The only medication sent home at discharge was buprenorphine (0.005 mg/kg sublingually q8h for three days). The owner was instructed not to administer amlodipine [(j)], atenolol, spironolactone or oral potassium gluconate [(c)]. The cat was scheduled for a recheck examination three days later.

Table 10 – In-house Blood Test Results - One Day Post Surgery

Date	Test	Laboratory Value 6:40 a.m.	Laboratory Value 1:58 p.m.	Reference Range
Day 7	PCV	30%	28%	27 – 46
	Total Protein	5.6 g/dL	6.4 g/dL	5.5 – 7.8
	Hct	30%	31%	27 – 46
	Hb	9.7 g/dL	10.2 g/dL	8.5 – 16.0
	Na^+	153.0 mmol/L	150.6 mmol/L	145.0 – 158.0
	K^+	3.93 mmol/L	3.87 mmol/L	3.4 – 5.6
	Cl^-	116.6 mmol/L	117.5 mmol/L	112.0 – 128.0
	iCa^+	1.16 mmol/L	1.14 mmol/L	0.90 – 1.30
	Glucose	107 mg/dL	76 mg/dL	64 – 118
	BUN	**42 mg/dL**	**46 mg/dL (H)**	20 – 30
	Creatinine	2.1 mg/dL	2.3 mg/dL	0.6 – 2.4
	TCO2	**24.8 mEq/L (H)**	22.6 mEq/L	17 - 23
	Anion Gap	**12.7 mEq/L (L)**	**11.5 mEq/L (L)**	13 - 27
	Urine Specific Gravity	1.032		1.015 – 1.060

The cat presented for a recheck appointment three days after discharge from the hospital. The owner reported that the cat had been doing very well at home – eating well and fully ambulatory, with no evidence of muscle weakness. He weighed 6.42 kg, the rectal temperature was 38.1° C, and the heart rate was 160 bpm with no arrhythmia ausculted. The surgical site was clean and dry, sutures were intact and there was minimal inflammation along the incision. In house laboratory results [(e)] (Table 11) showed normal BUN and creatinine, as well as normalization of all electrolytes and TCO2. Due to resolution of all other abnormalities associated with PHA and normalization of the blood pressure post-operatively, blood pressure was not obtained. The owner was advised to have sutures removed at the referring veterinarian in approximately 10 days. A recheck echocardiogram was also recommended in approximately three months to assess whether the left ventricle and left atrium remained enlarged. However, the owner declined the recommendation for a follow-up echocardiogram.

Histopathology results [(h)] were available approximately four days after surgery (Table 12), and reported an adrenocortical adenoma that was completely excised.

The owner reported via phone communication two weeks later that the cat was doing very well and she felt that he had made a complete recovery. A second phone communication occurred approximately three years later, and the owner reported that the cat was still in good health, with no evidence of recurrence of disease.

Table 11 – In-house Blood Test Results – Three Days After Discharge

Date	Test	Laboratory Value	Reference Range
Day 10	PCV	35%	27 – 46
	Total Protein	7.8 g/dL	4.5 – 7.8
	Hct	36%	27 – 46
	Hb	11.7 g/dL	8.5 – 16.0
	Na^+	152.0 mmol/L	145.0 – 158.0
	K^+	4.07 mmol/L	3.4 – 5.6
	Cl^-	119.0 mmol/L	104.0 – 128.0
	iCa^+	1.18 mmol/L	0.90 – 1.30
	Glucose	93 mg/dL	64 – 118
	BUN	20 mg/dL	20 – 30
	Creatinine	1.0 mg/dL	0.6 – 2.4
	TCO2	18.9 mEq/L	17 - 23
	Anion Gap	14.9 mE/L	13 – 27

Table 12 - Histopathology

SOURCE: a 2 x 4 cm tissue. History: Right adrenal mass

MICROSCOPIC FINDINGS: Adrenocortical adenoma

PROGNOSIS: Favorable

COMMENTS: A capsule appears to encircle the entire neoplastic focus, a feature typically considered associated with benignancy rather than malignancy. In the samples examined, there is no evidence of vascular invasion. There is no evidence of extension beyond the adrenal capsule. Cells comprising the neoplasm are uniform and histologically bland and monotonous. Mitoses average 0-1/hpf. Local excision appears to be complete

Discussion

This case describes a nine-year male-neutered domestic short hair presenting for evaluation of muscle weakness, hypokalemia and an arrhythmia. At initial presentation, the cat was found to be severely hypertensive (240 mm Hg). This is a level at which cats are at risk for end-organ damage, including retinal detachment and blindness. Although there were no ocular abnormalities noted on the general physical exam, a fundic exam should have been performed to check for hypertensive retinopathy/choroidopathy. Amolodipine therapy was commenced the day that hypertension was first detected, mitigating the risk of subsequent retinal damage.

A urinalysis was performed as part of the complete database, and the cat had hyposthenuric urine with mild hematuria; no white blood cells or bacteria were present. Despite the benign urine sediment, a culture should have been performed once hyposthenuria was identified, as dilute urine is more amenable to bacterial growth than well-concentrated urine. In addition, the absence of white blood cells and bacteria does not correlate well with infection in dilute urine.

The diagnosis of PHA was confirmed by a significantly elevated baseline serum aldosterone level with a concurrently low potassium. Ideally, plasma renin would have been measured at the same time, and an aldosterone to renin ratio calculated. An elevated aldosterone to renin ratio is most consistent with PHA, and differentiates primary from secondary hyperaldosteronism. However, a plasma renin assay for cats was not commercially available at the time. In addition, the presence of an adrenal mass combined with a high aldosterone concentration, persistent hypokalemia, and hypertension is sufficient to confirm the diagnosis of PHA. A repeat aldosterone level was not conducted in the recovery period, as the cat's serum potassium, blood pressure and muscle weakness all resolved after surgery without additional medical therapy. It is possible that the adrenal mass removed was a non-functional adenoma, and that the cause of the PHA was due to bilateral nodular hyperplasia. Certainly a recurrence of hypokalemia, muscle weakness or hypertension would have warranted a repeat baseline aldosterone test.

The cat was medically managed prior to surgery with spironolactone, amlodipine and supplemental potassium gluconate. In addition, he was treated with atenolol, a beta-adrenergic blocker, to help control PVCs. The arrhythmia may have been caused by prolonged hypokalemia, hypertension, underlying structural heart disease,

persistently elevated aldosterone, or a combination of these. When PVCs are non-cardiac in origin, treatment of the underlying cause of the arrhythmia is preferred to administering anti-arrhythmic medication. However, while the PVCs were intermittent, they had a rapid rate (greater than 300 bpm) and were occurring in runs of up to four at a time. There was concern that the rhythm might convert to sustained ventricular tachycardia with severe hemodynamic consequences. When the cat represented for surgery five days later, his heart rate was 180 bpm during the exam, slower than the 220 bpm recorded during the initial visit, but there appeared to be no change in the number or frequency of PVCs ausculted despite normalization of blood pressure and serum potassium. It appears that the cat was experiencing chronotropic benefits from the atenolol therapy, but not an anti-arrhythmic effect. In addition, the cat's arrhythmia resolved quickly after surgery, and it appears in retrospect that anti-arrhythmic therapy may not have been warranted.

Given the high peri-operative mortality rate associated with adrenal surgery due to hemorrhage, additional steps should have been taken prior to surgery to prepare for possible complications. The cat's blood type should have been checked prior to surgery to verify that the cat was not type B if a transfusion was warranted, as this blood type is often not readily available. Additionally, if acute hemorrhage did occur, time would have been lost by checking blood type during the hemorrhagic event. A central line or second IV catheter should also have been placed. Because the cat was having frequent blood draws before and after surgery, a central sampling catheter would have facilitated more rapid and less invasive blood draws. A central catheter could also have been used to monitor central venous pressure to help track hydration status and adjust IV fluid therapy. Finally, a second catheter would have provided redundancy had a catheter become non-patent for any reason. If the cat had hemorrhaged acutely and an IV catheter was discovered to be non-patent, the resulting severe hypotension might have made insertion of a second catheter extremely challenging, resulting in a delay in initiating life-saving therapy.

On the day of surgery, the cat's serum potassium concentration was within the reference range, yet the cat was placed on an isotonic crystalloid solution supplemented with 40 mEq/L potassium chloride for several hours prior to surgery. The primary reason was to avoid hypokalemia secondary to dilutional effects of a high rate of surgical fluids. The expected length of anesthesia was approximately two hours, and animals under inhalant anesthesia were placed on an increased rate of fluids (10 mL/kg/hour) to protect against hypotension due the vasodilatory effects of

inhalant anesthesia. Fluids used during surgery typically do not include added potassium to avoid an inadvertent overdose of potassium chloride if a fluid bolus was required during surgery. The extra potassium supplementation prior to surgery appears warranted, given that the cat was mildly hypokalemic at the end of surgery despite pre-loading.

The cat's renal parameters (BUN and creatinine) began to increase approximately seven hours after surgery, but no adjustment was made to the rate of IV fluids at that time, nor was urine initially collected to assess urine specific gravity and to determine if the azotemia was renal or pre-renal in origin. If a central line had been present, central venous pressure (CVP) might have been used to differential pre-renal (volume depletion resulting in a negative CVP) from renal causes (normal CVP). Without the ability to monitor CVP, serial weights after urination might also have helped determine if the cat was losing more fluid through urination than was being provided via IV fluid support. A urinary catheter with a closed collection system could also have provided an accurate method of tracking fluid in and out, but the discomfort associated with a urinary catheter coupled with the risk of iatrogenic infection outweighed the benefit in this case. The morning after surgery, the cat's renal parameters had experienced another mild increase. Urine was obtained for a urine specific gravity to determine if the cause was prerenal or renal, and the urine specific gravity was 1.034. There was no pre-surgical value for comparison, but the cat's urine was substantially more concentrated than at initial presentation, when urine specific gravity was reported at 1.005. The concentrated urine for a cat on IV fluids for 24 hours suggested a strong pre-renal component to the azotemia, and it seems clear that the IV fluid rate should have been increased to expand circulating volume. It would have been prudent to have kept the cat hospitalized for an additional 24 hours to track renal parameters to confirm that the azotemia was pre-renal in origin and that it was being corrected prior to discharge. However, due to financial considerations associated with hospitalization and the fact that the cat was eating and drinking, the fluid rate was decreased in anticipation of discharge from the hospital. The renal values were rechecked approximately seven hours later, and they had increased only slightly from the morning. The decision was made to discontinue IV fluids and to administer subcutaneous fluids to the cat prior to discharge.

The dose of buprenorphine used post-operatively and sent home with the owner, 0.005 mg/kg q8h, was low for a cat, both in terms of dosage and frequency. The patient was likely experiencing significant discomfort given the surgery

that had been performed the prior day. Recommendations for the administration of buprenorphine are four to six times higher than the dose the cat received, and this reflected a clinical error.

The cat returned for a recheck examination three days after discharge. Blood pressure was not obtained at this visit because all of the other abnormalities associated with PHA (hypokalemia, forelimb lameness and cardiac arrhythmia) had resolved post-surgery, and the cat's blood pressure had returned to normal in the post-operative period. The decrease in blood pressure after surgery might have been due to hemorrhage and hypovolemia, however. Given the adverse consequences associated with untreated hypertension, a recheck blood pressure would have been warranted.

Summary

A nine-year-old male-neutered domestic shorthair cat presented for evaluation of intermittent forelimb lameness, recurring hypokalemia and a cardiac arrhythmia. On physical examination, no orthopedic or neurologic abnormalities were identified. A sinus cardiac rhythm interrupted by short runs of premature beats was ausculted. The cat's systolic blood pressure was found to be severely elevated. An ECG showed paroxysmal ventricular tachycardia. An abdominal ultrasound revealed a large right adrenal mass. An echocardiogram showed evidence of mild cardiac disease. The diagnosis of PHA was confirmed by an elevated serum aldosterone level. The cat was medically managed for four days with amlodipine [(j)], potassium gluconate[(c)], spironolactone and atenolol until a unilateral right adrenalectomy was performed. The cat made an excellent recovery, with resolution of all abnormalities, and remained symptom-free three years later. The prognosis for cats with PHA caused by a unilateral aldosterone secreting tumor is good if they survive the peri-operative period.

Endnotes

a. Metacam® Oral Suspension, 1.5 mg/mL, Boehringer Ingelheim, Ingelheim am Rhein, Germany

b. VetScan i-STAT 3 Analyzer, Abaxis, Union City, CA, USA

c. Tumil K, Virbac AH, Fort Worth, TX, USA

d. Doppler Ultrasonic Flow Detector 811-B, Parks Medical Electronics, Aloha, OR, USA

e. VetScan i-STAT 8 Analyzer, Abaxis, Union City, CA, USA

f. GE Vivid 7 PRO, GE Medical Systems, Milwaukee, WI, USA

g. Physio-Control LIFEPAK 9 Cardiac Monitor, Redmond, WA, USA

h. ANTECH Diagnostics, Irvine, CA, USA

i. Endocrinology Section, Animal Health Diagnostic Laboratory, Michigan State University, East Lansing, MI, USA

j. Norvasc®, Pfizer Animal Health, St. Louis, MO, USA

k. Normasol® R, Abbott Laboratories, North Chicago, IL, USA

l. PropoFlow™ Injectable, Abbott Animal Health, Abbott Park, IL, USA

m. Ultane®, Abbott Animal Health, Abbott Park, IL, USA

n. BAIR Hugger Warming Unit, Model 505, Arizant Healthcare, Eden Prairie, MN, USA

o. Cardell Veterinary Monitor 9405, Midmark, Tampa, FL, USA

p. PDS II Suture, ETHICON Inc, Somerville, NJ, USA

q. Monocryl Suture, ETHICON, Somerville, NJ, USA

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