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"Puddles" is a 15-year-old FS Domestic Shorthair that presented to the emergency service on 9-17-2022 for two days duration of not being able to raise her head. She had otherwise been a healthy cat with no medical problems noted from previous medical records.

Physical examination findings include a weight of 4.4 kg, BCS – 5/9, rectal temperature-101.8 F, oral- mm's pink, CRT-2 seconds, heart rate- 200 bpm with an intermittent gallop sound, respiratory rate- 36 bpm, abdominal palpation- unremarkable with no pain elicited. Severe musculoskeletal weakness. Integument, eyes, ears - no significant findings.

Doppler blood pressure- 195 mmHg Retinal examination- no abnormal findings

Lab work (9-17-2022):

СВС	Result Reference Range		Units	
RBC	7.84	5.80-11.0		M/uL
НСТ	37%	28.0-47.0		%
HGB	11.5	8.6-16.0		g/dL
MCV	48	37.7-50.0		fL
MCH	14.7	12.3-17.2		pg
MCHC	30.8	28.9-42.2		g/dL
Platelet	227	145-484		K/uL
WBC	9.6	3.7-20.5		K/uL
Seg neut	8.3	1.30-15.7		K/uL
Lymph	1.08	1.00-7.90		K/uL
Mono	0.11	0.16-1.12		K/uL
Eos	0.06	0.06-1.23		K/uL
Packed cell volume	35	25-45		%
Total solids	5.9	6-8.2		mg/dl

Chemistry Profile (9-17-2022)

	Result	Reference Range	Units
Glucose	97	70-150	g/dL
ALT	141	20-158	U/L
ALKP	11	10-90	U/L
TBili	0.1	0.1-0.6	mg/dL
Chol	117	90-205	mg/dL
SDMA	10	0-14	ug/dl
BUN	19	10-30	mg/dL
Creat	1.4	0.3-2.1	mg/dL
Phos	3.2	3.4-8.5	mg/dL
Calcium	8.7	8.0-11.0	mg/dL
Total prot	5.9	5.2-8.2	g/dL
Alb	2.3	2.2-4.4	g/dL
Glob	3.6	2.5-4.5	g/dL
Na	152	142-164	mmol/L

К	2.1	3.7-5.8	mmol/L
Cl	112	109-122	mmol/L
Total T4	2.4	1.5-4.8	ug/dl

Urinalysis (9-17-2022 cystocentesis)		
	Result	Reference range (where applicable)
Color	Yellow	N/A
Clarity	Clear	N/A
SG	1.011	1.018-1.045
Glucose	Negative	Negative
Bilirubin	Negative	Negative
Ketone	Negative	Negative
Blood	Negative	Negative
рН	6.0	
Protein	Negative	Negative-trace
WBC	0 HPF	0-5 HPF
RBC	3-5 HPF	0-5 HPF
Bacteria	None observed	Negative
Epi cell	None observed	
Casts	None observed	
Crystals	None observed	

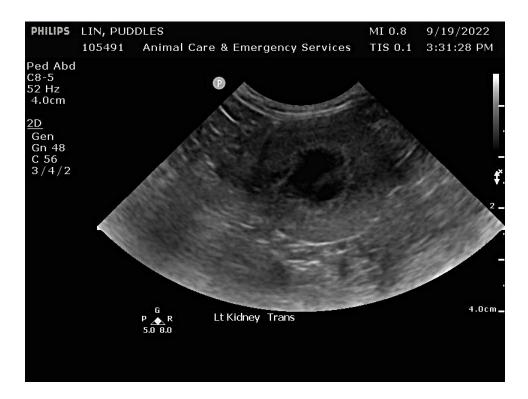
Primary differentials for an older cat with severe weakness and severe hypokalemia include primary hypoaldosteronism and chronic kidney disease. Toxicity such as albuterol consumption can also cause severe hypokalemia. A complete abdominal ultrasound was performed.

Abdominal ultrasound

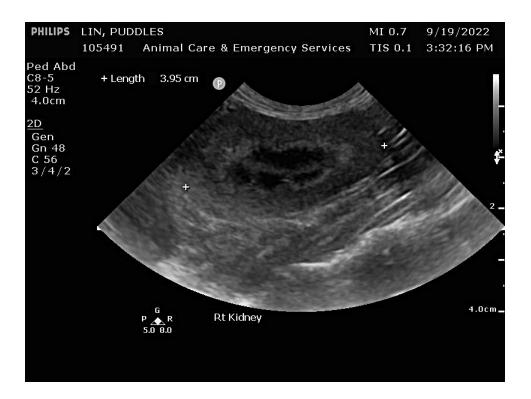
A Philips CX-50 ultrasound unit utilizing a curvilinear C8-5 MHz and linear L12-3 MHz probes was used. The following pertinent images are presented:



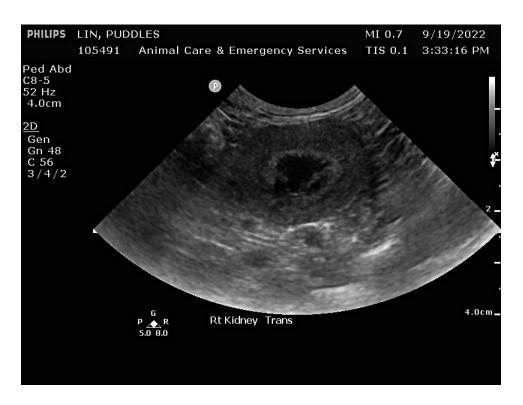
Sagittal view of the left kidney. The cortex is hyperechoic, and the length (3.89 cm) is within normal limits.



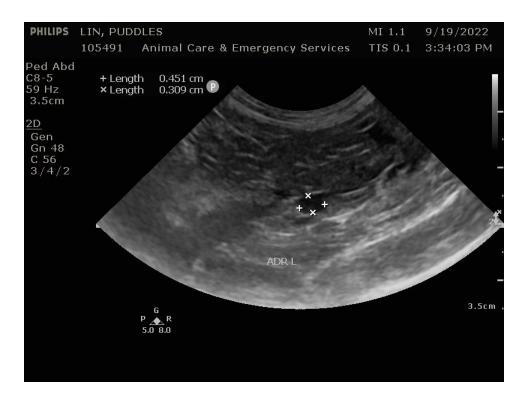
Transverse view of the right kidney. The renal cortex is hyperechoic and there is no renal pelvis distension.



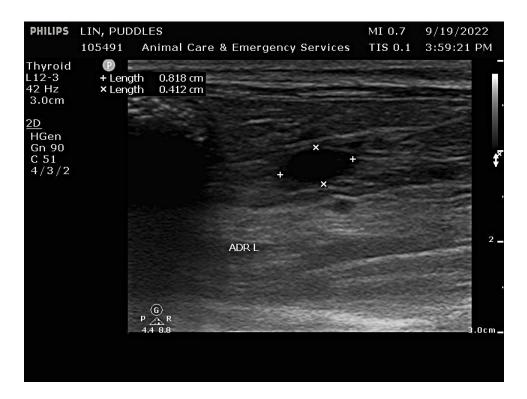
Sagittal view of the right kidney. The cortex is hyperechoic, and the length (3.95 cm) is within normal limits.



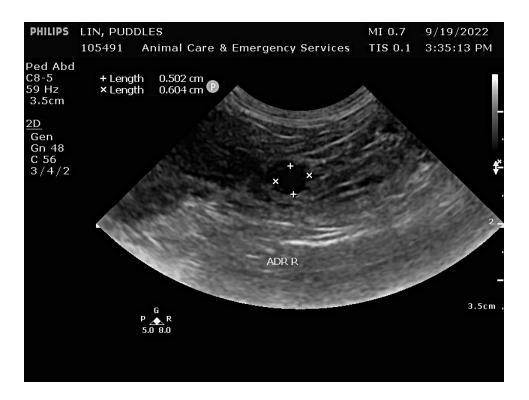
Transverse view of the right kidney. The cortex is hyperechoic and there is no renal pelvis dilation.



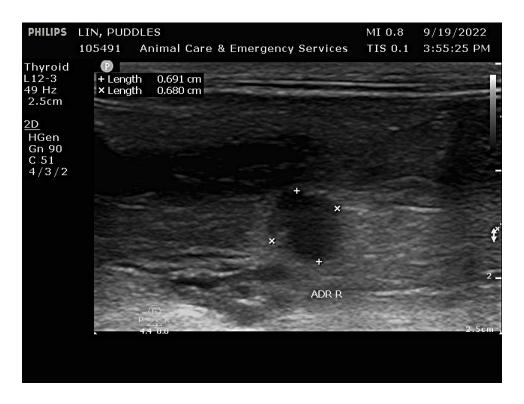
Transverse view of the left adrenal gland. The echogenicity is normal, and the length (4.51 mm) and width (3.09 mm) are within normal limits



Transverse view of the left adrenal utilizing the linear probe. The echogenicity is normal, and the length (8.18 mm) and width (4.12 mm) are within normal limits though there is a wide range of normal limits. There is acoustic shadowing from feces in the colon.



Transverse view of the right adrenal. The echogenicity is normal, and the gland is more circular $(5.02 \times 6.04 \text{ mm})$ and abnormally enlarged.



Transverse view of the right adrenal utilizing the linear probe. The echogenicity is normal, and the gland is more circular (6.91 x 6.80 mm) and abnormally enlarged.

Interpretation summary

The two primary abnormalities are the hyperechoic kidneys and the enlarged, misshapen right adrenal gland. Both kidneys have a hyperechoic cortex. Hyperechoic kidneys are most commonly associated with deposition of fat and can be related to underlying chronic kidney disease or infection. The misshapen and enlarged right adrenal gland has the primary differential of adenocarcinoma, adenoma, or hyperplasia.

Case progression

Puddles presented with generalized weakness due to hypokalemic polymyopathy. Primary hyperaldosteronism was highly suspected, and a plasma aldosterone concentration (PAC) was submitted. The value was 2,710 pmol/L. Primary hyperaldosteronism is considered the diagnosis in a cat with persistent hypokalemia, hypertension, an adrenal mass on ultrasound (or CT) and a PAC >1,000 pmol/L.

Treatment and response to therapy

Puddles was placed on IV fluids with potassium supplementation of 60 mEq/L. Oral potassium gluconate at a dose of 2 mEq three times a day was also administered. The primary medical treatment is spironolactone, which is a mineralocorticoid receptor blocker. This medication needed to be compounded and there was a delay in administration for 24 hours. The potassium remained between 2.1-2.3 during this time, despite supplementation, though Puddles' weakness improved.

Hypertension was treated with amlodipine 0.625 mg po twice daily and her blood pressure returned to normal after one dose. Puddles was discharged prior to receiving the spironolactone.

Discussion

Primary hyperaldosteronism (PH) is likely the most common adrenocortical disorder in cats and occurs in older cats (mean 13 years).¹ Excessive secretion of aldosterone is due to either a neoplastic or non-neoplastic (hyperplasia) zona glomerulosa tissue of one or both adrenal glands.¹ The pathophysiologic consequences of excessive aldosterone include sodium and water retention that can lead to hypertension, and increased potassium excretion resulting in hypokalemia. Muscle weakness can occur at blood plasma concentrations <2.5 mEq/L.¹ Affected cats can have a variety of clinical signs related to hypokalemia including plantigrade stance in the pelvic limbs, difficulty jumping or display ventroflexion of the neck, flaccid paresis with hyporeflexia, muscle hypotonia, and difficulty breathing have been reported.^{2,3} Cats can also present for signs of hypertension including blindness due to retinal detachment and retinal hemnorrhage.¹

One of the most important aspects of making the diagnosis of PH is imaging with ultrasound being the most readily available. Computerized tomography (CT) is also an imaging technique that can be used. Since excessive aldosterone secretion is from a neoplastic or non-neoplastic tissue of the adrenal, documentation of an abnormal adrenal gland or glands is extremely important in making the diagnosis. In addition, since surgical removal of an abnormal adrenal gland is the treatment of choice, imaging can possibly offer evidence of any invasion of the caudal vena cava by the abnormal adrenal gland.

The normal adrenal glands in the cat are similar in shape, unlike in dogs. They appear as oval or bean shaped structures, are well defined and hypoechoic relative to the surrounding fat.^{4,5} Due to their small size, a medium to high frequency (>7 MHz) linear or microconvex transducer is recommend and the highest possible frequency should be used to optimize resolution.⁶ In some cats, a thin hyperechoic line can be seen dividing the gland into two concentric layers with the outer layer hypoechoic and the inner layer hyperechoic.⁶ Both glands were successfully identified in Puddles using the microconvex

probe and the linear probe. Resolution was better with the linear probe, though two distinct layers were not identified in the normal left adrenal gland. Measurement of both glands was more accurate using the linear probe as well.

The normal size of the feline adrenal glands has been reported in several studies, summarized in Table 1.⁶ The left adrenal gland in Puddles had measurements that fell within normal limits. There was a difference in the measurement between the microconvex and linear probes, which is expected based on the ability of the linear probe to provide better resolution. The length measurement using the linear probe was more within the normal range, though enlargement is not ruled out.

Table 1 Normal adrenal gland reference intervals reported in the cat			
Study (in chronological order)	Study population	Short-axis dimension (height) (mm)	Long-axis dimension (length) (mm)
Cartee et al 19938	10 healthy cats	Mean thickness 4.0 ± 0.2	10.7 ± 0.4
Zimmer et al 2000 ⁴	20 healthy cats	2.9–5.3	4.5–13.7
Zatelli et al 2007 ⁹	24 sick cats with non-adrenal illnesses	Thickness left: 2.8–4.7 Thickness right: 3.4–7.1	Left: 7.1–19.5 Right: 5.4–13.7
Combes et al 2012 ¹¹	30 healthy cats aged 6-14 years	Cranial pole height: 1.5–5.9 Caudal pole height: 2.3–5.2	5.8–14
Combes et al 2013 ³	145 healthy cats and sick cats with chronic non-adrenal illnesses	Cranial pole 3.0–4.8 Caudal pole: 3.0–4.5	8.9–12.5

The right adrenal gland was consistently enlarged using both probes. The gland had lost the normal oval appearance and was more rounded. Interpretation of the length was not possible, as all the length measurements fell within normal limits based on several of the studies.

Unilateral adrenalectomy is the treatment of choice for confirmed unilateral PHA.¹ Invasion of the adrenal gland to the caudal vena cava, especially the right adrenal, can make surgical removal much more difficult. Vascular invasion of the caudal vena cava was confirmed at surgery in 7 cats, though ultrasound did not detect invasion in any of those cats.⁷ Failure to detect a visible invasion of the vena cava with ultrasound does not exclude it's presence nor does it mean the adrenalectomy will be easier.^{8,9} Finally, there are instances of inaccurate adrenal ultrasound results, one in a cat with a right adrenal mass and a normal left adrenal gland that went to surgery to remove the right adrenal, and it was found at necropsy 13 days later that both adrenals contained adrenocortical adenomas.⁸

Conclusion

Ultrasound identified an abnormal right adrenal gland, though based on a wide range of normal values and no studies reporting the measurements of enlarged adrenal glands, Puddles could have bilateral adrenal enlargement. These findings were significant in a cat with persistent hypokalemia and hypertension in the main differential of primary hyperaldosteronism. The PAC provided enough information to make this the diagnosis.

References

1. Djajadiningrat-Laanen S, Galac S, Kooistra H. Primary hyperaldosteronism: expanding the diagnostic net. *J Vet Intern Med* 2008;22(6): 1283-8.

2. Haldane S, Graves TK, Bateman S, et al. Profound Hypokalemia Causing Respiratory Failure in a Cat with Hyperaldosteronism. *J Vet Emerg Crit Care* 2007 June; 17(2):202-207.

3. Hammond TN, Holm JL. Successful use of short-term mechanical ventilation to manage respiratory failure secondary to profound hypokalemia in a cat with hyperaldosteronism. *J Vet Emerg Crit Care* 2008 October;18(5):517-525.

4. Nyland TG, Widmer WR, Mattoon JS. Adrenal glands. In, Mattoon JS, Nyland TG, eds. *Small Animal Diagnostic Ultrasound*, 3rd edition. Elsevier, St. Louis, 2015:541-556.

5. d'Anjou M-A, Penninck D. Adrenal glands. In, Penninck D, d'Anjou M-A, eds. *Atlas of Small Animal Ultrasonography*, 2nd edition. Wiley-Blackwell, Ames, 2015:251.

6. Griffin S. Feline abdominal ultrasonography: What's normal? What's abnormal? The adrenal glands. *J Feline Med Surg* 2021 Jan;23(1):33-49.

7. Lo AJ, Holt DE, Brown DC, et al. Treatment of aldosterone-secreting adrenocortical tumors in cats by unilateral adrenalectomy: 10 cases (2002-2012) J Vet Intern Med 2014; 28(1): 137-43.

8. Ash RA, Harvey AM, Tasker S. Primary hyperaldosteronism in the cat: A series of 13 cases. *J Fel Med and Surg* 2005;7(3):173-82.

9. DeClue AE, Breshears LA, Pardo ID, et a. Hyperaldosteronism and hyperprogesteronism in a cat with an adrenal cortical carcinoma. *J Vet Intern Med* 2005; 19(3): 355-8.