An SDMA case study: Twinkle

Patient: Twinkle, 13-year-old, spayed female domestic longhair

Presenting reason and history: Twinkle presented for a one-month history of vomiting every other day, decreased appetite, and weight loss. Her owners noted a slight increase in water consumption and larger clumps in the litter box. She had been seen for yearly wellness examinations, with a history of intermittent gastrointestinal signs, and was being fed a highly digestible commercial diet.

Physical examination: Twinkle was bright and alert. Vitals were assessed as normal, with body temperature was 38.3 °C, pulse was 170 beats per minute, and respiratory rate was 40 breaths per minute. Thoracic auscultation was normal. She was slightly guarded on abdominal palpation but had no notable pain, palpated abnormalities, or appreciated thickening of her gastrointestinal tract. Her body condition score (BCS) was slightly below normal at 3/9, and she had mild muscle wasting over her spine. She had lost 450 gr since her last visit, 1 year prior.

Diagnostic review—13th of May 2016

CBC

Haematology	13.05.16 20:39	
Click to view Differentials		
RBC	8.35	7.12 - 11.46 x10^12/L
Haematocrit	a 0.35	0.282 - 0.527 L/L
Haemoglobin	114	103 - 162 g/L
MCV	42	39 - 56 fL
MCH	13.7	12.6 - 16.5 pg
MCHC	326	285 - 378 g/L
% Reticulocyte	0.3	%
Reticulocytes	25	3 - 50 K/µL
WBC	12.4	3.9 - 19.0 x10^9/L
% Neutrophils	66.7	%
% Lymphocytes	25.6	%
% Monocytes	3.4	%
% Eosinophils	4.3	%
% Basophils	0.0	%
Neutrophils	8.271	2.62 - 15.17 x10^9/L
Lymphocytes	3.174	0.85 - 5.85 x10^9/L
Monocytes	0.422	0.04 - 0.53 x10^9/L
Eosinophils	0.533	0.09 - 2.18 x10^9/L
Basophils	0	0 - 0.1 x10^9/L
Platelets	354	155 - 641 x10^9/L

Urinalysis

Urinalysis	13.05.16 20:39	
Click to view Differentials		
Collection	CYSTOCENTESIS	
Colour	STRAW	
Clarity	HAZY	
Specific Gravity	1.015	
pH	6.5	
Urine Protein	a NEGATIVE	
Glucose	NEGATIVE	
Ketones	NEGATIVE	
Blood / Haemoglobin	TRACE	
Bilirubin	NEGATIVE	
Urobilinogen	NORMAL	
White Blood Cells	NONE SEEN	
Red Blood Cells	0-2	
Bacteria	NONE SEEN	
Epithelial Cells	RARE (0-1)	
Mucus	NONE SEEN	
Casts	NONE SEEN	

Chemistry panel

Chemistry	13.05.16 20:39	
Click to view Differentials		
Glucose	6.49	4 - 9.71 mmol/L
IDEXX SDMA Learn More	p 17	0 - 14 µg/dL
Creatinine	176.8	79.56 - 221 µmol/L
Urea	20.71	5.71 - 13.21 mmol/L
BUN: Creatinine Ratio	29.0	
Phosphorus	1.16	0.94 - 2.03 mmol/L
Calcium	2.54	2.05 - 2.79 mmol/L
Sodium	147	147 - 157 mmol/L
Potassium	3.9	3.7 - 5.2 mmol/L
Na: K Ratio	38	29 - 42
Chloride	116	114 - 126 mmol/L
Total Protein	66	63 - 88 g/L
Albumin	29	26 - 39 g/L
Globulin	37	30 - 59 g/L
Albumin: Globulin Ratio	0.8	0.5 - 1.2
ALT	252	27 - 158 U/L
Creatine Kinase	382	64 - 440 U/L
Haemolysis Index	q 1+	
Lipaemia Index	r N	

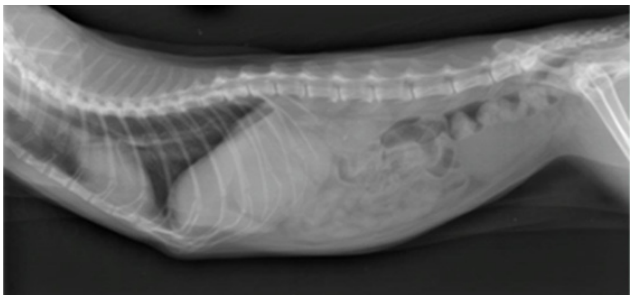
Total T_4

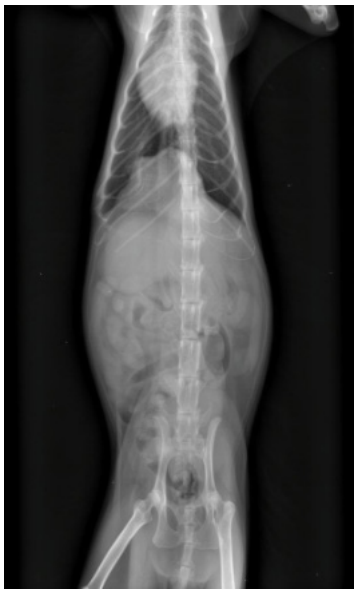
Endocrinology	13.05.16 20:39	
Click to view Differentials		
Total T4	e 19.31	10.3 - 60.49 nmol/L

Diagnostic plan

Differential diagnoses for Twinkle's clinical signs included primary gastrointestinal disease, triaditis, kidney disease, or other metabolic diseases. Her veterinarian recommended a complete blood count (CBC); chemistry panel, including the IDEXX SDMA® Test and electrolytes; complete urinalysis; and total T_4 as a first step to narrow the possible causes of her illness. Her owners also agreed to abdominal radiographs.

Abdominal radiographs:





Abnormalities were noted on her chemistry panel as well as her abdominal imaging, supporting several potential clinical conditions.

The increased ALT and AST sugged liver disease and hepatocellular damage due to inflammation or injury from diverse etiologies or metabolic disease with secondary hepatopathy. Skeletal myopathy was less likely with a normal creatinine kinase.[1] Given Twinkle's clinical signs, there was concern for pancreatitis causing inflammation, and/or cholangitis/cholangiohepatitis that could be infectious or sterile, or in combination with inflammatory bowel disease, as triaditis.

Her radiographs suggested a soft-tissue density in the right cranial quadrant, in the area of the liver. This finding is most suspicious for a right liver mass, with the most common causes being a benign lesion, a cyst, or neoplastic tissue.

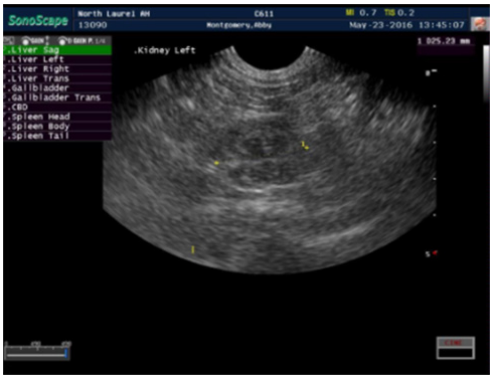
Twinkle's mildly increased SDMA* of 17 μg/dL suggested impaired glomerular filtration rate (GFR) with decline in normal kidney function. Based on her increased SDMA and urea and inappropriate urine specific gravity (USG) of 1.015, further investigation for primary or secondary effect on kidney function was warranted. The creatinine concentration may have been within normal limits and not reflective of her current kidney dysfunction due to muscle wasting. Creatinine can be falsely lowered in animals with loss of muscle mass, whereas SDMA is unaffected by changes in lean muscle mass and is often more reliable.[2,3]

Her radiographs also showed a smaller left kidney than right, with slightly irregular shape to both and probable small nephroliths in the right kidney. The inappropriate urine specific gravity and abnormal renal imaging with an increased SDMA supported primary kidney disease, though acute insult and functional worsening due to her concurrent liver disease could not be excluded.

Hyperthyroidism was unlikely based on her normal total T_4.

Further diagnostics—23th of May 2016

Twinkle's veterinarian suggested an abdominal ultrasound to investigate her suspected liver and kidney disease.



Twinkle's ultrasound revealed that she had a moderately-sized soft-tissue mass in the right lobe of her liver. It did not appear to obstruct the biliary outflow tract or to be causing substantial inflammatory reaction. Her gallbladder had moderate echogenic debris with normal wall thickness. This can be seen with cholangitis or bacterial cholangiohepatitis.[4] There were subtle changes to the pancreas. It was slightly thickened with a subtle nodular appearance and irregular margins, and there was hyperechoic (bright) peripancreatic fat, suggesting inflammation. These sonographic findings were consistent with pancreatitis.[4,5]

Both her right and left kidneys were smaller than normal and had loss of corticomedullary definition, suggesting chronic disease rather than acute injury, with no pyelectasia, reducing the likelihood of pyelonephritis.[4]

The SNAP® fPL™ Test was abnormal, and a Spec fPL® Test was indicated for quantification.

Chemistry	24/5/16 8:18 AM
SNAP fPL	Abnormal

Based on the findings, Twinkle's owners elected to treat her with antibiotics for potential bacterial infection of the liver and gallbladder, along with antiemetics for potential chronic pancreatitis. It was suggested that Twinkle return in 2 weeks for a recheck CBC and chemistry panel with the IDEXX SDMA® Test. Her owners did not wish to aggressively address the mass in her liver, rather treat potential medical conditions. Possible follow-up investigation of this mass would include repeat imaging to evaluate change, with options for fine-needle aspiration and/or biopsy.

Follow-up laboratory testing was indicated to determine if her medical care was successful and to evaluate for persistence of impaired GFR and probable kidney dysfunction. Persistent increases in SDMA in combination with other signs of kidney dysfunction (increased creatinine, inappropriate USG) often represent true decline in GFR associated with kidney disease.[6]

Twinkle completed 4 weeks of antibiotics, but she did not return for recheck laboratory testing for several months. When she was seen for recheck, her owners reported a vast improvement in her clinical signs. She was eating well and had not vomited in several weeks. On physical examination, Twinkle had regained her 450 gr of lost weight. Her owners consented to recheck CBC and chemistry panel with the IDEXX SDMA® Test.

Diagnostic review—3rd of September 2016

CBC—within reference intervals

Chemistry	03.09.16 05:17	
Glucose	8.83	4 - 9.71 mmol/L
IDEXX SDMA (Learn More)	m 20	0 - 14 µg/dL
Creatinine	194.48	79.56 - 221 µmol/L
Urea	23.2	5.71 - 13.21 mmol/L
BUN: Creatinine Ratio	29.5	
Phosphorus	1.39	0.94 - 2.03 mmol/L
Calcium	2.42	2.05 - 2.79 mmol/L
Sodium	149	147 - 157 mmol/L
Potassium	3.5	3.7 - 5.2 mmol/L
Na: K Ratio	43	29 - 42
Chloride	122	114 - 126 mmol/L
Total Protein	60	63 - 88 g/L
Albumin	26	26 - 39 g/L
Globulin	34	30 - 59 g/L
Albumin: Globulin Ratio	0.8	0.5 - 1.2
ALT	201	27 - 158 U/L
AST	76	16 - 67 U/L
ALP	16	12 - 59 U/L
GGT	<1	0 - 6 U/L
Bilirubin - Total	1.71	0 - 5.13 µmol/L
Bilirubin - Unconjugated	0	0 - 3.42 µmol/L
Bilirubin - Conjugated	n <1.71	0 - 3.42 µmol/L
Cholesterol	3.54	2.35 - 7.89 mmol/L
Amylase	1,704	623 - 2,239 U/L
Lipase	121	11 - 242 U/L
Creatine Kinase	153	64 - 440 U/L
Haemolysis Index	n N	
Lipaemia Index	o N	

Twinkle continued to have a mild increase in her liver enzyme activity, with possible slight improvement in both ALT and AST. Given their persistent increase, there was likely still ongoing liver disease, possibly associated with the mass.

Her SDMA remained increased. Twinkle's persistent increase in SDMA combined with inappropriate USG was strong evidence of ongoing impairment of GFR. In Twinkle's case, despite her normal creatinine, there was evidence of primary kidney disease: the persistent increase in SDMA and structural kidney changes. Following an initial mild increase in SDMA, with established persistence, 50% of cats will have an increased creatinine by 1 year. Given this information, it is especially important to emphasize sooner and more frequent follow-up laboratory testing to recheck renal biomarkers in cats such as Twinkle. By recognizing continued decline in kidney function earlier, consideration for appropriate management can be better instituted.[7]

Chemistry	03.09.16 05:17	13.05.16 20:39	10.08.15 20:24	26.08.14 23:52	08.07.14 12:53
IDEXX SDMA (Learn More)	20	p 17	s 12		
Creatinine	194.48	176.8	141.44	123.76	141.44

Given her persistently increased SDMA, along with a trend of increasing creatinine, inappropriate USG, and abnormal renal imaging, Twinkle was diagnosed with chronic kidney disease (CKD). The International Renal Interest Society (IRIS) CKD guidelines provide guidance on staging and treatment of CKD patients.[8] Twinkle was assessed as IRIS CKD Stage 2. Although not performed, a systolic blood pressure and urine protein:creatinine (UPC) ratio would be indicated to substage her CKD.

Based on this assessment, her veterinarian suggested an early renal therapeutic diet along with changing her antibiotic to better address any potential bacterial infection of her liver or pancreas. It was also recommended that Twinkle be rechecked in several weeks to monitor her liver function.

Further follow-up

Twinkle was assessed serially over the following months. Her liver enzyme activity was much improved, due perhaps to a decline in liver injury or inflammation, as a response to antibiotics, or other change. Her kidney values continued to progressively increase, and she was azotemic (creatinine increased) on recheck several months later. With appropriate kidney diet and phosphate management, she maintained relatively stable IRIS CKD Stage 2 disease for several months.

Chemistry	06.01.17 20:42	11.12.16 05:46	03.09.16 05:17	13.05.16 20:39
IDEXX SDMA (Learn More)	g 17	j 22	m 20	p 17
Creatinine	229.84	256.36	194.48	176.8
Urea	20.35	33.56	23.2	20.71
BUN: Creatinine Ratio	21.9	32.4	29.5	29.0
Phosphorus	0.77	2.84	1.39	1.16
Calcium	2.84	2.59	2.42	2.54
Sodium	154	157	149	147
Potassium	4.9	4.3	3.5	3.9
Na: K Ratio	31	37	43	38
Chloride	117	120	122	116
Total Protein	65	69	60	66
Albumin	29	31	26	29
Globulin	36	38	34	37

Diagnostic review

Twinkle's case emphasizes the importance of recognizing persistent increases of SDMA and understanding the clinical implications. It also emphasizes the importance of determining whether decline in GFR is due to a primary or secondary kidney insult. Twinkle's story began with a mildly increased SDMA (15–19 µg/dL), which was repeatably increased (17 µg/dL and 20 µg/dL). While these increases are subtle, heightened awareness of what a repeated abnormal result might indicate is very important. Concentrations of SDMA between 15–19 µg/dL are shown to often be persistent in feline patients.[9] Establishing persistence of SDMA increases is extremely important as some patients in this population continue to have stable kidney disease while others will develop progressive kidney disease. Of those patients where persistence can be identified and SDMA remains abnormal, approximately 50% will have an increased creatinine by one year.[8] Twinkle is an example of a cat who initially had stable kidney disease, which then showed moderate progression within in the 7 months. Appropriate follow-up testing helped recognize this now progressive disease, which was first indicated biochemically by only a mild persistent increase in SDMA.

It is important to use SDMA, together with other indicators of kidney dysfunction, to help support a diagnosis. In Twinkle's case, urinalysis and abdominal imaging were helpful to confirm primary kidney disease. Biomarkers, such as creatinine and urea, continue to be important complementary diagnostic tools. In Twinkle's case, SDMA was the first and most consistent biochemical marker of progressive kidney disease. It allowed her veterinarian to recognize the need for further diagnostics (imaging), monitoring, and treatment for her kidney disease, concurrent with her other illness. Without SDMA, Twinkle might have waited 6 months or more to have impaired GFR from kidney disease diagnosed and proper management instituted.

*Symmetric dimethylarginine.

References

1. Stockham SL, Scott MA. *Fundamentals of Veterinary Clinical Pathology*. 2nd ed. Ames, IA: Blackwell; 2008.
2. Hall JA, Yerramilli M, Obare E, Yerramilli M, Yu S, Jewell DE. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in healthy geriatric cats fed reduced protein foods enriched with fish oil, L-carnitine, and medium-chain triglycerides. *Vet J*. 2014;202(3):588–596. doi:10.1016/j.tvjl.2014.10.021
3. Hall JA, Yerramilli M, Obare E, Yerramilli M, Melendez LD, Jewell DE. Relationship between lean body mass and serum renal biomarkers in healthy dogs. *J Vet Intern Med*. 2015;29(3):808–814. doi:10.1111/jvim.12607
4. Thrall DE. *Textbook of Veterinary Diagnostic Radiology*. 7th ed. St Louis, MO: Elsevier; 2018
5. Williams JM, Panciera DL, Larson MM, Werre SR. Ultrasonographic findings of the pancreas in cats with elevated serum pancreatic lipase immunoreactivity. J Vet Intern Med. 2013;27(4):913–918. doi:10.1111/jvim.12117
6. International Renal Interest Society. IRIS CKD Staging Guidelines (modified 2019). www.iris-kidney.com/guidelines. Accessed May 20, 2020.
7. Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA.
8. Mack-Gertig R, Hegarty E, McCrann DJ. Agreement of renal biomarkers: Longitudinal evaluations of increased SDMA and creatinine in cats and dogs [ACVIM Abstract NU10]. Paper presented at: 2020 American College of Veterinary Internal Medicine Forum; 2020.
9. Mack-Gertig R, Hegarty E, McCrann DJ. The probability of persistence of an increased SDMA in cats and dogs [ACVIM Abstract NU07]. Paper presented at: American College of Veterinary Internal Medicine; 2020.