Anuric Renal & Hepatic Failure in a Dog

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Betsy, a 5-year-old spayed boxer, was presented for a 2-day history of vomiting, anorexia, and azotemia.

History & Examination

Betsy appeared dull and depressed but responsive. Mucous membranes were hyperemic, and capillary refill time was <1 second. Clinical dehydration was not detected. BCS was 5/9 with mild abdominal distension. Mild hypothermia (98.6ºF [37ºC]) was present, but heart and respiratory rates were normal. Severe generalized abdominal pain and ptyalism were noted.

Betsy was up-to-date on core vaccinations. More than a year before presentation, leptospirosis vaccination with serovars Canicola, Icterohaemorrhagiae, Pomona, and Grippotyphosa had been administered. Betsy received monthly heartworm and topical flea preventives but no other medications. She had access to several acres of wooded property and had suffered superficial skin wounds from a raccoon a week before presentation. Although a rabies booster was indicated, it was not administered. Betsy was hospitalized and treated with IV fluids and maropitant (1 mg/kg SC once a day), as well as enrofloxacin (5 mg/kg IV once a day) and ampicillin

BCS = body condition score

CBC = complete blood count

(20 mg/kg IM 3 times a day) for presumptive infection, but no improvement was seen. Abdominal distention developed, and Betsy was referred for specialty care. The referring veterinarian observed that Betsy did not urinate overnight despite receiving fluid therapy.

Diagnostic Results

CBC was unremarkable, but serum chemistry profile identified several abnormalities (***Table 1***). Urinalysis revealed trace glucosuria, 1+ proteinuria, and a urine specific gravity of 1.026. A urine culture yielded no bacterial growth. Baseline ammonia was significantly elevated. Severe hypertension was present (240 mm Hg systolic Doppler) despite administration of hydromorphone. Fundic examination was normal, and no evidence of uveitis was noted. Thoracic radiography revealed a diffuse, unstructured interstitial pattern, generalized mild bronchial pattern, and mild pleural effusion.

Abdominal ultrasonography revealed a small urinary bladder, bilateral hyperechoic renal cortices, ascites, and a hyperechoic pancreas. A SNAP (idexx.com) cPL (canine pancreas-specific lipase) was abnormal. Abdominocentesis yielded a pure transudate with fluid potassium (4.16 mEq/L) and creatinine (6.0 mg/dL) values equal to serum chemistry values. A urinary catheter was placed, but no urine was obtained despite administration of 5 L of IV fluids over the previous 24 hours. Leptospirosis titers were submitted.

TABLE 1

SIGNIFICANT LABORATORY RESULTS

Diagnostic Test	Result	Reference Range
BUN (mg/dL)	107	8-24
Creatinine (mg/dL)	5.6	0.5-1.4
Potassium (mEq/L)	4.0	3.5-5.5
Alanine aminotransferase (U/L)	116	10-90
Alkaline phosphatase (U/L)	727	11-140
Bilirubin (mg/dL)	4.4	0.2-0.6
Albumin (g/dL)	2.0	2.5-3.9
Cholesterol (mg/dL)	124	140-360
Ammonia (µg/dL)	128	1.7-5.1
Urine specific gravity	1.026	1.001-1.070
Urine glucose	Trace	Negative
Urine protein	1+	Negative
Abdominal fluid protein (g/dL)	1	Pure transudate (<2.5)
Abdominal fluid cells (/µL)	<1000	Pure transudate (<1500)
Abdominal fluid creatinine (mg/dL)	6.0	Abdominal fluid creatinine:serum creatinine <2.0
Abdominal fluid potassium (mEq/L)	4.16	Abdominal fluid potassium:serum potassium <1.4

Abdominal ultrasonography revealed a small urinary bladder, bilateral hyperechoic renal cortices, ascites, and a hyperechoic pancreas.

ASK YOURSELF

QUESTION 1
What are the treatment options to improve urine output in oliguric or anuric renal failure?

QUESTION 2
What are the most common diagnostic differentials for hypertension in dogs?

QUESTION 3
Which diagnostic test(s) is(are) recommended for canine leptospirosis?

QUESTION 4
How long after recovery from leptospirosis should vaccination occur?

Diagnosis

Acute renal failure and liver failure due to presumptive leptospirosis

Treatment & Outcome

Betsy was hospitalized for 14 days with IV fluid therapy to match intake and output and to resolve azotemia. Fluid overload, anuria, and hypertension resolved 6 hours after the start of treatment. A furosemide constant rate infusion (CRI; 1 mg/kg/hr) was necessary for the first 24 hours to maintain normal urine output. Treatment for leptospirosis was initiated with ampicillin–sulbactam, although ampicillin alone is the recommended leptospirosis treatment. IV antibiotics were continued until the patient ate well, at which time doxycycline (5 mg/kg PO twice a day) was administered for 3 weeks. Supportive care was also provided (***Table 2***). Betsy was discharged after 14 days of hospitalization with oral doxycycline, *S*-adenosylmethionine (SAMe) + silybin

TABLE 2

TREATMENT AT A GLANCE

Drug (Dosage)	Indication
Ampicillin–sulbactam (30 mg/kg IV 3 times a day)*	Leptospiremia in anorexic patient
Doxycycline (5 mg/kg PO twice a day)	Leptospiremia, leptospiruria
Furosemide (2 mg/kg IV bolus, then 1 mg/kg/hr CRI)*	Fluid overload, anuria
Maropitant (1 mg/kg SC once a day)*	Nausea, vomiting
Ondansetron (0.2-1 mg/kg IV 3 times a day)*	Nausea, vomiting
Omeprazole (1 mg/kg PO twice a day)*	Antacid, uremic gastritis
Famotidine (0.5-1 mg/kg PO once or twice a day)	Antacid, uremic gastritis
Aluminum hydroxide (30-100 mg/kg/day PO, divided with meals)	Hyperphosphatemia
S-adenosylmethionine (SAMe) + silybin (20 mg/kg PO once a day)	Glutathione precursor
N-acetylcysteine (140-180 mg/kg IV [diluted to 5%] over 20 min, followed by 70 mg/kg IV or PO every 6 hours for a minimum of 7 treatments)*	Glutathione precursor
Vitamin E (12 units/kg PO once a day)*	Antioxidant **Caution:** May exacerbate a vitamin K-dependent coagulopathy, especially with high doses of vitamin E
Vitamin K (1 mg/kg SC twice a day)*	Coagulopathy associated with liver failure

*Treatment administered in-hospital only

(20 mg/kg PO once a day), famotidine (0.5 mg/kg PO twice a day), and aluminum hydroxide (100 mg/kg PO divided daily with meals). Mild azotemia and mild hyperphosphatemia persisted at discharge. Initial leptospirosis titers were *Leptospira interrogans* serovar Grippotyphosa (1:100), *L interrogans* serovar Bratislava (1:400), and *L interrogans* serovar Autumnalis (1:100). Three weeks later, convalescent titers revealed an 8-fold rise in *L interrogans* serovar Grippotyphosa titers (1:800). Recheck bloodwork at 1 and 3 months was normal.

Discussion

Leptospirosis is a worldwide zoonotic disease.[1] Acute renal failure with or without acute hepatic failure commonly develops. Pancreatitis, disseminated intravascular coagulation, hepatic failure (without renal involvement), and pulmonary hemorrhage syndrome have also been documented.[1]

Leptospirosis is seen most commonly in late fall and after periods of heavy rainfall.[2] Organisms are shed in the urine of reservoir hosts (eg, raccoons, rodents) and transmitted through contact of mucous membranes or broken skin with contaminated water or soil—where the organism can survive for extended periods—or directly through ingestion of infected tissues.[2] The incubation period is ≈1 week, and leptospiremia is present for 3 to 4 days before the organisms reach the renal tubules, where they are shed in the urine.[2] Doxycycline is the treatment of choice and should be initiated as soon as oral therapy is tolerated to resolve urine shedding and decrease the risk to humans.[2] Penicillins are effective at clearing leptospiremia and can be used until doxycycline is tolerated; however, they do not clear the carrier state.[2]

Treatment with doxycycline is recommended for 2 to 3 weeks, and prognosis can be fair at 50% to 80% survival.[2] Complete renal recovery may take 3 to 4 weeks, and residual renal damage may persist.[2]

CRI = constant rate infusion
SAMe = *S*-adenosylmethionine

DID YOU ANSWER?

QUESTION 1

What are the treatment options to improve urine output in oliguric or anuric renal failure?

Once the patient is hydrated, urine production should increase depending on IV fluid rates. However, oliguria (ie, urine production <0.5 mL/kg/hr) or anuria (ie, no urine production) may develop in acute renal failure.[3] Pharmacologic therapy to increase urine output and safely continue fluid therapy includes diuretics, mannitol, fenoldopam, and diltiazem (***Table 3***).[3] Furosemide should be attempted first at 2 mg/kg IV bolus; if it is successful, a CRI is recommended.[3] If furosemide is unsuccessful, mannitol 20% (0.5-1 g/kg IV bolus every 4-6 hours then 1-2 mg/kg/min CRI) may be attempted if the patient is adequately hydrated. Doses higher than 2 to 4 g/kg/day should be avoided because of risk for acute kidney injury.[3] Fenoldopam, a selective dopamine agonist, is used in humans, but its use in veterinary medicine has not been associated with improved survival or urine output.[4] Diltiazem has been shown to improve urine output in dogs with leptospirosis.[3] If medical therapy fails to achieve diuresis, referral for renal replacement therapy should be discussed.

TABLE 3

TREATMENT OPTIONS FOR ANURIA & OLIGURIA

Drug	Dose
Furosemide	0.66 mg/kg IV bolus, then 0.66 mg/kg/hr CRI OR 0.5-1 mg/kg/hr CRI OR 2 mg/kg IV bolus, increasing to 4-6 mg/kg IV hourly until diuresis
Mannitol 20%	0.5-1 g/kg IV bolus slowly every 4-6 hrs then 1-2 mg/kg/min CRI OR Repeat 0.25-0.5 g/kg bolus every 4-6 hrs
Fenoldopam	0.8 µg/kg/min CRI
Diltiazem	0.1-0.5 mg/kg IV slowly then 1-5 µg/kg/min CRI

NOTABLE *LEPTOSPIRA INTERROGANS* SEROVARS

- Canicola
- Icterohaemorrhagiae
- Bratislava
- Grippotyphosa
- Autumnalis
- Pomona
- Hardjo

MAT = microscopic agglutination test

PCR = polymerase chain reaction

QUESTION 2

What are the most common diagnostic differentials for hypertension in dogs?

The most common diagnostic differentials for hypertension in dogs include renal disease, hyperadrenocorticism, fear and anxiety, pain, and diabetes mellitus.[5] Less common causes of canine hypertension include acromegaly, primary hyperaldosteronism, pheochromocytoma, congestive heart failure, hypothyroidism, obesity, fluid overload, and side effects from medications such as phenylpropanolamine.[5] Arterial hypertension is especially common in acute kidney failure and may further worsen renal function by inducing glomerular damage.[5]

QUESTION 3

Which diagnostic test(s) is(are) recommended for canine leptospirosis?

The current standard for diagnosis of leptospirosis is serology using the microscopic agglutination test (MAT), in which serial dilutions of the patient's serum are mixed with live organisms of different serovars (see ***Notable* Leptospira interrogans *Serovars***). Antibody titer is reported as the highest dilution to cause agglutination of the organisms using darkfield microscopy.[2] Vaccination can cause a rise in antibody titer, which may persist for months. A 4-fold or greater rise with convalescent titers to 1 or more serovars (2-4 weeks after initial titer) is required for diagnosis.[2] Significant cross reaction occurs among serovars, and titers may not accurately identify the true infecting serovar.[2] Whole blood polymerase chain reaction (PCR) may be useful for early diagnosis when antibodies are not present during the 3-to-4-day leptospiremic phase.[2,6] After the leptospiremic phase, urine PCR may be used.[2,6] Vaccinations do not cause a false-positive PCR result.[6] False negatives may occur with both MAT and PCR testing, especially if they are performed after starting antibiotics.[2,6] An enzyme-linked immunosorbent assay (ELISA) was not performed on Betsy because it was not available at the time.

QUESTION 4

How long after recovery from leptospirosis should vaccination occur?

It is unknown if lifelong immunity occurs after infection, and dogs that recover are likely to be continuously exposed to the organism if continuously exposed to the same environment.[2] Therefore, vaccination is recommended 1 year after recovery, followed by continued annual revaccination.[2]

References

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