Casting Light on a Young Labrador's Illness

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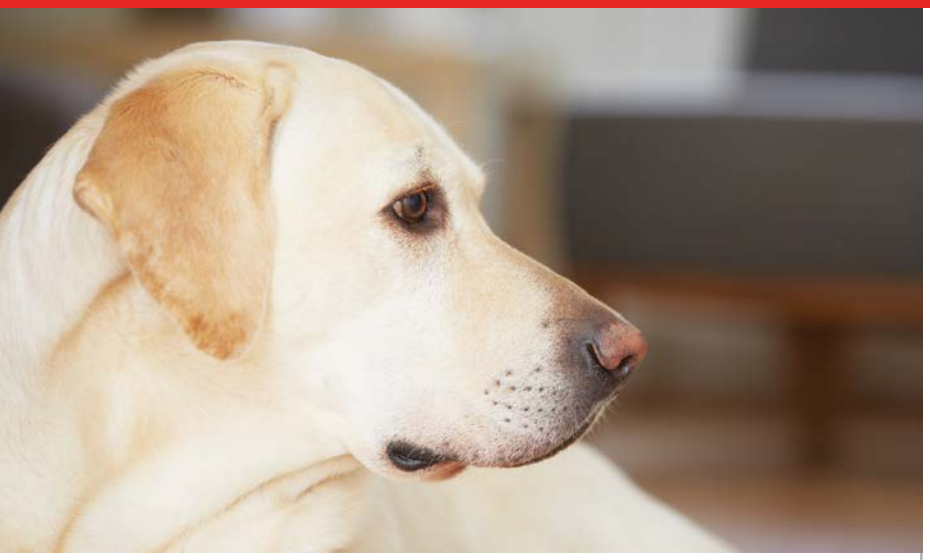


A previously healthy, 1-year-old spayed Labrador retriever was presented with a 1-month history of mild, intermittent lethargy and acute onset of vomiting and anorexia.

History & Examination

The owners reported that, before the onset of illness, the dog had an appropriate level of energy and spent a large amount of time outdoors.

The dog was bright, alert, and responsive. Body condition score was 3/5. Abdominal palpation elicited apparent pain, which was difficult to localize.

Diagnostic Findings

CBC showed mild, nonregenerative anemia and leukocytosis. An inflammatory leukogram was noted, with mild neutrophilia with left shift and monocytosis. Additional laboratory results are shown in ***Tables 1*** and ***2***; examination of urine sediment disclosed further findings (***Figures 1*** and ***2***, page 61).

ASK YOURSELF

- What 2 types of tubular structures (***Figures 1*** and ***2***, page 61) are present in the urine sediment?
- What is the clinical significance of each type?
- Which additional diagnostic tests are indicated in this patient?

TABLE 1

SERUM CHEMISTRY ANALYSIS

Parameter	Result	Reference Interval
ALBUMIN	2.4 g/dL	2.9–3.8
PHOSPHORUS	11.3 mg/dL	2.7–5.6
CREATININE	9.5 mg/dL	0.6–1.7
BUN	122 mg/dL	8–25

TABLE 2

URINALYSIS ON A FREE-CATCH SAMPLE

Parameter	Results	Reference Interval or Value
COLOR	Colorless	Yellow to amber
CLARITY	Clear	Clear or slight haze
SPECIFIC GRAVITY	1.008	Usual: 1.015–1.045* Range: 1.001–>1.075*
pH	6.0	5.5–7.5
PROTEIN, DIPSTICK	1+	Negative to trace, depending on specific gravity
GLUCOSE	Negative	Negative
KETONES	Negative	Negative
BILIRUBIN	Negative	Negative to 1+, depending on species and specific gravity
HEMOPROTEIN	Negative	Negative
HYALINE OR GRANULAR CASTS	1–3/lpf	0–1/lpf
EPITHELIAL CELLS	0–2/lpf	0–5/lpf
WBC	0–3/hpf	0–3/hpf
RBC	Rare	0–5/hpf
BACTERIA	None	Depends on collection method
CRYSTALS	None	Depends on type of crystal

hpf = high power field (40× objective), lpf = low power field (10× objective)

*Must be interpreted in context of hydration status, BUN, and creatinine levels.

Sediment Cytology Interpretation

The structures present in the sediment are renal tubular casts. The presence of casts in urine is called *cylindruria*. A low number of hyaline or granular casts (0 to 1/lpf) may be normal in urine sediment. However, when increased numbers are seen with an abnormally low urine specific gravity, as in this patient, renal tubular damage is probable.

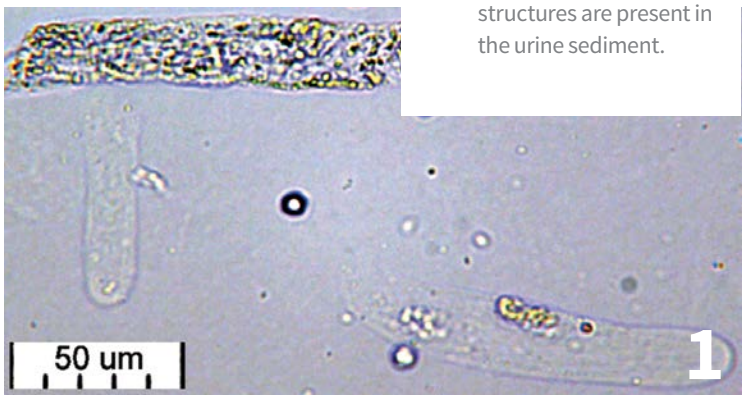
Cylindruria is not a sensitive marker of renal disease and may not be present even in cases of severe renal injury. However, this finding is markedly specific to renal tubular injury, as the structures are casts formed as a mold of the renal tubular lumen. Renal tubular injury may be associated with increased urine sediment casts, but the number of casts does not indicate the potential reversibility or prognosis of the disease[1] as renal tubular epithelium is capable of regeneration. Hyaline casts and granular casts are present in ***Figures 1*** and ***2***. Hyaline casts are at the bottom of ***Figure 1*** and left of ***Figure 2***. Granular casts are present at the top of ***Figure 1*** and the right of ***Figure 2***.

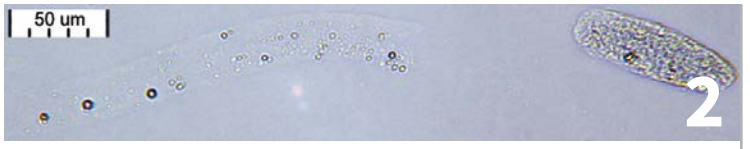
Hyaline casts (***Figure 3***) contain protein and are typically comprised of Tamm-Horsfall mucoprotein, which is produced continuously by renal tubular cells and accumulates in the distal nephron. Other pathologic causes of proteinuria, such as prerenal hyperproteinemia or renal proteinuria (eg, hyperglobulinemia associated with lymphoid neoplasia or glomerulonephritis), may also contribute to hyaline cast formation.

Hyaline casts are homogenous, colorless, and transparent and have parallel walls with rounded ends.[2] They may be difficult to see because of their low refractive index and are sometimes confused with mucus. Unlike casts, mucus threads (***Figures 4*** and ***5***) have tapered ends and often have twisted borders.

A low number (0 to 1/lpf) of hyaline casts may

▼ Unstained wet mount, 20× objective. Three tubular structures are present in the urine sediment.





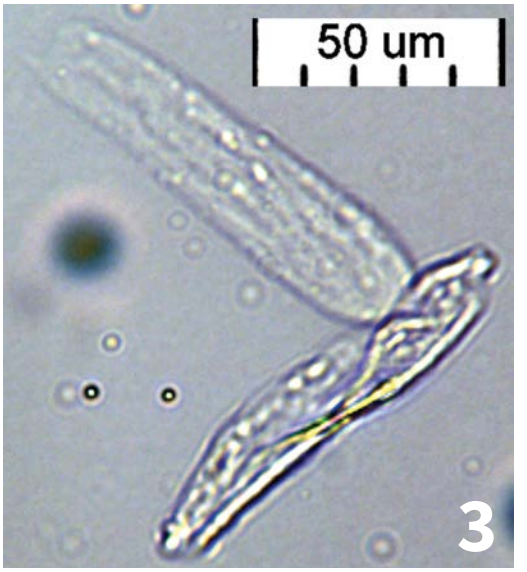
▲ Unstained wet mount, 20× objective. Two tubular structures are present in the urine sediment.

be found in the urine of normal patients. An increased number may be associated with prerenal or renal proteinuria. The cause for increased hyaline casts in this case is renal proteinuria.

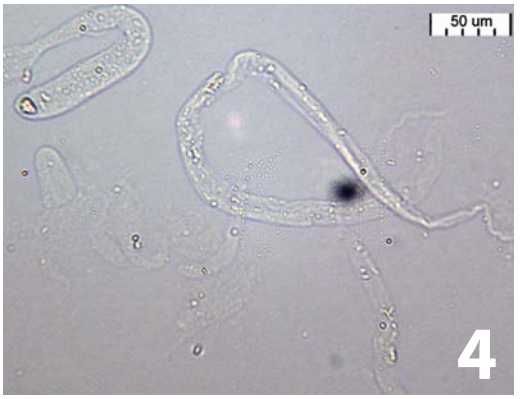
Intact cells are added to mucoprotein within renal tubules because of normal turnover or pathologic cell death caused by inflammation, ischemia, toxic insult, or other causes. Casts with recognizable cells (cellular casts) are seen in urine sediment if such a cast flows from the tubular lumen before sufficient time has passed for the cells to degrade into granular material.

Cells trapped within mucoprotein transform from intact cells to the intermediate granular material, and, finally, to cholesterol remnants of cell membranes. Waxy casts comprise these cholesterol remnants and signify chronic renal tubular damage.

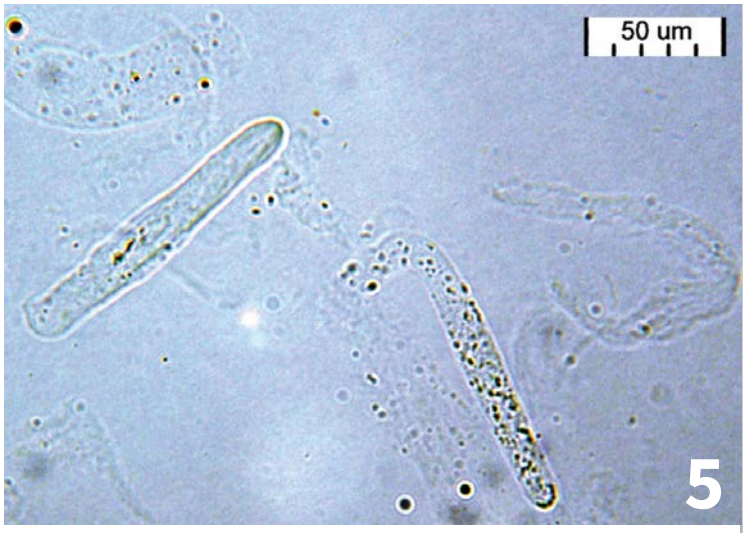
Granular casts contain Tamm-Horsfall mucoprotein and entrapped degraded cells, which create the granular appearance. These casts typically have parallel walls and rounded ends. A low number of granular casts (0 to 1/lpf) can



▲ Unstained wet mount, 20× objective. A hyaline cast (**top**) surrounded by many lipid droplets. Note the uniformly parallel walls and rounded ends. The cast is adjacent to a fiber (**bottom**). Fibers are distinguished from casts by their non-uniform width, angular termini, and higher refractivity.



▲ Unstained wet mount, 20× objective. Numerous mucus strands are present. In contrast with the hyaline casts, there is greater variation in width of the mucus strands. The mucus strands are twisted with tapered ends.



▲ Unstained wet mount, 20× objective. Two hyaline casts are surrounded by mucus strands. Note the rounded ends and parallel walls of the casts.

be routinely seen because of normal tubular epithelial cell turnover; increased granular casts suggest renal tubular injury (***Figures 6*** and ***7***). In this case, *Leptospira* spp infection caused tubular damage and cylindruria characterized by increased hyaline and granular casts.

Diagnosis & Interpretation

Acute Kidney Injury

Leptospirosis is a zoonotic disease of worldwide significance caused by bacteria in the genus *Leptospira*. Leptospires are thin, motile spirochetes that infect a variety of domestic and wildlife hosts. More than 250 antigenically distinct subtypes, called *serovars*, have been identified.[3-5] The infecting serovars are within the species *Leptospira interrogans* and *Leptospira kirschneri*, the 2 species pathogenic to dogs. Infecting serovars depend on geographic location and potential for exposure to reservoir hosts, and those known or suspected to cause disease in dogs in the United States include *L icterohaemorrhagiae, L canicola, L pomona, L grippotyphosa*, and *L bratislava*.[5]

Transmission of leptospires may occur directly but is more likely to occur indirectly from exposure to infected water, soil, or food. Spirochetes may survive for months in moist environments. Increased transmission rates may be seen seasonally or with rainfall, depending on geographic region.[3,4]

Leptospires can penetrate intact mucous membranes of the mouth, nose, or eyes, as well as abraded or water-softened skin. Replication occurs in the vasculature followed by spread to multiple other tissues.[3]

Clinical presentation is variable. Some dogs display mild or no clinical signs; others show signs of severe illness, often as a result of renal injury. Leptospirosis should be considered in dogs with renal or hepatic failure, uveitis, pulmonary hemorrhage, acute febrile illness, or abortion.[5]

Clinical Findings & Diagnosis

Acute kidney injury was supported by the concurrent findings of acute vomiting, anorexia, and renal pain in a previously healthy patient with abnormalities on serum chemistry analysis and urinalysis that were consistent with renal dysfunction (ie, marked azotemia, hyperphosphatemia, isosthenuria, proteinuria, cylindruria).

Leptospira spp antibody titer panel showed a markedly high reciprocal titer (>6400) against *Leptospira* serovar *grippotyphosa* along with consistent clinical findings. Typically, acute and convalescent titers are drawn 1 to 2 weeks apart and are used for diagnosis; a single titer may be low or undetectable early in infection, and previous exposure or vaccination may cause a high initial titer. Although a second

titer was not run in this case for confirmation, the diagnostic test results in conjunction with the clinical presentation were strongly suggestive of a diagnosis of leptospirosis, and the patient was managed as such.

A 4-fold change is considered diagnostic for acute infection, although antibiotic administration may blunt the detected response.[5] PCR and specialized culture are alternatives for confirmation of the diagnosis. Additional diagnostic test results in this case included mild pyelectasia and perirenal effusion on abnormal ultrasonography and negative routine urine culture.

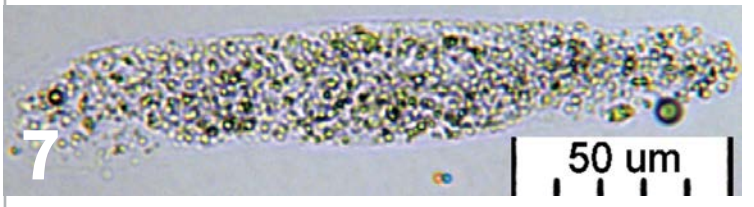
The patient's renal pain, inflammatory leukogram, and mild non-regenerative anemia were explained by leptospirosis and associated inflammation. The mild thrombocytopenia was likely due to vasculitis, which occurs in the majority of affected dogs.[5]

Azotemia is frequently present in dogs with leptospirosis. The mild hypoalbuminemia was likely caused by albuminuria. Additionally, with active inflammation, albumin may decrease as it is a negative acute phase protein—a protein that decreases in concentration when inflammation is present.

Other biochemical abnormalities that may be associated with leptospirosis include elevated liver enzymes and electrolyte abnormalities. Urinalysis findings seen in this case (isosthenuria, proteinuria, and cylindruria) have also been associated with leptospirosis. This patient's urine protein to creatinine ratio ranged from less than 0.5 to 1.5 (reference, <0.5) during hospitalization.

Hyposthenuria, glucosuria, bilirubinuria, hematuria, and pyuria are additional potential findings.[5]

▼ Unstained wet mount, 20× objective. A granular cast with parallel walls, rounded ends, and internal granular appearance is present with a single calcium oxalate dihydrate crystal (**left**).



▲ Unstained wet mount, 20× objective. A granular cast with parallel walls, rounded ends, and internal granular appearance is present.

Treatment & Follow Up

Treatment is aimed at clearance of the spirochetes from the kidney. If the patient is able to tolerate doxycycline orally or if injectable doxycycline is available, the drug should be administered at 5 mg/kg q12h for 14 days. IV ampicillin may be administered at 20 mg/kg q6h until the patient can tolerate oral doxycycline, at which time, doxycycline should be administered at 5 mg/kg q12h for 14 days.

Concurrently, renal support, including IV fluid therapy or dialysis, is required in most cases.[3]

Additional support for secondary GI signs and correction of electrolyte abnormalities may be necessary in some cases. In this patient, antibiotics (including doxycycline) and IV fluids were administered promptly and continued through the patient's nearly 2-week hospitalization. Two hemodialysis treatments were administered.

Initial supportive care included administration of enteral fluid through an esophageal feeding tube and oral aluminum hydroxide as a phosphate binder. The hyperphosphatemia resolved, and the patient was discharged. Mild persistent azotemia was noted, but no clinical abnormalities were present. The patient was monitored by its regular veterinarian.

Clinical findings were identified in this patient that are frequently associated with leptospirosis, including the presence of tubular casts as a marker of renal tubular injury. Although kidney injury in this case was obvious based on multiple clinical findings, some cases of early tubular injury may be identified using cylindruria as a marker that precedes azotemia.

DID YOU ANSWER?

- Hyaline and granular renal tubular casts.
- Hyaline casts may be seen in high numbers with causes of increased prerenal or renal proteinuria. Granular casts may be seen with renal tubular epithelial cell damage. A low number (0 to 1/lpf) of either may not be clinically significant.
- Tests for diagnosis of leptospirosis (ie, titers, PCR, culture), urine culture, determination of urine protein to creatinine ratio, and imaging.

Additional information about proper precautions can be found at **cliniciansbrief.com/column/clinic-forms/leptospirosis-protecting-your-patients-staff**.

It is important to note that leptospirosis is a zoonotic disease, and proper precautions must be maintained within the hospital and once the patient is discharged for at least 2 weeks after initiation of antimicrobial treatment. Client and team education is critical to ensure the safety of in-contact humans and other animals.

References

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