Protein-Losing Nephropathy & Lameness in a Dog

A 6-year-old, intact male mixed-breed dog presented for left forelimb lameness, malaise, and fever.

**History.** There was no history of illness or trauma, but the dog was lethargic and reluctant to engage in normal activities. He was current on immunizations against rabies, distemper/hepatitis/parvovirus, and leptospirosis. Upon presentation, he was eating less than normal, but was not vomiting or exhibiting polyuria/polydipsia.

**Physical Examination.** The dog was quiet but alert and hydrated. He had an elevated rectal temperature of 103.6°F. Notable findings included non-weight-bearing lameness of the left forelimb. No crepitus or effusions were found during palpation of the joints and spinal hyperpathia was not elicited. The dog’s central and peripheral nervous systems were intact based upon a complete neurologic examination.

**Initial Diagnostics.** Blood analysis revealed Lyme C6 peptide antibodies (SNAP 4Dx Test; IDEXX Laboratories, Inc, www.idexx.com), moderate azotemia, hypoalbuminemia, hyperphosphatemia, and hyperglobulinemia. Routine urinalysis collected via catheterization showed 3+ proteinuria with a specific gravity of 1.012. The dog also had a blood pressure of 260 mmHg as measured by a Doppler unit.

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**ASK YOURSELF...**
- What are some possible causes of the clinical signs in this dog?
- What are other important clinico-pathologic parameters to consider in a sick and lame dog?
**Diagnosis:** Renal failure with suspected glomerulonephritis associated with borreliosis, also known as Lyme nephritis

**Further Diagnostics.** The pet was hospitalized for further diagnostics and treatment. An abdominal ultrasound was unremarkable, but urine protein:creatinine ratio was elevated (see Table). A urine culture was negative.

**Treatment.** The dog was started on antibiotics (doxycycline, 10 mg/kg Q 24 H), antihypertensives (amlodipine, 0.25 mg/kg divided Q 12 H; enalapril, 0.5 mg/kg Q 24 H), an antacid (famotidine, 0.5 mg/kg Q 24 H), and pain medication (tramadol, 2 mg/kg Q 12 H).

In this case, amlodipine was specifically added to reduce systemic hypertension and enalapril was administered to decrease peripheral vascular resistance and reduce proteinuria by efferent glomerular vasodilation. Famotidine, an H₂-antagonist, was administered to reduce gastric acid production.

After 24 hours, the dog also received hydralazine (one dose, 0.5 mg/kg IV) due to worsening hypertension (> 300 mmHg). Blood pressure normalized overnight, and the dog was released from the hospital on doxycycline, enalapril, amlodipine, Pepcid AC, and low-dose aspirin (0.5 mg/kg Q 24 H). He began eating a high-quality/low-protein diet, initiated to delay ongoing renal damage.

**Outcome.** Subsequent evaluations of renal values showed consistently marked azotemia (see Table). Clinically, the patient became progressively more lethargic over the following month and anorectic despite services provided by a nutrition expert; his left forelimb lameness progressed and he developed palpable carpal effusion. Cytological analysis and culture of joint fluid showed marked sterile suppurative inflammation. The pathologist’s interpretation was consistent with an immune-mediated process or tick-borne arthropathy. The patient was euthanized due to a guarded to poor prognosis associated with a protein-losing nephropathy with renal failure.

**The Disease.** Lyme disease is caused by the spirochete *Borrelia burgdorferi* and is transmitted by the *Ixodes* species of tick (eg, black legged or deer tick). The organism is associated with several clinical manifestations in dogs, but in general, it is estimated that 95% of seropositive dogs in endemic areas do not have clinical signs. A protein-losing nephropathy (PLN) in a dog with azotemia and that is seropositive for *B burgdorferi* could represent a potentially fatal kidney disease referred to as Lyme nephritis or Lyme nephropathy. In general, detection of *B burgdorferi* spirochetes during the clinical phase of illness would be considered the “gold standard” test for Lyme disease. However, since *Borrelia* spirochetes are rarely found by PCR techniques or cultured from blood, urine, joints, cerebrospinal fluid, or kidneys, testing in dogs focuses upon antibody detection. It is also

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**Diagnostic Testing**

<table>
<thead>
<tr>
<th>Variable</th>
<th>(7/15) Result 1</th>
<th>(7/26) Result 2</th>
<th>(8/07) Result 3</th>
<th>Reference Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood urea nitrogen (mg/dl)</td>
<td>99</td>
<td>83</td>
<td>120</td>
<td>6-25</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>3.0</td>
<td>2.7</td>
<td>3.9</td>
<td>0.5-1.6</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>2.3</td>
<td>2.3</td>
<td>2.1</td>
<td>2.7-4.4</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
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<td>7.1</td>
<td>9.3</td>
<td>2.5-6.0</td>
</tr>
<tr>
<td>Globulin (g/dl)</td>
<td>4.6</td>
<td>3.9</td>
<td>3.6</td>
<td>1.6-3.6</td>
</tr>
<tr>
<td>Urine specific gravity</td>
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<td></td>
<td></td>
<td>1.015-1.050</td>
</tr>
<tr>
<td>Urine red blood cells (per hpf)</td>
<td>51-100</td>
<td></td>
<td></td>
<td>0-3</td>
</tr>
<tr>
<td>Urine protein:creatinine ratio</td>
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<td></td>
<td></td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>Urine culture</td>
<td>Neg</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Lyme C₆ antibody</td>
<td>Pos</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

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**DID YOU ANSWER. . .**

- The source of lameness was not localized upon initial exam. Differentials for joint disease include immune-mediated arthritis, degenerative joint disease, systemic lupus erythematosus, rheumatoid arthritis, septic arthritis, and synovial neoplasia. Other important considerations would be neck pain (root signature), a bony tumor, osteomyelitis, trauma, or polymyositis.
- Important initial clinicopathologic parameters in a lethargic, febrile, and lame dog include Lyme C₆ antibody status; serum BUN/creatinine, albumin, and phosphorus; urine screening for concentration, protein, or blood; and systemic blood pressure. If renal involvement is confirmed, then a full chemistry panel, complete blood count, urine culture, urine protein:creatinine ratio, and comprehensive “tick” (including *Ehrlichia canis* and *Anaplasma phagocytophilum* antibody tests) and leptospirosis serology are often indicated. Abdominal ultrasound and/or thoracic radiographs rule out concurrent disease and other causes of fever and lethargy.
not clear what role the organism plays in producing renal disease since Koch’s postulates for Lyme nephritis in dogs has yet to be established. In fact, one study has shown that out of 40 dogs with unique immune-mediated membranoproliferative glomerular lesions perceived to be associated with borreliosis, only two had spirochetes in their kidneys upon necropsy.

**Diagnosis.** Traditionally, whole-cell antibody testing or Western blot analysis have shown differences between vaccine-induced antibodies and natural exposure, but these tests have limitations in predicting if a dog is in a carrier, acute, or chronic phase of infection.

In-house screening tests (ie, SNAP 4Dx Test) now detect antibodies against the synthetic C₆ peptide, a protein derived from the VlsE outer-surface protein. This protein is highly specific for exposure to *B burgdorferi* and does not cross react with antibodies created by currently available Lyme vaccines.

*C₆* peptide antibodies are detectable as early as 3 weeks after exposure. As laboratory testing has shown that clinical signs associated with Lyme disease in dogs may occur 2 to 5 months after experimental infection, further investigation is warranted to determine whether or not acute and convalescent *C₆* peptide antibody levels taken 4 to 6 months apart (Lyme Quant C₆ Test; IDEXX Laboratories, Inc, www.idexx.com) correlate with clinical disease.

**Vaccination.** Vaccinating dogs with Lyme exposure and, in particular, Lyme nephritis is controversial. Most argue against the use of current Lyme vaccines in a patient with Lyme nephritis because of the risk of exacerbating immune-mediated complex formation. In addition, one source from a Lyme endemic area estimates that one-third of their Lyme nephropathy patients were vaccinated, suggesting that the vaccine offers little to no protection against the most dangerous form of canine borreliosis.

See Aids & Resources, back page, for references, contacts, and appendices.

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**Discharge Treatment**

Doxycycline (for 21 days, maybe longer in cases with PLN), enalapril, amlodipine, Pepcid AC, low-dose aspirin (0.5 mg/kg Q 24 H), and high-quality/low-protein diet (eg, Eukanuba Early Stage or Hill’s Pet Nutrition k/d diets)

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