CASE BY CASE: PARASITOLOGY

Diagnosis and Treatment of Lyme Borreliosis in Dogs: A Case-Based Approach

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Lyme borreliosis is caused by the spirochete *Borrelia burgdorferi,* which is transmitted by ticks of the *Ixodes* genus.[1] In the United States, Lyme borreliosis is most commonly identified in the Northeast and upper Midwest due to the host preferences of *Ixodes* ticks endemic to those regions.[2] It is usually diagnosed in the spring and summer due to tick activity and human and canine outdoor recreation.[3] The most frequently recognized syndromes associated with Lyme borreliosis in dogs are acute polyarthritis and glomerulonephritis.

Confusion surrounds the diagnosis and treatment of Lyme borreliosis, in part because most seropositive dogs remain asymptomatic,[4] which limits veterinary professionals' ability to study naturally occurring disease. In addition, although a *Borrelia*-associated fever and arthritis syndrome has been induced in dogs,[5,6] no experimental model exists for Lyme (*Borrelia*) nephritis,[3,7,8] which limits our understanding of the pathophysiology. As a result, guidance for diagnosis and treatment depends largely on consensus opinion. This case-based approach highlights best practices in diagnosis and treatment of Lyme borreliosis in the context of 3 common clinical scenarios.

CASE 1: POLYARTHRITIS

Case 1 was a 27-kg, 4-year-old castrated male pointer with a 48-hour history of lethargy and unwillingness to walk. He was mildly febrile (39.9 °C [103.8 °F]) and had moderate carpal effusion, mild tarsal effusion, and moderate prescapular lymphadenopathy. His gait was

Abstract

Diagnosis of Lyme borreliosis requires a combination of diagnostic testing and clinical judgment. This article provides 3 case examples of presenting complaints, physical examination findings, and screening laboratory abnormalities that accompany Lyme borreliosis. There is no singular confirmatory test. Treatment for the clinical syndromes most commonly associated with Lyme borreliosis—polyarthritis and glomerulonephritis—is doxycycline, plus immunosuppressives for dogs with rapidly progressive glomerular disease. Asymptomatic dogs with positive serologic results do not require treatment but should be screened for proteinuria for 1 year.

Take-Home Points

- No single test can prove that Lyme borreliosis is the cause of illness; therefore, the diagnosis requires a combination of diagnostic testing and clinical judgment.
- A lack of reported tick exposure is not sufficient to rule out Lyme borreliosis.
- The recommended treatment for Lyme borreliosis in dogs is a 4-week course of doxycycline.
- Polyarthritis resulting from Lyme borreliosis is expected to respond rapidly to treatment with doxycycline; if rapid improvement is not noted, other causes of polyarthropathy should be considered.
- The glomerular disease associated with Lyme borreliosis can be severe, progressive, and rapidly fatal.
- In dogs with severe, rapidly progressive glomerular disease and positive *Borrelia* serology, immunosuppression is frequently necessary along with doxycycline treatment. Immunosuppression is ideally based on renal histopathology, although biopsy may not be possible for all patients.
- Most dogs with positive *Borrelia* serologic results are asymptomatic; these dogs should be screened for proteinuria during the first year after positive serology is identified, and prophylactic doxycycline treatment is not indicated.

tentative and short strided. He had recently been taken hunting, although no tick infestation was reported.

Lab work revealed mild thrombocytopenia, minimally concentrated urine, and *B burgdorferi* antibodies (TABLE 1). The findings of polyarthropathy and positive *Borrelia* serology raised suspicion for polyarthritis caused by Lyme borreliosis. However, because of the high prevalence of asymptomatic dogs with positive serologic results, further investigation to rule out alternative causes of polyarthropathy was recommended. Carpal and tarsal radiographs revealed no erosive changes. Arthrocentesis was recommended, but the client declined in favor of doxycycline with a plan to proceed with arthrocentesis if improvement was not seen. Initial treatment was doxycycline (5.5 mg/kg PO q12h) with gabapentin (7.4 mg/kg PO q12h) and codeine (1.1 mg/kg PO q12h) for pain control.

After 48 hours, the client reported dramatic improvement in the patient's willingness to walk. By the next week, his tentative gait, joint effusion, and lymphadenopathy had resolved. The client had discontinued analgesics several days earlier when the dog was no longer perceived to be painful, but the doxycycline was continued for 4 weeks. Recheck examination 3 weeks after doxycycline discontinuation revealed no recurrence of painful gait, joint effusion, or lymphadenopathy. Urinalysis was monitored every 4 months for the first year after diagnosis to screen for development of proteinuria, but no proteinuria was detected.

CASE 2: NEPHRITIS

Case 2 was a 6.8-kg, 7.5-year-old spayed female Maltese mix that was presented to her primary care

TABLE 1 Laboratory Values for Case 1: Dog With Polyarthritis

TEST (REFERENCE RANGE)	VALUE	NOTES
Blood chemistry	Within reference range	
Platelet count, platelets/µL (170 000–377 000)	167 000	Platelet clumping on slides noted; platelet count estimated to be within reference range
USG (1.015–1.05)	1.053 with 1+ protein	
UPC (<0.5)	0.2	
SNAP 4Dx	*Borrelia burgdorferi* Ab + *Anaplasma* species Ab – *Ehrlichia canis* Ab – *Dirofilaria immitis* Ag –	

Ab = antibodies; Ag = antigen; UPC = urine protein:creatinine ratio; USG = urine specific gravity

veterinarian for chronic diarrhea. A chemistry panel revealed azotemia and mild hypoalbuminemia; urine was mildly dilute with an inactive sediment and 3+ protein (**TABLE 2**). Treatment was initiated with benazepril (0.3 mg/kg PO q24h). Three months later, repeat lab work revealed progressive azotemia, progressive hypoalbuminemia, and persistent proteinuria. A prescription renal diet was prescribed and the patient was referred for further diagnostics.

At the time of referral, the patient was feeling well. A chemistry panel revealed stable azotemia and progressive hypoalbuminemia. A complete blood count revealed marked thrombocytopenia, and the urine specific gravity was within reference range but with increased protein. A urine bacterial culture was negative. The urine protein:creatinine ratio (UPC) was markedly elevated. SNAP 4Dx (IDEXX, idexx.com) testing was positive for antibodies to *B burgdorferi*. The patient was markedly hypertensive, and C_6 antibody titer was elevated. Abdominal ultrasonography revealed a mild loss of corticomedullary definition with no other renal or extrarenal abnormalities.

Doxycycline was initiated (5.7 mg/kg PO q12h) for 4 weeks and benazepril was continued (0.3 mg/kg PO q24h). Amlodipine (0.25 mg/kg PO q24h) was initiated for treatment of hypertension and clopidogrel (1.8 mg/kg PO q24h) was initiated for thromboprophylaxis, based on concern for hypercoagulability in dogs with protein-losing glomerular disease,[9] which may put them at risk for thromboembolic complications.[10,11]

At a recheck examination 2 weeks later, hypertension was improved but persistent and blood urea nitrogen and creatinine were unchanged. Amlodipine was increased to 0.5 mg/kg PO q24h.

Three days after doxycycline completion, lab work revealed stable azotemia, persistently marked proteinuria, persistently marked thrombocytopenia, and decreased blood pressure. C_6 titer was lower but still above reference range. Renal biopsy was recommended to further characterize the glomerulopathy but was not performed due to the risks posed by thrombocytopenia. Instead, empiric immunosuppressive treatment (mycophenolate mofetil

TABLE 2 Laboratory Values for Case 2: Dog With Nephritis

TEST (REFERENCE RANGE)	INITIAL	3 MONTHS LATER	AT REFERRAL	3 DAYS AFTER DOXYCYCLINE COMPLETION	3 MONTHS AFTER IMMUNOSUPPRESSIVE THERAPY INITIATION
Platelet count, platelets/µL (170 000–377 000)			30 000	32 000	
BUN, mg/dL (9–31)	66	81	79	77	68
Creatinine, mg/dL (0.5–1.3)	2.7	4.4	4.2	4.3	3
Albumin, g/dL (2.7–3.9)	2.3	1.9	1.7		
C_6 titer, U/mL (<30)			281	103	
USG (1.015–1.05)	1.01 with inactive sediment and 3+ protein	persistent 3+ protein	1.02 with inactive sediment and 4+ protein		
UPC (<0.5)			13.2	12.8	6
Blood pressure, mm Hg (90–160)			240	180	140
SNAP 4Dx			*Borrelia burgdorferi* Ab + *Anaplasma* species Ab – *Ehrlichia canis* Ab – *Dirofilaria immitis* Ag –		

Ab = antibodies; Ag = antigen; BUN = blood urea nitrogen; UPC = urine protein:creatinine ratio; USG = urine specific gravity

at 9 mg/kg PO q12h) was elected. Telmisartan therapy (0.6 mg/kg PO q24h) was initiated and benazepril was discontinued. Two weeks later, hypertension was controlled, thrombocytopenia was resolved (280 000/µL), and azotemia was stable.

Three months after institution of immunosuppressive therapy, the patient was polyuric and polydipsic but otherwise feeling well. Proteinuria was markedly improved, azotemia was persistent but improved, and hypertension remained controlled. The patient returned to her primary care veterinarian for ongoing care; however, 13 months later she was euthanized due to complications of progressive kidney disease.

CASE 3: ASYMPTOMATIC, SEROLOGY-POSITIVE

Case 3 was a 10-year-old spayed female terrier presented for routine vaccinations. She was feeling well and physical examination was unremarkable other than a chronic grade 3/6 left apical systolic heart murmur. A SNAP 4Dx test performed for yearly heartworm screening was positive for *B burgdorferi* antibodies but negative for *Anaplasma* species and *Ehrlichia canis* antibodies and negative for *Dirofilaria immitis* antigen.

To follow up on the positive *Borrelia* serology, full laboratory work was performed. Chemistry panel and complete blood count were within reference ranges. Urinalysis revealed specific gravity within reference range (1.033) and trace protein. A UPC ratio of 0.1 ruled out clinically significant proteinuria.

Urinalysis was repeated every 4 months for the next 12 months. Any protein detected on urinalysis was followed up with a UPC ratio. Clinically significant proteinuria did not develop during the 12-month monitoring period. At the next annual screening, the SNAP 4Dx result remained positive for *B burgdorferi* antibodies but the patient remained healthy.

DISCUSSION

According to the American College of Veterinary Internal Medicine's (ACVIM) consensus statement on Lyme disease in dogs, diagnosis requires basing clinical judgment on evidence of exposure, consistent clinical signs, consideration of other differentials, and response to treatment.[8] The cases discussed here highlight the variability of clinical presentations associated with Lyme borreliosis.

A positive *Borrelia* antibody test in a dog with proteinuria suggests, but does not confirm, that *Borrelia* is the cause of glomerulopathy. One study even suggests that proteinuria is an uncommon finding in dogs with *Borrelia* antibodies[12]; therefore, a thorough diagnostic investigation of proteinuria is warranted.[13] Nevertheless, because glomerulonephritis caused by Lyme borreliosis can be rapidly progressive, doxycycline treatment should be initiated concurrently with standard therapy and investigation of glomerular disease.[7] Detailed descriptions of standard therapy and investigation of glomerular disease are published elsewhere and typically involve a combination of antihypertensives, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, antithrombotics, and prescription renal diets.[14]

For dogs that are clinically stable and nonazotemic, initial management can involve antibiotics and standard glomerular disease therapies. Renal biopsy should be recommended for dogs with azotemia or rapidly progressive disease.[3,7] Although renal biopsy cannot prove a cause-and-effect relationship between *Borrelia* and glomerular disease,[15] one justification for renal biopsy in these dogs is to enable differentiation between immune-mediated glomerular disease, which would be expected to respond to immunosuppression, and causes that would not be expected to respond to immunosuppression. If renal biopsy is not elected or is not safe to perform (as for Case 2), or if glomerular disease is too severe or rapidly progressive to await biopsy results, cautious immunosuppression may be warranted along with antibiotic therapy.[3,7] The recommended first-line immunosuppressive for glomerular disease is mycophenolate mofetil, with the optional short-term addition of glucocorticoids for severe, rapidly progressive cases.[16]

The recommended first-line antibiotic treatment for Lyme borreliosis is doxycycline, although optimal dose and duration of treatment are not known. The current recommendation is to continue treatment for 4 weeks.[3] For Lyme borreliosis–associated polyarthritis, a robust response is expected within 48 hours; a lack of response within this time frame should prompt investigation for other causes of polyarthropathy.[8] Controversy exists around using C_6 antibody titers to guide treatment duration. Measuring C_6 titers before and 6 months after starting treatment may be useful as a decrease of 50% or more likely indicates decreased antigenic load as a result of effective treatment. On the other hand, evidence that the magnitude of C_6 titer correlates to the

magnitude of current disease or the likelihood of developing future disease is lacking.[3] In addition, the magnitude of the decrease tends to be smaller with lower initial C_6 values, in which case the threshold of a decrease of 50% or more might not be achieved despite effective treatment. Nevertheless, some clinicians prolong doxycycline treatment until clinical resolution is achieved or until the C_6 antibody titer decreases into the target range.[3,7]

Most serology-positive dogs are asymptomatic.[4] A recommended approach is to screen for development of proteinuria every 3 to 4 months for the first year after seropositivity is identified,[3,8] which enables early intervention for proteinuria, potentially preventing ongoing glomerular damage. For asymptomatic, serology-positive dogs, measurement of C_6 antibody titers is not recommended and there is no evidence that prophylactic doxycycline treatment is beneficial.[3]

Prevention of Lyme disease is multimodal. Ectoparasiticides are recommended to prevent tick attachment or to kill ticks quickly after attachment as the likelihood of *Borrelia* and other tick-borne pathogen transmission increases with longer attachment time.[17,18] Recreation habits and landscaping can be modified to minimize exposure to tick habitat.[3] Dogs should be examined after exposure to tick-infested areas and ticks should be removed promptly. Vaccination is effective against both experimental[19] and natural[20] infection. The ACVIM consensus update on Lyme borreliosis in dogs and cats did not report a consensus on whether vaccination is recommended.[3] The decision to vaccinate should be made on an individual basis while considering patient risk factors. TVP

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