Exceptional Case

Lyme disease-associated glomerulonephritis

Finnian R. Mc Causland¹, Sophie Niedermaier², Vanesa Bijol³, Helmut G. Rennke³, Mary E. Choi¹ and John P. Forman¹

¹Renal Division, Brigham and Women’s Hospital, Boston, MA, USA, ²Department of Neonatology, Hauner Children’s Hospital, Munich, Germany and ³Department of Pathology, Brigham and Women’s Hospital, Boston, MA, USA

Correspondence and offprint requests to: Finnian R. Mc Causland; E-mail: fmccausland@partners.org

Abstract

We report two cases of Lyme disease-associated glomerulonephritis. A 57-year-old female presented with rash, volume overload, hypertension and rapidly progressive glomerulonephritis. Biopsy confirmed an immune complex-mediated, membranoproliferative lesion. She was treated successfully with steroids and antibiotics. In a second case, a 40-year-old male, with a previously known microscopic hematuria, presented with rash, arthralgias, new proteinuria and gross hematuria following a tick bite. Biopsy revealed focal proliferative IgA nephropathy. Treatment with steroids and antibiotics resulted in rapid resolution of findings. Acute Lyme disease may contribute to the development of de novo, or activation of previously quiescent, immune-mediated glomerular disease.

Keywords: glomerulonephritis; IgA; Lyme disease; membranoproliferative

Background

Lyme disease is caused by the spirochete Borrelia burgdorferi. The true incidence is likely underestimated due to underreporting and misdiagnosis. In humans, renal involvement is uncommon; however, here, we present two cases of Lyme disease-associated glomerular injury.

Case presentations

A 57-year-old female artist presented with shortness of breath. She noted a shoulder rash 2 weeks previously with nonspecific complaints of nausea, fatigue, headache and myalgias, before developing dyspnea on moderate exertion, ankle edema and weight gain of 5 kg. Acute Lyme disease was diagnosed and oral doxycycline was commenced, in addition to loop diuretics.

Her background history was unremarkable. She was married and denied using tobacco, alcohol or illicit drugs. She was hypertensive (184/90 mmHg), afibrile and volume overloaded by physical examination. Initial laboratory results are depicted in Table 1. Echocardiography demonstrated moderate mitral regurgitation, with ejection fraction of 65%. A renal ultrasound was unremarkable but urine dipstick revealed 2+ heme and 2+ albumin, with numerous dysmorphic red cells. Intravenous ceftriaxone was commenced due to concern for disseminated Lyme disease. A continued rise in serum creatinine (80–159 µmol/L), low complement C3 (0.74 g/L) and active urine sediment prompted treatment with high dose oral steroids and an urgent renal biopsy. Findings included global hypercellularity, mesangial expansion and subendothelial deposits consistent with an immune complex-mediated membranoproliferative glomerulonephritis (MPGN) (Figure 1). Six months following treatment, she had a bland urine sediment and serum creatinine of 71 µmol/L.

A 40-year-old male fitness trainer from Massachusetts presented with gross hematuria. One week previously, he was bitten by a tick, subsequently developing myalgias, sore throat, headache and fever to 39.4°C. Past history was notable for microscopic hematuria, diagnosed incidentally 2 years earlier, at which time he was normotensive, without proteinuria and had a serum creatinine of 88 µmol/L. He denied taking regular medications, had no allergies and had no family history of kidney disease. He was a non-smoker, rarely drank alcohol and denied illicit drug use. He was normotensive (112/81mmHg), afibrile and had a heart rate of 74 b.p.m.; physical examination was unremarkable otherwise. Presenting laboratory values are in Table 1. The urine sediment revealed dysmorphic red cells and red cell casts. High dose oral steroids were commenced and a renal biopsy revealed focal proliferation, one cellular crescent and mesangial IgA reactivity, consistent with IgA nephropathy (Figure 1). In the interim, he developed a macular rash in his left axilla, consistent with acute disseminated Lyme disease (confirmed by serology), for which he received oral doxycycline. Two months later, his creatinine was 106 µmol/L and urine protein/creatinine ratio had fallen from 1.0 to 0.16.

Discussion

B. burgdorferi is carried by ixodid ticks; in New England approximately 30–50% of adult ticks are infected and the
risk of transmission appears to correlate with the length of feeding [1]. Early localized Lyme disease is characterized in 90% of individuals by the rash of erythema chronicum migrans. Systemic features include fever, myalgias, arthralgias, headache and malaise [2]. Early disseminated disease can present with multiple typical rashes, carditis, meningitis and cranial nerve palsies. Late disease usually presents months after the initial bite with a monoarticular arthritis [2].

The literature is scant regarding renal involvement of Lyme disease in humans. Kirmizis et al. described a 76-year-old man from the former Republic of Georgia, who presented with a macular rash, fever, hypertension, oliguria, edema, proteinuria and glomerular hematia. He had a protracted course including cranial and peripheral neuropathies, possible Guillain–Barré syndrome, serositis and acute kidney injury requiring hemodialysis. Renal biopsy was consistent with an MPGN pattern of injury and an extensive work-up eventually returned positive for B. burgdorferi. He responded well to ceftriaxone and high dose steroids, gaining dialysis independence [3].

A 65-year-old Irish man presented with a 3-week history of headache, nausea and a unilateral VI cranial nerve palsy. Laboratory values were notable for an elevated Erythrocyte Sedimentation Rate, transaminits, serum creatinine of 465 µmol/L and dipstick proteinuria. A work-up for infectious and autoimmune etiologies, including complement, was negative except for positive serology to B. burgdorferi. Findings on renal biopsy were consistent with MPGN and he was treated successfully with steroids and ceftriaxone; 1 month later, his serum creatinine was 135 µmol/L [4].

A 61-year-old female presented with volume overload, fatigue and hypertension with creatinine of 204 µmol/L, hypocomplementemia and nephrotic range proteinuria. She was diagnosed with Lyme disease 12 years earlier, suffering from chronic arthritis subsequently. Her serological work-up revealed detectable cryoglobulins, but negative hepatitis and HIV serology, and no evidence of a plasma cell dyscrasia. Renal biopsy was consistent with MPGN, which the authors ascribed to a late complication of Lyme disease. Despite treatment with steroids and angiotensin converting enzyme (ACE) inhibitors, she eventually required dialysis [5].

A final case described a 64-year-old Swedish man who developed nephrotic syndrome following a tick bite (15.56 g/day urinary protein) and presented with a serum creatinine of 148 µmol/L. Serology was positive for acute Lyme disease with membranous nephropathy on renal biopsy. He was treated successfully with doxycycline and an ACE inhibitor—follow-up urine protein/creatinine ratio was 0.65 [6].
Conclusion

Lyme disease is a relatively common infection in endemic areas of the world. Clinical manifestations rarely affect the kidneys. MPGN is frequently seen in disease processes with persistent or episodic antigenemia and circulating immune complexes; such conditions include chronic infections (e.g. hepatitis B and C, bacterial endocarditis, shunt infections) and autoimmune diseases. In our first case, the temporal relationship, multisystem presentation, characteristic histology and response to antibiotics and steroids are consistent with a \textit{B. burgdorferi} induced, immune complex-mediated, glomerulopathy.

Our second case raises the possibility that Lyme infection can lead to activation of a previously quiescent glomerular condition. It appears likely that this subject had underlying IgA nephropathy at baseline. The temporal relationship to Lyme infection (and subsequent quiescence with treatment) raises the possibility that the acute flare was caused by an intense activation of the immune response.

Lyme-associated glomerular disease should be considered in patients from endemic areas presenting with nephritis. In such cases, it is imperative to take a detailed history for tick exposure and for symptoms commonly associated with acute Lyme disease.

Conflict of interest statement. None declared.

References


Received for publication: 9.5.11; Accepted in revised form: 12.5.11

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig1}
\caption{Kidney biopsy findings, in Case 1 (A–C) and Case 2 (D–F). (A) Light microscopy reveals a membranoproliferative pattern of glomerular injury, with global hypercellularity, mesangial expansion and frequent double contours, PAS ×400; (B) Electron microscopy shows large subendothelial electron-dense deposits (black arrows), with segmental new basement membrane formation (black arrowhead), uranyl acetate and lead citrate ×8000; (C) Prominent granular and confluent mesangial and capillary loop immunofluorescence reactivity for IgG, anti-gamma ×400; (D) Focal proliferative glomerulonephritis, with mesangial proliferation and a small cellular crescent (black arrow), PAS ×400; (E) Mesangial fine granular electron-dense deposits (black arrowhead), uranyl acetate and lead citrate ×8000 and (F) Mesangial fine granular immunofluorescence reactivity for IgA, anti-alpha ×400.}
\end{figure}