Renal Vein Thrombosis in a Patient with Class V Lupus Nephropathy

David Ozeri1*, Eric Cochran2, Andrew Kesselman3, Robert Ishakis1 Anthony Nicastri2 and Ellen Ginzler1

1Department of Rheumatology, SUNY Downstate, USA
2Department of Pathology, SUNY Downstate, USA
3Department of Radiology, SUNY Downstate, USA
4Department of Chemistry, Towson University, USA

Abstract

This is a case of a 46 year old woman with systemic lupus erythematosus (SLE) and class V lupus nephritis with nephrotic range proteinuria and antiphospholipid antibodies that had an unusual presentation of renal vein thrombosis that masqueraded as serositis. This case highlights the importance of ruling out venous thromboembolic disease in patients with SLE and antiphospholipid antibodies and consideration of prophylactic full dose anticoagulation in patients with SLE, nephrotic syndrome that have seropositivity for antiphospholipids.

ABBREVIATIONS

SLE: Systemic Lupus Erythematosus; APS: Anti Phospholipid Syndrome; VTE: Venous Thrombo Embolism

CASE PRESENTATION

A 46 year old woman with a past medical history of SLE with discoid lesions and class V lupus nephritis (Figure 1-2) presented to her outpatient rheumatologist for follow up in a city hospital’s outpatient clinic. She complained of dyspnea on exertion for 2 weeks, arthralgia, fatigue, and lower extremity swelling. She also noted severe right sided pleuritic chest pain for 3 days.

The patient was being maintained on mycophenolate mofetil (1.5 g BID) and prednisone 20 mg daily. Hydroxychloroquine was previously discontinued due to evidence of maculopathy.

Past medical history was significant for discoid lupus diagnosed in 2004, SLE with class V lupus nephritis diagnosed in 2008, dyslipidemia (cholesterol 442 mg/dl, LDL 352 mg/dl), corticosteroid-induced diabetes and corticosteroid-induced avascular necrosis of the right hip for which she underwent arthroplasty.

Physical exam findings were remarkable for moderate respiratory distress and lower extremity edema. She had no rash, oral ulcers, or arthritis. The patient was referred to the Emergency Department for further workup.

Laboratory studies performed 7 days prior to the outpatient clinic visit included hemoglobin 11.2 g/dl, hematocrit 34.5 %, mean corpuscular volume 79.1 fl, platelets 100,000 K/cmm, C3 82 mg/dl, C4 21 mg/dl, serum creatinine 0.59 mg/dl (GFR 127 ml/min), albumin of 2.0 g/dl, and an ESR of 100 MM/15 min. Urinalysis showed (UA) 300+ protein with 2+ hemoglobin and 2-5 granular casts. Estimated 24 hour urine protein using the spot urine protein: urinecreatinine was 2.9 g (increased from 0.12 g 3 months prior).

Further studies in the ED included a positive test for d dimers.

Figure 1 Immuno fluorescence microscopy shows a granular pattern in the glomerular capillary wall (GCW). Granular GCW and tubular basement membrane (TBM) deposition of C1q, C3, IgG, IgA, IgM, kappa and lambda support a diagnosis of membranous lupus nephritis in this SLE patient in the setting of nephrotic range proteinuria.
A chest CT with angiography showed no evidence of a pulmonary embolism, however it showed a moderate right sided pleural effusion (Figure 3). Laboratory studies were repeated in the ED. BUN/Cr remained stable 13/0.61 mg/dl respectively, she again showed evidence of hypoalbuminemia with a albumin of 2.0 mg/dl, hypocomplementemia with a C3/C4 of 74/20 mg/dl respectively, and her ESR remained elevated at 102 MM/15 min. Urinalysis showed proteinuria with 2-5 hyaline casts, estimated 24 hour urine protein excretion increased to 23.3 g. She was treated with 60 mg of prednisone; in view of her prominent proteinuria in the setting of serositis she was deemed to have failed mycophenolatemofetil and patient was scheduled for Rituximab.

Chest CT with angiography was further reviewed by radiology and evidence of renal vein thrombosis was noted (Figure 4). Serologies for β2 glycoprotein and anticardiolipin (IgM) were positive and lupus anticoagulant was negative. The patient was subsequently treated with antithrombotic therapy with low molecular weight heparin. After 48 hours her pleuritic chest pain resolved.

**DISCUSSION**

Nephrotic syndrome has been associated with an increase in venous thromboembolic events (VTE) such as deep vein thrombosis, pulmonary embolism and renal vein thrombosis [1]. Bellamo et al estimated that the risk of developing renal vein thrombosis in patients with membranous nephropathy is 37% [2].

The conundrum of whether or not to prophylactically anticoagulate patients with nephrotic syndrome has been well documented [3-4]. Lee et al suggests that using albumin as a surrogate marker for risk of VTE in patients with nephrotic syndrome can help guide the decision to initiate full dose anticoagulation [4]. While there is evidence supporting initiating prophylactic full dose anticoagulation in patients with primary membranous nephropathy and nephrotic range proteinuria there is still no consensus as to whether full dose anticoagulation should be considered standard of care. Furthermore there is a need to elucidate whether this evidence can be extrapolated to other etiologies of nephrotic syndrome [3,4].

Antiphospholipid syndrome (APS) is defined by the presence of antiphospholipid antibodies (anticardiolipin antibodies, anti-β2 glycoprotein antibodies and lupus anticoagulant) associated with a thrombotic event [5]. There is a large spectrum of renal thrombotic manifestations associated with APS including renal vein thrombosis, renal infarction, renal artery stenosis, and chronic thrombotic microangiopathy [6]. The consensus for managing secondary prophylaxis in APS is antithrombotic therapy [7].

Approximately 40% of patients with systemic lupus erythematosus (SLE) have antiphospholipid antibodies. Patients with a combination of antiphospholipid antibodies and SLE will develop thrombosis at an annual rate of 3-4% [5]. In observational studies primary prophylaxis with low dose aspirin showed a protective effect [8]. Given the limited toxic manifestations of low dose aspirin it is frequently used as primary prophylaxis. Similarly hydroxychloroquine is believed to be safe for primary prophylaxis in patients with SLE and antiphospholipid antibodies for its antithrombotic effects [3,9].
Our case featured a woman that had an increased risk of thrombotic complications due to SLE itself, membranous nephritis, and nephrotic range proteinuria. Her risk factors therefore warranted primary prophylaxis. The presence of antiphospholipid antibodies and a thrombotic event makes the diagnosis of APS. However, in our case patient has several pro-thrombotic risk factors that may have contributed to the thrombotic event. It is therefore impossible to know if the thrombosis was due to APS. This concept has practical importance as diagnosis is important in defining the duration and intensity of therapy.

SLE is a heterogeneous disease that can manifest itself in many different organ systems. Treatments are aimed at decreasing systemic inflammation and preventing end organ failure [10]. Our case was especially interesting in that our patient showed signs of SLE flare with arthralgias, complement consumption and elevated ESR. Given her history of Class V lupus nephritis her proteinuria was initially attributed to active nephritis. However, the constellation of the right-sided pleural effusion, with a precipitous increase in proteinuria in the absence of acute kidney injury suggested the absence of bilateral kidney involvement. In such a case, ruling out acute renal vein thrombosis is crucial.

Another important question that this case provokes is whether patients with SLE, nephrotic syndrome and antiphospholipid antibodies should be recommended antithrombotic therapy in the form of vitamin K antagonists, novel oral anticoagulants or low molecular weight heparin as primary prophylaxis. There are no clinical trials that recommend full dose anticoagulation. The decision of when and how to anticoagulate these patients is therefore challenging for the treating physician. Observational reports and controlled clinical trials are necessary to answer this question.

REFERENCES