

The Copy Cat Disease: A Case of Lupus Podocytopathy

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ABSTRACT

Systemic Lupus Erythematosus (SLE) is a chronic inflammatory disease that can affect various organs. Specifically, when the kidneys are affected this can result in nephritic or nephrotic syndrome. Lupus podocytopathy (LP) is a type of nephrotic syndrome associated with SLE. This case looks at a 44 year old female who presented to the emergency department (ED) with bilateral lower extremity edema and was noted to have hypoalbuminemia and an elevated total protein/creatinine ratio. She was discharged from the ED with a diagnosis of nephrotic syndrome and advised to follow up with nephrology as an outpatient. Her outpatient labs were positive for antinuclear antibodies (ANA), anti-ribonucleoprotein antibodies (anti-RNP), and anti-smith antibodies. She returned to the ED two weeks later for hand cramping and was admitted for an acute kidney injury. She had an inpatient renal biopsy performed which showed 100% podocyte effacement, concerning for minimal change disease (MCD). However, the biopsy also showed a positive tissue ANA with no immune complex deposition. In the context of MCD and a positive tissue ANA, this patient was diagnosed with LP. She was treated with steroids and hydroxychloroquine with improvement in her kidney function and proteinuria. Lupus podocytopathy is a new entity that is not classified in the 2018 International Society of Nephrology/Renal pathology Society (ISN/RPS) classification system [1]. It is treated similarly to MCD, with steroids and possibly immunosuppressive agents. Clinicians should keep autoimmune conditions on their differential when evaluating and treating patients with nephrotic syndrome.

Keywords: systemic lupus erythematosus, podocytopathy, nephrotic syndrome, minimal change disease

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic disease that can cause systemic inflammation of multiple organ systems, including the kidneys. SLE may present with nonspecific constitutional symptoms, arthralgias, malar rash, and oral ulcers. As the disease progresses it has the potential to cause end organ damage, including renal failure, a leading cause of morbidity and mortality. Lupus nephritis (LN) can be histologically categorized from class I-VI via the 2018 International Society of Nephrology/Renal pathology Society (ISN/RPS) classification system [1-2]. Class I and II are milder forms that resolve when treated with steroids [3]. Class III is classified as focal proliferative, while class IV-V are more diffuse forms

of the disease and class VI is advanced sclerotic disease without residual activity [4]. One unique form of LN that was not included in the 2018 Lupus Nephritis classification system is lupus podocytopathy (LP) [4]. Lupus podocytopathy is a somewhat new phenomenon defined as SLE associated nephrotic syndrome that is secondary to minimal change disease (MCD) or focal segmental glomerulosclerosis (FSGS) [5]. MCD is the absence of immune deposits in glomerular capillary walls and presence of severe podocyte effacement [6]. LP represents approximately 1% of lupus nephritis biopsies [3]. This case is about a 44 year old female who was found to have nephrotic syndrome secondary to lupus podocytopathy that mimicked minimal change disease.

CASE

A 44 year old female with past medical history of trigeminal neuralgia and family history significant for SLE on her maternal side, who initially presented to the emergency department (ED) for bilateral lower extremity and abdominal swelling. Chest radiograph showed increased vascular markings and a small effusion, while labs were notable for an elevated brain natriuretic peptide (BNP) and albumin of 1.5. A urinalysis was performed which showed a urine protein of 500 and an elevated total protein/creatinine ratio of 5906 mg/g. Creatinine was slightly elevated to 1.04 from a baseline of 0.54, and thyroid stimulating hormone was 3.03. Nephrology and cardiology were consulted in the ED and recommended discharging the patient on furosemide with further outpatient workup for proteinuria. Early rheumatologic workup as an outpatient was notable for antinuclear antibodies (ANA) of 1:640 with a speckled pattern, positive anti-ribonucleoprotein antibodies (anti-RNP), and positive anti-smith antibodies. Negative serologic evaluation included negative double stranded DNA (dsDNA), normal serum protein electrophoresis with immunofixation, negative hepatitis B surface antigen and hepatitis C, negative antistreptolysin O and normal complement levels. Two weeks later, the patient returned to the ED for muscle cramps in her hands and legs bilaterally. Labs showed a worsening creatinine of 2.17 and urine protein of greater than 600. She was admitted to the hospital for an acute kidney injury. Rheumatology and nephrology were consulted. Shortly after admission, a renal biopsy was performed which showed via light microscopy histologically unremarkable glomeruli with minimal tubular atrophy and interstitial fibrosis. Immunofluorescence demonstrated tissue ANA correlating with the patient's positive serum ANA without significant glomerular staining for antisera. Electron microscopy showed 100% foot process effacement of podocytes with no immune-type electron dense deposits or endothelial tubuloreticular inclusions seen. The findings from the renal biopsy were consistent with minimal change disease. However, given the patient's positive serum ANA the biopsy represented lupus podocytopathy. Patient was subsequently started on prednisone 60 mg once a day with dapsone 100 mg for pneumocystis pneumonia prophylaxis. Due to the significant proteinuria, the patient was at an increased risk of developing systemic clots and was discharged home on warfarin and bumetanide. Rheumatology also started the patient on hydroxychloroquine. After follow-up one month later, the patient's urine total protein improved to 46.5, creatinine returned to baseline, and urine total protein/creatinine ratio decreased to 486.

DISCUSSION

Lupus podocytopathy is a special form of lupus nephritis that mimics either minimal change disease or FSGS, where there is foot process effacement without immune deposition [7]. In patients with undiagnosed SLE who are presenting with nephrotic syndrome lupus

podocytopathy can be difficult to diagnose. A renal biopsy will give a definitive diagnosis for nephrotic syndrome and is vital when determining appropriate treatment options. In this case, although the patient's biopsy demonstrated MCD, in the context of a positive ANA, anti-RNP, and anti-smith antibodies, lupus podocytopathy was the diagnosis. After one month of treatment with both steroids and hydroxychloroquine, the patient's urine protein and urine protein to creatinine ratio significantly improved. In a case report by Dube et al, they reported 7 patients with SLE and MCD [8]. All 7 patients presented with full nephrotic syndrome including peripheral edema, nephrotic range proteinuria and hypoalbuminemia and were subsequently found to have MCD [8]. Although there are no specific guidelines for diagnosing LP, possible criteria could be nephrotic syndrome with biopsy showing MCD and tissue or serum serology positive for lupus.

When diagnosing nephrotic syndrome, LP is a prime example of why autoimmune conditions should be on the differential. According to Chaudhury et al., there appears to be an association between LP and Class II Lupus Nephritis [7]. Although there is still much to learn about LP, we continue to treat it in the same manner as MCD, with high dose steroids [7]. In this case, the patient's urine protein did improve with initiation of steroids and hydroxychloroquine. In a study by Hu et al., they analyzed 50 cases that were identified as lupus podocytopathy, 47 of the 50 cases achieved remission with immunosuppressive therapy after 4 weeks [9].

The exact pathophysiology of LP is still unknown, although one hypothesis includes that podocytes are in fact immunologically active cells that also act as antigen presenting cells which precipitate an immune response [6]. There has also been documented cases of LP progressing to other forms of lupus nephritis [6]. Another hypothesis pertains to IL-13 overexpression and aberrant T cells that lead to podocyte injury [7]. The emphasis on T cell dysfunction could be the factor uniting SLE and MCD.

CONCLUSION

Although there is still much to learn about LP, there is a baseline understanding that diagnosis is definitive with a renal biopsy that is positive for MCD or FSGS. With this in mind, it is important to keep an open mind when a patient presents with nephrotic syndrome. The whole picture must be analyzed and a thorough history must be obtained to come to the proper diagnosis, especially when differentiating between LP and MCD.

Citations

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