LUPUS PODOCYTOPYPATHY AN UNDERRECOGNISED ENTITY

VASUDEVAN CHELLIAH
Department of Nephrology,
KILPAUK MEDICAL COLLEGE AND HOSPITAL

Abstract:
Nephrotic syndrome is one of the common manifestations of systemic lupus erythematosus. Usually SLE patients with nephrotic range of proteinuria show diffuse proliferative lupus nephritis and membranous lupus nephritis, ISN RPS (International society of nephrology Renal pathological society) classes IV and V, respectively on histopathological examination. Here we are reporting a case of SLE presented with nephrotic syndrome. Renal biopsy showed mesangial proliferative lupus nephritis (class II) with MCD(Minimal change disease) like diffuse effacement of foot processes of podocytes in the absence of glomerular capillary wall immune deposits on electron microscopy. Patient had a complete remission with short course of high dose oral prednisolone therapy. The association of podocytopathy and SLE may not be a coincidence and this should be considered as one of the manifestations of lupus nephropathy.

Keyword: Lupus podocytopathy, Minimal change disease, Prednisolone.

INTRODUCTION:
Incidence of clinically evident renal disease is 30 to 50% in patients with SLE at initial presentation. During follow up, 60% of the patients will develop lupus nephritis 1-4. Proteinuria is the most common presentation of lupus nephritis and it is usually below 1 g per day in mesangial proliferative lupus nephritis (ISN/RPS class II)5,6. Interestingly some SLE patients will present with nephrotic syndrome due to diffuse foot process effacement as in minimal change disease without any evidence of diffuse proliferative (class IV) or membranous (class V) lupus nephritis 7-17. Here we are reporting a case of podocytopathy associated with class II lupus nephritis. Lupus podocytopathy is not included in WHO as well as in the recent ISN/RPS classification 18.

CASE REPORT:
A 36 year old female presented with generalized edema and arthritis involving both ankles and knees of one month duration. She did not consume any NSAIDs. She had oral ulcers one year ago. Physical examination revealed pallor, anasarca and arthritis. Blood pressure was 110/70 mmHg. Examination of other systems was normal. Urine analysis showed
4+ proteinuria. 24 hours urine protein was 6.2 g. Urine microscopy revealed 1 to 3 pus cells and 7 to 8 RBCs / hpf. Serum creatinine was 0.9 mg/dl and total cholesterol 291 mg/dl. Total protein was 4.7 g/dl and albumin 2.9 g/dl. Hemogram showed Hb 9.6 g/dl, total WBC count 6800/µL and platelets 2.2 lakhs/µL. Serology revealed ANA positivity (1 in 100 homogenous pattern). AntidsDNA and Rheumatoid factor were negative. C3 was 124 mg/dl (normal 90 to 180) and C4-28 mg/dl (normal 10 to 40). HIV, HBsAg and antiHCV antibody were negative. Renal biopsy contained 18 glomeruli that showed mesangial hypercellularity with mild matrix expansion. Capillary loops were patent with no endocapillary proliferation. Tubulointerstitium and blood vessels were normal (Figure 1). Immunofluorescence study showed immune complex deposits of 3+ positivity for C1q, 2+ for IgG and C3 over mesangium. IgA and IgM were negative (Figure 2 & 3). Electron microscopy showed electron dense mesangial immune deposits (Figure 4), normal glomerular basement membrane and diffuse effacement of foot processes of podocytes with no glomerular capillary wall immune deposits (Figure 5). Renal biopsy was suggestive of mesangial proliferative lupus nephritis (ISN/RPS class II) with evidence of podocytopathy as in MCD.

Figure 1: Light microscopy shows mild mesangial hypercellularity and matrix expansion.

Figure 2: Immunofluorescence shows intense C1q positivity in the mesangium.

Figure 3: Immunofluorescence shows C3 positivity in the mesangium.
Figure 4: Electron microscopy shows electron dense immune deposits in the mesangium.

Figure 5: Electron microscopy shows diffuse foot process effacement. Patient was given oral prednisolone 1mg/kg/day which resulted in complete remission of nephrotic syndrome in 4 weeks. She also recovered from arthritis and other symptoms of SLE.

DISCUSSION:
We reported a case of biopsy proven mesangial proliferative lupus nephritis with evidence of podocytopathy. There are only a few case reports, around 22 cases, described in the literature. Dube et al, reported 7 cases with MCD and SLE\textsuperscript{14}. Majority of cases had a complete remission of nephrotic syndrome in addition to disappearance of symptoms of SLE after corticosteroid therapy\textsuperscript{10,16}. Our patient also recovered from arthritis and other symptoms of SLE. Similar to our case, most of the cases described in the literature are class II lupus nephritis.

Even though the exact pathogenetic mechanism of lupus podocytopathy is not known, it was hypothesized that IL-13 produced in excess amount by aberrant T cells\textsuperscript{19}, crosstalks between renal dendritic cells and Th cells, and thereby directly causing damage to the podocytes. It was shown in studies with rats that over expression of IL-13 could lead to podocyte injury with down regulation of nephrin, podocin and dystroglycan and a concurrent upregulation of B7 -1 in the glomeruli inducing a minimal change like nephropathy\textsuperscript{20}. The amount of foot process effacement has been shown to be >80% in patients with nephrotic syndrome compared to<20% in patients with non nephrotic proteinuria even though all patients had similar class II lupus nephritis on renal biopsy\textsuperscript{21}. To conclude, lupus podocytopathy is an underrecognised entity and it is a reversible cause of nephrotic syndrome in SLE. The association of podocytopathy and SLE may not be a coincidence and this should be considered as one of the manifestations of lupus nephropathy. It may be included in the current ISN/RPS classification because it has prognostic and therapeutic implications\textsuperscript{21}.

REFERENCES:
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