

Nephrotic syndrome due to mesangial proliferative lupus nephritis (ISN / RPS class II): A case report

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Introduction

Kidney is the mostly affected visceral organ in systemic lupus (SLE). Renal involvement is seen in 40- 85 % of patients with SLE (1). The International Society of Nephrology and Renal Pathology (ISN/RPS) classifies Lupus nephritis into six classes (I - VI). Clinical features vary from isolated abnormalities of the urinary sediment to full-blown nephritic or nephrotic syndrome or chronic renal failure. Patients with mesangial proliferative lupus nephritis (MPLN - ISN/RPS class II) are supposed to have a benign course with mild degree of proteinuria and intact renal function. Nephrotic range proteinuria is typically seen with lupus nephritis ISN/RPS class V and also with class III and IV (2). There are few reported cases in literature where nephrotic syndrome was associated with MPLN (3,4). We report a young girl presented with nephrotic syndrome and detected to have SLE with MPLN after investigations.

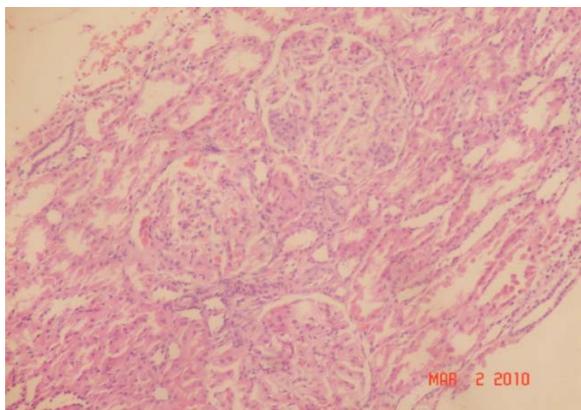
Case Report

A 18-year-old school girl admitted to our hospital with the complaints of progressive ankle swelling and bilateral periorbital swelling which was marked early in the morning for two months. She also complained of passage of frothy urine, alopecia, Raynaud's phenomenon and 6kg weight gain for the same duration. Furthermore, she complained of multiple erythematous skin eruptions over knees, elbows and scalp for two weeks. She had no past medical history of note. She had never used non-steroidal anti-inflammatory drugs (NSAIDs).

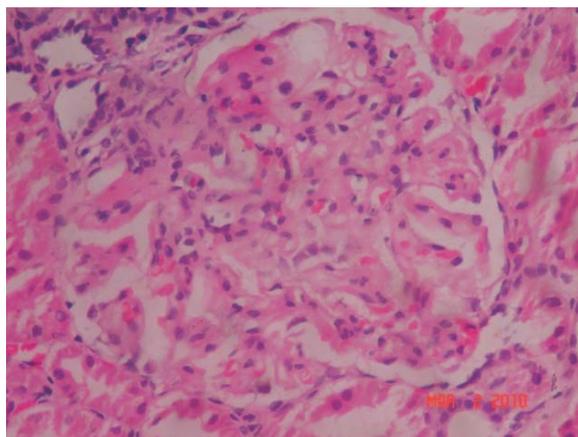
On physical examination she was found to be pale and had bilateral pitting ankle oedema. There were papular, erythematous skin eruptions over elbows, knees and scalp without scarring. Her blood pressure was 140/90 mmHg. Rest of the physical examination including optic fundi was normal.

Her ESR was 105mm in the first hour and complete blood count revealed anemia (hemoglobin 10.8g/dL) and thrombocytopenia ($112 \times 10^9/L$). Urine full report showed 3+ proteinuria with no casts or dysmorphic red cells. Her serum albumin level was 29g/L. Twenty four hour urine protein excretion was 7.3g. Serum creatinine level was normal (0.65mg/dL). Her serum cholesterol (320 mg/dL) and triglycerides (201mg/dL) were elevated. Also she had positive ANA and dsDNA tests but negative U1RNP. Her complement assay showed slightly reduced C3 and normal C4 levels. Biopsy of the skin lesion revealed sub acute cutaneous lupus. Percutaneous renal biopsy (Figure) was compatible with MPLN (activity index - 3/24 and chronicity index - 0/12).

She was started on frusemide 40mg b.d, atorvastatin 40mg nocte, hydroxychloroquine 200mg o.d, captopril 12.5mg b.d and prednisolone 60mg daily. After 2 weeks of therapy she lost 3 kg of weight and had 1+ proteinuria with normal blood pressure. After performing baseline bone densitometry she was started on alendronate 70mg weekly as well. Her proteinuria completely resolved after eight weeks of steroid therapy and prednisolone was tailed off and stopped over next eight weeks. She developed no new skin lesions. Being on regular follow up for the past two years, she never had a flare up of SLE or recurrence of proteinuria and her renal functions remain static.



(a)



(b)

Figure: Renal biopsy - light microscopy. **(a)** Three glomeruli showing mesangial expansion and hypercellularity [x100]. **(b)** Single glomerulus with hypercellular mesangium [x 400].

Discussion

Systemic lupus erythematosus is an inflammatory autoimmune disorder characterized by auto-antibodies against nuclear antigens (5). Lupus nephritis typically occurs in patients aged 20-40 years (6). Deposition of immune complexes and complement activation mediates the glomerular injury (7). More than 50% of the cases of lupus nephritis belong to ISN / RPS class III and IV. Another 10 - 15% cases are membranous type (class V) (7). Nephrotic range proteinuria is typically seen with lupus nephritis class V and also with class III and IV. It is generally agreed that patients with MPLN (ISN / RPS class II) have minimal clinical evidence of renal disease and mild haematuria or proteinuria with normal renal function (2).

The development of nephrotic syndrome in a patient with MPGN may signify transformation in to another form of lupus nephritis. But there are several case reports of MPLN causing nephrotic range proteinuria. Mesangial proliferative lupus nephritis is characterized by any degree of mesangial hypercellularity (defined as three or more mesangial cells per mesangial area in a 3 micron thick section) in association with mesangial immune deposits (8). The pathogenesis of nephrotic syndrome in mesangial nephritis is not well elucidated, because immune complexes are not detected in basement membrane. But it is postulated that immune complexes deposited in mesangium lead to release of cytokines that alter the glomerular permeability causing proteinuria (3,4). Lupus podocytopathy is another proposed mechanism responsible for heavy proteinuria due to extensive foot process effacement in MPLN (2).

Our patient fulfilled diagnostic criteria for SLE and had biopsy proven renal involvement with nephrotic syndrome. She had no history of using non steroidal anti inflammatory drugs which are well known to cause proteinuria. Since she had nephrotic range proteinuria at the time of renal biopsy, transformation into another type of lupus nephritis cannot be appreciated. Her renal biopsy was clearly indicative of MPLN. Furthermore activity index of 3/24 indicates less aggressive disease. Chronicity index of 0/12 also signifies good prognosis.

This patient had a rapid response to prednisolone with reduction of urine albumin excretion, which is a good prognostic marker. Being on regular follow up for the past 2 years, she never had a relapse of her proteinuria. But regular follow up is necessary to detect any relapse of proteinuria at which point repeat renal biopsy is warranted in order exclude transformation of her MPLN to another variety which has been described in earlier case reports.

Generally ISN / RPS class I and II require no specific therapy and expected to have good long term renal outcomes (9). However the optimal therapeutic approach to a patient with MPLN associated nephrotic syndrome is not well established because of sparse number of recorded clinical cases and variability of clinical course (3). Further studies are warranted in order to define the pathogenesis, optimal therapeutic regimes and prognosis of MPLN associated nephrotic syndrome in SLE patients.

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