CASE REPORT

Lupus Nephritis diagnosed by stand-alone renal histopathological findings in a middle-aged male

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a systemic autoimmune condition, characterized by the production of autoantibodies, predominantly against nuclear antigens. It primarily affects women of childbearing age. Men account for 4-22% of all cases in various series[1,2]. Lupus nephritis can be diagnosed with high sensitivity and specificity based on histopathological criteria alone[3]. We report lupus nephritis in a 50-year-old male diagnosed solely on renal histopathological findings.

Case Presentation.

A 50-year-old male presented to a nephrology outpatient clinic with a history of early morning puffiness of the face and bilateral lower limb swelling of one-month duration. He had also noticed foamy urine and that his urine output had decreased over the span of 1 month. He denied any history of gross hematuria, arthralgias, arthritis, oral ulcers, photosensitivity or skin rash. He denied any symptoms suggestive of Raynaud's phenomenon There was no history of drug abuse, diabetes, hypertension or ATT intake in the past. On examination, his pulse rate was 80 beats per min and his BP was 130/80 mmHg. He had pitting pedal edema up to bilateral knees. His systemic examination was unremarkable. His urine analysis showed 3+ albuminuria with bland urinary sediment. His blood urea and serum creatinine were 40 mg/dl and 1.10mg/dl (eGFR 78ml/min/1.73m2) respectively. His 24-hour urine protein was 8.0 gram per day. His serum protein and albumin levels were 3.7g/dl and 1.8 g/dl respectively. His viral markers were negative for hepatitis B, C, and HIV. Detailed investigations are shown in table 1.

Sodium	134 meq/l
Potassium	5.4 meq/l
Urea	40 mg/dl
Creatinine	1.10 mg/dl
Total protein	3.7 g/dl
Serum albumin	1.8 g/dl
Glucose	112 mg/dl
Bilirubin	0.2 mg/dl
AST	33 U/L
ALT	36 U/L
ALP	65 U/L
LDL cholesterol	276 mg/dl
Triglycerides	434 mg/dl
Hemoglobulin	11.1 g/dl
WBC	4800/cumm
Platelets	2.1 lac
Viral markers (HbsAg, AntiHCV, and HIV)	Non- reactive.
Urine analysis	Albumin 3+, RBCs- nil, Pus cells- 3 to 5/hpf
24hour urinary protein	8.0 gram/day

A diagnosis of adulthood onset nephrotic syndrome was made. Based on the clinical history and laboratory results, the likely renal histopathological lesion was presumed to be either membranous nephropathy, minimal chain disease or FSGS. Ultrasound-guided renal biopsy was taken from left kidney using spring-loaded Bard biopsy gun and tissue was

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sent for light microscopy, immunofluorescence microscopy, and electron microscopy.

Renal biopsy findings.

Light microscopy: Tissue was stained with hematoxylin-eosin, PAS, silver methenamine, Masson-trichrome, and Congo red. The biopsy core contains 13 glomeruli. All glomeruli appear enlarged and reveal diffuse variable mesangial and endocapillary hypercellularity with intracapillary and mesangial neutrophil infiltration. Peripheral capillary loops show patchy thickening, intramembranous mottling and about 4 glomeruli reveal subendothelial fuchsinophillic deposits with splits/ double contour formation. Active tuft necrosis, crescent formation, or intra-capillary thrombi were not observed. Interstitial fibrosis and tubular atrophy observed in 15 % of the sampled cortex. (Figure 1)

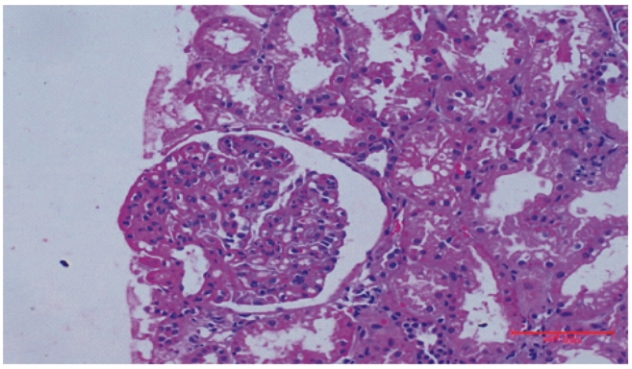


Fig 1. Light microscopic image showing single glomerulus displaying mesangial and endocapillary hypercellularity with patchy tubular injury (see text)

Immunofluorescence microscopy showed full house staining with IgG 3+ (IgG1 3+, IgG 2 2+, IgG3 2+, IgG4 negative), IgA 2+, IgM 2+, C3 2+, C1q 2+, κ 3+, λ 3+.

Granular staining for IgG, C1q, κ, and λ was noted along few tubular basement membranes.

Electron microscopy findings.

Glomerular basement membrane thickness varied from 381.6nm to 1839.5nm. The foot process of visceral epithelial cells showed widespread effacement (about 70%). Several mesangial, sub-endothelial, sub-epithelial and intramembranous electron deposits noted. Some tubulo-reticular inclusions identified in glomerular and peritubular capillary endothelial cell cytoplasm (Figures 2 and 3).

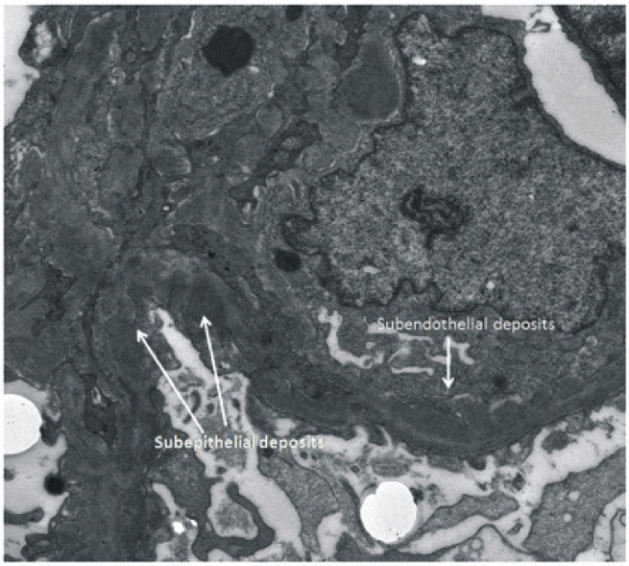


Fig 2: Electron microscopic image showing subepithelial and subendothelial deposits (large and small white arrows)

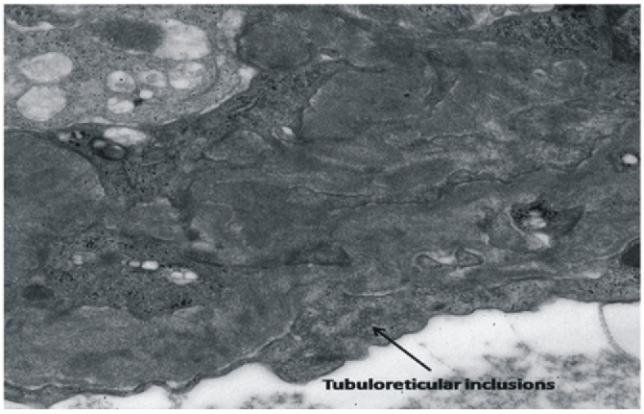


Fig 3: Electron microscopic image showing tubule-reticular inclusions (Black arrow)

Based on renal biopsy finding of full house immunofluorescence, significant C1q staining, extra-glomerular immune deposits, combined sub-endothelial and sub-epithelial deposits, and endothelial tubulo-reticular inclusions, diagnosis of lupus nephritis ISN/RPS class IV(A)+V was made

Subsequently patient's ANA, C3, C4 and ENA profile were done. ANA came out positive at endpoint titer of 1:360 (Hep 2 method), C3 and C4 were low (56.30mg/dl and 8.30mg/dl respectively) Anti dsDNA was negative and U1RNP was 3+.

DISCUSSION

Systemic lupus erythematosus is an autoimmune disease

that can essentially involve any organ or tissue. SLE tends to affect the young woman of child-bearing age and the incidence rate of SLE is 6-10 times more prevalent in women than in men[4]. Lupus nephritis is one of the most severe manifestations of SLE, being observed in 30-75% of patients present either at the time of diagnosis of SLE or later during the disease course. Lupus nephritis contributes significantly to morbidity and mortality in patients with SLE, either as a consequence of kidney disease itself or secondary to infectious complications due to intensive immunosuppression use[5-7]. Lupus nephritis is less frequent in late-onset SLE (≥50 years) with less than 30% getting affected[8]. Nephrotic syndrome is the most common renal manifestation of SLE in men as was seen in our patient.Class IV lupus is the most common histopathological form[9]. Our patient has class IV+V lupus as per ISN/RPS classification of lupus. A recent study done by Kudose S et al showed five renal histopathological findings with reasonably high sensitivity and specificity for the diagnosis of lupus nephritis (2+ intensity staining for C1q, full-house staining, extraglomerular deposits, combined subendothelial and subepithelial deposits, and tubuloreticular inclusions). When three of the five criteria are met, the specificity for the diagnosis of lupus nephritis is 0.95, and it increases to 0.98 with four criteria[3]. Our patient had all the five histopathological findings. Thus, the diagnosis was made solely on histopathological criteria. Immunological work up was not done at the start since lupus in men is uncommon and more so at or beyond 50 years of age. Immunological work up was subsequently done to have immunological markers for the identification of immunological remission and non-invasive assessment of subsequent relapse (if any). Historically, SLE in males has been associated with greater severity and poorer prognoses, particularly as a result of the presence of serositis and greater renal, neurologic, and hematologic impairment[1,10,11]. However, a recent study done by Andrés U et al showed no differences in remission or progression of LN in males when compared with a cohort of female patients with LN[9]. Our patient was given pulse methylprednisolone 1gram daily for 3 days followed by oral prednisolone 1mg/kg body weight. Mycophenolate mofetil was started at 3g per day along with hydroxychloroquine 6.5mg/kg body weight and supportive treatment. The patient was put on septran and acyclovir prophylaxis. The patient responded with a decrease in proteinuria from baseline of 8.0 gram per day to 700mg per day at month 3 of treatment.

This case is unique in the sense that lupus nephritis is rare in elderly men. Further, our patient didn't satisfy 4 of the 11 criteria as suggested by the American rheumatology association for diagnosis of SLE. The diagnosis was made entirely based on renal histopathological findings. This high lighten the fact that stand-alone renal histopathological findings are highly specific for making the diagnosis of lupus nephritis.

Further, our patient had proliferative lupus with bland urinary sediment which is a very rare finding.

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