

Unmasking Focal Segmental Glomerulosclerosis in A Patient With Lupus Nephritis: A Rare Clinicopathological Overlap

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Abstract

Background

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disorder in which lupus nephritis (LN) represents one of the most serious complications. Persistent nephrotic-range proteinuria despite appropriate immunosuppressive therapy should prompt consideration of concurrent renal pathology. Focal segmental glomerulosclerosis (FSGS) is an uncommon but clinically significant lesion that may coexist with lupus nephritis and adversely influence renal prognosis.

Case Presentation

A 28-year-old Middle Eastern male with biopsy-proven lupus nephritis diagnosed at the age of 18 years presented with progressively worsening nephrotic-range proteinuria despite maintenance therapy with mycophenolate mofetil (MMF). Laboratory evaluation revealed persistent proteinuria of 2.39 g/24 hours, serum creatinine of 2.5 mg/dL, normal complement levels (C3 and C4), negative anti-double-stranded DNA antibodies, and negative anti-Smith antibodies, suggesting inactive lupus disease. Owing to persistent renal dysfunction despite stable serological markers, repeat renal biopsy was performed. Histopathological examination demonstrated focal segmental glomerulosclerosis with intimal fibrosis and no evidence of active lupus nephritis. MMF was discontinued because of poor tolerance to higher doses, and treatment was modified with intravenous rituximab along with optimized supportive nephroprotective therapy. During follow-up, renal function remained stable without further clinical deterioration.

Conclusion

This case highlights the importance of considering superimposed FSGS in patients with lupus nephritis who continue to exhibit persistent proteinuria despite apparent immunological remission. Repeat renal biopsy remains invaluable in differentiating active lupus nephritis from secondary glomerular pathology and facilitates individualized treatment decisions that may improve long-term renal outcomes.

Keywords: Systemic lupus erythematosus, Lupus nephritis, Focal segmental glomerulosclerosis, Proteinuria, Renal biopsy, Rituximab.

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by immune-complex deposition and multisystem inflammation. Renal involvement occurs in nearly half of patients and remains one of the leading causes of morbidity and mortality (1,2). Lupus nephritis is classified according to the International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification, and treatment is primarily guided by histopathological findings (5–7).

Although persistent proteinuria is commonly attributed to active lupus nephritis, clinicians should remain alert to alternative renal pathologies, particularly when serological markers indicate inactive disease (2,5). Focal segmental glomerulosclerosis (FSGS) is characterized by segmental sclerosis involving a proportion of glomeruli and may develop as either a primary disease or secondary to chronic glomerular injury (4). The coexistence of FSGS with lupus nephritis is uncommon but carries important therapeutic and prognostic implications (3,8,9).

We report a rare case of biopsy-proven lupus nephritis complicated by superimposed FSGS, emphasizing the diagnostic value of repeat renal biopsy in patients with persistent proteinuria despite adequate immunosuppressive therapy (8–10).

Case Presentation

A 28-year-old Middle Eastern male with a known history of systemic lupus erythematosus and biopsy-confirmed lupus nephritis presented with progressive worsening of nephrotic-range proteinuria despite long-term treatment with mycophenolate mofetil. He had initially been diagnosed with lupus nephritis at 18 years of age and had remained on maintenance immunosuppressive therapy.

Routine laboratory evaluation demonstrated increasing 24-hour urinary protein excretion reaching 2,394 mg/day, with deterioration in renal function reflected by a serum creatinine of 2.5 mg/dL. Serological investigations showed normal complement C3 (137 mg/dL) and C4 (36 mg/dL) levels, negative anti-dsDNA antibodies (2.2 IU/mL), negative anti-Smith antibodies (<0.2 AI), and anti-chromatin antibodies of 0.7 AI, indicating inactive lupus disease.

Because the degree of proteinuria was disproportionate to the serological activity, repeat renal biopsy was performed. Histopathological examination revealed segmental glomerulosclerosis involving focal glomeruli with associated intimal fibrosis, while there was no evidence of active immune-complex-mediated lupus nephritis (4,5). These findings suggested secondary focal segmental glomerulosclerosis as the cause of persistent proteinuria.

Considering the biopsy findings and the patient's intolerance to higher doses of MMF because of headache and muscle pain, MMF was gradually discontinued. Intravenous rituximab (1 g) was initiated together with supportive measures including renin-angiotensin system blockade, blood pressure optimization, and regular nephrology follow-up (5,8).

The patient remained clinically stable during subsequent follow-up, with serum creatinine stabilizing between 2.4 and 2.5 mg/dL and no further progression of renal dysfunction.

Discussion

Lupus nephritis remains one of the most significant causes of chronic kidney disease in patients with systemic lupus erythematosus (2). Persistent proteinuria is usually interpreted as ongoing disease activity; however, chronic glomerular damage or superimposed renal diseases should be considered when serological markers remain inactive (3,5).

Focal segmental glomerulosclerosis is characterized by sclerosis affecting portions of selected glomeruli and results from podocyte injury (4). In patients with lupus nephritis, FSGS may develop secondary to chronic immune-mediated renal damage or adaptive glomerular hyperfiltration. Histologically, FSGS is distinguished by segmental scarring and podocyte injury without active immune-complex deposition (3,4).

Our patient demonstrated persistent proteinuria despite normal complement levels and negative anti-dsDNA antibodies, making active lupus nephritis unlikely. Repeat renal biopsy therefore proved essential in establishing the diagnosis of concurrent FSGS (5,8). Identification of this lesion significantly altered management, leading to discontinuation of ineffective escalation of MMF and initiation of rituximab with supportive nephroprotective measures.

Few published reports describe the coexistence of lupus nephritis and FSGS (8–10). Available evidence suggests that patients with overlapping pathology often experience greater proteinuria, faster progression to chronic kidney disease, and poorer long-term renal outcomes than those with isolated lupus nephritis (9,10). Consequently, repeat renal biopsy should be considered in patients whose clinical course is discordant with serological findings (5,8).

Conclusion

This case illustrates a rare but clinically important coexistence of focal segmental glomerulosclerosis and lupus nephritis. Persistent proteinuria despite serological remission should prompt reconsideration of the underlying diagnosis rather than automatic intensification of immunosuppressive therapy (5,8). Repeat renal biopsy remains the cornerstone for identifying superimposed renal pathology and guiding individualized management (5–7). Early recognition of FSGS in lupus nephritis may improve renal preservation and optimize long-term patient outcomes (4,8–10).

References

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