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Case Report

"Full house" lupus nephritis with negative serology: a case report

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ABSTRACT

Kidney disease is the leading cause of morbidity and mortality in systemic lupus erythematosus (SLE). Among the histological types of lupus nephritis, membranous lupus nephritis accounts for only one-fifth of all cases, with immunofluorescence being essential for diagnosis. The long-term prognosis of lupus nephritis is uncertain, with a significant percentage progressing to stage 5D chronic kidney disease (10 to 20%). Existing evidence on the relative efficacy of different therapies is limited. The authors present the clinical case of a 28-year-old male patient with a kidney biopsy revealing lupus nephritis, in the absence of other clinical and laboratory manifestations of SLE. Until a few years ago, 40% of patients with severe forms of lupus nephritis progressed to death or chronic kidney failure within five years of disease onset. Today, this pessimistic prognosis has improved significantly thanks to anatomical, clinical, and therapeutic approaches.

Keywords: Lupus nephritis, Systemic lupus erythematosus, Kidney biopsy, Steroids

INTRODUCTION

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with significant epidemiological, clinical, and immunological heterogeneity.[1]

Its etiology is unknown; however, genetic factors and an abnormal immune response likely interact to cause the disease. The primary mechanism of tissue injury appears to be the deposition of circulating immune complexes; other mechanisms such as anti-tissue antibodies and the formation of immune complexes *in situ* may also be involved.[2]

As a systemic disease, multiple organs and/or systems can be compromised. Renal involvement is a common complication of this disease, significantly influencing the prognosis and increasing the morbidity and mortality of patients who suffer from it. For this reason, it has been the subject of the special emphasis in the presentation of this case.

Mesengial proliferative lupus nephritis (MPNL), or class II, affects between 10 and 20% of patients with renal manifestations of SLE. Unlike classes III and IV, it frequently arises in the absence of other clinical and laboratory manifestations of SLE, making differential diagnosis with idiopathic membranous nephropathy (IMN) difficult. Like INM, it usually presents with nephrotic syndrome and a histological pattern indistinguishable from the idiopathic form.[3] Immunofluorescence is essential for diagnosis.[3]

The long-term prognosis for LNM is uncertain, with a significant percentage progressing to stage 5D chronic kidney disease (10-20%). The CVS and thromboembolic risk is high.[3] The natural history of the disease and risk factors for progression are not well established, making the decision on the initiation and type of the therapy difficult.

Antiproteinuric measures, alkylating agents, calcineurin inhibitors, mycophenolate mofetil and rituximab are some of therapeutic options. Existing evidence on relative efficacy of different therapies are limited.[4]

In the new international society of nephrology/renal pathology society (ISN/RPS) classification of lupus nephritis (2004), class II lesions are defined by pure mesangial hypercellularity of any degree and/or expansion of the mesangial matrix, as evidenced by conventional light microscopy, with mesangial immune deposits.

There may be a few subendotelial/subepithelial deposits detected by immunofluorescence or electron microscopy but not visible by conventional light microscopy.[5]

CASE REPORT

A 26-year-old patient with no significant medical history presents with a 5-day history of odynophagia accompanied by watery rhinorrhea, nausea, malaise, and no fever. Physical examination reveals no abnormalities; later, the patient exhibits severe lower back pain. During hospitalization, the patient exhibits polydipsia and polyurea. Urinalysis reveals protein levels of 500 mg/dL with no impaired renal function. Renal ultrasound reveals enlarged kidneys. The 24-hour proteinuria result was 3275 mg with a volume of 3000 milliliters.

Nephrotic syndrome is suspected due to the presence of proteinuria, with a new elevated sample value compared to that at admission: 24-hour proteinuria, with results of 526 mg/24 hours and a urine volume of 9450.00 ml/24 hours. Renal function worsened with a creatinine of 2.7 mg/dL compared to 1.3 mg/dL at admission. Serum complement C3 and C4 fractions were normal. ANA and anti-dsDNA titers were undetectable: total calcium: 8.8; phosphorus: 5.5; triglycerides: 74; cholesterol: 148; albumin: 3.88. Without a known cause of deterioration in kidney function, a kidney biopsy is indicated.

Renal biopsy shows renal parenchyma consisting of cortex, which had 32 glomeruli, no global sclerosis, no segmental sclerosis, presenting slight increase in mesangial matrix, preserved cellularity, no filling defects or spikes were identified, no endo or extra capillary proliferation. No glomerulomegaly. Table 1 shows the immunofluorescence study.

Table 1: Direct immunofluorescence.

S. no.	Variables
1	**IgG:** fine and coarse granular deposits ++/+++ in mesangium
2	**IgA:** fine and coarse granular deposits ++/+++ in mesangium
3	**IgM:** fine and coarse granular deposits +/+++ in mesangium
4	**C3:** fine and coarse granular deposits ++/+++ in mesangium
5	**C1q**: fine and coarse granular deposits ++/+++ in mesangium
6	**Kappa**: fine and coarse granular deposits +/+++ in mesangium
7	**Lambda**: fine and coarse granular deposits +/+++ in mesangium

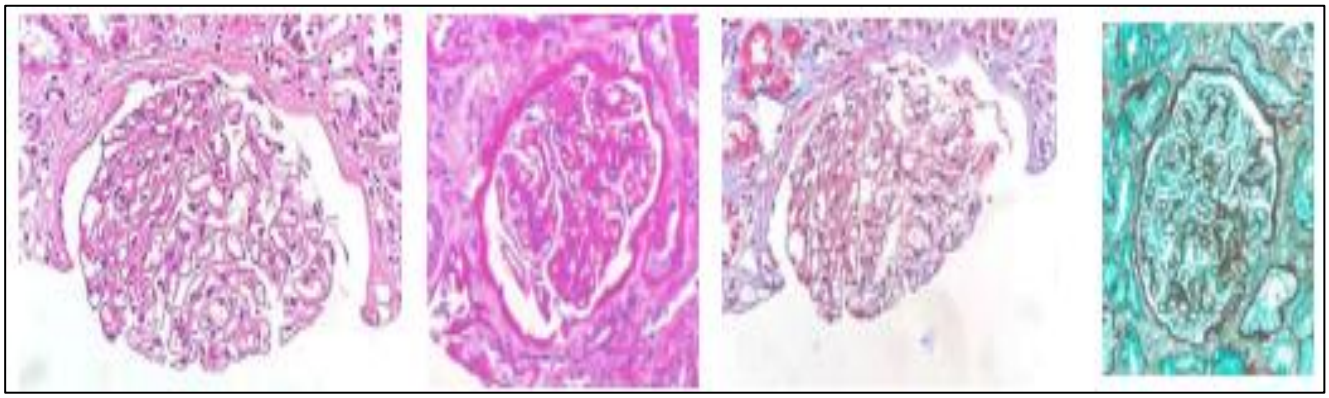

Figure 1: **Renal biopsy and histopathological result.**

Glomerular tuft with mesangial cell proliferation and segments of endocapillary proliferation with a small circumscribed crescent.

DISCUSSION

Lupus nephritis is an autoimmune condition marked by the generation of autoantibodies and immune complexes that deposit within renal structures, leading to inflammation and tissue damage. These antibodies may target nuclear antigens (such as DNA and associated proteins) as well as cytoplasmic or membrane components. Once deposited in the glomeruli, immune complexes trigger complement activation and the release of pro-inflammatory cytokines, which contribute to progressive renal injury. The diagnosis of SLE requires a comprehensive assessment of clinical

and laboratory findings, as no single test is sufficient for confirmation. Even renal biopsy, while crucial, cannot by itself establish the diagnosis.[6]

A crucial finding in this case is the "full house" immunofluorescence pattern, characterized by polyclonal and polycomponent deposits of IgG, IgA, and IgM, along with C3 and C1q, in addition to kappa and lambda chains, predominantly in the mesangium. This pattern is highly suggestive of lupus nephritis and, in the appropriate context, has greater diagnostic weight than serology alone, especially when ANA and anti-dsDNA antibodies are negative.[6]

The literature describes entities such as "non-lupus full house nephropathy" or "seronegative lupus nephritis," in which kidney exhibits a typical SLE immunophenotype without initial systemic criteria; in a proportion of these patients, extrarenal manifestations or seroconversion (ANA/anti-dsDNA) may become apparent during follow-up. Therefore, a negative serologic result does not exclude renal SLE, particularly when C1q deposits are observed alongside multiple immunoglobulins, an unusual finding in most non-lupus glomerulopathies.[7]

The etiology of SLE remains unclear, although genetic susceptibility, hormonal influences, infections, and environmental exposures appear to contribute. Some cases are associated with inherited complement deficiencies, while others may be drug-induced. A failure in the clearance of autoreactive lymphocytes and apoptotic debris also plays a central role in perpetuating autoimmunity, fueling chronic inflammation.[6]

Renal involvement results both from circulating immune complex deposition and from *in situ* immune complex formation. These mechanisms promote complement activation and the infiltration of inflammatory cells, thereby aggravating tissue injury. In addition, antiphospholipid antibodies may induce intrarenal thrombosis, compounding the glomerular damage.[7]

Lupus nephritis is a type 3 hypersensitivity reaction. This occurs when immune complexes form. The characteristics of autoantibodies relevant to lupus nephritis are: i) Anti-dsDNA antibodies can cross-react with the glomerular basement membrane; ii) Higher affinity autoantibodies can give rise to intravascular immune complexes that are deposited in the glomeruli; iii) Cationic autoantibodies have a higher affinity for the anionic basement membrane; iiii) Complement activation by autoantibodies of certain isotypes. These autoantibodies form immune complexes within the vessels that are deposited in the glomeruli.

Alternatively, autoantibodies can form immune complexes *in situ* by binding to antigens already located on the glomerular basement membrane. These immune complexes induce an inflammatory response by activating the complement system and recruiting inflammatory cells. Glomerular thrombosis is another phenomenon that plays a role in the pathogenesis of lupus nephritis, particularly in patients with antiphospholipid syndrome. It is thought to result from an interaction between antibodies and negatively charged phospholipid proteins.[7]

Although SLE can occur at any age, it is most prevalent among young adults, with a strong female predominance (9:1 ratio) and higher incidence in individuals of African descent. Extrarenal manifestations vary widely, affecting the skin, joints, hematological system, nervous system, serosal surfaces, and cardiopulmonary organs

Renal presentations range from mild asymptomatic hematuria or proteinuria to nephrotic syndrome or rapidly progressive renal failure. Approximately two-thirds of patients with lupus nephritis may develop nephrotic syndrome during the disease course. Serum creatinine and urea levels fluctuate depending on the extent and severity of histological injury. Hypocomplementemia is commonly observed during active disease phases and may correlate with disease activity in certain cases.[1-3]

Patient survival and preservation of renal function have improved significantly in recent decades. Treatment is based on corticosteroids and other immunosuppressants. Kidney disease is one of the leading causes of death in SLE. When chronic kidney failure occurs and hemodialysis is initiated, there is improvement in extrarenal manifestations in many patients. Kidney transplantation is a good option in cases of end-stage organ damage; disease recurrence in graft is not very common, and transplant survival is similar to that of other patients. Immunosuppression received by transplant recipients is, at least in part, responsible for clinical improvement in SLE.[7]

Many patients present with proteinuria ranging in intensity, usually accompanied by hematuria, sometimes with red blood cell casts. When active glomerular lesions are present, leukocyte casts may be present. Serum BUN and creatinine levels may or may not be elevated depending on the type and severity of the renal lesions. Generally, elevated levels are present in cases of active lesions (classes III and IV) or chronic damage.

In many cases of mesangial lupus nephropathy and pure membranous GN (class V), renal function is preserved. Hypocomplementemia is present in most patients with active disease, and in some, complement levels correlate with renal disease activity. A variety of autoantibodies can be detected in serum: ANAs, anti-dsDNA, anti-Sm (highly specific but insensitive), anti-RNP, anti-Ro, anti-La, anti-histone, and others; anti-DNA antibodies appear to be important in the pathogenesis of active lupus negphritis.[7]

The differential diagnosis of the "full house" pattern includes glomerulonephritis associated with infections (e. g., postinfectious), IgA nephropathy with accessory deposits, C1q nephropathy, and forms of membranoproliferative glomerulonephritis associated with chronic infections (HBV/HCV) or autoimmunity.

However, the robust coexpression of C1q with the three immunoglobulins and the histological context of mesangial proliferation strongly favor lupus nephritis. Normocomplementemia, as in this case, does not rule out lupus renal activity, especially in classes II and V, and may present in early stages or with limited renal manifestations.

From a practical perspective, recognition of the "full house" pattern in the biopsy guides therapeutic approaches toward specific regimens for lupus nephritis, even with initial negative serologies, once infectious causes and other etiologies have been ruled out. Furthermore, it supports a plan of close monitoring with serial repeat ANA, anti-dsDNA, anti-Sm, and complement (C3/C4) tests, as well as antiphospholipid antibody screening, given the risk of seroconversion and new systemic manifestations over time. In summary, in this patient, the "full house" pattern confers sufficient pathogenetic plausibility and diagnostic support to manage the case as mesangial lupus nephritis (ISN/RPS class II), despite the initially negative serum antigens/autoantibodies.[7]

Therapeutic advances over the past decades have significantly improved survival and renal outcomes. Corticosteroids remain the cornerstone of treatment, often combined with immunosuppressive agents such as cyclophosphamide, mycophenolate mofetil, rituximab, or calcineurin inhibitors tailored to disease severity. For patients progressing to end-stage renal disease, renal replacement therapies such as dialysis and transplantation are effective options, with graft survival comparable to that of other patient populations

Treatment and follow-up

The patient was initiated on high-dose corticosteroid therapy in combination with mycophenolate mofetil as the primary immunosuppressive regimen. Supportive measures included the administration of ACE inhibitors to reduce proteinuria and strict blood pressure control. During follow-up, the patient demonstrated a gradual reduction in proteinuria and stabilization of serum creatinine levels. Outpatient nephrology visits and regular monitoring of renal and immunological markers confirmed sustained improvement and no major complications during the first six months after diagnosis.

CONCLUSION

Lupus nephritis is an uncommon presentation in young male patients and poses diagnostic challenges when serological markers are absent. Histopathological confirmation is critical for prognosis and therapeutic decision-making. While there is no universally established treatment protocol, corticosteroids combined with immunosuppressants remain the foundation of management. Long-term follow-up is essential to prevent relapses and delay progression to end-stage renal disease.

This case highlights the importance of the ‘full house’ pattern in immunofluorescence as a key diagnostic element when serologies for SLE are negative. The concomitant presence of IgG, IgA, IgM, C3, and C1q in the mesangium guided both the diagnosis and the therapeutic strategy toward lupus nephritis, after ruling out infectious causes and other glomerulopathies. We emphasize the need for serial immunological and clinical follow-up, given the possibility of seroconversion and the fact that renal involvement may precede systemic manifestations of SLE.

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