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Lupus Nephritis Presenting with Mixed Nephrotic and Nephritic Syndrome : A Case Report

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ABSTRACT

Lupus nephritis (LN) is a severe manifestation of Systemic Lupus Erythematosus (SLE) that may present with mixed nephritic and nephrotic features. Diagnosis can be challenging when renal biopsy is not immediately feasible. Case Presentation: An 18-year-old female presented with dyspnea, pleuritic chest pain, generalized edema, and recurrent seizures. She exhibited persistent nephrotic-range proteinuria, active urinary sediment, severe hypoalbuminemia, hypocomplementemia, and strongly positive antinuclear antibodies, while anti–double-stranded DNA antibodies were negative. Imaging revealed bilateral pleural effusions and increased renal parenchymal echogenicity. Based on the 2019 EULAR/ACR criteria, she fulfilled 14 points, supporting a diagnosis of SLE. The clinical and laboratory findings were consistent with probable lupus nephritis presenting as mixed nephritic and nephrotic syndrome. She was treated with corticosteroids, mycophenolate mofetil, hydroxychloroquine, antihypertensive agents, electrolyte correction, and supportive therapy, resulting in clinical stabilization during hospitalization. This case illustrates the diagnostic complexity of lupus nephritis in a young female presenting with overlapping nephritic and nephrotic features when renal biopsy cannot be performed immediately. The presence of persistent nephrotic-range proteinuria, active urinary sediment, hypocomplementemia, high-titer ANA, and systemic manifestations fulfilled the 2019 EULAR/ACR classification criteria for SLE, supporting a clinical diagnosis of probable lupus nephritis. In accordance with current guidelines, early initiation of immunosuppressive therapy was justified to prevent irreversible renal damage. This case underscores the importance of integrating clinical, serologic, and laboratory findings for timely decision-making and highlights the need for close follow-up and renal biopsy once clinically feasible to optimize long-term outcomes.

KEYWORDS *Lupus Nephritis; Systemic Lupus Erythematosus; Nephrotic Syndrome; Nephritic Syndrome*

INTRODUCTION

Lupus nephritis (LN) is one of the most serious organ manifestations of Systemic Lupus Erythematosus (SLE). SLE is a chronic, multisystem autoimmune disease characterized by immune dysregulation and the production of autoantibodies, leading to immune complex formation and deposition across various organs (Teoh et al., 2025). Among its myriad manifestations, LN represents one of the most severe, posing a considerable risk for long-term renal impairment and progression to Chronic Kidney Disease (CKD) or End-Stage Kidney Disease (ESKD) (Roveta et al., 2024).

Women, particularly those of reproductive age, are disproportionately affected, with nearly 90% of SLE patients being female (Siegel & Sammaritano, 2023). Approximately 40–50% of SLE patients worldwide develop clinically apparent lupus nephritis during the course of their disease. The clinical spectrum of LN is highly heterogeneous, ranging from asymptomatic urinary abnormalities to rapidly progressive glomerulonephritis. Patients may present with features of nephritic syndrome, nephrotic syndrome, or a combination of both, reflecting immune-complex–mediated glomerular inflammation and injury.

Early recognition of LN is critical, as delayed diagnosis and treatment are strongly associated with poorer renal outcomes. Although renal biopsy remains the gold standard for

confirming LN, classifying histopathological variants (ISN/RPS), assessing activity versus chronicity, and guiding immunosuppressive management, real-world constraints often limit its feasibility—particularly in resource-limited settings or in patients presenting with hemodynamic instability, edema, or coagulopathy (Aljohani et al., 2024). In such circumstances, clinicians must rely on a combination of clinical judgment, laboratory findings (e.g., proteinuria, urinary sediment, complement levels), serologic markers (e.g., ANA), and classification criteria such as the 2019 EULAR/ACR guidelines to establish a provisional diagnosis and initiate early therapy.

In addition to renal involvement, SLE may present with extrarenal manifestations such as pleural effusion, cytopenias, neuropsychiatric symptoms, and constitutional complaints (Anders et al., 2020). Pleural effusion is one of the most common pulmonary manifestations of SLE, while seizures may occur as part of neuropsychiatric lupus (NPSLE) or as a result of metabolic derangements secondary to renal dysfunction. Differentiating these etiologies is essential for appropriate management (Rovin et al., 2024; Yap & Tang, 2023).

This case report discusses an 18-year-old female who presented with mixed nephrotic and nephritic syndrome, persistent heavy proteinuria, active urinary sediment, hypocomplementemia, pleural effusion, and neuropsychiatric symptoms (seizures). Given the limitations in performing a renal biopsy at that time, the 2019 EULAR/ACR classification criteria for SLE were applied, leading to a working diagnosis of probable lupus nephritis. This case highlights several critical issues: the diagnostic complexity of LN in the absence of histopathologic confirmation, the heterogeneity of SLE presentations, and the urgency of initiating timely immunosuppressive therapy to prevent irreversible renal damage. Moreover, it underscores the challenges encountered in real-world, resource-constrained clinical settings, emphasizing the need for heightened clinical suspicion, early detection, and comprehensive management strategies.

The objective of this case report is to describe the diagnostic approach and clinical management of a patient with suspected lupus nephritis presenting with mixed nephrotic and nephritic syndrome when renal biopsy was not immediately feasible, and to evaluate the utility of the 2019 EULAR/ACR classification criteria in guiding clinical decision-making. The benefits of this report are twofold. Clinically, it offers insights for practitioners facing similar diagnostic dilemmas in resource-limited environments, highlighting the importance of integrating clinical, serologic, and laboratory findings to initiate timely immunosuppressive therapy and prevent irreversible renal damage. Academically, this case contributes to the growing literature on lupus nephritis by illustrating its diagnostic and management challenges in atypical presentations and reinforcing the practical use of classification criteria as effective diagnostic tools when histopathologic confirmation is temporarily unavailable.

METHOD

Case Report

An 18-year-old female with a history of nephrotic syndrome and status epilepticus presented to the emergency room at RSUD Tabanan with worsening shortness of breath accompanied by bilateral chest pain over the preceding day. The dyspnea had begun two days before admission and was exacerbated when she lay on her left side. She also reported a non-productive cough without phlegm, sputum, or hemoptysis that had started two days earlier. On

the night prior to admission, she experienced two generalized tonic–clonic seizures lasting approximately five minutes each, separated by a one-hour interval during which she regained full consciousness. The patient reported progressive edema involving the lower extremities, upper extremities, and abdomen over the past two weeks. Additional symptoms included fatigue, arthralgia, and progressive non-scarring alopecia over the last two months. She described marked activity intolerance and had experienced unintentional weight loss of 6 kg since her last hospitalization one month earlier. One month prior, she had been hospitalized for generalized edema and seizures and was diagnosed with nephrotic syndrome and status epilepticus. At discharge, urinalysis showed +3 proteinuria. One week later, during a nephrology clinic follow-up, urinalysis again revealed persistent +3 proteinuria, leukocytes 2–4/HPF, and abundant erythrocytes. She had been prescribed prednisone, folic acid, captopril, atorvastatin, furosemide, albumin, hydroxychloroquine, and phenytoin. She denied any history of autoimmune disease, hypertension, diabetes, or heart disease, and there was no family history of similar conditions.

On examination, her blood pressure was 160/100 mmHg, pulse 99/min, respiratory rate 24/min, temperature 36°C, and oxygen saturation 98% on 3 L/min oxygen via nasal cannula. Her BMI was 17.86 kg/m². Physical examination revealed pale conjunctivae, dry oral mucosa, non-scarring alopecia, and diminished breath sounds with dullness to percussion at both lung bases. Abdominal examination demonstrated shifting dullness without hepatosplenomegaly. Pitting edema was present in both lower extremities, and tenderness was elicited on palpation of the elbows and knees. Neurological examination was unremarkable.

Laboratory evaluation demonstrated normocytic normochromic anemia (Hb 9.7 g/dL, MCV 88 fL, MCH 28 pg) and leukocytosis of 13,600/µL. Urinalysis showed +3 protein, 6–8 leukocytes/HPF, abundant erythrocytes, 6–10 flat epithelial cells/HPF, 2–4 renal tubular epithelial cells/HPF, and 1–2 granular casts/HPF. The albumin-to-creatinine ratio was markedly elevated at 1586.32 µg/mg (normal <30 µg/mg), with hypoalbuminemia of 1.7 g/dL (normal 3.4–4.8 g/dL) and a normal urine creatinine of 0.74 mg/dL. Serum electrolytes revealed hypokalemia of 2.7 mmol/L (normal 3.5–5.0 mmol/L). Renal ultrasonography showed normal-sized kidneys with increased parenchymal echogenicity and blurred corticomedullary differentiation bilaterally. Serologic testing revealed strongly positive ANA (>1:1000, speckled pattern), negative anti-dsDNA (34.3 IU/mL), and reduced complement C3 (79 mg/dL). Based on the 2019 EULAR/ACR classification criteria, the patient fulfilled a total of 14 points, consisting of proteinuria >0.5 g/day (4 points), pleural effusion (5 points), non-scarring alopecia (2 points), and decreased complement C3 (3 points), with ANA positivity serving as the entry criterion.

The overall constellation of persistent nephrotic-range proteinuria, active urinary sediment, hypocomplementemia, systemic features, and serositis supported a clinical diagnosis of probable lupus nephritis presenting with combined nephritic and nephrotic syndrome. Additional findings included Stage II hypertension, pleural effusion, hypokalemia, and recurrent seizures, with the latter raising suspicion for vasculitis, although metabolic causes remained under consideration.

During hospitalization, the patient received thoracentesis, electrolyte correction with intravenous potassium chloride, cefotaxime 1 g every 8 hours, 25% albumin infusion, omeprazole 40 mg daily, prednisone 60 mg daily (20 mg every 8 hours), mycophenolate

mofetil 500 mg twice daily, hydroxychloroquine 200 mg daily, vitamin D 100 mcg twice daily, lisinopril 10 mg daily, amlodipine 10 mg daily, atorvastatin 20 mg daily, aspirin 100 mg daily, spironolactone 25 mg daily, and phenytoin 100 mg every 8 hours, along with folic acid supplementation.

RESULT AND DISCUSSION

Lupus nephritis (LN) remains one of the most severe manifestations of SLE and contributes substantially to long-term morbidity and mortality. (Aringer et al., 2019; Vrabie et al., 2025) LN affects approximately 40–60% of patients with SLE, with higher incidence in adolescents and young adults. Recent epidemiological analyses between 2020–2025 demonstrate that LN remains more prevalent in females, particularly in populations of Asian and African ancestry, with earlier onset and more aggressive courses than in Western populations. (Fanouriakis et al., 2024; Fatima & Tsokos, 2024) The patient described in this case—a young female (18 years old) with a mixed nephritic and nephrotic presentation, persistent heavy proteinuria, active urinary sediment, hypocomplementemia, serologic autoimmunity (high-titer ANA), pleural effusion, and recurrent seizures—exemplifies several diagnostic and therapeutic challenges in the contemporary management of suspected lupus nephritis (LN).

The diagnosis of LN is ideally confirmed through renal biopsy, which remains the gold standard for classifying disease according to the ISN/RPS classification and guiding treatment intensity. (Gasparotto et al., 2020; Yao et al., 2020) However, international guidelines, including KDIGO 2024, acknowledge that biopsy may be delayed or temporarily deferred due to clinical instability, severe edema, bleeding risk, or resource limitations. (Justiz-Vaillant et al., 2024) In such circumstances, a synthesis of clinical, serologic, and laboratory findings must guide management decisions. In this patient, persistent nephrotic-range proteinuria, active urinary sediment with hematuria and granular casts, reduced complement C3, and strongly positive ANA provided compelling evidence of glomerular immune complex disease consistent with LN.

The patient fulfilled the 2019 EULAR/ACR classification criteria for SLE with 14 points, including ANA positivity, hypocomplementemia, serositis, non-scarring alopecia, and significant proteinuria. Multiple studies confirm that the 2019 criteria offer superior sensitivity (96%) and specificity (93%) compared to the 1997 ACR criteria, particularly in early disease or in patients with predominant renal manifestations. (Dima et al., 2022; Liu et al., 2022) Although anti–dsDNA antibodies are traditionally associated with LN, recent literature shows that 15–30% of biopsy-proven LN cases lack elevated dsDNA titers, emphasizing that complement consumption (particularly reduced C3) may correlate more strongly with renal activity. (Ji et al., 2020; Morales & Sandino, 2023) Thus, the absence of dsDNA elevation does not exclude LN, especially in patients demonstrating strong clinical and laboratory evidence of immune complex–mediated glomerulonephritis. Complement consumption, particularly low C3 (and/or C4), is a robust marker of immune complex activity and often correlates with renal flares (Mok, 2023; Yap et al., 2024).

The patient presented with combined nephritic and nephrotic features, including massive proteinuria, hematuria, active urinary sediment, hypoalbuminemia, and edema. KDIGO 2024 guidelines highlight that mixed presentations are highly suggestive of

proliferative LN (ISN/RPS Class III or IV), with or without membranous features (Class V), and require prompt immunosuppressive therapy even before biopsy if renal histology is delayed or unavailable. Ultrasound findings of increased parenchymal echogenicity further support chronic inflammatory injury. In addition, her persistent hypertension is consistent with known hemodynamic consequences of LN and further increases the risk of long-term renal impairment.

Serositis in the form of pleural effusion, as observed in this patient, is a well-recognized extrarenal manifestation of active SLE and is strongly associated with high disease activity and renal flares. Current studies (2021–2024) show that pleural effusion occurs in 30–50% of active SLE cases and correlates with complement consumption and renal involvement. Furthermore, non-scarring alopecia—a mucocutaneous criterion—is associated with disease flares and systemic activity. The patient's fatigue, arthralgia, and weight loss are consistent with systemic inflammation, which commonly precedes major organ involvement.

The patient's seizures warrant particular consideration. Neuropsychiatric SLE (NPSLE) affects 10–20% of patients, with seizures representing a common manifestation. However, the differential diagnosis must include electrolyte disturbances, uremia, hypertensive encephalopathy, and medication effects. In this case, severe hypokalemia likely contributed to lowering the seizure threshold, although NPSLE could not be excluded. Recent literature advocates for multidisciplinary evaluation to clarify etiology and guide management. The presence of generalized edema, nephrotic syndrome, and electrolyte disturbances may additionally lower the seizure threshold, further complicating the clinical picture.

Management decisions in the absence of biopsy must balance the risks of treatment delay with the risks of immunosuppression. The use of mycophenolate mofetil (MMF) is consistent with KDIGO 2024 and EULAR recommendations, which favor MMF as first-line induction therapy for proliferative or mixed LN due to superior renal response, better tolerability, and a lower risk of infertility compared with cyclophosphamide. The immunosuppressive regimen used in this case—prednisone, MMF, and hydroxychloroquine—is consistent with evidence-based induction therapy. Hydroxychloroquine remains a cornerstone treatment for SLE, with robust evidence supporting its role in reducing flare rates, thrombotic risk, and long-term organ damage.

Albumin infusion and diuretics were appropriate for symptomatic management of hypoalbuminemia and fluid overload. Correction of hypokalemia with parenteral potassium was indicated, as severe hypokalemia increases the risk of arrhythmia and seizure recurrence. Additional supportive management, including ACE inhibitors (lisinopril), amlodipine, and spironolactone, was appropriately used to reduce proteinuria and control hypertension, in line with renal-protective strategies recommended by KDIGO 2024 supportive care guidance for LN. Early blood pressure control is essential, as uncontrolled hypertension is a major predictor of poor renal outcomes. Thoracentesis was indicated given the symptomatic pleural effusion and respiratory compromise.

Long-term prognosis in LN correlates strongly with early renal response, defined as a significant reduction in proteinuria and stabilization or improvement of kidney function within six months. Close follow-up with serial evaluation of urine protein excretion, kidney function, complement levels, and serologic markers is necessary to guide ongoing therapy.(1,9) Once

clinically feasible, renal biopsy remains strongly recommended to establish histologic class, assess chronicity, and optimize long-term treatment.

In summary, this case illustrates a clinically compelling instance of probable lupus nephritis in which biopsy was not immediately possible. Despite the absence of renal histology, the integration of clinical, serologic, and laboratory evidence justified empiric induction therapy in accordance with current international guidelines. Aggressive immunosuppressive therapy is essential to prevent irreversible renal damage and recurrent life-threatening complications. Continuous monitoring of complement levels, urinary protein excretion, renal function, and systemic involvement is critical to assess treatment response and adjust therapy appropriately over time.

CONCLUSION

Lupus nephritis was diagnosed in a young female presenting with mixed nephritic and nephrotic syndrome in the absence of immediate histopathological confirmation. The constellation of persistent nephrotic-range proteinuria, active urinary sediment, hypocomplementemia, high-titer antinuclear antibodies, serositis, and systemic manifestations fulfilled the 2019 EULAR/ACR classification criteria for systemic lupus erythematosus and strongly supported a clinical diagnosis of probable lupus nephritis. Although renal biopsy remains the gold standard for definitive diagnosis and histological classification, real-world clinical constraints such as patient instability, severe edema, and limited resources may necessitate reliance on clinical judgment supported by serologic and laboratory findings. In such scenarios, early initiation of immunosuppressive therapy in accordance with current international guidelines is crucial to prevent irreversible renal damage and improve long-term outcomes.

This case underscores the importance of maintaining a high index of suspicion for lupus nephritis in young women with persistent proteinuria and systemic features, even in the absence of anti–double-stranded DNA positivity. It also emphasizes the role of a multidisciplinary approach and close longitudinal monitoring to guide therapy, assess response, and determine the appropriate timing for renal biopsy once clinically feasible. Early recognition and timely intervention remain key determinants of renal survival and overall prognosis in patients with suspected lupus nephritis.

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