International Journal of Scientific Reports
Das UK et al. Int J Sci Rep. 2024 Nov;10(11):410-413
http://www.sci-rep.com
pISSN 2454-2156 | eISSN 2454-2164
DOI: https://dx.doi.org/10.18203/issn.2454-2156.IntJSciRep20243054

Case Report

Male systemic lupus erythematosus, rapidly progressive glomerulonephritis, and iatrogenic acute bone marrow failure: a case report

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Received: 16 September 2024
Accepted: 17 October 2024

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ABSTRACT

Lupus nephritis (LN) is a significant complication of systemic lupus erythematosus (SLE), marked by kidney inflammation due to autoimmune activity, leading to proteinuria, hematuria, and potentially renal failure. Rapidly progressive glomerulonephritis (RPGN) is a rare, critical manifestation of LN characterized by a rapid decline in kidney function. This condition can lead to irreversible renal damage and is often fatal without prompt treatment. In this case, a 62-year-old man initially presented with fever, cough, and body aches, which were treated as an acute upper respiratory infection. Despite initial improvement, he developed persistent nausea, vomiting, and signs of renal dysfunction. Laboratory investigations revealed anemia, high erythrocyte sedimentation rate (ESR), electrolyte imbalances, and elevated creatinine. Imaging and endoscopy ruled out malignancy, and a differential diagnosis of multiple myeloma was excluded through plasma protein electrophoresis. Serological tests confirmed SLE, and subsequent renal biopsy revealed LN with RPGN features. Despite aggressive treatment with corticosteroids and cyclophosphamide, the patient's condition rapidly deteriorated, leading to respiratory distress and intensive care unit (ICU) admission. He ultimately succumbed to his illness, underscoring the unpredictable and severe nature of RPGN in LN. This case highlights the importance of early diagnosis and intensive management to prevent rapid disease progression and improve patient outcomes.

Keywords: Lupus nephritis, Systemic lupus erythematosus, Rapidly progressive glomerulonephritis, Renal biopsy, Immunosuppressive therapy, Respiratory distress

INTRODUCTION

Systemic lupus erythematosus (SLE) is a complex autoimmune disorder characterized by chronic inflammation that can affect multiple organ systems, including the kidneys. Lupus nephritis (LN), a severe manifestation of SLE, occurs when immune complexes are deposited in the glomeruli, leading to kidney inflammation, proteinuria, and hematuria. This condition can progress to rapidly progressive glomerulonephritis (RPGN), a rare but aggressive form of glomerular disease that results in a swift decline in renal function. RPGN, if not promptly treated, often leads to irreversible kidney damage and requires intensive immunosuppressive therapy.[1,2]

This case report discusses a 62-year-old male patient with SLE who developed RPGN and iatrogenic acute bone marrow failure following immunosuppressive treatment. The patient's clinical course underscores the challenges in managing SLE with severe renal involvement and highlights the potential risks associated with aggressive treatment strategies, including the development of life-threatening complications such as bone marrow failure. Early detection, close monitoring, and a multidisciplinary

approach are essential in managing these complex cases to prevent fatal outcomes.[3-6]

CASE REPORT

A 62-year-old man presented with a 7-day history of fever, cough, body aches, and runny nose, followed by two weeks of persistent nausea and vomiting. Initially, he experienced fever and cough, which later progressed to breathing difficulties. He sought medical advice from a primary care physician, who diagnosed him with an acute upper respiratory tract infection and prescribed symptomatic treatment, including paracetamol, fexofenadine, doxophylline, and a 7-day course of cefixime. His symptoms partially improved; the fever subsided, and the cough reduced in intensity. However, after the fever resolved, he developed persistent nausea and vomiting, which significantly affected his food intake. He denied other symptoms such as musculoskeletal pain, headaches, abdominal pain, distension, or constipation, except for occasional mild low back pain, which he attributed to his long-standing occupation as a pharmacy worker, often requiring him to stand for extended periods. He was a nonsmoker, normotensive, non-diabetic, with no known chronic illnesses or regular medications.

Physical examination was unremarkable, with vital signs within normal limits: temperature 98.4 °F, pulse rate 88 beats per minute, blood pressure 140/85 mm Hg, and respiratory rate 16 breaths per minute. Systemic examination revealed normal heart sounds, clear lung fields, and no organomegaly. Initial laboratory investigations, including a complete blood count (CBC), urine routine and microscopic examination (urine R/M/E), and chest X-ray (CXR), were performed. The CBC revealed a total WBC count of 11,000/cmm, hemoglobin of 10.4 g/dl, platelet count of 260,000/cmm, and an ESR of 87 mm in the first hour. Urine R/M/E showed RBCs 6-8/hpf, albumin +, and no casts, while the CXR was clear. Additional tests ruled out common infections: malarial parasites were absent, Widal test titers were insignificant, and ICT for *Salmonella typhi* IgG and IgM was negative. Postprandial plasma glucose was 5.7 mmol/l, and HbA1c was 6.2%. Blood film examination indicated anemia of chronic disease.

A month later, repeat urine R/M/E showed increased albumin, RBCs 8-12/hpf, pus cells 4-8/hpf, and no casts. CBC reported a hemoglobin of 10.2 g/dl, WBC count of 4,550/cmm, platelet count of 170,000/cmm, and a significantly elevated ESR of 100 mm in the first hour. Serum electrolytes revealed hyponatremia (Na+ 126 mmol/l), hypokalemia (K+ 3.2 mmol/l), hypochloremia (Cl- 89 mmol/l), and bicarbonate levels of 28 mmol/l. Given the patient's age, persistent nausea, vomiting, and elevated ESR, an upper GI endoscopy was performed to rule out gastric malignancy, which showed no abnormalities. Multiple myeloma was then considered as a differential diagnosis. However, plasma protein electrophoresis revealed polyclonal gammopathy, ruling out myeloma and suggesting SLE, despite the absence of clinical stigmata such as malar rash, photosensitivity, or arthritis.

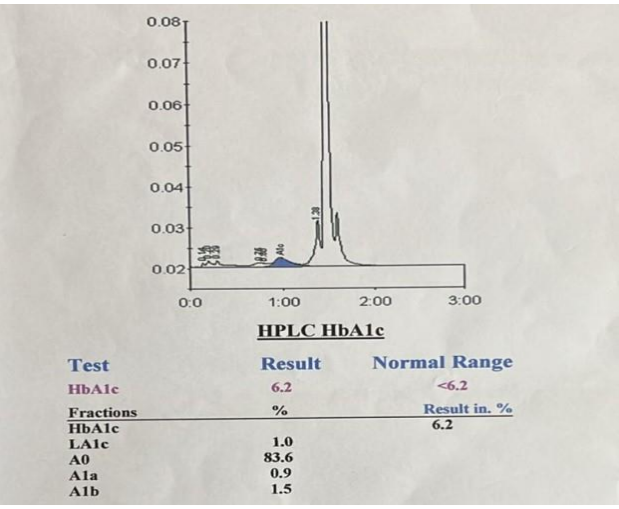

Figure 1: Biochemistry report.

Serological tests confirmed the diagnosis of SLE, with positive ANA (11.20 u/ml) and anti-dsDNA (162.0 IU/ml). Suspecting renal involvement, further tests revealed a serum creatinine level of 5.4 mg/dl, elevated blood urea, and BUN, leading to a clinical diagnosis of lupus nephritis. The patient was advised hospitalization for further evaluation and management. Screening tests for hepatitis B, hepatitis C, and HIV were negative. Coagulation studies showed normal bleeding and clotting times. Serum complement levels were low (C4: 0.26 gm/l, C3: 0.6 gm/l), and parathyroid hormone (PTH) levels were 95.20 pg/ml. Despite microscopic hematuria, urine was negative for dysmorphic RBCs. A 24-hour urine collection revealed total protein of 1.61 gm. Serum P-ANCA was positive (154.0 U/ml), while C-ANCA was negative (1.0 U/ml).

A renal biopsy was performed, with histopathology and immunohistochemistry pending. Meanwhile, the patient's condition rapidly deteriorated, developing oliguria and other uremic symptoms, necessitating initiation of hemodialysis every 3-4 days. Based on the rapid decline in renal function and the development of uremic symptoms, a diagnosis of RPGN secondary to lupus nephritis was made. Immunosuppressive therapy with cyclophosphamide and systemic corticosteroids (prednisone 40 mg daily) was initiated to halt the progression of renal disease.

Unfortunately, the patient developed severe pain at the biopsy site, worsening symptoms, and respiratory distress. A chest X-ray revealed bilateral lung consolidation. A follow-up CBC showed pancytopenia with total RBCs 2.43 million/cmm, hemoglobin 7.1 g/dl, WBC count 400/cmm, and platelet count 10,000/cmm, with an ESR of 96 mm in the first hour. Renal histopathology revealed global and segmental glomerulosclerosis, patchy tubular

injury, foci of tubular atrophy and interstitial fibrosis, moderate arterial medial thickening, and small vessel vasculitis. Direct immunofluorescence (DIF) was negative, likely due to insufficient glomeruli in the sample.

Despite ongoing dialysis and ICU care, the patient's condition continued to deteriorate, culminating in respiratory failure. He was transferred to the ICU, where he passed away the following morning.

DISCUSSION

SLE is characterized by the development of autoantibodies against self-nuclear components, driven by a complex interplay of genetic, environmental, immunological, and infectious factors, such as Epstein-Barr virus (EBV), leading to the loss of immune tolerance. These autoantibody-autoantigen complexes accumulate due to impaired clearance mechanisms in SLE, resulting in their deposition in various organs and tissues, which triggers inflammation, damage, and subsequent loss of function. SLE can affect any organ or tissue, particularly the skin, kidneys, liver, joints, blood vessels, heart, blood, and brain, leading to a wide range of clinical manifestations that can pose diagnostic challenges for clinicians.[7] The American College of Rheumatology (ACR) has identified 11 criteria for diagnosing SLE, with at least four of these criteria required for a diagnosis. However, recent updated guidelines by the European League Against Rheumatism (EULAR)/ACR have included antinuclear antibody (ANA) as the entry criterion for SLE diagnosis.[8]

SLE predominantly affects women of childbearing age, with only 10% of SLE patients being male. Literature on male SLE is limited, and when men are affected, the disease tends to be more severe, with higher morbidity and mortality. Organ failure, such as lupus nephritis (LN), may be the sole manifestation. LN typically develops within five years of SLE diagnosis and can progress to end-stage kidney disease (ESKD) in 5-20% of patients within ten years. Renal biopsy remains the gold standard for diagnosing LN, allowing classification of renal involvement into six categories.[9] Common early presentations of SLE include mucocutaneous, musculoskeletal, and systemic symptoms such as fever, fatigue, and rash. Approximately 40% of SLE patients develop LN, with a significant risk of progressing to ESKD within a decade.[10]

The case described involved a 62-year-old male who presented with uremia, a sign of ESKD, without any other typical SLE symptoms. Remarkably, he exhibited no classical symptoms of chronic kidney disease (CKD) prior to an acute febrile illness, which culminated in persistent vomiting and subsequent oliguria. The rapid deterioration in renal function led to a diagnosis of rapidly progressive glomerulonephritis (RPGN). The detection of positive ANA and anti-dsDNA antibodies, along with a very high ESR, microscopic hematuria, and proteinuria, confirmed the diagnosis of SLE with lupus nephritis.[11] Given the rapid decline in renal function within a month, a diagnosis of RPGN secondary to lupus nephritis was established. Due to the poor prognosis associated with this condition, treatment with oral cyclophosphamide and corticosteroids was initiated, alongside hemodialysis. The histopathological report revealed glomerulosclerosis, with no significant immunological reactions.[12]

Current guidelines for treating lupus nephritis recommend initiating treatment with immunosuppressive agents in combination with systemic corticosteroids. However, it remains unclear whether these medications are beneficial in cases of end-stage kidney disease due to lupus nephritis. In this patient, the initiation of oral cyclophosphamide alongside corticosteroids was followed by the development of acute bone marrow failure one week into treatment.[13] Early diagnosis and intervention may slow disease progression. Ongoing research is focused on developing new drugs that target immune system molecules and inflammatory pathways affecting vital organs.[14]

Voclosporin, an oral calcineurin inhibitor, has been approved for treating active adult LN in combination with other immunosuppressants. It is the first oral medication approved in the United States for this indication. Compared to cyclosporine, an earlier generation calcineurin inhibitor, voclosporin offers improved potency and metabolic stability in calcium-regulated phosphatase inhibition, blocking lymphocyte proliferation and T-cell-mediated immune responses, maintaining podocyte actin cytoskeleton integrity, and reducing proteinuria.[15,16] A real-world study demonstrated better efficacy with voclosporin compared to a placebo when combined with mycophenolate mofetil (MMF) and low-dose steroids. Findings from phase 2 and phase 3 clinical trials underscore the significant advancement voclosporin represents in managing patients with active LN.[17]

CONCLUSION

SLE is relatively rare in the male population, and classical clinical features are often absent. In these patients, vital organ involvement, particularly renal impairment, is common. RPGN should be promptly addressed to prevent progression to end-stage kidney disease. Careful selection of therapeutic agents is crucial for halting disease progression while minimizing the risk of severe adverse effects. Mycophenolate mofetil, an alternative medication, may be considered for such patients as it does not typically induce bone marrow suppression.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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factors during induction treatment of lupus nephritis. Arthritis Rheum. 2011;63(9):2421-31.
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Cite this article as: Das UK, Chowdhury EH. Male systemic lupus erythematosus, rapidly progressive glomerulonephritis, and iatrogenic acute bone marrow failure: a case report. Int J Sci Rep 2024;10(11):410-3.