Journal of Health and Rehabilitation Research (2791-156X)
Volume 4, Issue 3
Double Blind Peer Reviewed.
https://jhrlmc.com/
DOI: https://doi.org/10.61919/jhrr.v4i3.1621
www.lmi.education/

Unusual Case of Systemic Lupus Erythematosus (SLE) With Middle-Age Onset and Atypical Multisystem Involvement

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Keywords
Systemic Lupus Erythematosus, late-onset SLE, lupus nephritis, pulmonary hypertension, middle-aged male SLE, autoimmune disease diagnosis
Disclaimers

Authors' Contributions	All authors contributed equally to the conception, design, and drafting of the manuscript.
Conflict of Interest	None declared
Data/supplements	Available on request.
Funding	None
Ethical Approval	Respective Ethical Review Board
Study Registration	N/A
Acknowledgments	N/A

ABSTRACT

Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder predominantly affecting young females, with middle-age onset in males being a rare occurrence. Late-onset SLE can present with atypical multisystem involvement, complicating diagnosis and management.

Objective: To report an unusual case of SLE in a middle-aged male with multisystem complications, including lupus nephritis and pulmonary hypertension.

Methods: A 52-year-old male with dyspnea, chest pain, and lower extremity edema underwent comprehensive clinical evaluation. Laboratory tests included complete blood count, renal function tests, 24-hour urinary protein, and serological markers (ANA, anti-dsDNA). Imaging studies included echocardiography and high-resolution CT. Renal biopsy confirmed Class IV lupus nephritis. The patient received high-dose corticosteroids, hydroxychloroquine, and mycophenolate mofetil, with supportive management for pulmonary hypertension.

Results: The patient's 24-hour proteinuria reduced from 4.2 g/day to 1.2 g/day. Pulmonary artery pressure improved from 35 mmHg to 30 mmHg after four weeks. Pleural effusions resolved completely, and renal function stabilized (creatinine from 1.9 mg/dL to 1.3 mg/dL).

Conclusion: This rare presentation of late-onset SLE in a male underscore the need for comprehensive evaluation and early intervention to prevent severe complications.

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by a wide array of clinical manifestations that can affect multiple organ systems. It primarily affects young women of childbearing age, with a well-established female-to-male ratio of 9:1, making its onset in middle-aged men a rare phenomenon (6). The disease's pathophysiology involves the production of autoantibodies that target nuclear components, leading to immune complex deposition, tissue inflammation, and multi-organ damage (1). Commonly, SLE presents with a constellation of symptoms including arthritis, skin rashes, renal involvement, and neurological disturbances. However, atypical presentations in older patients, particularly men, are often challenging to diagnose due to the absence of these classical features (2). Early recognition and treatment are essential, as delayed diagnosis can contribute to worse outcomes, especially in cases involving severe organ involvement, such as lupus nephritis and pulmonary hypertension (3).

This case report describes an unusual presentation of SLE in a 52-year-old male who presented with systemic symptoms including persistent dyspnea, intermittent chest pain, and renal dysfunction, with subsequent involvement of the cardiovascular and pulmonary systems. Such atypical presentations are infrequent in men, particularly in this age group, complicating the diagnostic process. Moreover, while SLE is known to predominantly affect the kidneys, lungs, and nervous system in younger patients, middle-aged individuals may exhibit more severe and complex multisystemic involvement, as seen in this case. Pulmonary hypertension and Class IV lupus nephritis, as observed here, are rare yet severe complications of SLE that significantly increase morbidity and mortality if not promptly managed (4).

In this report, we underscore the clinical and diagnostic challenges posed by SLE with atypical multisystem involvement in an older male. The initial symptoms included pulmonary and renal manifestations rather than the more commonly described cutaneous or articular presentations. Diagnostic workup revealed a constellation of findings indicative of severe lupus nephritis and pulmonary hypertension, with serological markers such as positive ANA and anti-dsDNA antibodies, supporting the diagnosis (5). Early renal biopsy, showing Class IV lupus nephritis, and echocardiography, confirming mild pulmonary hypertension, were critical in guiding appropriate management. Aggressive immunosuppressive therapy was initiated, including high-dose corticosteroids and mycophenolate mofetil, in combination with supportive measures for pulmonary and cardiovascular complications

Manuscript Submitted under JHRR ID 1621: September 23/2024 | Accepted: September 29/2024

(8). The patient's response to this treatment regimen highlights the importance of a tailored therapeutic approach in managing late-onset SLE with multisystem involvement (7).

Given the rarity of SLE onset in older males, there is a lack of robust data on disease progression, optimal management strategies, and long-term outcomes in this subgroup. Current literature predominantly focuses on younger women, thus limiting generalizability to other demographics. This case emphasizes the need for heightened clinical suspicion and comprehensive diagnostic evaluation in atypical cases, as well as further research to elucidate the pathophysiology and prognosis of late-onset lupus in men (9). Identifying such cases early, employing timely interventions, and closely monitoring for complications can substantially improve clinical outcomes and quality of life for these patients.

MATERIAL AND METHODS

This case report was conducted in accordance with ethical standards outlined by the Declaration of Helsinki, and informed consent was obtained from the patient for publication of the clinical details and accompanying images. The patient, a 52-year-old male, presented to the outpatient department with complaints of persistent dyspnea, intermittent chest pain, and bilateral lower extremity swelling, accompanied by occasional joint pain and unintentional weight loss over the past three months. A detailed medical history was obtained, including information on lifestyle factors, comorbidities, and family history of autoimmune disorders, none of which were reported. The patient underwent a comprehensive physical examination, including assessment of vital signs and a focused systemic examination, revealing bilateral pedal edema and inspiratory crackles in the lung bases.

Routine laboratory investigations included complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), renal function tests, liver function tests, and urinalysis. The CBC revealed anemia (Hb 10.2 g/dL), with ESR elevated to 75 mm/hr and CRP mildly elevated at 1.8 mg/dL (1). Renal function tests showed elevated serum creatinine (1.9 mg/dL) and significant proteinuria (3+), which was further evaluated using a 24-hour urinary protein test, revealing protein excretion of 4.2 g/day (2). Urinalysis showed red blood cell casts, indicating glomerular pathology. Given the suspicion of an autoimmune etiology, serological tests were performed, including antinuclear antibody (ANA) and anti-double-stranded DNA (dsDNA) antibodies, both of which were positive with a high titer (ANA 1:320, anti-dsDNA 200 IU/mL) (3). Complement levels (C3 and C4) were found to be low, further supporting the diagnosis of systemic lupus erythematosus.

Imaging studies were conducted to evaluate systemic involvement. Chest X-ray demonstrated bilateral pleural effusions, and a high-resolution computed tomography (HRCT) scan revealed small pleural effusions with patchy ground-glass opacities, suggestive of lupus pneumonitis (4). An echocardiogram was performed, which showed mild pulmonary hypertension with an estimated pulmonary artery pressure of 35 mmHg. To confirm renal involvement, a renal biopsy was conducted, which demonstrated diffuse proliferative glomerulonephritis consistent with Class IV lupus nephritis, characterized by segmental endocapillary proliferation and subendothelial immune complex deposition (5).

Based on the clinical findings and diagnostic workup, the patient was diagnosed with systemic lupus erythematosus with multisystem involvement, including lupus nephritis and early pulmonary hypertension. The management plan involved high-dose corticosteroids (prednisone 60 mg/day) to control the acute disease flare, combined with hydroxychloroquine (400 mg daily) as a standard lupus-specific therapy. Mycophenolate mofetil (2 g/day) was initiated as a steroid-sparing immunosuppressant due to the severity of renal involvement. Supportive therapy included furosemide 40 mg daily for management of fluid retention and enalapril 10 mg daily for blood pressure control. Sildenafil was added for management of pulmonary hypertension (6).

Follow-up evaluations were scheduled at two-week intervals for the first month, with clinical assessments, laboratory tests, and repeat echocardiography to monitor treatment response. After two weeks of therapy, the patient's dyspnea significantly improved, and proteinuria decreased to 1.2 g/day. Repeat imaging showed resolution of pleural effusions, and follow-up echocardiography demonstrated stable pulmonary artery pressures. The patient continued on maintenance immunosuppressive therapy, with gradual tapering of corticosteroids based on clinical stability and laboratory results (7).

The primary outcome measures included improvement in dyspnea, reduction in proteinuria, stabilization of renal function, and control of pulmonary hypertension. Secondary outcomes included the absence of new organ system involvement and minimization of treatment-related adverse effects. Statistical analysis was not applicable due to the single-case nature of the study. All procedures were conducted in accordance with institutional guidelines and adhered to standard protocols for managing lupus nephritis and pulmonary hypertension (8).

This structured approach to diagnosis and management provided valuable insights into the complexities of late-onset systemic lupus erythematosus, highlighting the need for a comprehensive and multidisciplinary treatment strategy in atypical cases.

RESULTS

The clinical findings, laboratory investigations, imaging studies, and treatment response are presented below in a tabulated format for clarity and comprehensive representation.

The patient presented with multisystem involvement including pulmonary, renal, and cardiovascular symptoms. Initial laboratory results revealed significant proteinuria, elevated serum creatinine, positive ANA, and anti-dsDNA antibodies, with reduced complement levels, indicative of active lupus nephritis. Renal biopsy confirmed Class IV

lupus nephritis, while imaging revealed pulmonary hypertension and lupus pneumonitis. These findings were tabulated for clarity in Tables 1-3. The patient was started on high-dose corticosteroids, hydroxychloroquine, and mycophenolate mofetil, along with supportive therapy for renal and pulmonary complications.

Table 1: Baseline Clinical Characteristics and Presentation

Parameter	Findings
Age (years)	52
Gender	Male
Chief Complaints	Dyspnea, chest pain, bilateral leg swelling
Duration of Symptoms	3 months
Family History of Autoimmune Diseases	None
Lifestyle Factors	Nonsmoker, non-alcoholic
Physical Examination	Bilateral pedal edema, inspiratory crackles, joint tenderness
Vital Signs	BP: 145/90 mmHg; Pulse: 95 bpm; RR: 22 breaths/min; SpO2: 92% on room air

Table 2: Laboratory Investigations at Baseline

Test	Result	Reference Range
Hemoglobin (Hb)	10.2 g/dL	13.0 – 17.0 g/dL
Erythrocyte Sedimentation Rate (ESR)	75 mm/hr	< 20 mm/hr
C-Reactive Protein (CRP)	1.8 mg/dL	< 0.5 mg/dL
Serum Creatinine	1.9 mg/dL	0.7 – 1.3 mg/dL
24-hour Urinary Protein Excretion	4.2 g/day	< 0.15 g/day
Urinalysis	RBC casts, Proteinuria (3+)	Negative for RBC casts, Proteinuria < 1+
Antinuclear Antibody (ANA)	Positive, 1:320	Negative
Anti-dsDNA Antibodies	Positive, 200 IU/mL	< 30 IU/mL
Serum Complement C3	Low	90 – 180 mg/dL
Serum Complement C4	Low	10 – 40 mg/dL

Table 3: Imaging Studies and Renal Biopsy Findings

Investigation	Result
Chest X-ray	Bilateral pleural effusion
High-Resolution CT (HRCT)	Small pleural effusions, patchy ground-glass opacities
Echocardiogram	Mild pulmonary hypertension, Pulmonary artery pressure: 35 mmHg
Renal Biopsy	Class IV lupus nephritis (Diffuse proliferative glomerulonephritis)

Table 4: Treatment Response and Follow-Up Results

Parameter	Baseline	2 Weeks Follow-Up	4 Weeks Follow-Up
Dyspnea Severity	Severe	Mild	Absent
Proteinuria (24-hour)	4.2 g/day	1.2 g/day	<0.5 g/day
Serum Creatinine	1.9 mg/dL	1.6 mg/dL	1.3 mg/dL
Pulmonary Artery Pressure	35 mmHg	32 mmHg	30 mmHg
Pleural Effusion (Chest X-ray)	Bilateral effusion	Mild left effusion	Resolved
Treatment Regimen	Prednisone, Hydroxychloroquine, Mycophenolate mofetil	Same regimen, reduction in corticosteroid dose	Maintenance therapy with further steroid taper

By the second week of follow-up, there was a marked improvement in dyspnea, a reduction in proteinuria from 4.2 g/day to 1.2 g/day, and stabilization of pulmonary artery pressures (Table 4). The pleural effusions showed progressive resolution, and by the fourth week, they were completely resolved on repeat imaging. The patient's serum creatinine also improved, returning closer to normal limits.

Overall, the patient demonstrated a favorable response to the combination of immunosuppressive therapy and supportive measures, highlighting the importance of aggressive management in cases of late-onset SLE with severe multisystem involvement. Further follow-up is planned to monitor long-term disease progression and therapy optimization.

DISCUSSION

The presented case illustrates an uncommon manifestation of systemic lupus erythematosus (SLE) in a middle-aged male, characterized by atypical multisystem involvement, including severe lupus nephritis and early pulmonary hypertension. This presentation posed significant diagnostic and therapeutic challenges, as SLE typically affects young females of childbearing age and seldom manifests initially with pulmonary and cardiovascular complications in older males (6). While renal involvement is

a hallmark of SLE, with up to 50-60% of patients developing lupus nephritis during the disease course, the occurrence of Class IV lupus nephritis in males over the age of 50 is exceptionally rare and poorly documented in the literature (3). Moreover, the concurrent presence of pulmonary hypertension, which has been reported in only 5-14% of SLE patients, further complicates the clinical scenario and significantly worsens prognosis if left untreated (7).

The diagnosis of SLE in this patient was based on a combination of clinical features and serological findings, including positive ANA and anti-dsDNA antibodies along with low complement levels, which are consistent with active disease. These findings are corroborated by previous studies highlighting the importance of serological markers in establishing the diagnosis, particularly in atypical cases where classical symptoms such as cutaneous manifestations and arthritis are absent (2). The renal biopsy, confirming Class IV lupus nephritis, underscored the need for aggressive immunosuppressive therapy, as this subtype is associated with a high risk of renal failure and systemic complications (3). Previous reports have shown that Class IV lupus nephritis often requires intensive treatment with a combination of corticosteroids and steroid-sparing agents such as mycophenolate mofetil or cyclophosphamide to achieve remission and prevent disease progression (3).

Pulmonary hypertension in SLE is a relatively rare but severe complication, often secondary to pulmonary vasculitis, interstitial lung disease, or thromboembolic events (7). The early identification and management of pulmonary hypertension in this patient were crucial, as untreated cases have a high mortality rate. The use of sildenafil, a phosphodiesterase-5 inhibitor, has been shown to improve pulmonary hemodynamics and exercise capacity in patients with SLE-associated pulmonary hypertension, as supported by multiple case series and observational studies (9). This patient's positive response to sildenafil, in conjunction with immunosuppressive therapy, aligns with previous findings indicating that early intervention can stabilize or even reverse pulmonary hypertension in SLE, thereby improving long-term outcomes (7).

Despite the favorable clinical response observed in this patient, the case highlights several limitations in the management of atypical SLE. First, the absence of classical lupus manifestations delayed the initial diagnosis, underscoring the need for heightened clinical vigilance and consideration of SLE in the differential diagnosis of multisystemic disease, even in older male patients. Second, the potential for adverse effects with prolonged immunosuppressive therapy, particularly in the context of multisystem involvement, remains a significant concern. This case emphasizes the importance of regular monitoring for treatment-related complications, such as infections, osteoporosis, and cardiovascular risks, which are more prevalent in older adults receiving high-dose corticosteroids and cytotoxic agents (3). One of the strengths of this case was the comprehensive diagnostic approach, including serological testing, renal biopsy, and echocardiography, which enabled a timely and accurate diagnosis. The early initiation of a tailored therapeutic regimen, with close follow-up and adjustment based on clinical response, was critical in achieving remission and preventing further organ damage. However, the rarity of SLE in older males and the absence of specific guidelines for managing late-onset lupus limit the generalizability of this approach. Current therapeutic recommendations are largely based on studies in younger female populations, highlighting the need for further research to establish optimal management strategies for atypical presentations of SLE in different demographic groups (6).

This case also underscores the need for individualized treatment plans that consider the severity of organ involvement, patient comorbidities, and risk factors for adverse outcomes.

In cases of severe lupus nephritis and pulmonary hypertension, as seen here, a combination of high-dose corticosteroids, mycophenolate mofetil, and supportive therapies such as sildenafil may be required to achieve disease control.

Nonetheless, long-term studies are needed to evaluate the safety and efficacy of these regimens in older patients and to determine whether alternative agents, such as belimumab or rituximab, might offer better tolerability and comparable outcomes in this subgroup (8).

Future recommendations include increased awareness of the diverse manifestations of SLE across different age groups and genders, particularly in settings where atypical presentations may be misdiagnosed.

Education for healthcare professionals should emphasize the variable clinical spectrum of SLE and the importance of a multidisciplinary approach in managing complex cases. Additionally, further research is warranted to explore the pathophysiological mechanisms underlying late-onset SLE and to identify potential biomarkers that may aid in early diagnosis and risk stratification (9).

In conclusion, this case reinforces the necessity for prompt recognition and aggressive management of severe SLE complications, even in populations traditionally considered low-risk for the disease, to improve prognosis and quality of life.

CONCLUSION

This case of systemic lupus erythematosus with atypical multisystem involvement in a middle-aged male highlights the importance of maintaining a high index of suspicion for SLE, even in demographics less commonly affected by the disease.

Early recognition and aggressive treatment of severe complications such as lupus nephritis and pulmonary hypertension are critical for preventing irreversible organ damage and improving patient outcomes.

The findings underscore the need for personalized treatment strategies and vigilant long-term monitoring to address the unique challenges of late-onset SLE, thereby enhancing overall healthcare delivery and patient quality of life.

Further research is essential to guide the management of such atypical presentations and refine therapeutic protocols for diverse patient populations.

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