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**Case Report**

# Late-onset systemic lupus erythematosus masquerading as rheumatoid arthritis with multisystem involvement: a diagnostic challenge

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## ABSTRACT

Late-onset systemic lupus erythematosus (SLE), occurring after the age of 60 years, often presents with atypical features, which leads to delayed diagnosis. This report highlights how an atypical presentation led to misdiagnosis as rheumatoid arthritis, resulting in delayed recognition and diagnostic challenge of late-onset SLE. A 61-year-old Indian woman presented with a 1-year history of bilateral inflammatory symmetrical polyarthralgia involving both small and large joints which was initially treated as rheumatoid arthritis without significant improvement. Over time, she developed worsening fatigue, cold intolerance and bilateral periorbital swelling with mild bilateral pedal oedema. Investigations revealed pancytopenia, raised inflammatory markers, hypocomplementemia; strongly positive ANA (4+, homogeneous pattern, 1:640), along with positivity for anti-Ro52, anti-SSA, anti-ribosomal P protein, and ANCA-P. She had mild left ventricular systolic dysfunction (Ejection fraction of 45%), suggesting possible autoimmune cardiac involvement. HRCT thorax revealed features of interstitial lung disease (ILD) suggesting non-specific interstitial pneumonitis (NSIP) pattern. Based on clinical, serological, and immunological findings, the patient fulfilled the 2019 EULAR/ACR criteria for SLE with a score of 18, confirming the diagnosis of late-onset SLE. This case emphasizes the diagnostic difficulty of late-onset SLE, especially when classical cutaneous manifestations are absent and the disease closely resembles rheumatoid arthritis. Early consideration of autoimmune evaluation in elderly patients with unexplained multisystem involvement may help prevent delayed diagnosis and progressive organ damage.

**Keywords:** Systemic lupus erythematosus, Late-onset SLE, Rheumatoid arthritis mimic, Antinuclear antibodies, Elderly, Diagnostic challenge, EULAR/ACR criteria

## INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoantibody associated autoimmune disease with diverse clinical manifestations. Immune complex-mediated tissue injury involving multiple organ systems is the hallmark. Although SLE is classically considered a disease of young women, nearly 10-20% of cases occur after the age of 50 years and are termed late-onset SLE.[1]

Late-onset SLE often presents differently from the classical disease seen in younger patients. Cutaneous manifestations such as malar rash, photosensitivity, and discoid lesions are less common, whereas constitutional symptoms, serositis, musculoskeletal complaints, and haematological abnormalities are more frequently observed.[1,2] Because these manifestations overlap with several age-related disorders, diagnosis is often delayed in elderly individuals.[3]

Rheumatoid arthritis is among the most common conditions mistaken for late-onset SLE because both diseases may initially present with predominant joint symptoms. However, the two conditions differ significantly in treatment, monitoring, and long-term prognosis.[3] We present a case in which the patient was

initially managed as rheumatoid arthritis for more than one year before further evaluation revealed late-onset SLE. During this period, the disease progressed with haematological involvement and echocardiographically confirmed ventricular dysfunction, highlighting the diagnostic challenge of SLE in elderly patients.

## CASE REPORT

A 61-year-old woman presented with a 12-month history of bilateral symmetrical inflammatory polyarthralgia involving both small and large joints. She was initially treated as rheumatoid arthritis and put on disease modifying drugs including methotrexate and non-steroidal anti-inflammatory drugs. However, she showed no significant clinical improvement. Further evaluation revealed a positive autoimmune background, and family history was notable for immune-mediated disease in her daughter.

Over the preceding three months, her illness evolved beyond articular manifestations. She developed progressive fatigue, cold intolerance, and bilateral periorbital puffiness. She denied photosensitivity, oral ulcers, skin rash, Raynaud's phenomenon, pleuritic chest pain, and alopecia. On examination, she appeared pale, with bilateral symmetrical periorbital oedema associated with overlying erythema. Musculoskeletal examination revealed no active synovitis or joint deformities. There was no peripheral lymphadenopathy, and haemodynamic parameters were within normal limits.

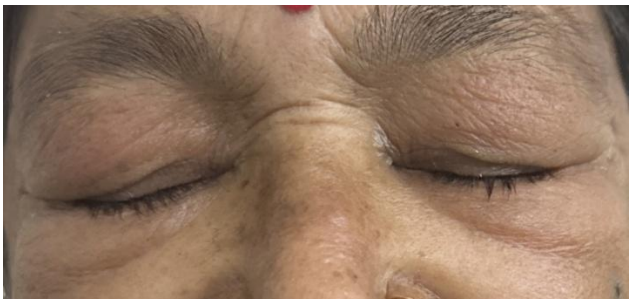

**Figure 1: Bilateral symmetrical periorbital oedema with facial puffiness and mild overlying erythema.**

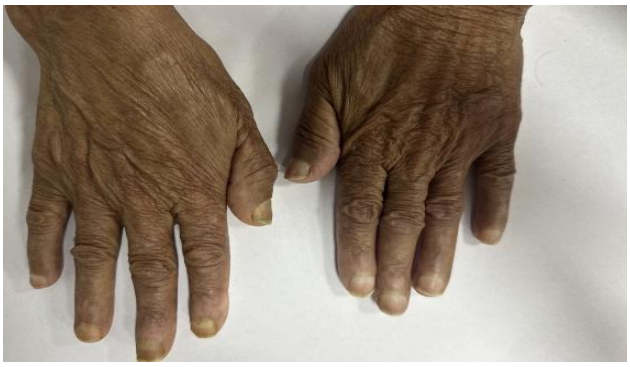

**Figure 2: Bilateral non-deforming polyarthritis with mild diffuse swelling of the small joints of the hands.**

***Laboratory investigations***

Haematological and biochemical data and Immunological data are set out in Tables 1 and 2 respectively.

**Table 1: Haematological and biochemical investigations.**

| Parameters | Results |
|---|---|
| **Haemoglobin** | 8.5 g/dl |
| **White blood cell count** | $2.93\times10^3/\mu l$ |
| **Platelet count** | $49\times10^3/\mu l$ |
| **Peripheral blood film** | Moderate anisocytosis; normocytic normochromic; leucopoenia with eosinophil predominance |
| **Serum creatinine** | 0.81 mg/dl |
| **eGFR** | 71.9 ml/min/1.73m² |
| **Urine protein: creatinine ratio** | 21 |
| **ALT / AST** | 14/31 IU/l |
| **TSH** | 7.1 mIU/l |
| **ESR** | 105 mm/h |
| **CRP** | 10.9 mg/l |
| **LVEF (echocardiography)** | 45% |

Initial laboratory evaluation revealed pancytopenia with peripheral blood smear demonstrated moderate anisocytosis in a predominantly normocytic normochromic background, along with relative eosinophilia. The overall morphological picture favoured peripheral immune-mediated destruction rather than primary bone marrow pathology or active haemolysis. No significant renal or hepatic involvement at presentation. Thyroid profile was suggestive of subclinical hypothyroidism as an associated finding. Chest X-ray showed low lung volumes with mild bi-basal atelectatic/fibrotic changes**.** HRCT thorax revealed bilateral basal reticulations/ground-glass opacities suggestive of fibrotic NSIP pattern.

Echocardiography demonstrated global hypokinesia with left ventricular systolic dysfunction, with an ejection fraction of 45%. Coronary and primary structural cardiac pathologies were excluded clinically, favouring an inflammatory myocardial process.

The immunological screen (Table 2) identified intensely positive ANA by indirect immunofluorescence (4+, homogeneous nuclear staining, titre 1:640). Extractable nuclear antigen subtyping confirmed anti-Ro52 (2+), anti-SSA (1+), anti-ribosomal P protein (2+), and anti-nucleosome (1+) reactivities. Anti-mitochondrial antibody M2 registered borderline positivity (1+). Serum C3 and C4 were each below their respective lower reference limits, consistent with consumption via the classical pathway. Rheumatoid factor was positive with mildly raised value

but anti-cyclic citrullinated peptide antibodies were absent. Anti-double-stranded DNA status was negative.

Drawing together the clinically coherent constellation of articular involvement, trilineage cytopenia, left ventricular contractile failure, hypocomplementemia, and disease-specific autoantibody reactivity, weighted scoring under the 2019 EULAR/ACR classification criteria for SLE yielded 18 points-well in excess of diagnostic threshold-thereby establishing the diagnosis of late-onset SLE.

**Table 2: Immunological investigations.**

| Tests | Results | Clinical significance |
|---|---|---|
| **ANA (IIF)** | 4+, homogeneous, 1:640 | Intensely positive; primary serological entry criterion for SLE |
| **Anti-Ro52** | 2+ | Raises possibility of secondary Sjögren syndrome overlap |
| **Anti-SSA** | 1+ | Marker of broad systemic immune dysregulation |
| **Anti-ribosomal P protein** | 2+ | Highly disease-specific for SLE |
| **Anti-nucleosome** | 1+ | SLE-restricted target; tracks disease activity |
| **Anti-mitochondrial Ab (M2)** | 1+ (borderline) | Longitudinal monitoring for primary biliary cholangitis warranted |
| **Anti-dsDNA** | Negative | Confirm result |
| **Anti-CCP** | Negative | Weighs against rheumatoid arthritis |
| **Rheumatoid factor** | Mildly positive | Non-specific autoimmune marker; may occur in SLE |
| **Complement C3** | Low | Classical pathway consumption by circulating immune complexes |
| **Complement C4** | Low | Classical pathway consumption by circulating immune complexes |

**Table 3: Differential diagnosis.**

| Differential diagnosis | Features suggestive of diagnosis | Reason for exclusion |
|---|---|---|
| **Seronegative rheumatoid arthritis** | Symmetrical small-joint pain and stiffness | Negative anti-CCP antibodies, absence of erosive disease, poor response to treatment, and multisystem involvement |
| **Sjögren's syndrome** | Anti-SSA and anti-Ro52 positivity with arthralgia | No definite sicca symptoms; SLE-specific antibodies present |
| **UCTD** | Positive ANA with systemic symptoms | EULAR/ACR score strongly supported definite SLE |
| **Mixed connective tissue disease** | Overlapping autoimmune features | Anti-U1 RNP negative; no myositis or oesophageal symptoms |
| **Myelodysplastic syndrome** | Pancytopenia in elderly patient | No dysplasia or blasts on peripheral smear |
| **Lymphoma** | Fatigue and cytopenias | No lymphadenopathy or organomegaly |
| **Hypothyroidism** | Fatigue, cold intolerance, periorbital puffiness | Could not explain pancytopenia and autoimmune profile |
| **Viral / idiopathic cardiomyopathy** | Reduced ejection fraction with hypokinesia | Associated active autoimmune disease favoured lupus myocarditis |
| **Primary biliary cholangitis** | Borderline AMA-M2 positivity | Normal liver enzymes and no cholestatic features |
| **Drug-induced lupus** | Previous NSAID/DMARD exposure | Presence of hypocomplementemia and SLE-specific antibodies favoured primary SLE |

*Abbreviations: RF-rheumatoid factor; anti-CCP-anti-cyclic citrullinated peptide; ANA-antinuclear antibody; SLE-systemic lupus erythematosus; EULAR/ACR-European League Against Rheumatism/American College of Rheumatology; UCTD-undifferentiated connective tissue disease; AMA-M2-anti-mitochondrial antibody M2; NSAID-non-steroidal anti-inflammatory drug; DMARD-disease-modifying anti-rheumatic drug.

***Treatment and follow up***

The patient was initiated on low-dose oral prednisolone 2.5 mg once daily for lupus-associated cytopenias. Hydroxychloroquine 200 mg once daily and sulfasalazine 500 mg twice daily were added for management of inflammatory arthritis, while inhaler therapy was continued for associated NSIP. Following treatment initiation, patient showed gradual clinical improvement with reduction in constitutional symptoms and improvement in haematological parameters. At subsequent follow-up, the patient remained clinically stable with improvement in joint and respiratory symptoms.

## DISCUSSION

Late-onset SLE, defined as disease onset after 50 years of age, is an uncommon but important clinical entity that

often presents with atypical manifestations and delayed diagnosis.[1,4] In contrast to younger patients, elderly individuals with SLE frequently lack classical mucocutaneous features such as malar rash and photosensitivity, making diagnosis more challenging.[1,5] Instead, constitutional symptoms, polyarthralgia, and haematological abnormalities are more commonly observed.[4,5]

In the present case, the patient was initially treated as seronegative rheumatoid arthritis because of symmetrical small-joint involvement. However, persistent symptoms despite therapy, absence of erosive joint disease, and absence of erosive disease and negative anti-CCP antibodies prompted further evaluation for connective tissue disease.[6] The presence of pancytopenia, hypocomplementemia, strongly positive ANA, and disease-specific autoantibodies ultimately supported the diagnosis of late-onset SLE.

Haematological involvement is a well-recognized manifestation of SLE and may occur due to immune-mediated peripheral destruction or bone marrow suppression.[7] The reduced complement levels in this patient further indicated active immune complex-mediated disease activity.[8] Autoantibodies such as anti-ribosomal P protein and anti-nucleosome antibodies are highly associated with SLE and may correlate with systemic disease activity.[9]

Cardiac involvement in SLE ranges from pericarditis to myocarditis and cardiomyopathy.[10] In this patient, reduced left ventricular ejection fraction with global hypokinesia in the absence of other obvious cardiac causes suggested possible lupus-related myocardial involvement. Early recognition and treatment are important to prevent irreversible organ damage.

This case highlights the importance of considering SLE in elderly patients presenting with unexplained cytopenias, constitutional symptoms, and inflammatory polyarthritis, particularly when the clinical course is atypical for rheumatoid arthritis. Early autoimmune evaluation and multidisciplinary assessment can help reduce diagnostic delay and improve patient outcomes.[1,4]

## CONCLUSION

Late-onset SLE can mimic common rheumatological disorders and may lack classical mucocutaneous features, leading to delayed diagnosis and preventable organ damage. This case highlights the importance of considering SLE in elderly patients with unexplained multilineage cytopenias, inflammatory arthralgia refractory to standard therapy, and positive autoimmune serology. Early comprehensive evaluation, including extended autoantibody testing, complement levels, and cardiac assessment, along with multidisciplinary collaboration, is essential for timely diagnosis and preservation of organ function.

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