Case Report

When the skin speaks scleroderma but the antibodies whisper lupus: A case report

Arun Bargali[1], Ayushman Bindal[2], Sumit Pachori[3], Abhigyan Bindal[4], Harsh Pratap Singh[5]

From [1]Senior Resident, Department of Clinical Immunology and Rheumatology, [5]Post Graduate Resident, Department of Internal Medicine, Sawai Man Singh Medical College and Hospital, Jaipur, Rajasthan, [2]Post Graduate Resident, Department of Dermatology, Lady Harding Medical College, [3]Assistant Professor, Department of Internal Medicine, Maulana Azad Medical College and Lok Nayak Hospital, [4]Post Graduate Resident, Department of Radiodiagnosis, Maulana Azad Medical College, New Delhi, India

ABSTRACT

Overlap syndrome is the coexistence of clinical features of more than one connective tissue disease in a single patient, often accompanied by a mixed serological profile. Systemic sclerosis with overlapping lupus serology may present predominantly with scleroderma manifestations while fulfilling immunological criteria for systemic lupus erythematosus. We report the case of a 40-year-old woman who presented with progressively worsening dyspnea over 7 years, skin tightening, dysphagia, non-productive cough, and winter-predominant painful bluish discoloration of the fingers. Examination revealed tight skin with a modified Rodnan skin score of 21/51, Raynaud's with digital gangrene, raised jugular venous pressure, and bilateral inspiratory crepitations. Investigations showed type 1 respiratory failure, anemia, leukocytosis, and basal reticular opacities on imaging. High-resolution computed tomography of the chest revealed a non-specific interstitial pneumonia (NSIP) pattern of interstitial lung disease (ILD). Serological analysis demonstrated a positive antinuclear antibody with a homogeneous pattern and positive anti-double-stranded DNA, smD1, and nucleosome on immunoblot. Nailfold capillaroscopy showed dilated loops and avascular areas, consistent with secondary Raynaud's phenomenon. Pulmonary function test was suggestive of moderate restriction. A diagnosis of scleroderma-dominant overlap syndrome with secondary Raynaud's phenomenon and NSIP-pattern interstitial lung disease was established. The patient was managed with low-dose corticosteroids, hydroxychloroquine, tadalafil, bosentan, mycophenolate mofetil, and rituximab, with clinical improvement observed on follow-up.

Key words: Interstitial lung disease, Overlap syndrome, Raynaud phenomenon, Systemic lupus erythematosus, Systemic sclerosis

Systemic sclerosis (SSc) and systemic lupus erythematosus (SLE) are distinct connective tissue diseases with heterogeneous clinical spectra, immunological profiles, and patterns of organ involvement [1]. In a subset of patients, features of more than one autoimmune rheumatic disease coexist, giving rise to overlap syndromes that defy rigid classification criteria [1]. SSc-SLE overlap is an uncommon but clinically significant entity, often characterized by scleroderma-dominant manifestations with serological markers suggestive of lupus [2]. These patients may present with Raynaud's phenomenon, digital ischemia, gastrointestinal dysmotility, inflammatory arthritis, and interstitial lung disease [3]. Interstitial lung disease, particularly the nonspecific interstitial pneumonia (NSIP) pattern, represents a major determinant of morbidity and mortality in connective tissue disease overlap syndromes [4]. The dissociation between clinical phenotype and serological profile poses diagnostic and therapeutic challenges and may delay appropriate treatment [1]. Early recognition is essential, as management often requires an individualized immunosuppressive strategy that balances features of both diseases.

We report a case of scleroderma-dominant overlap syndrome with lupus serology complicated by severe Raynaud's phenomenon and NSIP-pattern interstitial lung disease.

CASE REPORT

A 40-year-old woman from Delhi presented to the emergency department with progressive dyspnea evolving over 7 years. Initially mild (Modified Medical

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Correspondence to: Dr. Arun Bargali, Senior Resident, Department of Clinical Immunology and Rheumatology, Sawai Man Singh Medical College and Hospital, Jaipur, Rajasthan- 302004, India. E-mail: pratyush9411@gmail.com

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Research Council grade 1), her breathlessness gradually worsened to grade 3, with a rapid deterioration to grade 4 over the preceding 20 days. There was no associated chest pain, palpitations, or peripheral edema. Concurrently, she reported a 7-year history of progressive skin tightening beginning in the fingers and extending proximally, along with long-standing dysphagia characterized by discomfort during swallowing, oral dryness, and pain. She also described episodic bluish discoloration of the fingers precipitated by cold exposure and winter months. In addition, she had bilateral knee pain for 5 years, predominantly morning stiffness that improved with activity, without associated swelling, redness, or warmth. Over the 20 days before admission, she developed a non-productive cough and painful bluish-black discoloration of multiple fingers bilaterally, worsening with cold exposure, without blistering or discharge.

Upon examination, she was afebrile with tachycardia (pulse rate 128/min, regular), blood pressure of 152/96 mmHg (right arm, supine), and tachypnea (respiratory rate 30/min) with an irregular abdominothoracic breathing pattern. Oxygen saturation on room air was unrecordable. She had features of Raynaud's phenomenon with digital gangrene. There was no pallor, icterus, peripheral lymphadenopathy, digital clubbing, or pedal edema. Jugular venous pressure was elevated. The modified Rodnan skin score (mRSS) was 21/51. Respiratory examination revealed bilateral coarse inspiratory crepitations over the infra-axillary, infra-mammary, and infra-scapular regions. Cardiovascular examination demonstrated normal heart sounds without murmurs. The abdomen was soft and non-tender with no organomegaly, and neurological examination was unremarkable.

Laboratory evaluation showed anemia, leukocytosis, and elevated erythrocyte sedimentation rate (Table 1). Arterial blood gas analysis revealed type 1 respiratory failure. Chest radiography demonstrated basal reticular opacities. Electrocardiography and transthoracic echocardiography were within normal limits. Upper gastrointestinal endoscopy performed for dysphagia showed no structural abnormalities. Nailfold capillaroscopy (NFC) revealed dilated capillary loops, avascular areas, and bushy capillaries, consistent with a microangiopathic pattern (Fig. 1). Spirometry was suggestive of a moderate restrictive ventilatory defect, with reduced forced vital capacity (FVC) (60% of predicted) and forced expiratory volume in 1 second (FEV_1) (63% of predicted) with a preserved FEV_1/FVC ratio. High-resolution computed tomography (HRCT) of the chest demonstrated diffuse interlobular septal thickening and reticular opacities involving bilateral lung parenchyma, with focal areas of ground-glass attenuation (left more than right) and fibrotic changes involving the right upper and middle lobes (Fig. 2). Radiographs of the hands were normal. However, complete lung-volume measurements, diffusion capacity for carbon monoxide (DLCO), and serial pulmonary function data were unavailable, limiting comprehensive assessment of interstitial lung disease (ILD) severity and longitudinal progression.

Table 1: Routine blood investigations of patient, including inflammatory markers

Parameter	Patient's value	Normal range
Hemoglobin	8.2 g/dL	13–16 g/dL
TLC	13,500/cc	4,000–11,000/cc
DLC	74/23/2/1	—
Platelet count	1.72 lakh/µL	1.5–4 lakh/µL
ESR	65 mm/h	—
CRP	2.1 mg/dL	<3 mg/dL
Total bilirubin	0.5 mg/dL	0.2–1.3 mg/dL
ALT	34 U/L	<50 U/L
ALP	107 U/L	38–126 U/L
CPK total	36 U/L	10–120 U/L
CPK-MB	6 U/L	5–25 U/L
AST	39 U/L	17–59 U/L
Blood urea	20 mg/dL	15–39 mg/dL
Serum creatinine	0.8 mg/dL	0.66–1.25 mg/dL
Sodium	136 mmol/L	135–145 mmol/L
Potassium	4.4 mmol/L	3.5–5 mmol/L
D-dimer	304 ng/mL	—
Urine routine examination	Normal	—
24-h urine protein	75 mg/day	—
RF	Negative	—
Anti-CCP antibody	Negative	—

TLC: Total leukocyte count, DLC: Differential leukocyte count, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, ALP: Alkaline phosphatase, CPK: Creatine phosphokinase, AST: Aspartate transaminase, RF: Rheumatoid factor, CCP: Cyclic citrullinated peptide

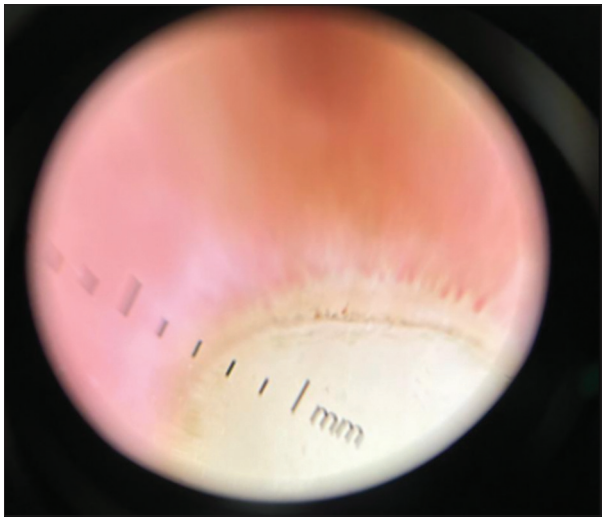


Figure 1: Nailfold capillaroscopy showing dilated tufted capillaries suggestive of secondary Raynaud's phenomenon

Immunological evaluation revealed a homogeneous antinuclear antibody (ANA) pattern with positivity for anti-double-stranded DNA (anti-dsDNA), anti-Smith, and antinucleosome antibodies on immunoblot. Antibodies against Scl-70, centromere, Ro, and La were negative. The detailed ANA profile is summarized in Table 2.

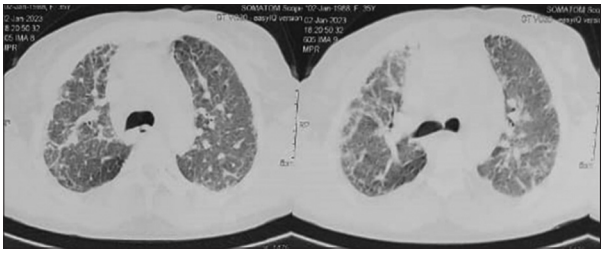


Figure 2: High-resolution computed tomography chest showing diffuse interlobular septal thickening and reticular opacities in bilateral parenchyma with few areas of ground-glassing (Left > Right) and associated fibrotic changes in the right upper and middle lobe. Features suggestive of fibrotic non-specific interstitial pneumonia-interstitial lung disease

Table 2: ANA and ENA profile of patient

ANA/ENA	Patient report	Normal value
ANA by immunofluorescence	Homogeneous positive (1:160)	Negative
Anti-double-stranded DNA	Positive	Negative
SmD1	Positive	Negative
Anti-SSA (Ro52, Ro60)	Negative	Negative
Anti-SSB (La)	Negative	Negative
Anti-Scl-70	Negative	Negative
Anti-Histone	Negative	Negative
Anti-U1 RNP	Negative	Negative
Anti-nucleosome	Positive	Negative
Anti-centromere	Negative	Negative
Anti-Jo-1	Negative	Negative
Anti-Mi-2	Negative	Negative
Anti-Ku	Negative	Negative
Anti-PCNA	Negative	Negative

ANA: Antinuclear antibody, ENA: Extractable nuclear antigen, PCNA: Proliferating cell nuclear antigen

The patient fulfilled the 2013 American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) classification criteria for SSc, with skin thickening extending proximal to the metacarpophalangeal joints, which independently conferred a score of 9 points. Additional supportive features included Raynaud's phenomenon, abnormal nailfold capillaries, and HRCT-confirmed ILD. Although the patient fulfilled the ANA entry criterion for the 2019 EULAR/ACR SLE classification criteria and had positive anti-dsDNA and anti-SmD1 antibodies, she accrued 6 points and did not fulfill the ≥10-point threshold or have a qualifying clinical SLE criterion. Thus, the diagnosis of SSc-SLE overlap was based on definite SSc with strongly lupus-specific serology, rather than fulfillment of formal classification criteria for both diseases.

The patient was initiated on supplemental oxygen and nebulization, along with empiric antibiotic therapy for suspected superadded respiratory infection. Hydroxychloroquine and low-dose systemic corticosteroids were commenced for immunomodulation. Tadalafil and bosentan were initiated for severe Raynaud's phenomenon complicated by digital ischemia. In view of clinically significant ILD with hypoxemic respiratory failure and radiological evidence of fibrotic lung involvement, mycophenolate mofetil was initiated, and rituximab was administered as induction therapy at a dose of 1 g intravenously on days 1 and 15.

The patient demonstrated significant clinical improvement, with improvement in respiratory symptoms and overall clinical status and continues to remain under regular outpatient follow-up. Given the presence of fibrotic ILD and severe systemic vasculopathy, continued surveillance with serial pulmonary function testing, including FVC and DLCO where available, assessment of exercise capacity, and periodic HRCT evaluation when clinically indicated is planned. Ongoing screening for pulmonary hypertension and other cardiopulmonary complications is also warranted.

DISCUSSION

Overlap syndromes represent a subset of connective tissue diseases in which patients exhibit clinical and/or immunological features of more than one defined rheumatic disorder. Among these, SSc-SLE overlap is relatively uncommon but clinically important because of its heterogeneous presentation, variable disease course, and therapeutic implications [1]. Unlike mixed connective tissue disease, SSc-SLE overlap lacks a single defining autoantibody and is diagnosed based on the coexistence of clinical and/or immunological features of both disorders [1]. The present case illustrates a scleroderma-dominant overlap syndrome, with long-standing Raynaud's phenomenon complicated by digital gangrene, progressive skin tightening with a high mRSS, gastrointestinal dysmotility, and ILD. The presence of lupus-specific autoantibodies – anti-dsDNA, anti-SmD1, and anti-nucleosome antibodies – fulfilled immunological criteria for SLE despite the absence of classical lupus organ manifestations such as nephritis or neuropsychiatric disease. Such discordance between clinical phenotype and serology has been described in overlap syndromes and may pose diagnostic challenges, particularly in early or evolving disease [5].

The uniqueness of this case lies in the marked discordance between the dominant clinical phenotype and the autoantibody profile. Despite a severe SSc-predominant phenotype characterized by extensive skin involvement, severe Raynaud's phenomenon with digital gangrene, scleroderma-pattern nailfold microangiopathy, and fibrotic NSIP-pattern ILD, the patient demonstrated a distinctly lupus-specific serological profile. This occurred in the absence of major classical SLE organ manifestations. Furthermore, the absence of major SSc -associated antibodies, including anti-Scl-70 and anticentromere antibodies, added to the diagnostic complexity. Thus, the case highlights the importance of integrating clinical manifestations, disease-specific serology, microvascular findings, and organ involvement rather than relying on a single dominant phenotype or autoantibody profile.

ILD is a major determinant of morbidity and mortality in SSc and overlap syndromes [4]. The NSIP pattern observed in this patient is the most common ILD subtype associated with SSc and SSc-overlap disorders and generally has a better prognosis than usual interstitial pneumonia [6]. However, fibrotic NSIP with clinically significant respiratory involvement warrants early immunosuppressive therapy to limit further irreversible lung damage [4]. The absence of pulmonary hypertension on echocardiography was reassuring, although continued surveillance remains essential because of the long-term risk of pulmonary vascular disease in SSc-spectrum disorders [7].

The pulmonary assessment was limited by the absence of complete lung-volume measurements, DLCO values, serial pulmonary function testing, and longitudinal HRCT evaluation. Although pulmonary function testing demonstrated a moderate restrictive ventilatory defect, the extent and rate of functional decline could not be objectively assessed. Similarly, the absence of serial imaging precluded definitive evaluation of radiological progression. Nevertheless, the combination of type 1 respiratory failure, restrictive physiology, and HRCT evidence of fibrotic NSIP-pattern ILD indicated clinically significant pulmonary involvement. These limitations should be considered while interpreting disease severity and treatment response. Serial assessment of FVC and DLCO, evaluation of exercise capacity, and repeat HRCT when clinically indicated are important for monitoring progression and response to therapy.

The prognosis of SSc-SLE overlap is heterogeneous and is largely determined by the dominant disease phenotype and extent of internal organ involvement. In this patient, fibrotic ILD with type 1 respiratory failure, severe Raynaud's phenomenon complicated by digital gangrene, and marked nailfold microvascular abnormalities may indicate an increased risk of long-term morbidity. Although NSIP generally has a more favorable prognosis than UIP, the presence of fibrosis and hypoxemic respiratory failure warrants close surveillance because progressive ILD may result in irreversible functional impairment and contribute substantially to long-term mortality.

Conversely, the absence of pulmonary hypertension on echocardiography, preserved renal function, normal 24-h urinary protein excretion, and the lack of clinical evidence of lupus nephritis or neuropsychiatric lupus are relatively favorable findings. The patient also demonstrated significant early clinical improvement following immunomodulatory and vasodilator therapy. However, the absence of serial FVC and DLCO measurements, longitudinal imaging, and long-term follow-up precludes definitive conclusions regarding sustained pulmonary stabilization or overall prognosis. Continued surveillance for progressive ILD, pulmonary hypertension, recurrent digital ischemia, and additional organ involvement is therefore essential.

Severe Raynaud's phenomenon with digital ischemia and gangrene reflects advanced microvascular involvement, a defining feature of SSc. NFC demonstrated dilated loops and avascular areas, supporting a scleroderma-pattern microangiopathy and helping distinguish secondary from primary Raynaud's phenomenon [8]. In the present patient, marked capillary architectural abnormalities together with digital gangrene indicated substantial microvascular disease. These findings may also have prognostic relevance because severe capillary loss and advanced microangiopathy have been associated with increased vascular complications and progressive systemic involvement.

There are no standardized treatment guidelines for SSc-SLE overlap, and management is individualized according to the dominant clinical phenotype and organ involvement [1]. In the present case, low-dose corticosteroids and hydroxychloroquine were used to address lupus-related immunological activity, while mycophenolate mofetil and rituximab were employed for progressive ILD, consistent with emerging evidence supporting their efficacy in SSc-associated ILD [9,10]. Tadalafil and bosentan were initiated for severe Raynaud's phenomenon and digital ischemia. The favorable early clinical response supports a phenotype-driven, multidisciplinary approach; however, sustained ILD stabilization requires longitudinal assessment using serial FVC and DLCO measurements and, where clinically indicated, follow-up HRCT imaging. The short duration of follow-up and limited longitudinal pulmonary data are important limitations of this report.

CONCLUSION

This case underscores the need for heightened clinical suspicion for overlap syndromes in patients with scleroderma features and atypical serology. Its principal educational value is the demonstration that a severe SSc-dominant phenotype may coexist with strongly lupus-specific serology despite the absence of classical SLE-related organ involvement. The coexistence of severe vasculopathy, scleroderma-pattern microangiopathy, fibrotic NSIP-pattern ILD, and lupus-specific autoantibodies emphasizes the need for an integrated clinical, serological, capillaroscopic, and radiological approach. Early recognition and timely organ-directed therapy may improve outcomes; however, long-term prognosis depends on the trajectory of pulmonary disease and the development of pulmonary vascular or other major organ involvement, necessitating continued multidisciplinary follow-up.

AUTHORS' CONTRIBUTIONS

Arun Bargali, Ayushman Bindal, Abhigyan Bindal and Harsh Pratap Singh: Designed the study, collected and analyzed the data, and prepared the first draft. Sumit Pachori: Reviewed and modified the manuscript.

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