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Case Series

Unraveling complex autoimmunity: a case series of rheumatologic overlap syndromes

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ABSTRACT

Overlap syndromes represent a complex interplay of multiple connective tissue diseases coexisting within a single patient, posing significant diagnostic and therapeutic challenges due to overlapping clinical, serologic, and immunologic features that defy classification into a single disease entity. We report a case series of ten patients evaluated at a tertiary care rheumatology unit in Northeast India, illustrating the heterogeneity of this clinical entity. The cohort included overlaps of systemic sclerosis with rheumatoid arthritis, Sjögren's syndrome with polymyositis, systemic lupus erythematosus with rheumatoid arthritis, systemic lupus erythematosus with Sjögren's syndrome, and systemic sclerosis with polymyositis, with organ involvement ranging from interstitial lung disease and pulmonary arterial hypertension to lupus nephritis, neuropsychiatric lupus, and lupus enteritis. Nine of the ten patients were female, and diagnosis relied on comprehensive autoantibody profiling alongside clinical evaluation. Management with corticosteroids, mycophenolate mofetil, cyclophosphamide, and hydroxychloroquine, guided by dominant organ involvement, achieved favourable outcomes in most patients; two patients with treatment non-adherence progressed to fatal complications. These cases emphasize the importance of maintaining a high index of suspicion for overlap syndromes in patients with multisystem autoimmune manifestations. Early recognition, detailed immunologic profiling, and multidisciplinary management are essential to prevent irreversible organ damage, guide personalized therapy, and optimize long-term outcomes in this challenging and increasingly recognized domain of clinical rheumatology.

Keywords: ANA profile, Dermatomyositis, Overlap syndrome, Polymyositis, Rheumatoid arthritis, Sjögren syndrome, Systemic lupus erythematosus, Systemic sclerosis

INTRODUCTION

Overlap syndrome is a complex clinical scenario characterized by the coexistence of features from two or more connective tissue diseases within the same patient. Connective tissue disorders such as systemic lupus erythematosus, Sjögren's syndrome, polymyositis, dermatomyositis, rheumatoid arthritis, and systemic sclerosis can coexist together, a phenomenon known as overlap syndrome.[1]

This challenges the traditional diagnostic boundaries because patients exhibit overlapping clinical, serologic, and immunologic features that do not fit neatly into a single disease category. This syndrome is often encountered in Rheumatology, where overlapping manifestations of diseases occur simultaneously or sequentially.[2]

The recognition of overlap syndrome is critical because it directly influences prognosis and therapeutic decisions. The pathogenesis of overlap syndrome likely involves a complex interplay of environmental triggers, genetic factors, and defects in immune regulation leading to multisystem autoimmunity.[3]

Autoantibodies characteristic of each underlying disease may be present together, resulting in a diverse and often confusing clinical picture. Clinically, patients with overlap syndrome may present with symptoms affecting multiple organ systems including skin, joints, muscles, blood vessels, heart, and lungs, necessitating a comprehensive and often multidisciplinary approach for diagnosis and management.[4]

Treatment strategies are decided according to the clinical features and may include corticosteroids, immunosuppressive agents such as mycophenolate mofetil, cyclosporine, or azathioprine, and biologic therapies. However, the heterogeneous nature of overlap syndromes makes treatment challenging, often requiring individualized regimens to balance efficacy and adverse effects.

Early diagnosis improves patient outcome, as delay in diagnosis and treatment can lead to irreversible organ damage and increased morbidity and mortality. The complex and rare nature of overlap syndromes makes them a diagnostic dilemma, emphasizing the need for high clinical suspicion and thorough immunologic evaluation in patients presenting with multisystem autoimmune features.

CASE SERIES

Case 1*: *Systemic sclerosis + rheumatoid arthritis overlap

A 29-year-old female from a village in Assam presented to our rheumatology OPD with complaints of skin tightness for the past 2 years and bluish discoloration of bilateral fingertips on exposure to cold for the past 2 years. She also had bilateral symmetric inflammatory polyarthritis involving the upper limbs, small-joint predominant, with sparing of the distal interphalangeal joints, morning stiffness, and neck pain. Joint pain was relieved at the end of the day with daily household activities. She denied any history of trauma, nausea, fever, headache, altered sensorium, vertigo, esophageal dysmotility, or chest pain. Deformity involving bilateral hands had been present for the past 1 year. She also reported nocturnal dry cough and exertional breathlessness for the past 6 months, which had aggravated over the preceding 3 weeks. There was no history of fever, productive cough, orthopnea, or paroxysmal nocturnal dyspnea.

On examination, blood pressure was 136/84 mmHg, pulse rate 86 per minute, and SpO_2 99% on room air. Bilateral basal fine end-inspiratory crepitations were present. Heart sounds S1 and S2 were heard with no murmur and no loud P2. GCS was 15/15. No pallor, icterus, edema, clubbing, or lymphadenopathy was noted. Boutonniere's deformity involving bilateral hands was present.

Laboratory investigations revealed hemoglobin 10.8 g/dL, total leukocyte count 6100/mm³ (neutrophils 83%, lymphocytes 14%, monocytes 2%, eosinophils 1%), and platelet count 2.2 lakhs. Urine routine examination showed 1-2 pus cells per HPF, with albumin and sugar absent. Creatinine was 0.6 mg/dL, urine albumin-creatinine ratio 27 mg/g, TSH 3.24, serum albumin 3.1 g/dL, serum globulin 5 g/dL with A:G ratio reversal. Chest X-ray showed bilateral basal fine reticular opacities. ECG showed normal sinus rhythm. HRCT thorax revealed nodular opacities involving bilateral lung fields with basal ground-glass opacification. ESR 65 mm/hr, CRP 11.9 mg/dL, procalcitonin<0.05, RBS 89 mg/dL, rheumatoid factor 265 IU/mL, anti-CCP strongly positive, HLA-B27 negative, ANA profile 1:3200 titre with 3+ intensity, anti-Scl-70 positive. 2D echocardiography showed normal systolic and diastolic function, ejection fraction 65%, no pulmonary arterial hypertension. Pulmonary function tests showed a restrictive pattern.

The patient was evaluated by a multidisciplinary team comprising internal medicine, rheumatology, pulmonary medicine, and cardiology specialists. A diagnosis of diffuse systemic sclerosis with rheumatoid arthritis overlap syndrome was made. She was initiated on tab mycophenolate mofetil 2 g/day, tab hydroxychloroquine 200 mg once daily at bedtime, tab nifedipine 10 mg twice daily, tab nintedanib 150 mg twice daily, tab calcium with vitamin D3, proton pump inhibitor, tab cotrimoxazole 800/160 mg on alternate days, and tab prednisolone 10 mg once daily for 3 weeks with subsequent tapering.

On 3-month follow-up, joint pain, swelling, breathlessness, and skin tightness showed improvement. However, bilateral hand Boutonniere's deformity persisted. The patient was continuing medications and physiotherapy, with overall improvement in general condition.

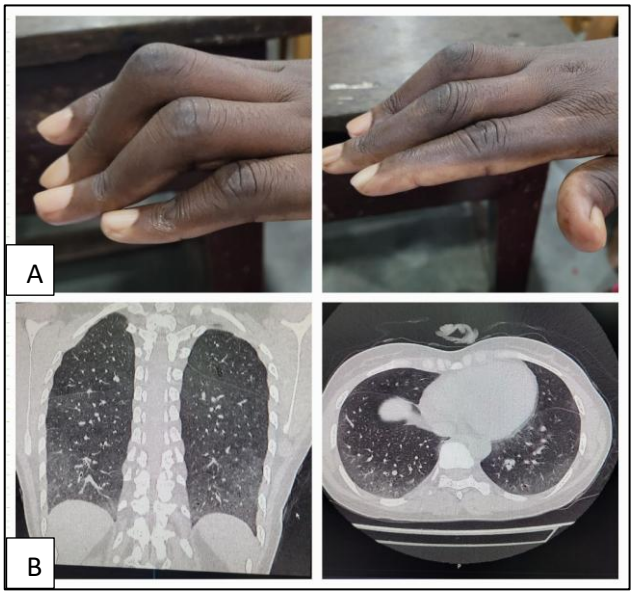

Figure 1 (A and B): Skin tightness with Boutonniere's deformity (top); bilateral basal ground-glass opacification with nodular opacities on HRCT thorax suggestive of interstitial lung disease (bottom).

Case 2: Sjögren's syndrome + polymyositis overlap

A 49-year-old female presented to the rheumatology OPD with low backache aggravated on bending forward and lifting heavy weights for the past 2 years, for which she had initially consulted an orthopedician. MRI of the dorsolumbar spine showed multiple-level disc bulges at the lower thoracic and lumbar regions. She also reported fatigue as the primary complaint for the past 1 year, associated with itching and foreign body sensation in the eyes, dryness of the mouth, and alopecia noticed for the past 6 months. She had generalized body ache and muscle pain relieved only transiently by analgesics, along with proximal muscle weakness of the bilateral lower limbs. No history of cough, evening rise of temperature, tuberculosis contact, significant weight loss, diarrhea, breathlessness, or dysphagia was noted.

On examination, blood pressure was 100/60 mmHg, pulse rate 89 per minute, SpO_2 99% on room air. Chest was bilaterally clear. Heart sounds S1 and S2 were heard. GCS was 15/15.

Laboratory investigations showed hemoglobin 10.9 g/dL, total leukocyte count 4800/mm³, platelet count 90,000, ESR 66 mm/hr, CRP <0.5 mg/dL, creatinine 0.9 mg/dL, AST/ALT 35/29 IU/L, serum albumin 3.5 g/dL, serum globulin 4.5 g/dL, urine routine examination showing albumin nil, sugar nil, pus cells 1-2/HPF, RBS 102 mg/dL, rheumatoid factor negative, anti-CCP negative, pANCA and cANCA negative, ANA profile 1:320 titre with 3+ intensity, antibodies against Ro52 and Jo-1 positive (3+ intensity). Chest X-ray and ECG were normal. TSH 2.6. 24-hour urine protein 0.28 g/day. Elevated LDH and elevated creatine kinase were noted. HRCT thorax showed a normal study. Schirmer's test showed severe dry eyes bilaterally.

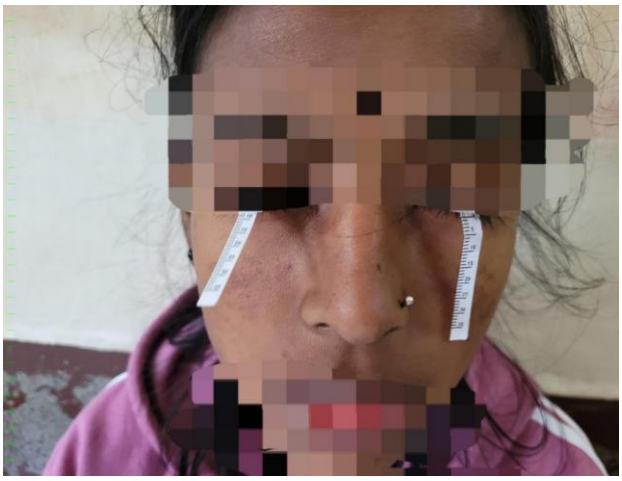

Figure 2: Schirmer's test of bilateral severe dry eyes.

A diagnosis of Sjögren's syndrome with polymyositis overlap was made. The patient was started on carboxymethylcellulose eye drops, tab mycophenolate mofetil 2 g/day, tab calcium with vitamin d3 once daily, tab prednisolone 40 mg/day with tapering in subsequent visits, and tab cotrimoxazole 800/160 mg on alternate days.

On 3-month follow-up, fatigue and muscle pain improved. Oral steroid dosage was tapered in subsequent visits while immunosuppressive agents were continued. The patient was doing well.

Case 3: Systemic lupus erythematosus + rheumatoid arthritis overlap

A 17-year-old female presented with bilateral knee, elbow, wrist, metacarpophalangeal, and interphalangeal joint pain and fever for the past 12 months. At presentation, she had deformity of both hands for the past 6 months and had been bedridden for 1 month. Associated features included alopecia and malar rash. On day 7 of admission, she developed altered sensorium. ANA profile showed antibodies against SS-A, Smith, ribosomal protein, Histone, and U1-RNP. CSF analysis ruled out infection. She had elevated ferritin and A:G ratio reversal. MRI brain showed multiple small white matter hyperintensities on T2-weighted imaging. Rheumatoid factor and anti-CCP were strongly positive. Urine albumin-creatinine ratio was 17 mg/g.

A diagnosis of SLE with Neuro-Lupus and Rheumatoid Arthritis overlap syndrome was made. The patient received Injection Methylprednisolone pulse dose (1 g/day) for 3 days followed by maintenance oral Prednisolone. Tab mycophenolate mofetil, tab hydroxychloroquine, tab calcium with vitamin D3, and sunscreen lotion were also added. She recovered with physiotherapy support; joint pain resolved, sensorium improved, and she was able to walk with support at discharge.

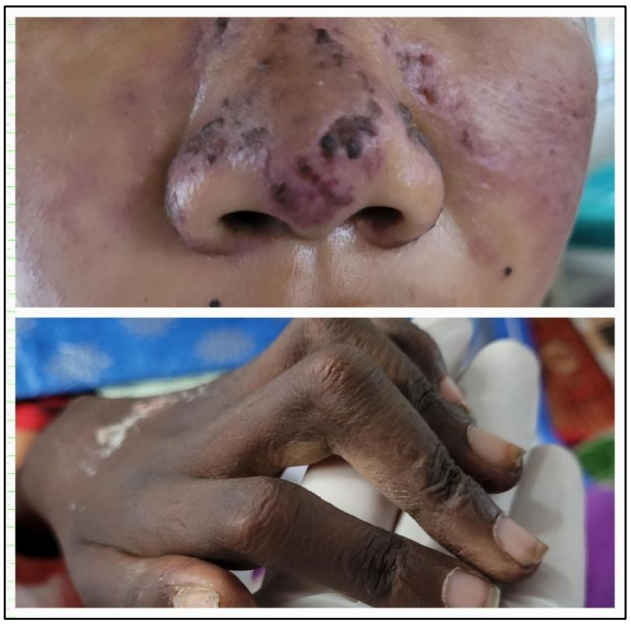

Figure 3: Malar rash and Boutonniere's deformity.

Case 4: Systemic sclerosis + rheumatoid arthritis overlap

A 41-year-old female presented with skin tightening, bilateral symmetric polyarthritis of 10 months duration, esophageal dysmotility, and impaired mouth opening. There were no signs of pulmonary arterial hypertension or Raynaud's phenomenon. On evaluation, antibodies against SS-A were 3+, nucleosome 1+. Rheumatoid factor and anti-CCP were elevated. Hyperferritinemia was present. HRCT thorax showed interstitial lung disease NSIP pattern. 2D echocardiography showed a normal study.

The patient was managed with hydroxychloroquine, low-dose prednisolone, mycophenolate mofetil, pantoprazole, and domperidone. On 3-month follow-up, skin thickening and tightness reduced minimally; however, joint pain resolved completely and the patient was able to carry out day-to-day activities.

Case 5: Systemic sclerosis + rheumatoid arthritis overlap

A 20-year-old female presented with bilateral symmetric polyarthritis of 1-year duration, with sparing of the distal interphalangeal joints and morning stiffness. She also had skin tightness and bluish discoloration of the fingertips on exposure to cold for the past 10 months. No complaints of esophageal dysmotility, chest pain, or breathlessness were noted. On evaluation, hemoglobin 9 g/dL, ESR 120 mm/hr, CRP <0.5 mg/dL, rheumatoid factor 15.60 IU/mL. ANA profile showed Scl-70 3+, Ro52 3+, U1-RNP 2+. anti-CCP was positive. Schirmer's test was negative. HRCT thorax and 2D echocardiography were normal.

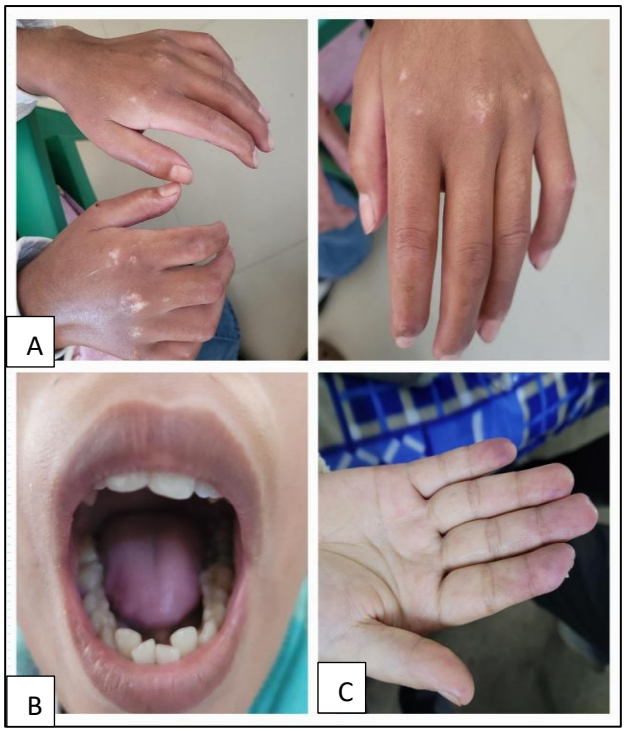

Figure 4 (A-C): Skin tightening, fish-mouth appearance, and Raynaud's phenomenon.

The patient was initiated on hydroxychloroquine, prednisolone 10 mg/day with tapering, mycophenolate mofetil 2 g/day, cotrimoxazole prophylaxis, and calcium channel blockers. Over 6-month follow-up, skin tightening gradually decreased and bluish discoloration of the extremities improved. However, the patient was subsequently lost to follow-up and was non-compliant with therapy. She developed gangrene of the right ring and middle fingers, left ring finger, and a right forearm abscess. She subsequently developed severe sepsis with septic shock and was admitted to the medicine ICU. Despite aggressive treatment with intravenous antibiotics, the patient succumbed to death on day 7 of admission, approximately 12 months after diagnosis.

Case 6: Systemic lupus erythematosus + rheumatoid arthritis overlap

A 33-year-old female school teacher presented with multiple small and large joint pain and swelling for 1 year, associated with non-scarring alopecia for 6 months. She also had bilateral pitting pedal edema and frothy urine for 6 months. She had been managed by a primary care physician with analgesics for 1 month without relief, and her pedal edema worsened in the preceding week. On evaluation, she had more than 10 joints involved with at least 1 small joint, strongly positive anti-CCP and rheumatoid factor, symptom duration exceeding 6 weeks, and abnormal ESR and CRP, yielding a score of 10 by 2010 ACR/EULAR criteria, fulfilling a diagnosis of rheumatoid arthritis.

Urine routine examination showed protein 3+. 24-hour urinary protein was 4.5 g/day. Blood investigations revealed hemoglobin 10.9 g/dL, total leukocyte count 10,240/mm^3, creatinine 0.9 mg/dL, sodium 134 mEq/L, potassium 3.9 mEq/L, albumin 2.1 g/dL, globulin 4.2 g/dL, ESR 150 mm/hr, CRP <0.5. Hepatitis B, Hepatitis C, and HIV 1 and 2 were negative. Procalcitonin was less than 0.5. Mantoux test was negative. ANA IF showed 3+ intensity with 1:360 titre. ANA profile revealed antibodies against dsDNA, Smith, and Ribosomal protein. C3 and C4 levels were significantly low. Chest X-ray and USG whole abdomen were normal. According to ACR/EULAR 2019 criteria, a diagnosis of SLE with Lupus Nephritis was also made.

A diagnosis of SLE with lupus nephritis and rheumatoid arthritis overlap syndrome was established. She received injection methylprednisolone 1 g in 100 mL normal saline intravenously once daily for 3 days, followed by injection cyclophosphamide 15 mg/kg after proper counseling and informed written consent. She was also initiated on losartan, oral prednisolone 1 mg/kg/day for 4 weeks with tapering at 5 mg per 2-week intervals, prophylactic antibiotics, and diuretics. Pedal edema resolved completely within 5 days. She was discharged on day 5 and has been followed up monthly for 6 planned cycles of cyclophosphamide.

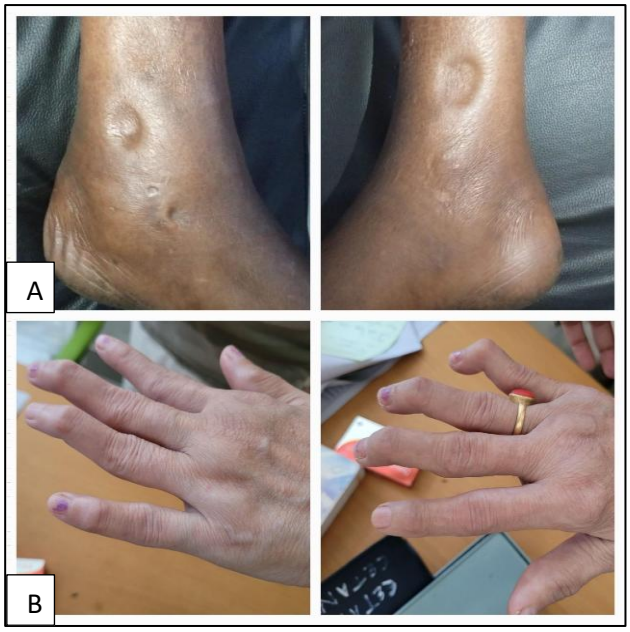

Figure 5 (A and B): Bilateral pitting pedal edema and swan-neck deformity of fingers.

Case 7: Systemic lupus erythematosus + Sjögren's syndrome overlap

A 32-year-old female presented with a facial rash for 1 year, multiple erythematous patches over the bilateral anterior legs, itching and watering of both eyes for 10 months, intermittent fever for 4 months, and painless oral ulcers for 1 week. She was brought to the emergency department with one episode of generalized tonic-clonic seizures with post-ictal altered sensorium. CT brain showed a normal study. She was given short-acting benzodiazepines, a loading dose of Levetiracetam 1 g, and broad-spectrum antibiotics. Suctioning of oropharyngeal secretions was performed and she was admitted to the medicine ICU.

At admission, GCS was E2V3M4. Blood pressure was 120/76 mmHg, pulse rate 76/minute, SpO_2 99% on face mask at 6 L/min O_2. Bilateral basal crepitations were present. Investigations showed hemoglobin 12 g/dL, total leukocyte count 6730 cells/mm³, platelet count 2.8 lakhs/mm³, creatinine 0.75 mg/dL, sodium 141, potassium 4.18, ESR 100 mm/hr, CRP <0.5, TSH 0.72, serum albumin 3.98 g/dL, serum globulin 4.2 g/dL. USG abdomen was normal. Chest X-ray showed bilateral minimal pleural effusion. Urine routine showed protein 2+; urine ACR 480 mg/g; 24-hour urine protein 800 mg/day. C3 and C4 were low. ANA profile showed 3+ intensity at 1:360 titre with antibodies against U1-RNP, Smith, ribosomal P protein, and Ro52. Hepatitis B, hepatitis C, and HIV 1 and 2 were negative. APLA profile was negative. Schirmer's test was positive. MRI brain showed T2 hyperintensities in the periventricular and subcortical areas with lacunar infarcts and micro-hemorrhages, suggestive of vasculitis.

A diagnosis of SLE with Sjögren's syndrome overlap was made. The patient received intravenous antibiotics for 5 days. Serum procalcitonin was <0.5; blood culture was negative. Sensorium improved to GCS E4V4M6 and SpO_2 was maintained on room air. She received injection methylprednisolone 900 mg in 200 ml normal saline over 1 hour for 3 days, followed by oral Prednisolone 60 mg/day for 4 weeks with tapering. Injection Cyclophosphamide 15 mg/kg in 300 mL Normal Saline was administered, preceded and followed by 500 mL normal saline infusion and intravenous Ondansetron. Injection Leuprolide was advised on day 15 for ovarian protection. Psychiatric consultation was obtained for agitation; Tab Quetiapine was prescribed. She was also given prophylactic antibiotics, ARBs, Calcium with vitamin D3, PPIs, and antiepileptics. She was discharged and reviewed in OPD after 1 month, receiving her 2nd cycle of cyclophosphamide. Erythematous lesions and oral ulcers resolved significantly. Fever and malar rash resolved completely.

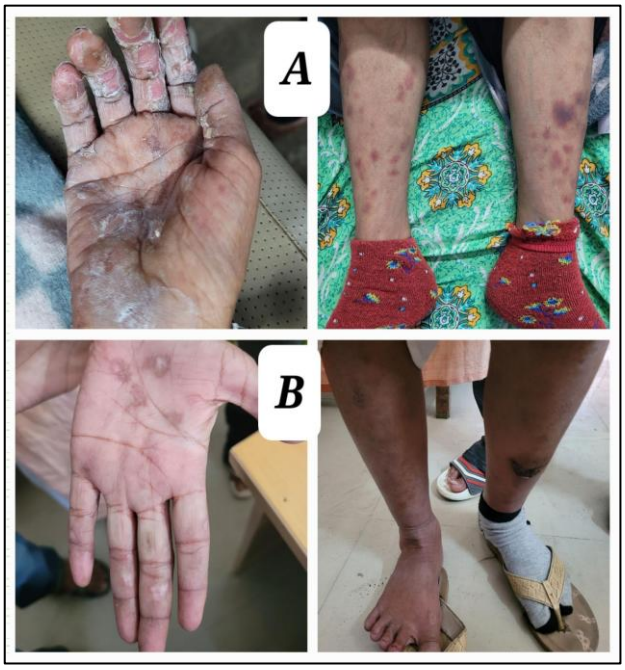

Figure 6 (A and B): A) Erythematous lesions over bilateral shin and hand; B) Resolved in subsequent visit.

Case 8: Systemic lupus erythematosus + rheumatoid arthritis overlap

A 25-year-old female homemaker presented with bilateral symmetric polyarthritis involving small and large joints (bilateral knee, ankle, elbow, metacarpophalangeal, and proximal interphalangeal joints) with sparing of the distal interphalangeal joints, morning stiffness, and non-scarring alopecia for 1 year. She also reported tingling and numbness with bluish discoloration of the extremities for the past 6 months, and a photosensitive facial rash for the past 6 months. No pedal edema or frothy urine was noted.

Examination showed BP 110/70 mmHg, pulse rate 96/minute regular, non-scarring alopecia, chest bilaterally clear, and Raynaud's phenomenon present. Laboratory investigations showed ESR 25 mm/hr, CRP 3 mg/dL, Rheumatoid Factor 57.06 IU/mL (normal <12), anti-CCP 94.02 (normal <17), ANA 3+ at 1:320 titre with nuclear speckled pattern, U1-RNP strongly positive 3+. Urine albumin was negative, 24-hour urine protein 30 mg. Hemoglobin 12.2 g/dL, total leukocyte count 12,200/mm³, platelet count 1.5 lakhs/mm³, creatinine 0.62 mg/dL, sodium 134, potassium 4.2, AST/ALT 23/21 IU/L, serum albumin 3.2 g/dL, serum globulin 2.6 g/dL, TSH 4.26. Hepatitis B, Hepatitis C, and HIV were negative. Chest X-ray and USG abdomen were normal. 2D echocardiography showed ejection fraction 60%, mild TR, and moderate PAH. HRCT thorax was normal. SLICC criteria and ACR/EULAR 2019 criteria were fulfilled.

A diagnosis of SLE with rheumatoid arthritis overlap syndrome was made. The patient was initiated on Tab Methotrexate 15 mg once weekly, tab folic acid 5 mg twice weekly, tab nifedipine 20 mg twice daily, tab tadalafil 10 mg once daily, tab prednisolone 10 mg once daily for 4 weeks with tapering, tab hydroxychloroquine 200 mg once daily at bedtime, sunscreen lotion, tab calcium with vitamin D3, and tab pantoprazole 40 mg once daily on empty stomach. On monthly follow-up, joint pain improved and she is able to carry out day-to-day activities.

Case 9: Systemic lupus erythematosus + rheumatoid arthritis overlap

A 27-year-old female presented with bilateral symmetric polyarthritis involving wrists, elbows, proximal interphalangeal joints, metacarpophalangeal joints, and cervical spine with sparing of distal interphalangeal joints for 1.5 years, and a photosensitive facial rash for 2 months. She had also experienced chronic diarrhea and bilateral pedal edema, for which she had been given 6 months of anti-tubercular therapy (ATT) by a local physician for suspected abdominal tuberculosis. Her symptoms did not improve with ATT.

On evaluation at our hospital, blood pressure was 130/80 mmHg, pulse rate 86/minute, with bilateral pitting pedal edema and a hard palate oral ulcer. Investigations showed ESR 80 mm/hr, CRP 1.13 mg/dL, hemoglobin 7.8 g/dL, total leukocyte count 4000/mm³, platelet count 1.2 lakhs, serum albumin 2.9 g/dL, globulin 3.5 g/dL with A:G ratio reversal, rheumatoid factor 13.10, anti-CCP positive. Corrected serum calcium 9.2, urine ACR 23 mg/g. Peripheral smear showed microcytic hypochromic red cells with adequate platelets and WBC. Hepatitis B, hepatitis C, and HIV 1 and 2 were negative. CT abdomen showed multiple enlarged para-aortic lymph nodes, the largest measuring 1.2×0.7 cm. Inguinal lymph node biopsy showed reactive hyperplasia. Upper GI endoscopy was normal. Colonoscopy showed grade 1 anal hemorrhoids. Mantoux was positive. HRCT thorax was normal. Serum C3 and C4 were low, and anti-dsDNA titres were high. ANA profile showed 3+ intensity at 1:720 titre with antibodies against centromere, Scl-70, Ro52, Ro60, U1-RNP, Smith, and histone.

A diagnosis of SLE with rheumatoid arthritis overlap was made. She had features of lupus enteritis, a visceral manifestation of SLE. She was initiated on injection methylprednisolone 15 mg/kg/day for 3 days followed by oral prednisolone 1 mg/kg/day for 4 weeks with subsequent tapering. Tab mycophenolate mofetil 2 g/day was added as a steroid-sparing agent. She also received calcium, PPI, oral cotrimoxazole prophylaxis, probiotics, and diuretics. Arthritis resolved by day 5 of admission. Enteritis symptoms persisted for the first 2 months and gradually improved with tapering steroids and mycophenolate mofetil.

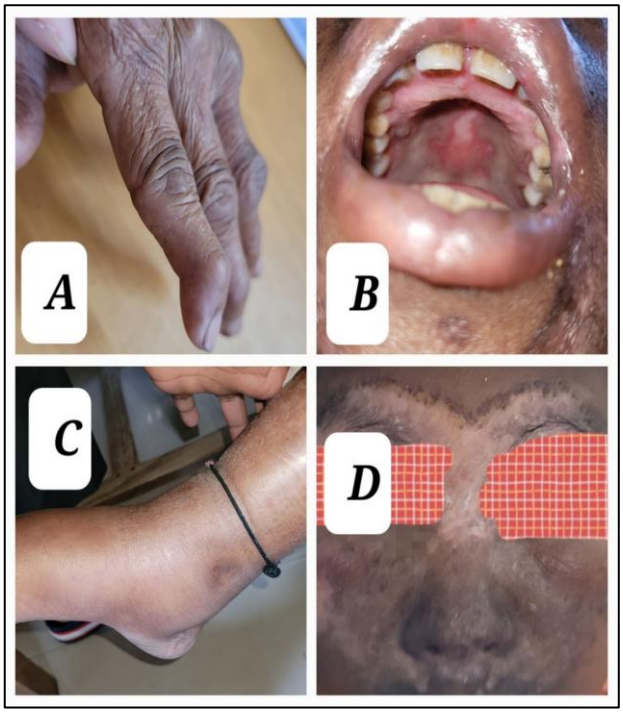

Figure 7 (A-D): A) Swan-neck deformity; B) Hard palate oral ulcer; C) Pitting pedal edema; D) Photosensitive facial rash.

Case 10: Systemic sclerosis + polymyositis overlap

A 42-year-old male with a known history of hypertension presented with joint pain, painful bluish discoloration of the extremities on exposure to cold, skin tightening, and breathlessness 2-2.5 hours after going to sleep, for the past 1 year. He also complained of generalized weakness, epigastric burning, exertional breathlessness for the past 3 months, and blackish discoloration of the right index finger for 7 days. Weakness was insidious in onset and gradually progressive, preventing him from rising from a squatting position and combing his hair. He had salt-and-pepper pigmentation of the bilateral hands, shins, neck, and trunk.

On examination, the patient had skin tightening, bilateral pitting pedal edema, gangrene of the right index finger, bilateral basal fine crepitations, raised JVP, loud P2, BP 160/100 mmHg, PR 98/minute, and was in NYHA Class III. Laboratory parameters showed hemoglobin 9.2 g/dL, ESR 100 mm/hr, CRP 12 mg/dL, urine microscopy normal. ANA profile showed 3+ intensity at 1:360 titre with antibodies against centromere, U1-RNP, and Jo-1. Serum CPK was elevated. HRCT thorax showed features of usual interstitial pneumonitis/interstitial lung disease with honeycombing and traction bronchiectasis, with a dilated main pulmonary trunk. 2D echocardiography showed severe PAH, severe TR, grade 2 LV diastolic dysfunction, and LV EF 55%. USG Doppler of the right upper limb showed absent flow in the distal radial artery branches.

A diagnosis of systemic sclerosis with polymyositis overlap was made. The patient was initiated on broad-spectrum intravenous antibiotics, tab mycophenolate mofetil 2 g/day, tab hydroxychloroquine 300 mg once daily at bedtime, tab tadalafil 10 mg once daily, tab furosemide 40 mg once daily, tab prednisolone 10 mg/day, and cotrimoxazole prophylaxis. Breathlessness and pedal edema resolved over 10 days. The patient was discharged on the above medications but was subsequently found to have expired 1 month after discharge, likely due to drug non-compliance and worsening pulmonary edema with heart failure.

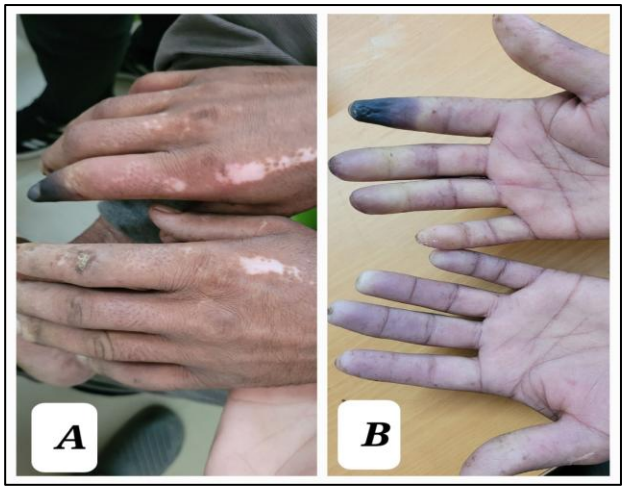

Figure 8 (A and B): A) Salt-and-pepper pigmentation over bilateral hands; B) Gangrene of right index finger with Raynaud's phenomenon.

DISCUSSION

Overlap syndromes represent a complex intersection of autoimmune connective tissue diseases, most frequently involving systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, Sjögren's syndrome, polymyositis, and dermatomyositis. Most of the patients in our series were female (9 out of 10), reflecting the well-established female preponderance of autoimmune overlap syndromes. Our ten-case series highlights the heterogeneity of clinical expression, serologic diversity, and variable organ involvement that characterize these entities. The clustering of disease-specific autoantibodies within the same individual reflects shared immunogenetic susceptibility and dysregulated B-cell-mediated autoimmunity.

In systemic sclerosis-rheumatoid arthritis overlap, pulmonary and vascular complications significantly influenced prognosis in our patient population. Pinto et al described comparable cases with severe cardiopulmonary and articular disease, emphasizing the importance of early aggressive immunosuppression to prevent irreversible organ damage.[1,15] Zimmermann et al demonstrated that anti-CCP positivity in systemic sclerosis patients identifies a true rheumatoid overlap phenotype rather than nonspecific serologic coexistence.[2,8-10]

Our lupus-rheumatoid arthritis overlap cases exhibited deforming inflammatory arthritis alongside immune complex-mediated organ involvement, consistent with reports of multi-antibody positivity (anti-dsDNA and anti-CCP) indicating authentic overlap rather than sequential disease evolution.[3,11,13] The association of Sjögren's syndrome with inflammatory myopathies in our series parallels findings by Migkos et al who highlighted Ro/Jo-1 antibody clustering and shared B-cell-driven mechanisms.[5,7,14] Rare triple overlaps reported by Mizuhashi et al further support the concept of overlapping immune pathways producing multisystem autoimmunity.[6]

Therapeutically, individualized regimens centred on corticosteroids and mycophenolate mofetil achieved favourable responses in most patients, aligning with contemporary organ-directed treatment strategies.[1,4,12] Mortality in two non-compliant cases underscores the higher morbidity associated with overlap syndromes. Early recognition, comprehensive serologic profiling, and multidisciplinary management remain essential to improving long-term outcomes.

CONCLUSION

This case series of ten patients underscores the clinical complexity and evolving nature of rheumatologic overlap syndromes, where distinct autoimmune entities converge within a single host. The coexistence of conditions such as systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, and Sjögren's syndrome reflects shared immunopathogenic pathways rather than mere coincidence. Our observations demonstrate that overlap syndromes often present with aggressive articular disease, early internal organ involvement, and diverse autoantibody profiles, demanding a high index of suspicion and comprehensive immunologic evaluation.

While most patients responded favourably to timely, organ-directed immunosuppressive therapy, delayed presentation and treatment non-adherence were associated

with severe complications and mortality, emphasizing the prognostic vulnerability of this subgroup. These cases highlight the importance of individualized therapeutic strategies tailored to dominant organ involvement, supported by multidisciplinary collaboration. Early recognition, regular follow-up, and sustained patient engagement are essential to prevent irreversible damage. Ultimately, a patient-centred and vigilant approach remains central to improving long-term outcomes in this challenging yet increasingly recognized domain of clinical rheumatology.

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REFERENCES

1. Pinto AS, Santos FC, Dinis SP, Madeira N, Ferreira JF, Vaz C. Systemic sclerosis and rheumatoid arthritis overlap syndrome-management of severe cardiac, pulmonary and articular involvement. Reumatologia. 2023;61(1):55-62.
2. Zimmermann C, Steiner G, Skriner K, Hassfeld W, Petera P, Smolen JS. The concurrence of rheumatoid arthritis and limited systemic sclerosis: clinical and serologic characteristics of an overlap syndrome. Arthritis Rheum. 1998;41(11):1938-45.
3. Gopal S, Vakati D, David K. Unraveling the complexity: a rare case of systemic sclerosis, rheumatoid arthritis, and systemic lupus erythematosus overlap syndrome. Cureus. 2024;16(9):e68405.
4. Bergamasco A, Hartmann N, Wallace L, Verpillat P. Epidemiology of systemic sclerosis and systemic sclerosis-associated interstitial lung disease. Clin Epidemiol. 2019;11:257-73.
5. Migkos MP, Sarmas I, Somarakis GA, Voulgari PV, Tsamis KI, Drosos AA. Sjögren syndrome associated with inflammatory muscle diseases. Mediterr J Rheumatol. 2018;29(2):92-6.
6. Mizuhashi Y, Hirata S, Sakata K. Overlap syndrome involving anti-OJ antibody-positive polymyositis, systemic lupus erythematosus and Sjögren's syndrome: a case report and literature review. Mod Rheumatol Case Rep. 2023;7(2):399-403.
7. Betteridge ZE, McHugh NJ. Myositis-specific autoantibodies: an important tool to support diagnosis of myositis. J Intern Med. 2016;280(1):8-23.
8. Fiori G, Pignone A, Cerinic MM. Overlap syndromes. Reumatizam. 2002;49(2):12-5.
9. Md Nawawi NZ, Kanoo LL, Peter AB, Alias AB, Baharuddin H, Ramli AS. Overlap syndrome involving rheumatoid arthritis and systemic sclerosis complicated by Hashimoto's thyroiditis and interstitial lung disease detected in primary care: a case report. AME Case Rep. 2025;9:135.
10. Kondoh Y, Bando M, Kawahito Y, Sato S, Suda T, Kuwana M. Identification and management of interstitial lung disease associated with systemic sclerosis (SSc-ILD), rheumatoid arthritis (RA-ILD), and polymyositis/dermatomyositis (PM/DM-ILD): development of expert consensus-based clinical algorithms. Expert Rev Respir Med. 2024;18(6):447-56.
11. Guseva NG. Overlap syndromes in rheumatology. Vestn Ross Akad Med Nauk. 2008;(9):36-40.
12. Mohammed MJ, Hashim HT, Al-Obaidi AD, Al Shammari A. A novel overlap syndrome: Rheumatoid arthritis, Sjogren's syndrome, antiphospholipid syndrome, and dermatomyositis. Clin Case Rep. 2023;11(4):e7274.
13. Jury EC, D'Cruz D, Morrow WJ. Autoantibodies and overlap syndromes in autoimmune rheumatic disease. J Clin Pathol. 2001;54(5):340-7.
14. Iaccarino L, Gatto M, Bettio S, Caso F, Rampudda M, Zen M, et al. Overlap connective tissue disease syndromes. Autoimmun Rev. 2013;12(3):363-73.
15. Dubai FM, Isa A. Overlap Syndrome in a Male Presenting With Progressive Lower Limb Weakness: A Case Report. Cureus. 2023;15(1):e33664.

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