Case Report

Diffuse Parenchymal Lung Diseases due to Overlap syndrome (Rheumatoid arthritis and Systemic Sclerosis) with Sjogren syndrome and Psoriasis: A Rare case report

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ABSTRACT

The diffuse parenchymal lung diseases (DPLDs) are a heterogeneous group of conditions affecting the pulmonary parenchyma (interstitial) and/or alveolar lumen. Since DPLD in overlap syndromes has a poor prognosis, extensive work up should be performed even when clinical evidence of only one autoimmune disease is present. DPLD is a frequent manifestation of connective tissue diseases (CTDs), with incidence and prevalence variously assessed in the literature but reported in up to 30% of patients, with higher frequency in rheumatoid arthritis (RA) and systemic sclerosis (SSc). However, Sjogren's syndrome (SS) is a chronic inflammatory disease characterized by lymphocytic infiltrates in the exocrine glands, mainly the salivary and lacrimal glands. DPLD is found in 3-11% of the patients with primary Sjogren's syndrome, often leading to life-threatening complications. When combined, the diagnosis is often missed or delayed, which can lead to an increased incidence of long-term morbidity and mortality. We present an interesting case of DPLD due to RA-SSc overlap syndrome and Sjogren syndrome – a 53-year-old non-diabetic, normotensive, non-smoker, cotton-wool cloth weaver, married, Muslim female presented with progressively increasing dry, distressing non-productive cough for 3 years which was persistent throughout the day without any seasonal or diurnal variation. She complaints of insidious onset, gradually progressive breathlessness, with mMRC grade-3 at present from initial mMRC grade-0. There was no history of orthopnoea, palpitation, chest pain or any swelling of body. She also complaints of symmetrical inflammatory polyarthritis for 6 months involving small joints of hands, wrist, elbow, feet; not associated with joint swelling, oral ulcer, photosensitivity. She developed painless, non-itchy salt and pepper skin pigmentation along with partly scaly over forehead, back of chest, around neck, upper and lower limbs but no muscle aches and proximal myopathy. We emphasized on inter-professional consultation in the diagnosis and treatment of such a rare case.

Keywords: *DPLD, Overlap syndrome, Sjogren syndrome.*

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INTRODUCTION

The diffuse parenchymal lung diseases (DPLDs) are a heterogeneous group of conditions affecting the pulmonary parenchyma (interstitium) and/or alveolar lumen, which are frequently considered collectively as they share a sufficient number of clinical physiological and radiographic similarities[1]. They often present with cough, which is typically dry and distressing, and breathlessness, which is often insidious in onset but thereafter relentlessly progressive. Physical examination reveals the presence of inspiratory crackles and in many cases digital clubbing develops. Pulmonary function tests typically show a restrictive ventilatory defect in the

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presence of small lung volumes and reduced gas transfer. The typical radiographic findings include, in the earliest stages, ground glass and reticulonodular shadowing, with progression to honeycomb cysts and traction bronchiectasis. While these appearances may be seen on a chest x-ray, they are most easily appreciated on HRCT, which has assumed a central role in the evaluation of DPLD[1-4].

Connective tissue diseases (CTDs) are an important cause of DPLD up to 30% of the cases, with a significant higher frequency in rheumatoid arthritis (RA) and systemic sclerosis (SSc); their clinical manifestations can be very significant, even with multi-compartmental involvement (e.g., interstitium, pleura, pulmonary arteries), and affect patients' survival[1,3].

Overlap syndrome refers to a group of conditions that have clinical features of, and meet classification for, more than one well-characterized rheumatic disease. Diagnosis depends on the diseases based on patients' symptoms and determining positive antibodies in their serological reports. However, their prognosis depends on several factors, e.g., histopathological reports, baseline lung function, auto-antibody levels, etc. Although rare, there can be an overlap between various autoimmune conditions, each of them independently contributing to pulmonary fibrosis (PF).[1-6] For example, ANCA positivity is associated with increased incidence of PF in RA patients. Similarly, increased incidence of PF is seen in SSc patients with ANCA positivity as well as in SSc-RA overlap patients[2,6]. As expected, the prognosis of PF in overlap syndromes is worse than individual entities. Also, SS-A, SS-B positivity in PF can predispose to development of primary SS seen in 3 to 11 % of the patients[3-5].

CASE SUMMARY

A 53-year-old non-diabetic, normotensive, non-smoker, cotton-wool cloth weaver, married- Muslim female presented with progressively increasing dry, distressing non-productive cough for 3 years which was persistent throughout the day without any seasonal or diurnal variation, with no aggravating or relieving factors. For the last 6 months she complaints of insidious onset, gradually progressive breathlessness, with mMRC grade-3 at present from initial mMRC grade-0. There was no history of orthopnoea, palpitation, chest pain or any swelling of body. She also complaints of symmetrical inflammatory polyarthritis for 6 months involving small joints of hands, wrist, elbow, feet; not associated with joint swelling, oral ulcer, photosensitivity. She developed painless, non-itchy salt and pepper skin pigmentation (Fig. 1), along with partly scaly over forehead, back of chest, around neck, upper and lower limbs but no muscle aches and proximal myopathy. On query, she mentioned of gradual skin thickening over forearm and dorsum of hands sparing other parts of body and dry eye, dry mouth as well as dryness of her vagina for 6 months. She also mentioned of pallor of hands and feet on cold exposure for few months, but she denies: alternate bowel habit, muscle aches, any foetal loss, weight loss, headache, seizures, loss of consciousness, reduced urination. Her bowel and bladder habits were normal. She had no history of contact with any tuberculosis patient. She was mildly anaemic, not cyanosed or clubbed, found exercise induced arterial hypoxaemia. Her pulse was 68 beats/min, BP was 120/70mm of Hg, and respiratory rate was 25 breaths/min. On examination of respiratory system, her breath sound was vesicular, bilateral basal end inspiratory fine crepitation was present, which was not altered by coughing, and bilateral chest expansibility symmetrically reduced. Skin thickening in dorsal aspects of both palm, Digital infarct was observed on pulp of fingers of both hands (Fig. 2) with difficulty to introducing 3 fingers in mouth with Grade-3 tenderness present in PIP, MCP and wrist joints symmetrically with restricted movements. Apart from those symptoms and signs, she was being treated with weekly methotrexate and folic acid for her psoriasis (Fig. 3), despite any improvement. However, she had no features of pulmonary hypertension or right heart failure; other system revealed no abnormalities. Her routine investigation revealed mild anaemia (Hb=9.9 mg/dl), high ESR (69 in first hour), high eosinophil counts (13%), normal blood sugar (RBS 5.5mmol/L), normal renal (serum creatinine 1.05 mg/dl) and liver (SGPT 15U/L) functions with proteinuria. Her chest radiograph showed in-homogeneous reticular opacities in both mid and lower zones (Fig. 4). Her lung function tests were done; spirometry revealed moderately severe restrictive abnormalities, while lung diffusion testing determined severely reduced DLCO. For confirmation, HRCT of chest was undertaken and showed multifocal extensive honeycombing, reticulations, fibrosis and ground glass opacities in different segments of both lungs with basal and peripheral subpleural predominance (Fig. 5).

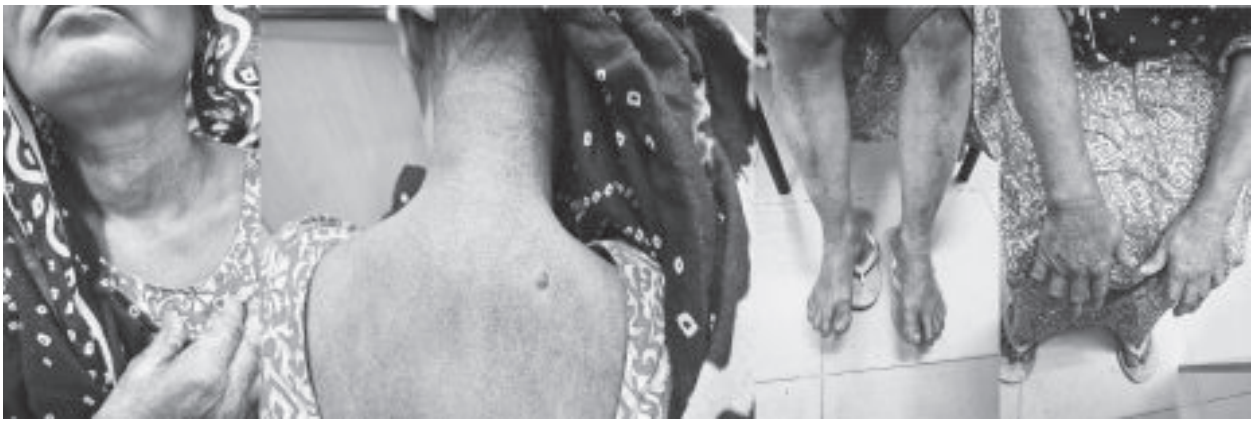

Fig.-1: *Salt and pepper pigmentation.*

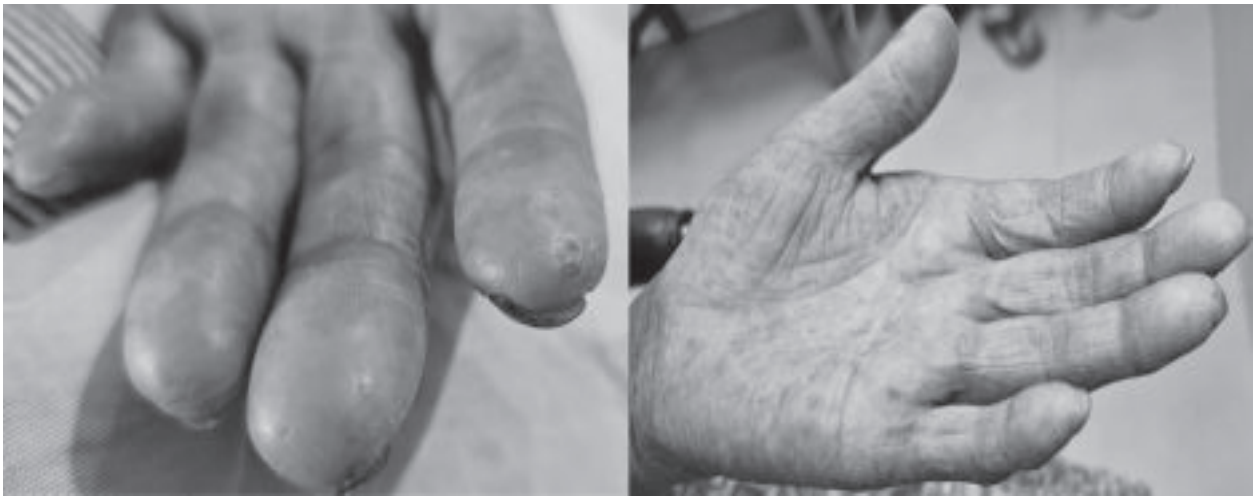

Fig.-2: *Skin thickening and digital infarct at finger tips.*

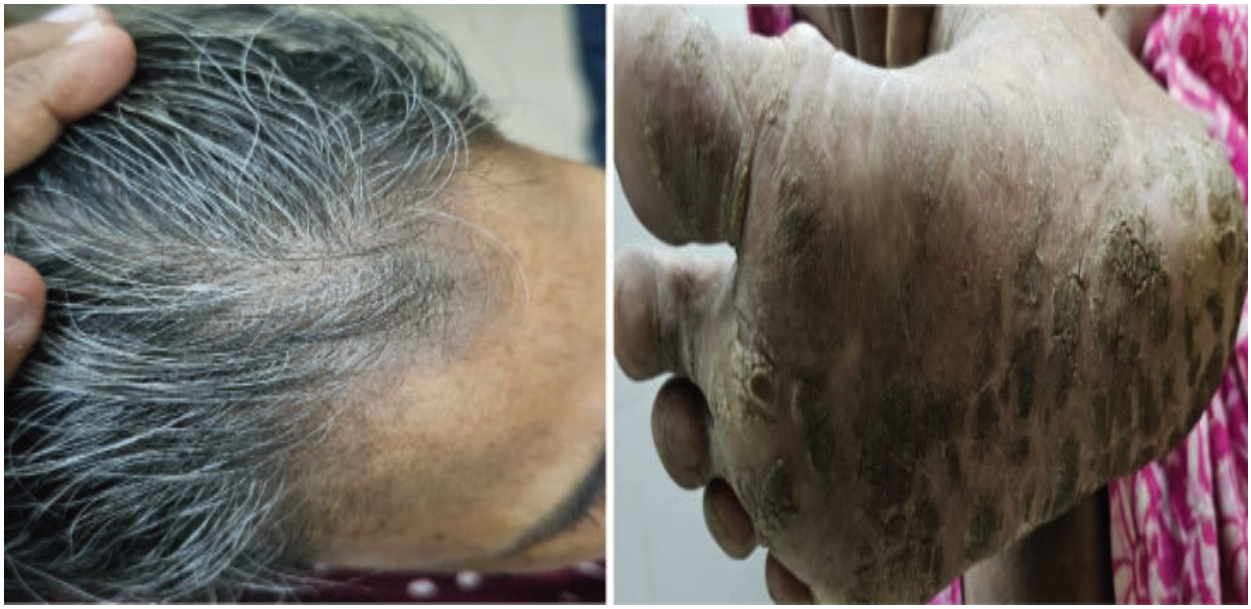

Fig.-3: *Psoriasis as observed on scalp and soles of feet.*

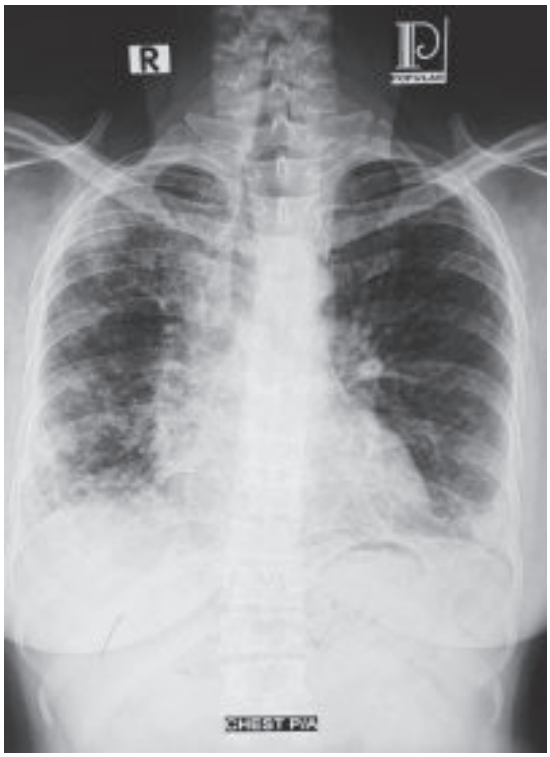

Fig.-4: *Chest x-ray P/A view showing in-homogeneous reticular opacities in both mid and lower zones.*

Table-I : *Autoantibodies screening report*

Name	Results
RA	64.5 IU/mL
Anti-CCP	<0.40 IU/mL
ANA	11.5 IU/mL
Anti-ds DNA	13 IU/mL
CPK	70 IU/L
SS-A	Positive
SS-B	Positive
PM-Scl	Positive

For aetiology of DPLD and as per clinical features of the patient, we searched related antibody screening for diagnosing possible connective tissue diseases (Table-I). The results were consistent with rheumatoid arthritis (RA) with systemic sclerosis (SSc) and Sjogren syndrome. Therefore, our final diagnosis was diffuse parenchymal lung disease (DLPD) due to overlap syndrome (rheumatoid arthritis and systemic sclerosis) with Sjogren syndrome and psoriasis.

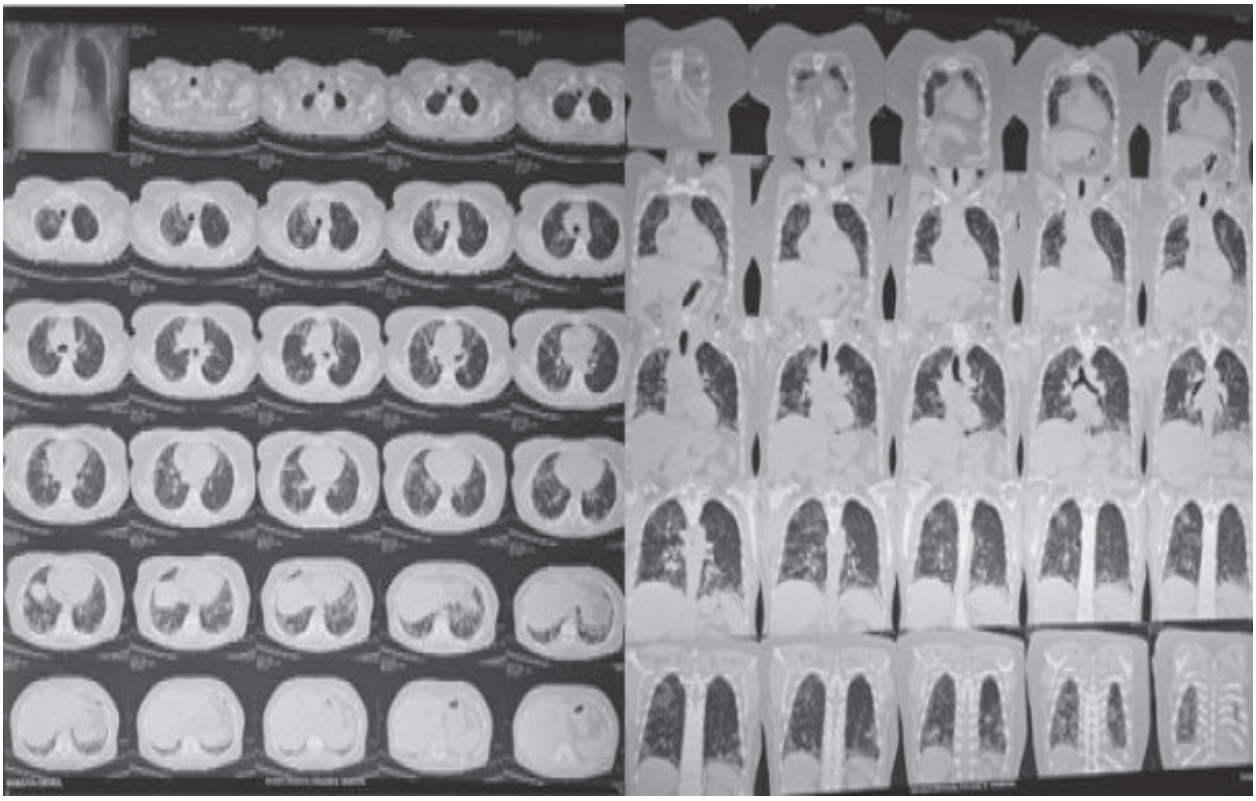

Fig.-5: *High resolution CT scan of lung showing diffuse parenchymal lung disease (DLPD).*

Patient was properly counselled about natural course and prognosis of the disease and advised to avoid cold exposure, vibrating tools, use of thermal insulating gloves/ socks, domestic pets and cotton exposure; gave emphasis on maintenance of high core temperature along with influenza and pneumococcal vaccination, for prophylaxis of GERD symptoms, also encouraged to take regular aerobic exercise. Specific treatments were advised in collaboration with specialists from Department of Medicine and Department of Dermatology of the same hospital. Oral baricitinib 4mg started instead of oral methotrexate. Anti-fibrotic agents (nintedanib), N-acetylcysteine, steroid, and immunosuppressive therapy were also considered for interstitial lung disease. Symptomatic treatment was given for dry mouth and eyes and psoriasis. She was discharged with proper follow-up advice. The patient received another follow-up after 2 weeks and her clinical conditions started to improve.

DISCUSSION

Diffuse Parenchymal Lung diseases (DPLD) are a diverse group of parenchymal pulmonary disorders characterized by varying degrees of inflammation and fibrosis. In RA, ILD is reported in 8–20% of cases and an interstitial lung abnormality (ILA), which may precede the development of true ILD, in 20%[2]; RA-ILDs are mainly observed in males, elderly and with a history of smoking[3,7]. However, in systemic sclerosis (SSc), the presence of ILD is even more common (e"80%); in addition, pulmonary hypertension (PH), also in the absence of diffuse lung disease, can be demonstrated by cardiac catheterization in 10% of cases. These conditions are the two main prognostic factors for SSc patients, in fact 40% of deaths in SSc are attributable to pulmonary pathology[4]. In 20% of patients with SSc, PFTs are still within normal range at the time of diagnosis but HRCT is already positive. 20% of SSc-ILDs turn out to have a progressive course[5].

In a review of 17 patients with SS, Suda et al. observed acute exacerbation in 6% of the patients[8]. A more benign clinical course with a 5year survival of 83% was observed in the series of Japanese patients. The optimal treatment for this kind of case is glucocorticoids in high doses, immunosuppressive drugs, and nintedanib in progressive fibrotic ILD[5].

CONCLUSION

In recent years, we have seen a growing interest in the pulmonary manifestations of ILD-CTDs, mainly due to the widening of the use of anti-fibrotic drugs initially introduced exclusively for IPF. We present this interesting case of DPLD due to RA-SSc overlap syndrome and Sjogren syndrome. It is important to keep it in our differential diagnosis for a patient presenting with worsening shortness of breath especially if the patient has an underlying history of joint pain and skin pigmentation. The patients usually have symptoms of dry cough and exertional dyspnea. General prognosis of this disease depends on the histopathologic subtype and the level of impairment of the lungs. Unfortunately, in our case, the prognosis is not that good. However, inter-department referral and relevant thorough investigations are essential to diagnose such meticulous diagnosis. We conclude that in a patient with systemic disorders, the possibility of pleomorphic respiratory involvement should be considered.

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