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Case Report

AN UNCOMMON CASE OF DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

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ABSTRACT

Systemic sclerosis (SSc) is a chronic connective tissue disorder of immune dysregulation characterised by widespread fibrosis of skin and internal organs, small vessel vasculopathy, and presence of intracellular autoantibodies. It is rare disorder with worldwide distribution sparing no ethnic group.

It has marked clinical heterogeneity in its presentation and severity. Systemic sclerosis is classified as limited cutaneous systemic sclerosis (lcSSc), diffuse cutaneous systemic sclerosis (dcSSc) and Systemic sclerosis sine scleroderma (SSS), a rare type without skin involvement. dcSSc has the worst prognosis because of internal organ involvement. There is no definitive therapy available to arrest or reverse the progression of fibrosis. Management is essentially symptomatic. Various immunosuppressive agents have been used in a bid to reduce the fibrosis and improve organ function.

We report a case of dcSSc who had signs of widespread dermal involvement along with distinct facial features and characteristic scleroderma biomarkers. Investigations have ruled out any definitive systemic involvement. The management has been as per the EULAR/ACR guidelines. The case is being reported for its rarity in general population and also to highlight the significance of mutually exclusive autoantibodies in classifying subsets of the disease.

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INTRODUCTION

Systemic sclerosis (SSc) is a chronic connective tissue disease of unknown aetiology characterized by widespread fibrosis of the skin and internal organs along with small vessel vasculopathy, dysregulation of immune system and production of specific autoantibodies.[1] The main feature is autoimmunity and inflammation causing vasculopathy in multiple vascular beds resulting in interstitial and perivascular fibrosis. The crux of the problem is small vascular bed inflammation with aberrant immune response (both innate and adaptive) leading to defective/uncontrolled reparative process of fibrosis and extracellular matrix deposition. [2, 3, 4] SSc has an estimated incidence of approximately 18 to 20 cases per million population per year. Its prevalence in Europe, USA, Australia and Argentina is 150-300 cases per million. The prevalence is lower in Scandinavia, Japan, UK, India, and Taiwan at about 120 cases per million.[5] The spectrum of SSc comprises of; (a) localised cutaneous systemic sclerosis (lcSSc) (b) diffuse cutaneous systemic sclerosis (dcSSc)(c) systemic sclerosis sine scleroderma and (d) overlap syndrome.[6,7] Each subset has its characteristic clinical features, natural history, and pattern of visceral involvement, and therefore the management approach needs to be individualised based on organ system involvement and investigation result.

We report a case of dcSSc who despite widespread cutaneous involvement for three years and positive serology, has no evidence of visceral involvement.

CASE REPORT

A37-year-old lady presented with gradually progressive hardening of the skin of face, hands, forearms, and legs for past three years. Her handgrip became weak owing to the swelling and tightness of the skin of fingers. She also noticed that her nose became pointed, upper lipthinned out and she could not open her mouth fully leading to difficulty in eating. Since last one year, she developed ulcers over tips of right index and left middle finger that healed leaving behind pitting scars. The skin changes also involved neck, anterior abdomen, and right knee joint. These included patches of skin thickening, scattered areas of hypo pigmentation with hair loss, sweating over dorsum of both hands, feet and around right knee joint. She denied any history of breathlessness, pain chest, or palpitations. There was no symptom suggestive of Raynaud's phenomenon.

Clinically she had dry ulceration over right middle fingertip with sausage shaped fingers and pulp atrophy of fingertips both hands. 'Salt and pepper' skin changes were present in patches over right ear pinna, dorsum of both hands, forearms, right knee joint, left medial malleolus and ankle joint, and feet. There were shiny indurated skin around neck, and anterior

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abdominal wall.(Figures 1,2,3) There was no clinical evidence of telangiectasia, or Raynaud's phenomenon.

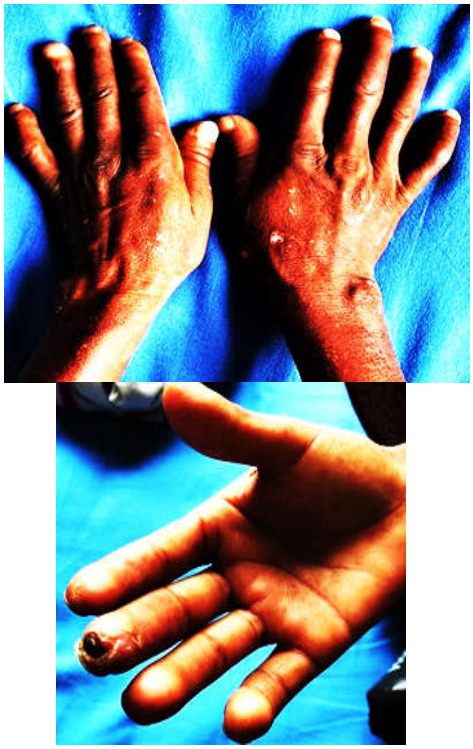

Figure 1 Puffed fingers, sclerodactyly, and digital ulcer

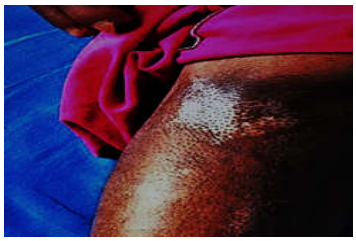

Figure 2 Salt and pepper skin

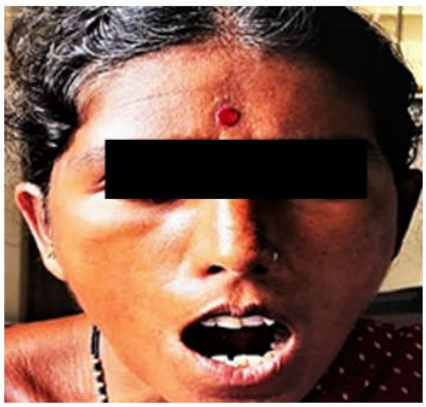

Figure 3 Puckered mouth with restricted opening

Investigations revealed normal blood counts, urinalysis, and serology. X-ray of hands revealed acral osteolytic lesions. (Figure 4) Autoantibody screening revealed significant positive ANA titre of 1:1000, and moderately positive anti-topoisomerase I (anti-Scl-70) IgG. Chest X-ray was normal. Spirometry showed evidence of early small airway obstruction.We could not carry out the HRCT chest and lung diffusing capacity (DLCO) due to financial and administrative reasons. Echocardiography excluded presence of pulmonary arterial hypertension. She was diagnosedas dcSSc according to 2013 ACR/EULAR criteria with a score of 18. [15]There is no evidence of other organ system involvement as yet.

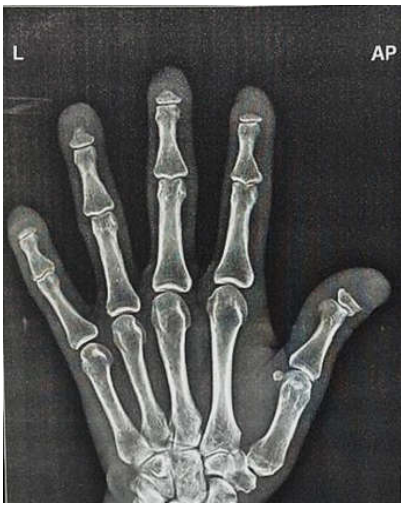

Figure 4 X-ray Hands showing Acral Osteolysis

Table 1 The ACR-EULAR Criteria for the classification of Systemic Sclerosis

Items	Sub-items	Weight / Score
Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints **(sufficient criterion)**		9
Skin thickening of the fingers^ (only count the highest score)	Puffy fingers Sclerodactyly of the fingers (distal to MCP but proximal to the PIPs)	2 4
Fingertip lesions^ (only count the highest score)	Digital Tip Ulcers Finger Tip Pitting Scars	2 3
Telangiectasia		2
Abnormal nailfold capillaries		2
Pulmonary arterial hypertension and/or Interstitial lung Disease* (*Maximum score is 2)	PAH (proven PAH by right heart catheterization) ILD (pulmonary fibrosis on HRCT or chest radiograph, or presence of `velcro' crackles on auscultation not due to another cause)	2
Raynaud's phenomenon		3
Scleroderma related antibodies** (any of anti-centromere, anti-topoisomerasel	Anti-centromere Anti-topoisomerasel	3
[anti-Sd 70], anti-RNA polymerase III)	Anti-RNA polymerase III	3(Max score 3)

Total Score:
Patients having a total score of 9 or more are being classified as having definite systemic sclerosis.
^Add the maximum weight (score) in each category to calculate the total score.

Management The patient has been managed with non-selective immunomodulation with methotrexate targeted to arrest skin fibrosis and also to prevent pulmonary fibrosis in lung which is likely to occur. Skin emollients, and calcium channel blocker (nifedipine) were used for the ischaemic digits; and proton pump inhibitor, pantoprazole, was used for dyspeptic symptoms.

DISCUSSION

Scleroderma or systemic sclerosis (SSc) is characterized by autoimmune dysregulation, leading to systemic inflammation,

vasculitis, and progressive fibrosis involving virtually every organ system. [8]'Thickened skin texture' as its first description is attributed to Hippocrates in 400 BCE. The term 'scleroderma' was first applied in 1836 by Fantonetti. It was used to describe the human skin and joint disease presenting with tightened dark leathered skin leading to impaired joint mobility. [9]Scleroderma or systemic sclerosis is a rare disease, more common in females (ratio 4.6:1) and most prevalent in individuals aged 30-50 years.[10] It is characterized by chronic variable course and varied clinical manifestations. Though patterns may vary, Skin is involved in all except in a specific subgroup termed *sclerodermasine scleroderma*(SSS).

SSc is sub classified in two major subtypes based on the extent and pattern of involvement: limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc). Each subtype has distinct natural history, clinical and laboratory features. Being a multisystem diseasevirtually every organ can be affected but mainly lungs, GIT, kidneys and heart are involved to a variable frequency, pace and severity of the clinical picture. [11]dcSSc typically presents over 1-3 years with widespread skin texture changes, puffy oedematous extremities, generalized pruritus and constitutional and inflammatory symptoms. Vasospastic symptoms are usually not prominent in the early stages. Significant visceral disease is common in dcSSc.

Our patient has definite dcSSc, based on pattern of skin involvement and presence of autoantibodies. She has widespread skin involvement, restricted mouth opening, but no evidence of GIT, respiratory, cardiac, or renal involvement. So far she has no respiratory symptoms and X-ray chest does not show any evidence of pulmonary fibrosis. However, spirometry was suggestive of small airway obstruction. Obstruction of small airways may indicate a possible prominent bronchiolar involvement within systemic sclerosis–related interstitial lung disease. [12, 13] Raynaud's phenomenon is seen in 99% of lcSSc and 98% of dcSSc. The presence of ATA have been reported in 15-42 % of SSc patients with a specificity ranging from 90-100%. ATA are strongly associated with dcSSc and poor prognosis.[14] Schneeberger D *et al* studied 5390 patients of SSc and found that only 0.2% (12) lacked both, the RP and anti-topoisomerase antibodies.[15] Though, our patient denied history suggestive of RP, she has the clinical sequela of vasculopathy in the form of ischaemic digital ulcers and pitting scars. She has predominantly marked skin involvement of proximal as well as distal parts of the body. Our patient does not have any evidence of cardiac, renal or lung involvement as yet. However, the evidence of small airway obstruction may be the indication of early pulmonary involvement. Treatment with methotrexate for diffuse skin lesions has beenbased on EULAR recommendations considering the absence of other organ system involvement. [16]

Conclusion: We have reported an interesting case of dcSSc, who despite widespread skin lesions, does not have any other organ system involvement so far, except evidence of small airway obstruction on spirometry. Inability to carry out HRCT chest, DLCO and nail-bed capillaroscopy is the major limitation of this case report. The aim of reporting is to present an uncommon disease with heterogeneous clinical manifestations, highlight the approach for stratification by investigations (autoantibodies/autoimmune serology), importance of sub-classification, andmanagement plan.

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