Sine Scleroderma

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Abstract

Systemic sclerosis (SSc) is a connective tissue disorder of unknown aetiology. A small subset (10%) of patients with limited systemic sclerosis have all other features of the disease without any skin involvement and is known as systemic sclerosis sine scleroderma (ssSSc). Severe Critical Limb Ischaemia is rare in sine scleroderma. The present case showed severe critical limb ischaemia with severe PAH, Esophageal dysmotility, Glomerulonephritis (a rare association) with hypertension. Although skin thickening is considered as a hallmark of systemic sclerosis, there should be a high index of clinical suspicion in patients presenting with possible manifestations of systemic sclerosis without sclerodermatous cutaneous involvement because early diagnosis and treatment can reduce the morbidity and mortality in it.

Introduction

Systemic sclerosis (SSc) is a connective tissue disorder of unknown aetiology. Skin thickening is considered as a hallmark of it, which distinguishes it from other connective tissue disorders. On the basis of pattern of skin involvement, it is broadly classified into diffuse and limited variety. Diffuse systemic sclerosis (dcSSc) involves skin of extremities, face and trunk while limited systemic sclerosis (lcSSc) involves only distal extremities and face with no involvement of trunk. A small subset (10%) of patient with limited systemic sclerosis has all other features of the disease without any skin involvement and is known as systemic sclerosis sine scleroderma (ssSSc).

Case Report

A 70 year old female presented to emergency department of R.N.T. medical college with complaints blackish discolouration of fingers of hand over last 4 months. It started from ring finger of left hand, gradually progressing to involve middle finger of right hand and then middle finger of left hand. Past history of bluish and reddish discoulouration of fingers on exposure to cold water, cold wind since 2 years, suggestive of Raynauds phenomena. No past history of any medical or surgical disease. No history of similar complaints amongst any family members. Patient was non-alcoholic and non-smoker.

On examination

General examination-pulse rate 84/min, regular, normal volume, no radio radial delay, no radio femoral delay, arterial wall normal, all peripheral pulses present and equally palpable. Blood pressure 200/100 in right arm, sitting posture; respiratory rate 20/min and she was afebrile. Her JVP was raised. Pallor was present. No edema, icterus, clubbing. Dry gangrene of right index finger and middle finger and left ring finger of present (Figure 1 A and B).

Cardiovascular examination revealed loud P2 with no murmur. Rest systemic examination revealed no abnormality.

Blood parameters revealed HB=9.0g/dl, ESR=35, TC=5,000/mm³, platelet=2.26 lacs/mm³, SE sodium=135, SE potassium =6.0, SE urea=48, SE creatinine=0.38, LFT=WNL, CRP +(11.57, upper limit being 5).

Urine examination: positive for protein (1+), RBCs (20-22/HPF), pus cells (10-20/HPF), calcium oxalate crystals ++, 24 hours urine albumin = 0.81gm/day (significantly greater). X-ray showed distal osteolysis (Figure 2).

USG abdomen : mild cholelithiasis, rest findings were normal.

Her echo revealed: mild concentric LVH, normal LV systolic function (EF=60%), type 1 diastolic dysfunction, severe PAH, no clot/veg/embolus.

Colour doppler study of bilateral upper and lower limbs was normal.

CECT chest : fibrotic changes in bilateral upper lobes.

All these investigation suggested
vasculitis, we got her ANA profile done with following results- positive for anticentromere antibodies by EIA (200 RU/ml, normal range from laboratory being 0-20 RU/ml). Other autoimmune conditions were ruled for overlap syndrome (RF/DS-DNA/APLA/SCL-70/RNP/SSA/SSB/ANCA).

We also got a skin biopsy done which had normal hpe findings.

**Upper GI endoscopy revealed pangastropathy, barium swallow study-lower esophageal dysmotility** (Figure 3).

Finally she was diagnosed to have sine scleroderma. She was started on losartan 50 mg OD, nifedepin 20 mg BD. After 2 weeks of follow up she still complained of pain in her fingers. We added sildenafil 50 mg BD. After consultation with rheumatologist and dermatologist she was given cyclophosphamide pulse therapy (500 mg once in every 4 weeks). Patient’s symptoms have improved considerably with no further progression of ischaemia. She was also given a CTVS opinion for amputation of gangrenous digits for which she refused and was willing to wait for autoamputation.

**Discussions**

Systemic sclerosis is a chronic connective tissue disease that typically affects skin and internal organs by widespread micro vascular damage and excessive deposition of collagen. Annual incidence of it in USA is about 20 cases per million adults. Women are around 4 times more likely than men to develop it. To facilitate its accurate diagnosis, American College of Rheumatology has given preliminary classification criteria in 1980, according to which there is one major and three minor criterias. Major criteria include skin thickening proximal to MCP joints whereas minor criterias include sclerodactyly, digital pitting scars and bibasilar pulmonary fibrosis. Utility of these criteria is to distinguish it from other connective tissue disorders. It’s further classified into limited and diffused variety based on the presence and extent of skin involvement.

Limited systemic sclerosis involves skin distal to elbow and knees only, whereas diffuse variety involves proximal extremities and/or trunk in addition to distal thickening. Face can be involved in both forms. In diffuse variety systemic complications like interstitial lung disease and renal crisis are more common whereas in limited variety pulmonary arterial hypertension is more common. Most of these patients have positive antinuclear antibody by indirect immunofluorescence (85-90%).

Amongst scleroderma specific antibodies, anti -Topoisomerase (Scl-70) and antiRNA polymerase III is more specific for diffuse variety whereas anti-Centromere is more specific for limited variety. Systemic sclerosis sine scleroderma is a variant of limited systemic sclerosis which has all other features of this disease except the skin involvement. The first report of it was published by Abrahm et al. in 1954 and the term was coined by Rodnan and Fennel in 1962. This disease is not a separate entity but a part of a single disease spectrum. Compared to limited cutaneous systemic sclerosis it has no significant difference in internal organ involvement, antibody type or prognosis but there is a greater frequency of pulmonary artery hypertension in it. According to Poormoghim et al. its diagnosis should be considered if he or she has all of following: 1) Raynaud’s phenomenon, 2) Positive ANA, 3) Any one of following- distal esophageal hypomotility, small bowel hypomotility, pulmonary interstitial fibrosis, pulmonary artery hypertension, cardiac involvement typical of scleroderma or scleroderma renal crisis and 4) no other defined connective tissue or other diseases as a cause of 1), 2), or 3). This diagnosis would be more convincing if ANA specificity was due to systemic sclerosis associated autoantibody.
Most frequently associated serum autoantibody associated with it is anticentromere antibody. There are scarce data in the literature for systemic sclerosis sine scleroderma.


Severe Critical Limb Ischaemia is rare in sine scleroderma. The present case showed severe critical limb ischaemia with severe PAH, Esophageal dysmotility, Glomerulonephritis (a rare association) with hypertension.

In conclusion, although skin thickening is considered as a hallmark of systemic sclerosis, there should be a high index of clinical suspicion in patients presenting with possible manifestations of systemic sclerosis without sclerodermatous cutaneous involvement because early diagnosis and treatment can reduce the morbidity and mortality in it.

References