Systemic Sclerosis Sine Scleroderma

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Abstract
Systemic sclerosis sine scleroderma is a rare form of limited systemic sclerosis. These patients are without skin involvement, but do not differ in its clinical or laboratory features and prognosis from classical systemic sclerosis. In the absence of cutaneous signs/symptoms, its diagnosis is delayed leading to significant morbidity and mortality. We report a case of sixty year old female who presented to us with dyspnoea on exertion and Raynaud’s phenomenon. She was investigated and was found to have this disorder with pulmonary artery hypertension.

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 60 year old female came to our emergency department with complaints of dyspnoea on exertion since last 6 months which was progressed from NYHA I to III. She also gave history of bluish discolouration of fingers in winters and in exposure to cold water since last four years. She denied having any other complaints. There was no other significant past medical history. Patient was a non smoker and non alcoholic.

On examination, her pulse rate was 100/min, BP was 100/60 mm Hg in right arm supine position, respiratory rate was 24/min and she was afebrile. Her JVP was raised and pedal oedema was present. Cardiac auscultation revealed loud P2 and pan systolic murmur over tricuspid area with no radiation. Pitted scars were present on fingers of hand but there was no skin tightening (Figure 1). Other system examination was normal.

Her ECG was showing right axis deviation with right ventricular hypertrophy (Figure 2). 2D Echo showed dilated RA and RV, severe tricuspid regurgitation with pulmonary arterial hypertension (PASP: 101 mm Hg).
Hg) with normal systolic functions (Figure 3). Pulmonary function test showed moderate restriction. Her X-ray hand showed acro-osteolysis (Figure 4). Barium swallow showed oesophageal dysmotility (Figure 5). HRCT chest showed dilated central pulmonary artery with no evidence of interstitial lung disease. Her ANA by IIF was positive (1:2560). Systemic sclerosis specific antibodies were sent and she came out to be positive for anti-centromere antibody.

So, it was a case of systemic sclerosis sine scleroderma. She was started on diuretics (torsemide 10 mg bd), endothelin receptor antagonist (bosentan 62.5 mg bd) and phosphodiesterase inhibitors (sildenafil 20 mg tds) and is doing well on drugs.

Discussion

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 anti RNA 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 oesophageal 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 disease 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. The German registry for systemic sclerosis frequency, subset and pattern of organ involvement reported 22 patients of it. Poormoghim et al. described 48 North American patients from Pittsburg scleroderma databank. Recently in 2012 Spanish registry reported case series of 69 patients. So till 2012 total of 139 cases of it are in the literature excluding isolated case reports. Toya et al. analysed 108 published cases of it and found peripheral vascular system involvement in all, gastrointestinal manifestations in 82% and pulmonary involvement in 66% of cases. In a study from Brazil in 2013 out of 947 patients with systemic sclerosis, 79 (8.3%) were classified as having systemic sclerosis sine scleroderma. Oesophageal involvement was most frequent (83.1%), followed by interstitial lung disease (56.9%) and pulmonary hypertension (22.8%).

To the best of our knowledge there are no case series published from India for ssSSc.

Sharma et al. reported calcinosis cutis as a presenting feature of it.10 Pauling et al. reported pulmonary artery hypertension as a presenting feature of it and recommended pulmonary vascular disease screening in all these patients as PAH is major cause of mortality in this condition. Present case report is also showing pulmonary artery hypertension as a presenting feature of it.

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