Systemic sclerosis presenting as CREST syndrome: A case report and review

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Abstract

Systemic sclerosis (SSc) is a chronic multisystem disorder of unknown etiology, characterized by diffuse fibrosis; degenerative changes; and vascular abnormalities in the skin (scleroderma), articular structures, and internal organs especially the esophagus, GI tract, lung, heart, and kidney. We report the case of a 31 years old female patient who came to the ED with complications of SSc after has been diagnosed with a limited cutaneous scleroderma. This case illustrates the varied multisystem presentation of SSc.

Introduction

Systemic sclerosis (systemic scleroderma) is a chronic connective tissue disease of unknown etiology that causes widespread microvascular damage and excessive deposition of collagen in the skin and internal organs. 1 The degree and rate of skin and internal organ involvement vary among patients. SSc has a worldwide distribution and affects all races. The prevalence of scleroderma is estimated to be between 4 and 253 cases per million persons. Factors such as age, sex, genetic background, and environmental exposure may influence susceptibility. The onset of disease is unusual in childhood and young men. Women are affected 3 times as often as men, and the incidence increases with age, peaking in the third to fifth decade.2 We report the case of a patient who came to the ED with findings suggestive of SSc complications who has been diagnosed with a limited cutaneous scleroderma.

Case report

A 31 years old female patient from senafe with remote history of systemic sclerosis and recurrent hospital admissions presented to the ED of Orotta hospital with shortness of breath and altered mental status. She had generalized body weakness, and dry cough associated with chest pain. She also complained heartburn and dysphagia. The patient denied fever, chills, nausea, vomiting or any loss of blood. She reported irregular menstruation for the past five years and cessation of her menses for the last five months. Two years back she presented to the Orotta hospital dermatology clinic with history of skin dryness, cold sensitivity of fingers and tightness of the face. She had history of pulmonary problems and given anti TB treatment for a duration of 8 months. She denied history of recurrent sore throat and any chronic illnesses like hypertension or diabetes mellitus. There is no history of similar illness in her family. Before one year she developed pericardial effusion and was admitted to the hospital. Echocardiography study revealed enlargement of right atrium and ventricle, and tricuspid regurgitation without valvular fibrosis. Along with full investigations and management diagnose was established as limited cutaneous scleroderma with RHF secondary to pulmonary arterial hypertension. She was discharged home with lasix 40 mg PO daily, digoxin 0.125 mg PO daily and prendisolone 5 mg in tapering dose. She had been following at the dermatology, cardiac and infectious clinics of the hospital with the periodically given medications. With time her condition worsened for which she had repeated admissions due to cardiopulmonary complications of systemic sclerosis (SS).

Physical examination revealed a chronically sick looking severely emaciated young woman afebrile with respiratory distress and altered mental status. The pulse was weak with unobtainable blood pressure and the Spo2 was 91%. She had decreased breath sounds with basal lung crepitations, murmur grade III/VI at the apex, raised JVP, hepatomegaly with ascites and extremities were edematous and cold with prolonged capillary filling. On cutaneous examination there was skin thickening, hyperpigmented patches with mask like face, erythematous macular lesions on the palmar and plantar areas along with hardening and cyanosis on the tip of the fingers as shown in the figures below.

Figure 1. Telangiectasias scattered on the palm with Raynoulds phenomenon.

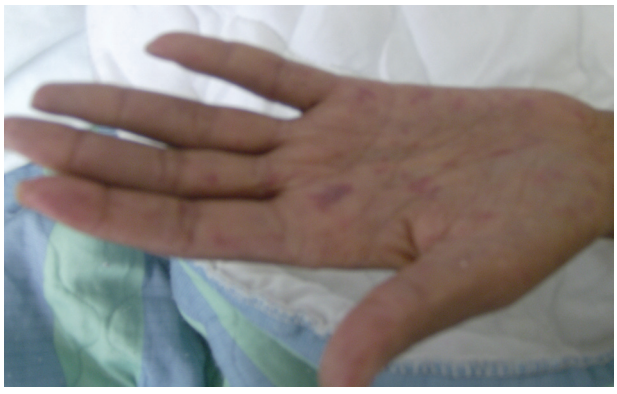
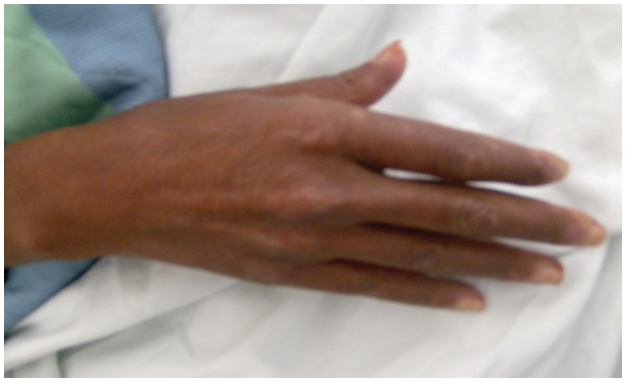


Figure 2. The affected skin in the hand appears shiny, taut, and thickened, tightly adhering to the underlying cutis



Previous investigations revealed; the chest x-ray showed interstitial fibrosis, accentuation of broncho-vascular marking with nodular spots and LFT, RFT and CBC were with in normal limit (WNL). Immunologic tests showed; ANA positive with titer 1:5120, ENA (negative), C3 141mg/dl (83-185), C4 27.1mg/dl (12-54), Anti-Scleroderma 17.6 units (0-24.9), Scleroderma Ab 0.2 units (0-0.9).

Her condition was grave as complication of her underlying illness and was admitted to the ICU with an impression of cardiogenic shock. On admission LFT, RFT values were deranged as shown in table1 below.

Table 1: Hepatic and renal testes of the patient during her last admission

Hepatic Function Panel	Patients Results	Reference Values
AST (SGOT)	210	0- 31u/L
ALT (SGPT)	219	0- 31u/L
Alkaline phosphate	95	39-117u/L
Total bilirubin	0.7	0.0-1.0mg/dL
Direct bilirubin	0.0	0.0-0.3mg/dL
Indirect bilirubin	0.7	
Albumin	2.3	3.4-4.8g/dL
Renal Function Panel		
BUN-serum	57	6-20mg/dl
Creatinine serum	1.8	0.4-1.1mg/dl
Sodium (Na) - serum	134	135-146mmol/L
Potassium (K) - serum	5.1	3.6-5.0mmol/L
Chloride (Cl) – serum	96	101-111mmol/L
Carbon dioxide (Co2)	24	21-31mmol/L
Anion gap	14	2-21miclU/ml

She was resuscitated and managed with oxygen 3L/min, restricted fluid, duptamine 250mg in 50cc of N/S in ../hr, digoxine 0.25mg once daily, lasix 20mg IV Bid and hydrocortisone 100mg IV Qid, Her condition improved with stable vital signs and she was transferred to medical ward for continuation of treatment.

Discussion

Systemic sclerosis varies in severity and progression, ranging from generalized cutaneous thickening (systemic sclerosis with diffuse scleroderma) to a form distinguished by restricted skin involvement (often just fingers and face) and slow progression, often several decades, before full manifestation of characteristic internal involvement. This latter form is termed limited cutaneous scleroderma or CREST syndrome (calcinosis cutis, Raynaud's phenomenon, esophageal dysfunction, sclerodactyly, and telangiectasia). 3

The most common initial complaints in systemic sclerosis are Raynaud's phenomenon manifested by episodic pallor followed by cyanosis and/or rubor of the distal portions of the digits after exposure to cold.4 Raynaud's phenomenon often predates other manifestations in the limited subtype and is often found concurrently in diffuse systemic sclerosis. 4,5 GI disturbances such as heartburn, dysphagia or respiratory complaints eg. dyspnea are occasionally the first manifestations of the disease. 3

The skin is almost always involved in systemic sclerosis. Induration is symmetric and may be confined to the fingers (sclerodactyly) and distal portions of the upper extremities, or it may affect most or all of the body. As the disease progresses, the skin becomes taut, shiny, and hyperpigmented; the face becomes masklike; and telangiectases appear on the finger, chest, face, lips, and tongue. Subcutaneous calcifications may develop (calcinosis circumscripta), usually on the fingertips (pulps) and over bony eminences. 3,4

Gastrointestinal manifestations are common in systemic sclerosis, and the most common is esophageal dysfunction. Dysphagia, manifested by various abnormal swallowing sensation, is initially caused by impaired esophageal motility but later can result from gastroesophageal reflux disease and secondary stricture formation. Barrett's esophagus occurs in 1/3 of patients with scleroderma; these patients have an increased risk of complications (eg, stricture, adenocarcinoma). 3,6

Pulmonary manifestations of systemic sclerosis include interstitial lung disease, pulmonary hypertension, pleuritis and pleural effusion, and aspiration pneumonia.7 Lung involvement generally progresses indolently, with substantial individual variability. Dyspnea and nonproductive cough in a patient with systemic sclerosis should raise the possibility of lung disease, and a work-up for interstitial lung disease should be performed. However, chronic cough may be the only sign of pulmonary disease in systemic sclerosis.3,4 Pulmonary hypertension is more frequently seen with limited systemic sclerosis than with diffuse disease and often occurs late in the disease course. It may result from long –standing

interstitial and peribronchial fibrosis or intimal hyperplasia of small pulmonary arteries. A common presenting symptom of pulmonary hypertension is dyspnea on exertion. Physical examination may reveal accentuation of the S2 and signs of right-sided heart failure (elevated jugular venous pressure, pitting edema, right ventricular heave). An echocardiogram or right-sided cardiac catheterization can confirm the diagnosis. 4,6

Patients with systemic sclerosis develop hypertension and atherosclerosis at similar or increased rates compared to those in the general population.8 The major cardiac complications are pericarditis with effusion, constrictive pericardium, arrhythmias, and congestive heart failure. Heart failure may develop because of pulmonary hypertension and secondary cor pulmonale or because diffuse fibrous replacement of cardiac muscles. Heart failure tend to be chronic and difficult to treat. 3

Scleroderma renal crisis is characterized by an abrupt rise in blood pressure over days to weeks and rapidly progressive renal failure if untreated, usually within the first 5 years of the disease. 9 It occurs virtually only in early diffuse systemic sclerosis. The spectrum of presentation ranges from normal or mildly elevated blood pressure to malignant hypertension, causing elevated plasma renin levels, elevated serum creatinine (seen in 50% of patients), proteinuria, and microangiopathic hemolytic anemia (seen in 50% of patients). 4

Diagnosis

The diagnosis of systemic sclerosis is based on the identification of features that distinguish it from other disease, and thus a detailed history and careful physical examination are required. The American College of Rheumatology has proposed criteria to assist in identifying those affected with the condition.10 Major criteria include scleroderma proximal to the metacarpophalangeal joints. Minor criteria are sclerodactyly, digital pitting scars, and bibasilar pulmonary fibrosis. To fulfill a diagnosis of systemic sclerosis, either 1 major or 2 minor criteria are needed. Clinical evidence of active disease in systemic sclerosis must be investigated. Pulmonary complaints should prompt an evaluation with chest radiography, pulmonary function testing, or HRCT of the chest. Cardiac symptoms may prompt an electrocardiogram, echocardiogram, a stress test, or cardiac catheterization. Serial echocardiograms are routinely done in systemic sclerosis to screen for pulmonary hypertension, and if positive, right heart catheterization is performed. Symptoms of gastrointestinal involvement may require evaluation with endoscopy. Capillary microscopy may be indicated for complaints of Raynaud's phenomenon.4,6

Laboratory Findings

Antinuclear antibodies have been detected in up to 90% of cases of systemic sclerosis.10 Anti-centromere antibodies are more likely to be associated with limited systemic sclerosis, whereas autoantibodies to topoisomerase-I (anti-Scl-70) are more likely to be associated with diffuse systemic sclerosis. However, these tests have low sensitivity, with anti-centromere antibodies having a sensitivity of approximately 30% and anti-Scl-70 having a sensitivity of approximately 40%.11 Hematologic studies are usually normal12 although autoimmune hemolytic anemia and neutropenia have been reported.13 More commonly, anemia of chronic disease or iron deficiency anemia is seen; the latter is associated with chronic bleeding in the gut from esophagitis or watermelon stomach or other telangiectasia.

Therapy in systemic sclerosis is directed at the organ/system involved. Localized skin lesions have been reported to respond to ultraviolet light therapy with improvement in skin tautness.14 Other treatment modalities for skin lesions include high-dose topical corticosteroids, topical antibiotic ointments, and oral analgesics. A recent study has shown that patients with scleroderma treated with 1 year of oral cyclophosphamide had modest improvement in lung function, functional status, and health-related quality of life as well as reduced dyspnea compared with patients who received placebo.15

Our case illustrates typical presentation of CREST syndrome as clearly described above. As the initial presentations of the disease are characterized with Raynaud's phenomenon and pulmonary manifestations, the patient clearly describes these features. In areas with epidemic of pulmonary tuberculosis, the pulmonary manifestation of SSs mimics with PTB and are often treated with anti TB as in our case. As the disease progresses the involvement of internal organs become evident, then patients develop systemic complications. This patient developed cardiopulmonary complications. She had pericardiac effusion associated with pulmonary hypertension leading to right heart failure. Still there are no manifestations suggestive of renal crises in this patient except serum Bun and cretinine elevation in her last admission. On laboratory findings the ANA is positive with anti-Scl-70 negative supporting the diagnoses of limited systemic sclerosis.

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