Diffuse Cutaneous Systemic Sclerosis: A Case Report

Janice Natasha C. Ng, M.D.*; Sime Raymond B. Fernandez, M.D.**; Victoria P. Guillano, M.D. ***; Bryan Edgar K. Guevara, M.D. ***

Abstract

Background: Systemic sclerosis (SSc) is a rare, connective tissue disease with multisystem involvement. This is due to immunological processes, vascular endothelial cell injury and extensive activation of fibrolast that commonly affects the skin and other internal organs such as the esophagus, lungs, heart, and kidneys. SSc has one of the highest mortality among the autoimmune rheumatic diseases, hence the emphasis on the early recognition and management to prevent significant progression of the disease.

Case: A 22-year-old female presented with a one-year history of multiple hard and hypopigmented patches on the face, neck, trunk and upper extremities. Further examination revealed mask-like facies, microstomia, frenulum sclerosis, Raynaud's phenomenon, pitted scars on the digital pulp of hands and sclerodactyly. Baseline blood chemistry, chest radiograph and electrocardiography were all negative for systemic involvement. Autoantibodies were positive for dsDNA, SS-A/Ro and Scl-70. Skin biopsy revealed sclerosing dermatitis, which was consistent with SSc.

Outcome: The patient was initially started with oral prednisone 0.5 mg/kg/day and was increased to 0.75 mg/kg/day for eight weeks. Prednisone was slowly tapered to 5.0 mg/day and methotrexate 15.0 mg/week was included in the management for eight weeks which resulted in decreased joint pains, halted the progression of skin induration, decreased in pruritus and palmar edema.

Conclusion: The characteristic dermatological findings of SSc are not only important signs to dermatologists, but these serves as diagnostic clues for clinicians from other disciplines as well. In our case, the presence of the autoantibody Scl-70 indicated the potential risk of pulmonary fibrosis and pulmonary arterial hypertension that accounts with high mortality. Hence, physicians should be aware of the possible risk of organ damage, even when asymptomatic because there is a high risk of disease progression. The importance of early recognition and a multidisciplinary approach lead to the good outcome in this case.

Keywords: scleroderma, systemic sclerosis, diffuse cutaneous systemic sclerosis, prednisone, methotrexate

Introduction

Systemic Sclerosis (SSc) is a rare, multisystem, connective tissue disorder based on autoimmunity, inflammation, widespread vasculopathy and progressive interstitial and perivascular fibrosis.[1] It has a worldwide distribution, more common in women than men with a female-to-male ratio between 3:1 up to 14:1.[2] The disease onset ranges between 30 and 50 years old.[3] The incidence is between 0.6-20 per million/year.[3] The Philippine Dermatologic Society (PDS) central data from 2011-2016, included only 16 diagnosed cases of SSc, 10 of which were diffuse cutaneous SSc and six cases were limited cutaneous SSc.[4]

Case

This is a case of a 22-year-old, female who presented with one-year history of multiple, pruritic, hypopigmented macules with associated hardening skin initially at the nape area; subsequently involving the face, trunk and upper extremities. Consultation was done, and was given tar ointment which didn't improve the lesions. Self medication with traditional oil and herbal capsules were done, which afforded no relief as well.

Four months prior to consultation, there was persistence of lesions now associated with bluish discoloration of fingers upon exposure to cold temperature. Patient continually applied the traditional herbal oil and continued to take herbal capsules three times a day, still with no relief of symptoms. Persistence of symptoms prompted consultation at our institution.

*Resident, Department of Dermatology, Southern Philippines Medical Center, Davao City, Philippines
**Resident, Department of Internal Medicine, Southern Philippines Medical Center, Davao City, Philippines
***Consultant, Department of Dermatology, Southern Philippines Medical Center, Davao City, Philippines

Corresponding author: Janice Natasha C. Ng, M.D., Southern Philippines Medical Center, Davao City, Philippines
Email: janiceng3@yahoo.com

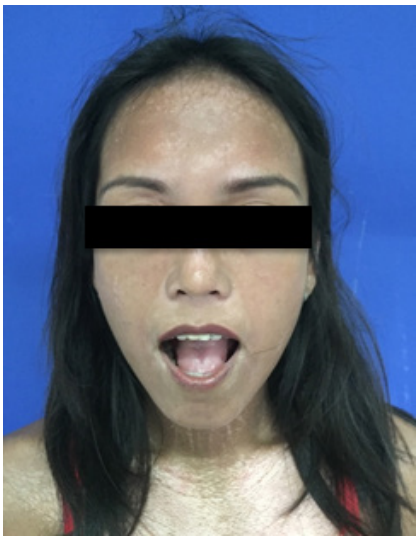

Figure 1. Mask like facies and microstomia

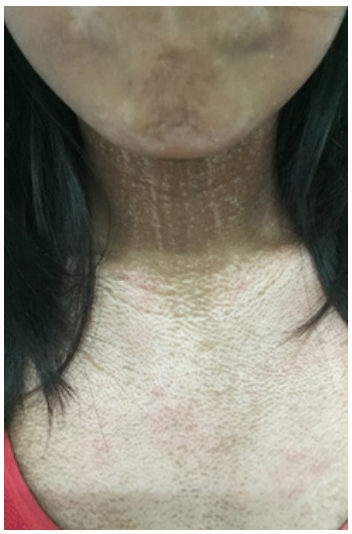

Figure 2. Salt and pepper sign

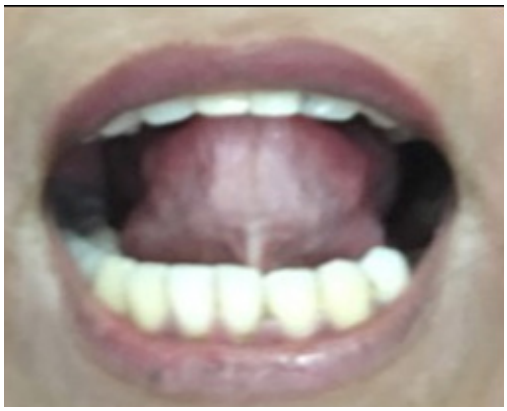

Figure 3. Frenulum sclerosis

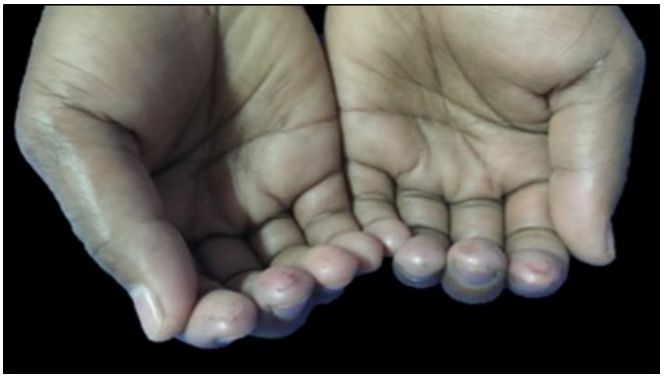

Figure 4. Pitted scars located on the 2nd, 3rd, 4th digital pulp of both hands with bilateral sclerodactyly on second digits

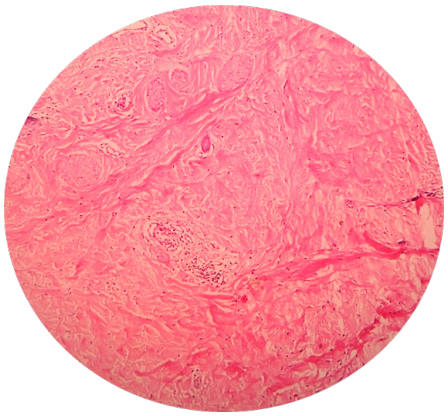

Figure 5. Skin punch biopsy- Dermal thickening and hyalinization of collagen bundles (H&E stain, 100x)

General physical examination was unremarkable with normal vital signs. Dermatologic examination showed mask like facies, microstomia (Figure 1), hypopigmented patches with sparing of the perifollicular skin "salt and pepper sign" (Figure 2) with hard overlying skin on the face, neck, trunk and upper extremities. Pitted scarring was noted on the second, third and fourth digital pulps of both hands (Figure 4) and bilateral sclerodactyly on the second digits of both hands. Oral mucosa showed frenulum sclerosis with no erosions or ulcerations (Figure 3). Scalp hair and nail findings were unremarkable.

Significant laboratory findings revealed elevated ESR at 21 mm/hr (normal range: 0 – 20 mm/hr) and positive antibodies (positive value, ratio > 1.2), such as anti-double stranded DNA (anti-dsDNA) with ratio of 1.36, anti- Sjögren's-syndrome-related antigen A/Ro (anti-SS-A/Ro) with ratio of 2.38 and anti-topoisomerase 1 (anti Scl-70) with ratio of 3.04. A 4.0-mm skin punch biopsy taken from a hypopigmented indurated patch located on the chest hyalinized dermis with thickening of collagen bundles and associated with perivascular inflammatory infiltrates composed predominantly of eosinophils. The histopathologic diagnosis was consistent with sclerosing dermatitis (Figure 5).

Patient was co-managed with internal medicine-rheumatology service. Initially, prednisone was started at 20.0 mg/day (0.5 mg/kg/day) for two weeks, however there was still persistence of bilateral wrist joint pain and pruritus. It was then increased to 35.0 mg/day (0.75 mg/kg/day) for an additional six weeks, which showed significant improvement of the joint and skin manifestations. Prednisone was slowly tapered to 5.0 mg/day and was started on methotrexate 2.5 mg/tablet, six tablets (15.0 mg/week) divided over a 48-hour period. In addition, folic acid 5.0 mg/tablet daily was given. She was also referred to rehabilitation medicine unit for the management of musculoskeletal impairments.

After eight weeks of methotrexate 15.0 mg/week with prednisone 5.0 mg/day, patient had no progression of skin

induration, joint pain, pruritus, and palmar edema. Patient was advised to follow-up every month to monitor disease progression.

Discussion

The American College of Rheumatology (ACR) published a preliminary classification criteria to classify patients with SSc which showed a 97% sensitivity and 98% specificity.[2] The diagnosis is ascertained, if either one major criteria (scleroderma proximal to the metacarpophalangeal or metatarsophalangeal joints) or at least two or more minor criteria (sclerodactyly, digital ulcerations and/or pitting digital scars and bibasilar pulmonary fibrosis) are present.[3] In our case, one major criteria and two minor criteria were fulfilled (sclerodactyly and digital ulcerations). She did not present with dyspnea and had unremarkable chest findings.

The natural course of the SSc may vary, a few patients may have spontaneous remission, however majority would undergo progression of skin and internal organ involvement, resulting in considerable morbidity and ultimately in death.[5] The diffuse cutaneous form carries the highest risk of fatality of the connective tissue diseases, with 20–34% survival at five years and 55% survival at 10 years.[1,6] The survival rate is negatively impacted by older age of onset, male sex, scleroderma renal crisis, pulmonary fibrosis, pulmonary arterial hypertension, cancer, and positive for anti-topoisomerase and anti-U1 antibodies.[7]

Our patient presented with a diffuse cutaneous subtype of SSc, but has a better prognosis, because of her age, sex and there was no internal organ involvement. Antibodies tested was positive for Scl-70, which is associated with pulmonary fibrosis (PF) and pulmonary arterial hypertension (PAH). The percentage of SSc patients dying from PF and PAH has increased (from 6% to 33%), which made it the most common cause of death.[8] It is important that we were able to diagnosed our patient at an early stage while still being asymptomatic. Further, we can regularly monitor the progression of the disease with regular follow-ups and tests such as chest radiography, lung function tests and electrocardiography.

Dermatologic findings play an important role on early recognition of SSc, as cutaneous involvement is a cardinal feature of the disease. The skin usually presents as a tight, indurated, and firmly bound to the subcutaneous tissue.[9] The hair follicles and sweat and sebaceous glands atrophy and the skin over the hands and face is most frequently involved.[9] Raynaud's phenomenon is the second most common manifestation of SSc and is present in more than 85% of patients.[9,10] It is characterized by recurrent spasms of small digital arterioles/arteries at fingers and toes, usually triggered by cold and emotional stress.[3] All these dermatologic findings were present in the case, which attributed to the early diagnosis of our case.

Pulmonary involvement presents with symptoms of tachypnea and exertional dyspnea that can be secondary to either pulmonary fibrosis or pulmonary hypertension.[9]

Gastrointestinal tract is the most frequent internal organ system involved in scleroderma at 90%, and in 10% of cases it is the presenting feature of the disease.[9,10] The esophageal symptoms results from reduced lower esophageal sphincter pressure and dysmotility of the lower two thirds of the esophagus leading to reflux, heartburn, and dysphagia to solid foods.[9] Fortunately for our patient, we were able to diagnose the case at an early stage wherein she didn't present with symptoms of internal organ involvement.

Management of diffuse SSc is challenging and the current treatments are of limited efficacy.[11] Common treatments for early diffuse systemic sclerosis includes systemic steroids, immunosuppressive medications such as methotrexate, mycophenolate, cyclophosphamide, azathioprine, and also intravenous immunoglobulin.[2,11] Since systemic sclerosis is a multisystem disease, a number of subspecialties are involved in the management.[3]

Our patient was successfully controlled with prednisone and methotrexate for eight weeks. Our plan is to continue methotrexate 15.0 mg/week for 12 more months and close monitoring through regular follow-ups and other laboratory work ups to rule out possible systemic involvement.

Conclusion

We presented a case of diffuse systemic sclerosis that was diagnosed early that prevented the progression to more severe presentation, such as the pulmonary fibrosis and pulmonary arterial hypertension. The cutaneous manifestations in systemic sclerosis are not only important among dermatologists, but also serves as diagnostic clues for internists to prevent complications of the disease and to achieve effective management. A multidisciplinary approach is important to give the best management to the patient. We recommend that frequent follow ups be done, since diffuse cutaneous systemic sclerosis has a greater risk for clinically significant major organ dysfunction.

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