Asian Journal of Health Research
Journal Homepage: https://a-jhr.com
Published by Ikatan Dokter Indonesia Wilayah Jawa Timur

OPEN ACCESS

Case Report

Cutaneous Manifestations of Scleroderma: A Case Report

Tessa Thendria*, Amira Suryani Rahmatika, Evy Ervianti, Sawitri, Dwi Murtiastutik, Trisiswati Indranarum, Hasnikmah Mappamasing, Septiana Widyantari
Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga/ Dr Soetomo General Academic Hospital, Surabaya, Indonesia

ARTICLE HISTORY
Received: 5 April 2023
Revised: 1 June 2023
Accepted: 2 July 2023

CORRESPONDING AUTHOR
Tessa Thendria
tessa_then@yahoo.com
Department of Dermatology and Venereology, Faculty of Medicine, Universitas Airlangga/ Dr Soetomo General Academic Hospital, Surabaya, Indonesia

KEYWORD
Scleroderma; Systemic Sclerosis; Autoimmune Disease

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ABSTRACT

Introduction: Scleroderma, or systemic sclerosis, is a rare multisystemic autoimmune disease characterized by vasculopathy, inflammation, and progressive fibrosis of the skin and organs. Cutaneous manifestations and Raynaud's phenomenon usually become the initial presentation of scleroderma.

Case Presentation: A 47-year-old woman presented with hardening and thickening of the skin on her arms and legs for 3 years, which spread to her face and trunk. The lesions initially appeared as multiple red patches, which progressed into white, thick, and hard patches. The patient had a history of recurrent Raynaud's phenomenon, a dry cough, and shortness of breath. In the physical examination, the patient had skin hardening with a salt and pepper appearance on her upper back and chest. The thoracic CT scan revealed interstitial lung disease. The patient was diagnosed with definitive scleroderma based on The European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) criteria with a score of 18. She had been treated with methotrexate, methylprednisolone, topical corticosteroids, and moisturizer. The skin lesion improved with the reduction of Rodnan's skin score from 31 to 19 after 4 months of treatment.

Conclusion: Cutaneous manifestations can be the earliest alarm and first manifestation of scleroderma. As the pathology is deep beyond the skin, a complete examination should be performed to find any organ involvement. Dermatologists play a significant role in the early identification of skin disorders and multidisciplinary referrals. Early diagnosis and prompt treatment could reduce morbidity and mortality in patients with scleroderma.

Cite this as: Thendria T, Rahmatika AS, Ervianti E, Sawitri, Murtiastutik D, Indranarum T, Mappamasing H, Widyantari S (2023) Cutaneous Manifestations of Scleroderma: A Case Report. *Asian J Heal Res*. 2 (2): 66–71. doi: https://doi.org/10.55561/ajhr.v2i2.103

INTRODUCTION

Scleroderma, or systemic sclerosis (SSc), is an autoimmune disorder characterized by progressive fibrosis, vascular changes, and systemic inflammation. The degree of cutaneous and organ involvement, severity, and outcome vary significantly among individuals [1]. The skin, gastrointestinal tract, pulmonary, cardiac, and renal systems are the most involved organs [2].

Scleroderma is a rare disorder. The prevalence is estimated at 2–233 patients per million people per year. Scleroderma affects women far more often than men. The disease generally occurs between the ages of 30 and 50. Black patients with scleroderma tend to have a younger onset than whites [3]. The major risk factor is a family history of systemic sclerosis. Environmental factors such as medication, chemicals, and toxins can induce scleroderma [4]. The combination of genetic predispositions provoked by environmental stressors leads to autoimmune reactions, vasculopathy, fibrosis, and extracellular matrix deposition [1].

The spectrum of skin manifestations and severity of organ involvement contribute to the heterogeneity of its presentation. Scleroderma is clinically diagnosed by the presence of Raynaud's phenomenon, skin thickening, and visceral involvement. Patients with systemic sclerosis frequently present primarily cutaneous complaints and are unaware of their systemic involvement. Cutaneous involvement manifests as skin sclerosis. Raynaud's phenomenon is caused by vasculopathy and is experienced by more

than 90% of SSc patients. Serology tests for autoantibody profiles guide the classification of disease subtypes and exclude other closely related conditions [5]. Organ-specific examination facilitates the evaluation of disease-related organ complications. Individuals with cardiorespiratory complications may develop dyspnea, dry cough, cyanosis, and dysrhythmia as a result of fibrosis and pulmonary arterial hypertension [6]. As the condition advances, around 5–10% of patients may develop hypertension, deteriorate renal function, and fall into acute kidney failure. Digestive tract problems in SSc patients induce delayed gastric emptying, gastrointestinal reflux, impaired absorption, and malnutrition [7].

The American College of Rheumatology (ACR) developed preliminary SSc diagnostic criteria in 1980. The major criteria are skin sclerosis proximal to the metacarpophalangeal and metatarsophalangeal joints. The minor criteria are sclerodactyly, digital ulceration or pitting scars, and Bibasilar pulmonary fibrosis [8]. The diagnosis of SSc can be established when one major and at least two minor criteria are found. The New European League Against Rheumatism Criteria (EULAGR) classifies scleroderma based on a certain score system. This score considers the early and milder signs of SSc based on atypical nail fold capillaries, fingertip lesions, and specific autoantibodies [1]. In 1988, Le Roy distinguished between limited and diffuse scleroderma. Patients with limited type typically experience recurrent attacks of Raynaud's phenomenon. The cutaneous alterations are present in the facial skin and extremities distal to the knee or elbow joint [8]. Meanwhile, skin involvement in diffuse-type scleroderma is progressive and extensive. The other scleroderma variants are undifferentiated SSc, SSc sine scleroderma, and SSc overlap syndrome [4].

In this case report, we would like to point out that patients with systemic sclerosis often present primarily with skin complaints and are unaware of their systemic involvement, as in this patient, who had been screened and was found to have pulmonary complications.Early diagnosis by a dermatologist can help prevent morbidity and mortality.

CASE PRESENTATION

We report a case of a 47-year-old woman presenting with thickening and hardening of the skin. The patient complained of her skin stiffness, thickening, and hardening for 3 years. Initially, the patient complained of rashes on both her arms and legs. The rash eventually faded, leaving whitish, stiff, tight, and dry skin. About 1-2 months later, similar lesions appeared on her face and trunk. The patient complained of tightness in her face. The patient also complained that her fingers had occasionally turned white and pale in the past 4 years. The color change was accompanied by numbness and tingling sensations. It occurred anytime she was stressed or in cold weather. Lately, she has had difficulty opening her mouth widely. Her fingers become stiff and difficult to move gradually. She struggled to dress since it was difficult to raise both of her arms. The patient has had a dry cough for six months, easily got tired when doing strenuous work. The dry cough has become more frequent in the last month, accompanied by shortness of breath. The patient denied any history of another medication intake prior to her condition. The patient denied any fever, hair loss, or swallowing difficulty. There is no history of similar conditions in her family.

Investigation

In a physical examination, her vital signs were normal. In her dermatological status, there was thickening of the skin on her face, trunk, and upper and lower extremities. The patient had a mask-like facial appearance (hypomimia) and a beak-shaped nose (Fig.1). A salt and pepper skin appearance was found on the upper back and chest (Fig.2). The patient had difficulty raising her arms with a limited range of motion, especially in the right arm. There were puffy fingers and contractures on her fingers (Fig.3). In the laboratory examination, there was an increase in the ANA test level to more than 1:400, while other hematologic, liver, and renal panels were within the normal range. The chest radiograph showed a reticular pattern on the right and left paracardia of the lungs. The patient's chest CT scan revealed interstitial lung disease.

The patient was diagnosed with definitive scleroderma based on The European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) criteria with a score of 18. Differential diagnoses of scleroderma are circumsript or localized scleroderma (morphea), eosinophilic fasciitis, lichen sclerosis et atrhopicans, sclerodermiform amyloidosis, Scleredema diabeticorum, Acrodermatitis chronica atrophicans, Scleromyxedema, and Cutanea Tarda Porphyria [17]. The skin biopsy was also performed and supported the scleroderma diagnosis. We referred the patient to the multidisciplinary specialists of internal medicine, pulmonary medicine, physical therapy and rehabilitation. The severity level of skin sclerosis was also assessed with the modified Rodnan skin score (mRSS), with a score of 31.

Treatment

The patient was treated with methotrexate (15 mg/week), methylprednisolone (4 mg/day), amlodipine (10 mg/day), and N-Acetylsystein (600 mg/day). The patient has also been prescribed a topical steroid of dexosimethasone 0.25% for the hardening and



Fig.1. The patient had no expression, a mask-like facial appearance, a beak-shaped nose, and a limited range of mouth opening



Fig.2. There was hardening of the skin with salt and pepper appearance on the upper back and chest (red circle)

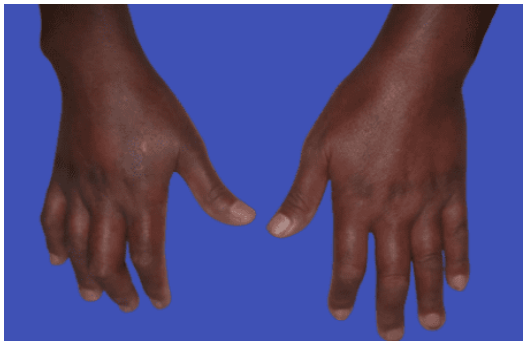


Fig.3. There were puffy fingers and flexion contractures of the fingers (sclerodactyly). No erosion or ulceration was observed

thickening skin lesions, and instructed to routinely apply moisturizer to her skin. The patient was advised to avoid cold weather by wearing gloves or socks, not smoking, and stretching her skin regularly.

Outcomes and Follow Up

After 4 months of treatment, the patient reported a decrease in Raynaud's phenomenon recurrence and an improved breathlessness and coughing. The patient also noticed that her skin was not as dry and stiff as it was during her initial visit. There was a significant improvement in the skin lesions, with softening of the skin on her abdomen and thighs. During the treatment, the patient had never reported any wounds or ulcerations on her skin. There was an improvement in the mRSS score to 19. The patient also had improvements in the arm's range of motion.

DISCUSSION

Systemic sclerosis is predominant in women, with a female-to-male ratio of 3:1 to 14:1. The age of disease onset ranges from 30 to 50. Our patient is a 47-year-old female. Female patients with scleroderma have an earlier onset compared to males. Epigenetic differences in X-chromosome inactivation in women and estradiol (E2) may play a role in the etiopathogenesis of SSc by inducing fibrosis in the skin and other organs [9]. The strongest risk factor for SSc is a positive family history. First-degree relatives have a 13-fold higher relative risk. Genetic markers of altered innate immunity involved in the connective tissue response of SSc are HLA DRB1 1302 and HLA-DQB1 0604/0605 [10]. Our patient had no family history of similar conditions or other autoimmune diseases.

The patient's fingers occasionally turned pale and white with a tingling sensation when exposed to cold weather or stress. This condition is associated with the Raynaud phenomenon. Raynaud's phenomenon is a distinctive diagnostic feature of SSc, reported in more than 90% of SSc patients [11]. It is characterized by recurrent vasospasm of small digital arterioles in the fingers and toes when induced by cold or stressful events. 12 Systemic sclerosis is typically preceded by Raynaud's phenomenon, which can last for many years. Raynaud's phenomenon resembles the underlying vasculopathy in SSc [2].

Patients with scleroderma have typical facial features such as a mask-like facial appearance, a beak-shaped nose, microstomia, radial furrowing around the mouth, and telangiectasia. Salt and pepper appearances are a pathognomonic cutaneous manifestation that presents as hypopigmented and hyperpigmented macules. Hair follicles and sweat glands are also reduced. As a result, the patient's skin becomes dry, causing hypohidrosis [8]. In patients with scleroderma, the extent and severity of skin sclerosis can be assessed by the modified Rodnan skin score. This scoring correlates with illness progression and severity. Increasing skin thickness is associated with new or worsening multi-organ complications and a poor prognosis. Patients with a high mRSS score are at a higher risk of morbidity and death. On our patient's first visit, we got a score of 31. A score of more than 20 is correlated with a high risk of systemic complications [12].

Scleroderma was diagnosed by typical skin thickening, Raynaud's phenomenon, visceral organ involvement, and a distinct autoantibody subset. The diagnosis of scleroderma is made based on ACR/EULAR scoring [8]. The patient had typical scleroderma skin, a history of Raynaud's phenomenon and lung involvement, skin thickening of the fingers of both hands extending proximal to the MCP joints, skin thickening with sclerodactyly, Interstitial lung disease, and Raynaud's phenomenon with a total score of 18. A score >9 is classified as having definitive scleroderma [8]. The ANA test result was more than 400. Anti-nuclear antibody (ANA) (positive if >1:160) is present in approximately 95% of patients with SSc [13]. Increased ANA titers demonstrate the role of autoimmunity in systemic sclerosis. In patients with unclear systemic symptoms, increased ANA titers are used as screening for systemic sclerosis. An elevation of a specific ANA profile is also linked to organ involvement, level of severity, and certain prognoses. Following the increasing ANA titers, specific antibody titers for systemic scleroses, such as anti-centromere (ACA) and anti-DNA topoisomerase I (anti-topo I) antibodies, formerly known as anti-Scl-70 antibodies, should also be measured [14]. We are not able to measure these tests for our patient due to facility limitations.

A histopathologic examination was performed to support the diagnosis. Morphea and systemic sclerosis share similar pathologic features of thickening and homogenized collagens in the dermis and subcutis, accompanied by vascular changes and the infiltration of inflammatory cells. The epidermis and adnexal components become atrophic. The reticular dermis is distinguished by wide sclerotic collagen bundles that surround and replace subcutaneous tissue [8].

The main approach in SSc treatment is to prevent disease progression and complications. The patient was treated with methotrexate (15 mg/week) and a systemic corticosteroid of methylprednisolone (4 mg daily). Scleroderma patients are at increased risk of renal complications; thus, prednisone should be administered at low doses (less than 10mg/daily). The mechanisms of SSC development are inflammation, vasculopathy, and fibrosis. Therefore, based on the pathophysiology, the patient was treated with immunosuppressants, vascular therapies, and antifibrotic drugs for the treatment of SSC. The immunosuppressants widely used are mycophenolate mofetil, cyclophosphamide, steroids, methotrexate, and biologic agents [11,15]. The patient is prescribed a calcium channel blocker of amlodipine 10mg daily to manage the vasculopathy related to Raynaud's phenomenon. The recommended vascular treatments in SSc are Calcium channel blocker (CCB), Angiotensin-converting enzyme (ACE) inhibitor, Angiotensin II receptor blocker (ARB), and prostacyclin [16].

The patient was given topical steroids and moisturizer for cutaneous involvement. Chronic inflammation in SSc causes atrophy of the skin and its adnexa and glands. It can cause dry skin, diminish sebum production, and increase susceptibility to trauma. Therefore, routine moisturizer application is essential [17]. The sclerosis in the hand may progress to joint contractures [4]. Chronic vasculopathy in SSC may cause skin ulcers on the fingers. The patient should be educated

about Raynaud's phenomenon by avoiding precipitating factors such as nicotine, emotional stress, sympathomimetics, and coldness [18].

The complications of scleroderma are sclerodactyly, ulceration, digital amputation, pulmonary fibrosis, pulmonary hypertension, inflammatory myocarditis, arrhythmia, heart block, restrictive heart failure, and acute or chronic renal failure [19]. Gastrointestinal tract involvement was reported in more than 60% of patients, including dysphagia, peptic stricture, peptic ulcer, pseudo-obstruction, and malabsorption. The 5-year survival rate for patients with scleroderma is expected to be 74.9% at 5 years and 62.5% at 10 years. The prognosis is determined by the involvement of internal organs. The primary cause of mortality was pulmonary complications [20].

CONCLUSION

The cutaneous manifestation may be the first and most pathognomonic feature of scleroderma. A patient with scleroderma should be investigated for organ involvement. Since the patients initially recognized the skin changes, most of them would visit a dermatologist first before seeing another specialist. Therefore, a dermatologist plays a significant role in the early identification of skin disorders and making multidisciplinary referrals. Early diagnosis and prompt treatment could reduce morbidity and mortality in patients with scleroderma.

ACKNOWLEDGMENT

We thank anonymous referees for their valuable suggestions.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

REFERENCES

1. Ferreli C, Gasparini G, Parodi A, Cozzani E, Rongioletti F, Atzori L. Cutaneous Manifestations of Scleroderma and Scleroderma-Like Disorders: a Comprehensive Review. Clinical Reviews in Allergy and Immunology. 2017;53(3):306–36.
2. Asano Y. Systemic sclerosis. Journal of Dermatology. 2018;45(2):128–38.
3. Bergamasco A, Hartmann N, Wallace L, Verpillat P. Epidemiology of systemic sclerosis and systemic sclerosis-associated interstitial lung disease. Clinical Epidemiology. 2019;11:257–73.
4. Moinzadeh P, Denton CP, Black CM, Krieg T. Systemic Sclerosis. In: Kang S, Amagai M, Bruckner A, Enk A, Margolis D, McMichae A, editors. Fitzpatrick's dermatology in general medicine. 9th ed. New York: McGraw-Hill; 2019. p. 1086–104.
5. Knobler R, Moinzadeh P, Hunzelmann N, Kreuter A, Cozzio A, Mouthon L, et al. European Dermatology Forum S1-guideline on the diagnosis and treatment of sclerosing diseases of the skin, Part 1: localized scleroderma, systemic sclerosis and overlap syndromes. Journal of the European Academy of Dermatology and Venereology. 2017;31(9):1401–24.
6. Ruaro B, Confalonieri M, Salton F, Wade B, Baratella E, Geri P, et al. The relationship between pulmonary damage and peripheral vascular manifestations in systemic sclerosis patients. Pharmaceuticals. 2021 May 1;14(5).
7. Sobolewski P, Maślińska M, Wieczorek M, Łagun Z, Malewska A, Roszkiewicz M, et al. Systemic sclerosis - Multidisciplinary disease: Clinical features and treatment. Vol. 57, Reumatologia. Termedia Publishing House Ltd.; 2019. p. 221–33.
8. Rongioletti F, Ferreli C, Atzori L, Bottoni U, Soda G. Scleroderma with an update about clinico-pathological correlation. Giornale Italiano di Dermatologia e Venereologia. 2018;153(2):208–15.
9. Peoples C, Medsger Jr TA, Lucas M, Rosario B, Feghali-Bostwick C. Gender differences in systemic sclerosis: relationship to clinical features, serologic status and outcomes. J Scleroderma Relat Disord. 2016;177(1(2)):177–240.
10. Singh D, Parihar AK, Patel S, Srivastava S, Diwan P, Singh MR. Scleroderma: An insight into causes, pathogenesis and treatment strategies. Pathophysiology. 2019;26(2):103–14.
11. Khanna D. Diagnosis and treatment of systemic and localized scleroderma. Expert Review of Dermatology. 2011;6(3):287–302.
12. Khanna D, Furst DE, Clements PJ, Allanore Y, Baron M, Czirjak L, et al. Standardization of the modified Rodnan skin score for use in clinical trials of systemic sclerosis. J Scleroderma Relat Disord. 2017;2(1):11–8.
13. Fabri M, Hunzelmann N. Differential diagnosis of scleroderma and pseudoscleroderma. JDDG - Journal of the German Society of Dermatology. 2007;5(11):977–83.
14. Hamaguchi Y, Takehara K. Anti-nuclear autoantibodies in systemic sclerosis : News and perspectives. Vol. 3, Journal of Scleroderma and Related Disorders. SAGE Publications Ltd; 2018. p. 201–13.
15. Zhao M, Wu J, Wu H, Sawalha AH, Lu Q. Clinical Treatment Options in Scleroderma: Recommendations and Comprehensive Review. Vol. 62, Clinical Reviews in Allergy and Immunology. Springer; 2022. p. 273–91.
16. Shah AA, Wigley FM. My approach to the treatment of scleroderma. Mayo Clinic Proceedings. 2013;88(4):377–93.

17. Careta MF, Romiti R. Localized scleroderma: Clinical spectrum and therapeutic update. Anais Brasileiros de Dermatologia. 2015;90(1):62–73.
18. Cappelli L, Wigley FM. Management of Raynaud Phenomenon and Digital Ulcers in Scleroderma. Vol. 41, Rheumatic Disease Clinics of North America. W.B. Saunders; 2015. p. 419–38.
19. Shenavandeh S, Naseri R. Assessment of hospitalization and mortality of scleroderma in-patients: A thirteen-year study. Reumatologia. 2017;55(4):163–8.
20. Meridor K, Sagy I, Molad Y. Anti-Ro/SS-A antibody is associated with worse pulmonary outcome and reduced overall survival in systemic sclerosis. Mod Rheumatol. 2022 Nov 1;32(6):1086–93.