Limited Cutaneous Scleroderma

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ABSTRACT

Introduction: Scleroderma is a rare autoimmune disease of connective tissue characterized by extensive fibrosis, inflammation, and vasculopathy. It classified as limited cutaneous and diffuse based on the degree of skin involvement. The management is still a challenge since it has a high morbidity and mortality rate. This case report aims to understand scleroderma and provide appropriate treatment that can improve the patient's prognosis.

Case report: A 55-year-old female came with complaints of stiff skin on the forearms, lower legs and face since approximately eight months ago, initially on the right and left forearms, then to face, right and left lower legs. On physical examination, there was sclerosis of the skin on the face, forearms and lower legs, and salt and pepper appearance with Rodnan score were 26. The result from histopathological examination were scleroderma. The patient was diagnosed with limited cutaneous scleroderma. The management consisted of methotrexate, folic acid, sulphur ferous, vitamins B1, B6, B12 intraorally and 10% urea cream topically. She also was informed to practice moving the hands and fingers slowly.

Conclusion: The diagnosis of limited cutaneous scleroderma is based on history, physical examination and investigations. It is still a life-threatening disease, however multidisciplinary management with early detection and treatment of complications can improve the prognosis.

Keywords: limited cutaneous scleroderma, systemic sclerosis

INTRODUCTION

Scleroderma or also known as systemic sclerosis is still a problem in the dermatology field. It is an autoimmune disease of connective tissue that can affect multiple organ systems, characterized by extensive fibrosis, inflammation, and vasculopathy. The clinical manifestations include the Raynaud phenomenon (RP), skin fibrosis and involvement of visceral organs, such as the lungs, heart, kidneys and gastrointestinal tract. Scleroderma is more common in women than men, with age-onset between 30-50 years old. The prevalence of scleroderma worldwide is estimated at 200 cases per 1 million population and the incidence is 20 cases per 1 million population. At the Sanglah Central General Hospital Denpasar, there was one new case during the period August 2019-August 2020.¹-³

The descriptive subclassification scleroderma consists of limited cutaneous and diffuse, which is primarily related to the degree of skin involvement. Diffuse scleroderma is defined as a progressive form of scleroderma with early-onset RP, usually within 1 year of the onset of skin thickening, while limited cutaneous scleroderma is characterized by a history of pre-existing RP and skin changes on the distal extremities of the knee and elbow joints, including the skin of the face. Although the aetiology of this disease is still unknown, it is assumed that there is a role for genetic, environmental and chemical factors.⁴ Management of scleroderma is also a challenge since it has a high morbidity and mortality rate. The treatment is symptomatic based on the organ involved and suppresses the immune system.⁴,⁵ Thus, we report a case of limited cutaneous scleroderma.

CASE REPORT

A Balinese 55-year-old female complained of stiff skin on the forearms, lower legs and face since eight months ago. She began to have difficulty moving her hands, followed by the fingers that start to swell, stiffen and pain, especially on the fingers of the right hand for six months. There were wounds on the fingertips of the right hand. Her face then felt stiff therefore causing difficulty to eat and drink. There were also white patches on both arms, back and neck. She lost 3 kg in the last three months. The patient has a history of discoloration of the fingers. It becomes pale or bluish when exposed to cold since about a year ago. For one month, she suffered frequent swelling of the right and left legs in the morning while working and getting better when resting at night. She also complained of less frequent urination. There was no
history of previous illness, drug and food allergies.

The general physical examination is normal. On the dermatological status in the frontal, right zygoma, anterior neck, posterior thoracoabdominal region, upper and lower extremities we observed multiple depigmented macules, well-defined margin, geographical shape, vary in size 0.2x0.3 cm-1x3 cm; in several areas, there were multiple hyperpigmented macule, well-defined margin, rounded shape, some confluent to form a geographical shape, vary in size 0.2x0.5 cm-3x6 cm (salt and pepper appearance) and in other areas, there were thin white scales. We also observed multiple erosions, well-defined, geographic shape, size 0.2x1 cm - 0.4x1 cm, in other areas, there are thin white scales.

On skin palpation of the face, the superior and inferior right and left extremities, we found hard and stiff skin. The right and left hands and right and left feet showed non-pitting edema and sclerodactyly of the 2nd and 3rd digits of the right hand. There were limitations to open the mouth (microstomia). Total Rodnan score examination was 26. The results of dermoscopy examination of the skin lesions revealed depigmented macules with perifollicular islands around them. On cold provocation examination, Raynaud’s phenomenon was found. From skin biopsy showed eosinophilic hypertrophic collagen bundles and degeneration of vacuoles and apoptotic bodies in the basal layer of the epidermis, thus concluded as scleroderma dd/ morphea dd/ lichen sclerosus et atrophicus. Complete blood count, liver function and kidney function were performed for evaluation.

The patient was diagnosed with limited cutaneous scleroderma and mild anemia. Management consisted of methotrexate tablets 3x5 milligrams per week with 12 hours interval intraorally, folic acid 5 milligrams tablets orally taken 12 hours after the last methotrexate, sulphna ferrous every 24 hours intraorally, vitamins B1, B6, B12 every 24 hours intraorally, and urea cream 10% administered topically every 12 hours.

**DISCUSSION**

Scleroderma (systemic sclerosis) is a multisystemic disease characterized by an autoimmune process, vascular endothelial cell injury, inflammation, and extensive fibroblast activation. Based on the extent of skin involvement, patients can be classified into limited cutaneous and diffuse scleroderma. The worldwide prevalence of scleroderma varies, estimating at 200 per one million population. The age of onset is mainly between 30–50 years which women are 3 to 14 times more often affected than men. Approximately
70% of people with scleroderma have limited cutaneous scleroderma, while the remaining are of the diffuse type. The aetiology of scleroderma is still unknown, but there are indications of a genetic role.3

It is expected there is damage that causing endothelial cells and platelets to release vasoconstrictors derived from platelet-derived growth factor and thromboxane A2. When vasoconstriction occurs, immune cells such as lymphocytes and monocytes migrate to damaged tissues and blood vessels and produce cytokines and growth factors. Hyperplasia of blood vessels, vasculopathy and ischemia occur. Tissue hypoxia plays a role in stimulating the activity of dermal fibroblasts, increasing the synthesis of collagen and extracellular matrix components, causing thickened skin and organ fibrosis.6

Early symptoms of scleroderma include swelling, tightness, and thickening of the skin that makes it feel hard. Examination reveals non-pitting edema, decreased joint flexibility and may be followed by patchy hypopigmented patches (salt and pepper appearance).7 The diagnosis of scleroderma is mainly based on typical clinical findings. The classification currently used is based on a collaboration between the American College of Rheumatology (ACR) and The European League Against Rheumatism (EULAR) in 2013. It has a diagnostic sensitivity of 91% and a specificity of 92%. Other clinical symptoms include sclerosis of the fingers (swollen fingers, sclerodactyly), fingertip lesions (ulcers, scars), telangiectasia, abnormal nail fold capillaries, pulmonary arterial hypertension and/or interstitial lung disease, Raynaud’s phenomenon, and positive scleroderma-associated antibodies.7-9 In this case, a total score of 19 met the criteria for scleroderma based on the 2013 ACR/EULAR diagnostic criteria.

Scleroderma is often differentially diagnosed with subtypes of scleroderma itself and generalized morphea because of its clinical manifestations in the form of sclerosing skin. In morphea there is no fingers involvement. In limited cutaneous scleroderma, skin fibrosis is limited to the face, fingers (sclerodactyly), and distal extremities, whereas in diffuse scleroderma, trunk and proximal extremities are also affected. In patients with limited cutaneous scleroderma, Raynaud’s phenomenon usually indicates skin involvement and other disease manifestations over months, while patients with diffuse scleroderma have rapid disease progression with extensive skin changes and early visceral organ complications. The acronym CREST (calcinosis, RP, esophageal dysmotility, sclerodactyly, and telangiectasia) is used for limited cutaneous scleroderma and has at least 2 of the 5 CREST signs for the diagnosis.10 Systemic involvement may occur in both diffuse or limited scleroderma.11

In all patients, the extent and severity of cutaneous sclerosis can be assessed by the modified Rodnan skin score. Skin score at baseline correlated with disease severity and outcome of limited cutaneous or diffuse scleroderma. Skin thickening and fibrosis form the basis of most classification criteria and subsets of this disease spectrum. Locations consisted of face, right and left upper and lower arms, thorax, abdomen, right and left hands, right and left fingers, and right and left thighs, right and left lower limbs, right and left legs. Skin thickness was categorized into grades 1, 2, or 3, according to mild, moderate, and severe based on skin palpation by a trained examiner.7 The patient’s Rodnan score in this case improved with follow-up, from 26 to 14 in 35 days indicating clinical improvement in the patient.

On histopathological examination, accumulation of collagen and lymphocyte infiltrates between collagen bundles in the dermis will be found, especially in the perivascular that can spread to the adnexal and subcutaneous tissue. In the early stages, collagen bundles appear in the reticular dermis. It appears pale, swollen, homogeneous and parallel to the skin surface, and often a perivascular lymphocytic infiltrate is seen. As the disease progresses, the vascularity and inflammation of the involved skin will decrease, while adnexal tissue including hair follicles and glands disappears. The rete ridge disappears and the epidermis thins. Subcutaneous fat will be replaced by fibrotic tissue. The histopathological picture of scleroderma is very similar to morphea, so it needs a clinical correlation to help make the diagnosis.5,12,13

An important element in the management of skin manifestations of scleroderma is to maintain circulation, joint mobility, and muscle strength. Skin affected by scleroderma tends to be very dry, tight, and prone to trauma. Thickening of the skin can be improved with physical therapy and exercise, lymphatic drainage, topical treatment with steroids, calcineurin blockers, and moisturizing creams. Systemic therapy consists of immune-suppressing drugs, systemic steroids for a short time only, and phototherapy ultraviolet A1 or psoralen and ultraviolet A. Dry and itchy skin is treated topically with corticosteroids, cannabinoid agonists, capsaicin, emollients, and phototherapy.14

The current management of scleroderma is based on the organ involved and the administration of immunosuppressants. In general, the immune system is known to play a role in the pathogenesis of scleroderma, so immunosuppressive therapy is useful. Several studies found a significant improvement in skin thickening with methotrexate administration.1,14

The use of methotrexate (MTX) for skin and joint involvement in scleroderma has largely been demonstrated to be effective in rheumatoid arthritis and other autoimmune diseases. The effect of MTX on skin development in early diffuse scleroderma was examined in two multicentre, using a double-blind, placebo-controlled method. A research investigated the administration of 15 mg of MTX intramuscularly per week. This study included patients with diffuse (n = 11) and limited cutaneous (n = 18) scleroderma with skin thickening that was less than three years. They also included patients with a longer duration of disease if there was any development of skin thickening, persistent digital ulceration or decreased lung function in the previous six months. The primary outcomes included improvement in the total Rodnan skin score greater than or equal to 30%. Pope et al. investigated 71 patients with diffuse and limited cutaneous type scleroderma with a duration that was less than three years, then treated them with placebo or MTX (15 mg - 17.5 mg orally per week) for 12 months. MTX had a beneficial effect on Rodnan’s modified skin score (mRSS)
(mRSS -5.3 in the MTX group vs +1.8 in the placebo group [p < 0.009]).\textsuperscript{15,16}

MTX is recommended by the European League Against Rheumatism (EULAR) and the European Scleroderma Trials and Research Group (EUSTAR) as the treatment of skin manifestations in early scleroderma. A recent consensus guideline study based on responses to an electronic survey sent to members of the Scleroderma Clinical Trials Consortium (SCTC) and the Canadian Scleroderma Research Group (CSRG) found that 62% of scleroderma specialists use MTX as first-line for the treatment of skin thickening and 60% using MTX as a first-line treatment for inflammatory arthritis.\textsuperscript{16}

In this case, treatment was given in the form of methotrexate tablets 3x5 milligrams per week with an interval of 12 hours intraorally, folic acid tablets 5 milligrams orally taken 12 hours after the last methotrexate, sulpha ferrous every 24 hours intraorally, vitamins B1, B6, B12 every 24 hours intraorally, 10% urea cream administered topically every 12 hours. The patient also was informed to practice moving the hands and fingers slowly. Based on Rodnan score there is improvement in patient.

CONCLUSION

The diagnosis of limited cutaneous scleroderma is based on history, physical examination and investigations. It is a high morbidity disease, however multidisciplinary management with early detection and treatment of complications can improve the prognosis.

CONFLICT OF INTEREST

The author declares there is no conflict of interest regarding publication of current report.

ETHIC IN PUBLICATION

The patient had received signed inform consent regarding publication of their respective photograph in journal article.

AUTHORS CONTRIBUTION

Author PGHW and MHL examine and follow up the patient, literature review, construct the manuscript and publication. Author PSSS contribute in the supervision and patient’s treatment.

REFERENCES