PROGRESSIVE SYSTEMIC SCLEROSIS WITH MULTIPLE COMORBIDITIES IN A 71-YEAR-OLD FEMALE

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ABSTRACT

INTRODUCTION: Progressive systemic sclerosis (PSS) is a connective tissue disorder with unknown etiology, characterized by increased collagen deposition leading to fibrosis, skin thickening and other pathological changes in organs. Females constitute at least two-thirds of all the cases. The disease commonly occurs in women aged 30-40 years. Other features of the disease include Raynaud's phenomenon, telangiectasia, calcinosis, myositis, arthritis, tenosynovitis, renal failure, esophageal dysmotility, pulmonary fibrosis, and heart failure.

MATERIALS AND METHODS: A 71-year-old female was hospitalized with ischemic and cyanotic fingertips in the Department of Rheumatology, St. Marina University Hospital, Varna, Bulgaria. She complained of pain in both hip joints when walking, erythema in the region of the distal phalanges of the hands and feet with individual ulcerations on the fingertips. Raynaud's phenomenon was positive. Other comorbidities that were included in her medical records were type two diabetes, hypertension, and past history of endometrial cancer. The physical exam revealed sclerodactyly, cutaneous sclerosis of hands and feet, and microstomia. Laboratory tests revealed high levels of very low-density lipoprotein (4.9) and high level of blood sugar (7.2). Immunology revealed high levels of antinuclear antibodies (+++), anti-centromere protein B (+++), anti-Sjögren's syndrome-A (Ro52) (+++).

RESULTS: The following medications were administered: methylprednisolone 40 mg intravenous, ranitidine 150 mg 2x1 per os, pulse therapy with cyclophosphamide amp 1000 mg in 500 mL saline, then followed by another bank of 500 mL saline, metoclopramide 10 mg - 1 ampoule intravenously, and heparin 2x500E intravenous.

CONCLUSION: The occurrence of the disease in such an advanced age is unlikely, while the risk of diabetes and neoplasia increases exponentially with the age. The uniqueness of the case herein lies with its late presentation, which could easily be misinterpreted as a complication of her concomitant diseases.

Keywords: rheumatology, progressive systemic sclerosis, Raynaud's phenomenon, microstomia

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INTRODUCTION

Systemic sclerosis (SSc) is a chronic systemic autoimmune disease characterized by microangiopathy, increased deposition of extracellular matrix with progressive fibrosis, both in the skin and in visceral organs that can involve the lungs, heart, kidneys, and the gastrointestinal tract (1).

Many factors, including environmental ones, can lead to immunologic system disturbances and vascular changes. Endothelial alterations may lead to a cascade of stimulatory changes that involve many cells, including fibroblasts, T-lymphocytes, macrophages, and mast cells. In turn, the activated cells secrete a variety of substances, including cytokines and their soluble receptors and enzymes and their inhibitors. These substances lead to changes in the extracellular matrix compounds, including fibronectin; proteoglycans; and collagen types I, III, V, and VII. Increased collagen production or disturbances in its degradation can cause excessive collagen deposition in tissues. The tissue lesions in various stages of scleroderma are characterized by early microvascular damage, mononuclear cell infiltrates, and slowly developing fibrosis. In later stages of scleroderma, the main findings are very densely packed collagen in the dermis, loss of cells, and atrophy. Although skin fibrosis is the distinguishing hallmark, the pathological changes in the lungs, gastrointestinal tract, kidneys, and heart determine the clinical outcome. In general, the extent of skin involvement and its rate of progression reflect the severity of visceral organ complications (2,3).

A striking feature of systemic sclerosis is its patient-to-patient variability, and heterogeneity has been observed in clinical manifestations, autoantibody profiles, the rate of disease progression, response to treatment and survival. Based on the extent of their skin involvement, patients are grouped into limited cutaneous systemic sclerosis (lcSSc) and diffuse cutaneous systemic sclerosis (dcSSc) subsets. In lcSSc, skin fibrosis is restricted to the fingers (sclerodactyly), distal extremities and face, whereas in dcSSc, the trunk and proximal extremities are also affected. In patients with lcSSc, Raynaud's phenomenon typically precedes skin involvement and other disease manifestations by months to years, whereas patients with dcSSc have rapid disease progression

with extensive skin changes and early development of visceral organ complications (2).

Autoantibodies are particularly helpful in systemic sclerosis for both diagnosis and classification. lcSSc is more commonly associated with centromere-specific antibodies, whereas dcSSc is more often associated with topoisomerase I- or RNA polymerase III-specific antibodies. However, not all patients with systemic sclerosis fall clearly into one of these two disease subsets, and some can change their subset assignment over time (2).

CASE PRESENTATION

A 71-year-old female was hospitalized with ischemic and cyanotic fingertips in the Department of Rheumatology, St. Marina University Hospital, Varna, Bulgaria. She complained of pain in both hip joints when walking. Erythema was observed in the region of the distal phalanges of the hands and feet with individual ulcerations on the fingertips and Raynaud's phenomenon was positive. Other comor-

Fig. 1

Fig. 2

Fig. 3

bidities, which were included in her medical records, were type two diabetes, hypertension and past history of endometrial cancer. The vital signs were blood pressure of 130/80 mmHg, and pulse of 75 bpm. On

Fig. 4

physical examination the skin was pale pink, indurated and upon testing, its tightness taking hold of a plica was hindered in the area of the hands, feet, and face. The visible mucosa was without deviations. The fingers were pale with low local temperature with multiple ulcerations and indurations. Laboratory test results: Hb: 103 g/L, leukocytes: $4.22 \times 10^9/L$, platelet count: $181 \times 10^9/L$, urea: 5.5 mmol/L; creatinine: 63 $\mu\text{mol/L}$; random plasma glucose: 7.1 mmol/L, VLDL: 4.9; Na: 144 mmol/L; K: 4.3 mmol/L, CRP

Table 1

2013 ACR / EULAR Criteria For The Classification Of Systemic Sclerosis (Scleroderma)*		
Item	Sub-items(s)	Weight/score [†]
Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints (<i>sufficient criterion</i>)	-	9
Skin thickening of the fingers (<i>only count the higher score</i>)	Puffy fingers	2
	Sclerodactyly of the fingers (distal to the metacarpophalangeal joints but proximal to the proximal interphalangeal joints)	4
Fingertip lesions (<i>only count the higher score</i>)	Digital tip ulcers	2
	Fingertip pitting scars	3
Telangiectasia	-	2
Abnormal nailfold capillaries	-	2
Pulmonary arterial hypertension and/or interstitial lung disease (<i>maximum score is 2</i>)	Pulmonary arterial hypertension	2
	Interstitial lung disease	2
Raynaud's phenomenon	-	3
SSc-related autoantibodies (anticentromere, anti-topoisomerase I [anti-Scl-70], anti-RNA polymerase III) (<i>maximum score is 3</i>)	Anticentromere 3 Anti-topoisomerase I Anti-RNA polymerase III	3

* The criteria are not applicable to patients with skin thickening sparing the fingers or to patients who have a scleroderma-like disorder that better explains their manifestations (e.g., nephrogenic sclerosing fibrosis, generalized morphea, eosinophilic fasciitis, scleredema diabeticorum, scleromyxedema, erythromyalgia, porphyria, lichen sclerosis, graft-versus-host disease, diabetic cheiroarthropathy).

[†] The total score is determined by adding the maximum weight (score) in each category.
Patients with a total score of ≥ 9 are classified as having definite scleroderma.

Sensitivity 91% Specificity 92%

Van den Hoogen et al. 2013 Classification Criteria for Systemic Sclerosis. Arthritis and Rheumatism. Vol. 65, No. 11, November 2013, pp 2737–2747

quantitative: 0.47 mg/L; antinuclear antibodies (ANA) (+++), anti-centromere protein B (antiCEMP-B) (++), anti-Sjögren's syndrome-A (Ro52) (anti-SS-A) (+++). Abdominal ultrasound revealed a persisting oval paraaortic lesion on the left with an approximate size of 38/42mm and a cortical cyst in the left kidney with an approximate size of 37/22mm.

RESULTS

The following medications were administered intravenously: methylprednisolone 40 mg, ranitidine 150 mg 2x1 per os, pulse therapy with cyclophosphamide amp 1000 mg in 500 mL saline, then followed by another bank of 500 mL saline, metoclopramide 10 mg - 1 ampoule intravenously, and heparin 2x500E.

DISCUSSION

Scleroderma is an autoimmune disorder involving multiple systems, thus making the course of this disease unpredictable. Though the exact nature of the disease is not known, high prevalence of circulating autoantibodies in serological investigations points toward an autoimmune mechanism (4).

In this case, a 71-year-old female patient was with main complaints of pain in both hip joints when walking, erythema in the region of the distal phalanges of the hands and feet with individual ulcerations on the fingertips. On physical examination, sclerosis lesions, sclerodactyly on fingers and toes, telangiectasia in the region of the hands and feet were reported.

Laboratory test results: CRP quantitative: 0.47 mg/L, antinuclear antibodies (ANA) (+++), anti-centromere protein B (antiCEMP-B) (++), anti-Sjögren's syndrome-A (Ro52) (anti-SS-A) (+++) with the conclusion: scleroderma.

In 2013, a revised classification criteria — the American College of Rheumatology (ACR)–European League Against Rheumatism (EULAR) criteria — were proposed to address some of the difficulties in the classification and diagnosis of scleroderma (Table 1). In this case, the patient had skin thickening of the fingers of both hands extending proximally to the metacarpophalangeal joints, sclerodactyly of the fingers, individual fingertip lesions with pitting scars, telangiectasia, Raynaud's phenomenon,

SSc-related autoantibodies, and the score was 24. The patient was then diagnosed with scleroderma.

CONCLUSION

The management for systemic scleroderma consists of 1) counseling and psychological support; 2) management of the skin and joints; 3) management of Raynaud's phenomenon; 4) drug therapy; 5) immunotherapy; and 6) management of complications.

- ◆ Counselling and psychological support are needed to alleviate the burden of the disease and in increasing the quality of life for the patient.
- ◆ Methylprednisolone 40 mg i.v. is administered as an anti-inflammatory agent.
- ◆ Ranitidine 150mg 2x1 p.o. is administered as an antiulcerative agent.
- ◆ Cyclophosphamide amp 1000 mg pulse therapy is used as an immunosuppressant.
- ◆ Metoclopramide 10 mg - 1 ampoule i.v. is used as an antiemetic.
- ◆ Heparin 2x500E i.v. is administered as an anticoagulant.

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