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Severe Pericardial Effusion Heralding Scleroderma Renal Crisis: A Case Report and the Literature Review

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Abstract

Introduction: Both scleroderma renal crisis and severe pericardial effusion are rare and life-threatening complications of systemic sclerosis. This article describes a case of scleroderma renal crisis heralded by severe pericardial effusion.
Case Presentation: The patient was a 39-year-old woman with a history of 8 years diffuse cutaneous scleroderma and extensive skin involvement who referred to Imam Khomeini Hospital Complex, Tehran, Iran, with worsening dyspnea and pleuritic chest pain. Echocardiography revealed severe pericardial effusion, which was drained by the pericardial window. Thereafter, the patient became gradually anuric and her blood pressure was uncontrolled despite maximum doses of antihypertensive agents, including captopril. The serum creatinine level was increased progressively; thus, hemodialysis started. Concomitantly, microangiopathic hemolytic anemia complicated the course of the disease, which responded to plasma exchange. Kidney biopsy revealed pieces of evidence indicating thrombotic microangiopathy.
Conclusions: This case report denotes to a probable association between scleroderma the renal crisis and severe pericardial effusion. Therefore, physicians should be vigilant about the renal crisis in patients with systemic sclerosis and pericardial effusion.

Keywords: Acute Kidney Injury, Cutaneous, Diffuse, Hemodialysis, Hemolytic Anemia, Pericardial Effusion, Window, Scleroderma, Systemic, Thrombotic Microangiopathies

1. Introduction

Systemic sclerosis (SSc) is a connective tissue disorder of unknown etiology, characterized by obliterative vasculopathy, inflammation, and fibrosis. In addition to the skin, other visceral organs such as gastrointestinal tract, lung, kidney, and heart could be involved in the course of the disease (1). In the early stages of the disease, the inflammatory features are dominant, and as the disease progresses, functional and structural alterations will be dominated. According to the degree of skin involvement and the rate of disease progression, the patients are classified into either diffuse (dcSSc) or limited (lcSSc) cutaneous scleroderma (2). Scleroderma renal crisis (SRC) is a relatively rare, but life-threatening complication of SSc. Its prevalence in the EUSTAR cohort on 637 patients with dcSSc was only 2.4% (3). The clinical presentations of SRC vary widely. Some patients might have a full blown picture, presenting as malignant hypertension and rapidly progressive oliguric renal failure. Others may present with a less aggressive course, modest elevation in blood pressure, and some degree of renal dysfunction (4, 5). Microangiopathic hemolytic anemia could complicate the course of SRC (1).

Mild, often asymptomatic pericardial effusion is common in patients with SSc. Depending on the diagnostic method and defined criteria, the prevalence of pericardial effusion in SSc varies from 15% to 43% in echocardiography study to more than 75% in necropsy series (6, 7). However, cardiac tamponade and severe pericardial effusion are very rare in SSc and are associated with poor prognosis (8). Since both SRC and severe pericardial effusion are rare complications of SSc, there are very few reports describing the association between such rare complications. In this study, we report a non-compliant woman with dcSSc who presented with dyspnea and severe pericardial effusion. Concomitantly, she developed hypertension and oliguric renal failure, and her course was also complicated by microangiopathic hemolytic anemia.

2. Case Presentation

A 39-year-old woman with a history of 8 years suffering from dcSSc was admitted with worsening dyspnea to Imam Khomeini Hospital Complex, Tehran, Iran on 4 October 2015. Our hospital is a governmental center that is affiliated to Tehran University of Medical Sciences. As a referral center, the patient was admitted to our hospital from Baneh, Kurdistan Province, Iran. The patient was poorly compliant with medications and did not have any medical follow-up since two years earlier. Dyspnea and dry cough progressed over this time and a significant weight loss was added to her symptoms. She complained of orthopnea and pleuritic chest pain. Features of dcSSc were evident, including shinny expressionless face, narrow tip nose, radial wrinkles around her small aperture mouth with protruding upper central incisors, finger- and elbow flexion contracture with tendon friction rub, distal pitting scars, and skin induration from the distal phalanges up to proximal of arms and trunk.

Upon arrival, her blood pressure was 150/95 mmHg, pulse rate 110 pulses per minute, respiratory rate 36 breaths per minute with oxygen saturation of 85% while breathing ambient air. Jugular venous pressure was elevated, and pulsus paradoxus was detectable. There were fine crackles in both lung bases and the cardiac sounds were muffled. Initial laboratory tests showed 15400/μL white blood cells (neutrophil dominant), hemoglobin level of 10.7 g/dL, platelet count 123000/μL, urea 65 mg/dL, creatinine 1.3 mg/dL, urinalysis revealed 2+ proteinuria with 2 - 4 white blood cells, and 8 - 10 red blood cells per high power field. The patient characteristics, including vital signs and laboratory data at the time of admission and during her course of the disease, are illustrated in Table 1. Blood pressure and pulse rate measurements were done by the oscillometric method using Microlife Watch BP Office (Microlife AG, Windau, Switzerland), which was calibrated before the use. The laboratory tests were done at the Laboratory Department of our hospital by devices and instruments, including Sysmex X 1800 and Hitachi 917. Serologic tests were performed by ELISA method using AESKULISA kit. The instruments, devices, and diagnostic kits were calibrated before analyzing blood and urine samples.

Following the admission, SRC was considered, and captopril started for the patient. Also, with the impression of sepsis, broad-spectrum antibiotics were administered. Chest X-ray revealed an increased cardiothoracic ratio and reticular changes of both lung fields. Electrocardiography showed low voltage sinus tachycardia. Echocardiography revealed severe pericardial effusion with a left ventricular ejection fraction of 45%, systolic pulmonary arterial pressure of 65 mmHg, and right ventricular dysfunction. Due to severe pericardial effusion, the patient was a candidate for emergency drainage of pericardial effusion. Thus, at the operation room, the surgical pericardial window was inserted and thereafter, about 400-mL sero-hemorrhagic fluid was drained. Following this procedure, the dyspnea improved significantly.

The urine output of the patient was 650 mL on the first day of the admission. Over the next days, the patient's condition deteriorated; she became edematous, and her urine output declined progressively. Then, the patient became anuric, and her blood pressure was unresponsive to maximum doses of captopril and amlodipine. Serum creatinine levels increased parallel to the decrease in urine output. Renal ultrasonography was normal, but just showed an increased cortico-medullary echo pattern. After insertion of the central vein double lumen catheter, hemodialysis was prescribed. Concomitantly, thrombocytopenia complicated the course of renal failure. The patient's platelet counts dropped to about 47000 /μL, and her serum lactate dehydrogenase (LDH) rose above 2000 IU/L. The peripheral blood smear showed pieces of evidence of microangiopathic hemolytic anemia, including fragmented RBCs and schistocytes (Figure 1). Antiphospholipid panel was negative, and ADAMTS13 activity level was normal. Daily plasma exchange with fresh frozen plasma replacement was started for the patient.

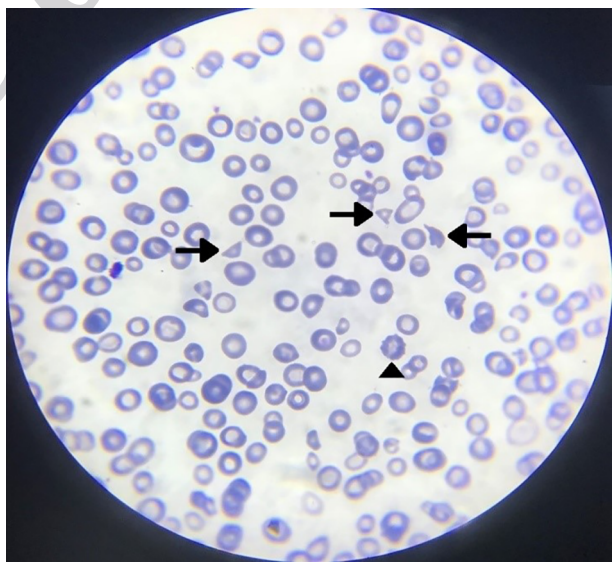

Figure 1. Peripheral blood smears ($\times$ 100) show fragmented red blood cells (arrows), echinocyte (arrowhead), thrombocytopenia, and anisopoikilocytosis

The patient's edema and blood pressures were controlled by hemodialysis. With plasma exchange, her platelet counts increased, and serum LDH levels, and the percentage of fragmented RBCs decreased progressively. Therefore, plasma exchange was tapered off. The patient remained anuric during her disease course. After the in-

Table 1. Summary of Patient Characteristics at the Time of Admission and During Her Course of the Disease

Patient Characteristics			
Important Points of History and Physical Exam			
Chief complaints	Worsening dyspnea, orthopnea, pleuritic chest pain		
Past medical history (PMH)	A history of 8 years with dcSSc		
Drug and allergy history	None		
Vital signs (on admission)			
Blood pressure	150/95 mmHg		
Pulse rate	110 beat/min		
Respiratory rate	36 /min		
Temperature	37.2°C axillary		
SpO_2	85% at ambient air		
Body mass index (BMI)	16.7 Kg/m^2		
Cardiovascular exam	Elevated JVP, pulsus paradoxus, muffled cardiac sounds		
Lung exam	Fine crackles in both lung bases		
Time Course of Clinical and Laboratory Values	**1st Day**	**5th Day**	**20th Day**
Urine output, cc/24 h	650	100	< 50
White blood cells (WBC), *1000/μ	15.4	7.6	4.4
Hemoglobin (Hb), mg/dL	10.7	9.6	10.2
Platelets, *1000/μ	123	47	116
Serum creatinine, mg/dL	1.3	3.1	4.7
LDH, U/L	1050	2007	458
PBS	Fragmented RBCs, low platelet count		
ANA, U/mL	81.4 (Positive > 10)		
Anti DS DNA, U/mL	10.5 (Negative < 16)		
P-ANCA, U/mL	3.5 (Negative < 8)		
C-ANCA, U/mL	2.5 (Negative < 8)		
ADAMTS 13 activity	123%		
ADAMTS 13 inhibitor	0.39 BuS/mL (Normal < 0.5)		

crease in the platelet count, CT-guided kidney biopsy was performed. On microscopic examination of the biopsy sample, the affected glomeruli showed capillary wall thickening, subendothelial widening, hilar thrombosis, and fibrinoid necrosis (Figure 2A). Branches of interlobular arteries revealed the mucoid expansion of intima and endothelial swelling (Figure 2B). No specific immune reaction on immunofluorescence study was noted. These histopathological findings were compatible with kidney injury due to acute thrombotic microangiopathy. Due to persistent anuria, permanent cuffed double lumen catheter was inserted for the patient and she was discharged with routine hemodialysis (3 sessions per week, each session 4 hours). However, the patient never referred to our center for future follow-up.

3. Discussion

As a heterogeneous disease with an autoimmune nature, SSc would result in the fibrosis of the skin and various internal organs. Our patient had a complicated course of the disease. Her skin involvement was extensive and in addition, GI tract, lungs, heart, and kidneys were also involved.

In SSc, all layers of the heart, including pericardium, myocardium, and endocardium could be involved. Clinically significant pericardial effusion is extremely rare in SSc and is associated with poor clinical outcome (9). In the largest case series of 40 patients with SSc and severe pericardial effusion, dyspnea was the most common symptom (75%). Most of the patients had dcSSc and the pericardial fluid was serohemoragic in more than 50% of patients (10).

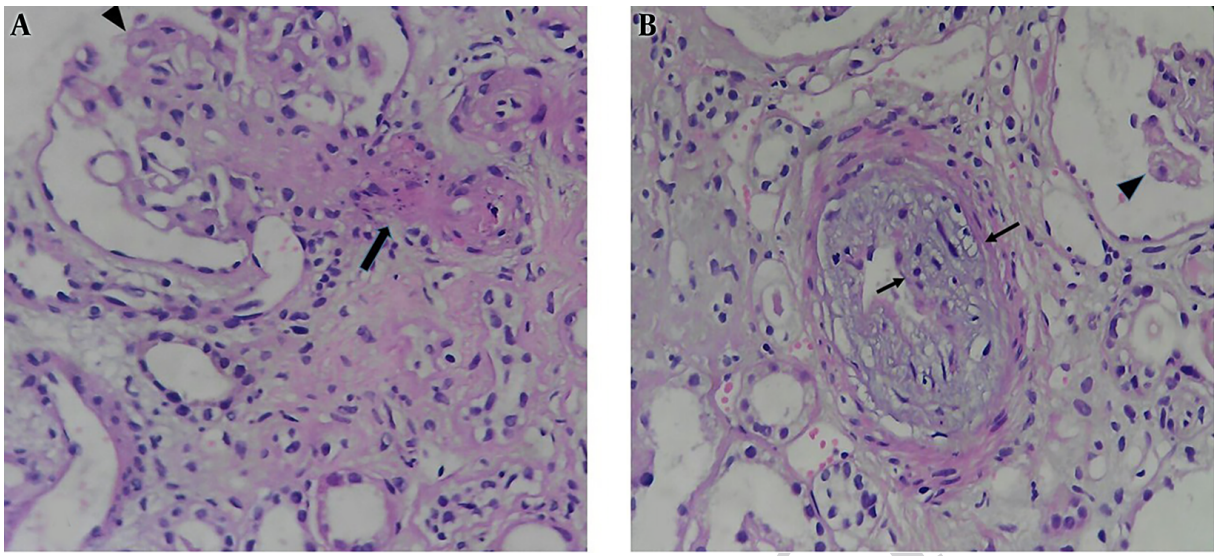

Figure 2. Microscopic examination of kidney biopsy. A) Affected glomeruli (× 100) show capillary wall thickening, subendothelial widening (arrowhead), and hilar thrombosis with fibrinoid necrosis (arrow). B) Branches of interlobular arteries (× 400) reveal the mucoid expansion of intima and endothelial swelling (between the arrows). No specific immune reaction to immunofluorescence study is noted. Overall histopathological findings were compatible with kidney injury due to acute thrombotic microangiopathy. The distinction of malignant hypertension and scleroderma solely on pathologic examination was not feasible

Likewise, our patient had dcSSc and presented with dyspnea and serohemoragic pericardial effusion. In Table 2, the characteristics of our case were compared with previously published case series and reports.

An important association was observed between pericardial involvement and renal failure in patients with SSc. Steen et al. in an early study reported that cardiac involvements, including congestive heart failure and pericardial effusion, preceded the onset of SRC by 6 months (13). In the study of Fernandez Morales et al., 12.5% of patients with severe pericardial effusion eventually developed SRC (10). The reasons for the association of such rare events are not completely understood yet. It might be due to renal cortical hypoperfusion and ischemia as a result of heart failure or abundant diuretic use in the setting of severe pericardial effusion. Also, pericardial effusion might reflect an extensive activity of the disease that ultimately involves the kidneys (11). Our patient had some degree of renal failure and urinary sediment abnormality at presentation, soon after admission she became anuric and remained so during the course of the disease.

The differential diagnosis of acute renal failure in patients with SSc is comprised of ANCA-associated vasculitis that might be confused with SRC (1). So kidney biopsy was performed for the patient, which showed pieces of evidence of acute thrombotic microangiopathy; all of these features are associated with SRC (14).

SRC is more likely to occur in patients with diffuse skin involvement, at early stages of the disease and during rapid skin thickening (1). Medium to high doses of glucocorticoids (prednisone doses of greater than 15 mg/day) could increase the risk of SRC development (15). Although our patient did not receive any glucocorticoids, her skin involvement was extensive with contracture of large joints and her disease was active and might be evidence of heart involvement. Antibodies against RNA polymerase III are independently associated with SRC development (16), but these autoantibodies were not checked in this patient.

Pieces of evidence regarding microangiopathic hemolytic anemia (including thrombocytopenia, elevated LDH, and fragmented RBCs in the PBS) were obvious in our patient. There are few case reports describing the association of scleroderma and thrombotic thrombocytopenic purpura (TTP) (17). The activity of ADAMTS 13 was normal and the course of the disease implies that other forms of thrombotic microangiopathies (e.g. TTP and HUS) are unlikely in the patient. Microangiopathic hemolytic anemia could complicate the course of SRC in about 50% of cases and should be treated with plasma exchange, as was done for our patient.

This study describes the co-occurrence of two rare complications of SSc, including SRC and severe pericardial effusion in our patient. We did not check the serologic markers such as RNA Polymerase III that might be one of the limitations of our study. Thus the association between serologic markers and SSc presentations and complications could not be assessed. In addition, our patient was noncompliant and never returned to our center again. There-

Table 2. Comparison of the Patient's Characteristic with Previously Published Case Series and Reports

Study Description	Demography	Type of SSc	Disease Duration	Amount of Pericardial Effusion (PE)	Presenting Symptoms	Onset of SRC
Case series describing patients with SSc and PE; Fernandez Morales et al. (10); 2016	Mean age 49.3; 83% female	55% dcSSc	PE later than SSc in 67.5%; PE concomitant with SSc in 22.5%; PE before SSc in 10%	Severe PE: 27%; cardiac tamponade 63%	Dyspnea 75%; chest pain 35%	12.5% developed SRC
Case report of SRC following PE; Shu E et al. (11); 2014	43 years old woman	dcSSc	9 weeks after diagnosis of dcSSc	Moderate PE	None	Two weeks after PE
Case report of cardiac tamponade as presentation of SRC; Pattanaik et al. (12); 2004	37 years old man	Not mentioned	One week after diagnosis of SSc	Cardiac tamponade	pleuritic chest pain and shortness of breath	Concomitant with PE
PE heralding SRC (current study)	39 years old woman	dcSSc	8 years	Severe PE	Worsening dyspnea and pleuritic chest pain	Concomitant with PE

Abbreviation: PE, pericardial effusion.

fore, we failed to provide appropriate follow-up data.

3.1. Conclusions

Our patient was a non-compliant woman with dcSSc and extensive skin involvement who presented with dyspnea and severe pericardial effusion. Her course was complicated by SRC and microangiopathic hemolytic anemia. Both SRC and severe pericardial effusion are rare complications of SSc. This case report and other case series denote to the association between these rare events. Thus the physicians should be vigilant about SRC development in patients with SSc and pericardial effusion.

Footnotes

Conflict of Interests: The authors have no conflict of interest to disclose.

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Patient Consent: The patient signed informed written consent for publishing this report.

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