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Management of scleroderma renal crisis with left ventricular diastolic dysfunction in a resource-limited setting: A rare case report

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Abstract

Scleroderma renal crisis with left ventricular diastolic dysfunction can lead to significant mortality. We presented the case of a 32-year-old female with anuria for 2 days. On further inquiry, she had joint pain, difficulty turning her head sidewise, and associated difficulty in finger movement. Also, hyperpigmentation with superimposed hypopigmentation was reported, which reduced during her pregnancy and worsened post-partum. Her family history suggested similar complaints in her mother. In addition, she had a blurring of vision. She had hypertension, microangiopathic hemolytic anemia, deranged renal function, and retinopathy on ophthalmologic examination. Radiological investigations revealed pulmonary edema, pleural effusion, and left ventricular diastolic dysfunction. Hence, a diagnosis of scleroderma renal crisis complicated by left ventricular diastolic dysfunction was made. She was managed conservatively using anti-hypertensive medications and hemodialysis, which resulted in gradual improvement. Our case highlighted the management approach to this rare presentation with anti-hypertensives and hemodialysis in a resource-limited setting.

Keywords

Scleroderma, renal crisis, cardiac complication, case report, management

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Introduction

Scleroderma renal crisis (SRC) characterized by malignant hypertension and renal failure is a fatal complication of systemic sclerosis (SSc) with a low prevalence rate of 5%–10% and a mortality rate as high as 30%.[1,2] Although its pathophysiology is unclear, SRC is associated with endothelial cell injury resulting in tissue ischemia and reduced renal perfusion.[1] This is followed by activation of the renin–angiotensin system with further aggravation of tissue ischemia and hypoperfusion, ultimately leading to acute kidney failure.[1] Additional presentation of SRC includes congestive heart failure, pulmonary edema, and microangiopathic hemolytic anemia (MAHA).[2,3] The mainstay pharmacological treatment options include angiotensin-convertor enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and calcium channel blockers (CCBs).[1] In addition, indications for dialysis and renal transplantation may be warranted in patients with kidney injury progressing to end-stage renal failure.[3] The SRC with variable signs and symptoms overlapping with other forms of autoimmune and renal diseases makes it difficult to diagnose.[1] In addition, there is a lack of a standard treatment algorithm for SRC, which makes it challenging to select the best course of treatment.[4] Our case highlights the approach to diagnosis and treatment of SRC in

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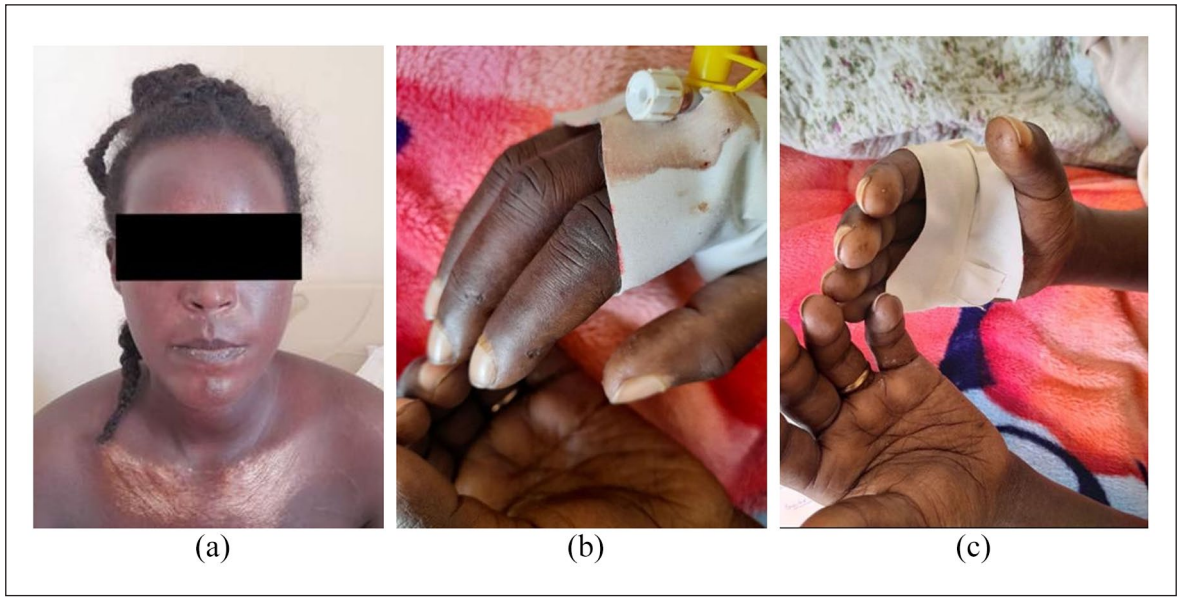

Figure 1. (a) Diffuse hyperpigmentation with hypopigmentation around the chest, nose, and lips of the patient. (b) Ulcerations on patients' fingers. (c) Ulceration on the tip of the patient's fingers.

the setting of associated left ventricular diastolic dysfunction (LVDD).

Case presentation

A 32-year-old female presented to our hospital with anuria for 2 days. On further inquiry, she revealed pain in her knees and elbow for 2 years, difficulty turning her head sidewise, and associated difficulty in finger movement. Also, she had gradual darkening of the skin of her entire body with superimposed hypopigmentation over her face, bilateral forearms, and chest, which improved during her third pregnancy and worsened post-partum. Moreover, the tips of her fingers used to be painful during cold weather and sometimes formed small vesicles, which later ulcerated to form painful scars. Over the past month, she started to experience bilateral blurring of vision with floaters and flashes of lightning. Her family history revealed the occurrence of skin hyperpigmentation in her mother. She occasionally drinks alcohol but does not smoke or use recreational drugs. Her baseline blood pressure before the current problem was 120/80 mm Hg.

On presentation, her vitals were blood pressure of 180/110 mm Hg, pulse rate of 110 beats per minute, respiratory rate of 20 breaths per minute, and temperature of 36.5°C. She had conjunctival pallor, and bilateral pedal pitting edema. Her oral examination revealed a three-finger trismus with a fish mouth appearance. Her skin was thickened and hyperpigmented over the face, neck, bilateral arm, forearm, thigh, and leg (Figure 1); there was patchy hypopigmentation over her chest, nose, and lips (Figure 1). The tips of her fingers had punched out ulcerations that were tender to touch (Figure 1). Modified Rodnan skin score was 30 out of 51.[5] Other systemic examinations were unremarkable.

Her initial investigations (Table 1) showed low hemoglobin levels, schistocytes on peripheral blood morphology, elevated serum creatinine, thrombocytopenia, elevated serum lactate dehydrogenase (LDH), and hyponatremia. The urinalysis showed mild proteinuria (1.5 g/dL in 24 h) and red blood cells. Also, anti-nuclear antibody (ANA) titers were positive. Erythrocyte sedimentation rate and C-reactive protein were elevated, and rheumatoid factor was negative. The ultrasonography of the abdomen and pelvis revealed bilateral cortical renal thinning. Also, ophthalmoscopic examination showed Stage IV hypertensive retinopathy with exudative retinal detachment.

Based on clinical evaluation and laboratory findings, the patient was diagnosed with diffuse scleroderma renal crisis. She was admitted to the intensive care unit (ICU) and was initially treated with oral captopril 25 mg, followed by the addition of oral nifedipine 10 mg for better blood pressure control. After the failure of this therapy, the patient was started on intravenous metoprolol 2.5 mg, given three times over 5-min intervals, which decreased the blood pressure to 150/90. After this, oral metoprolol 100 mg once daily for the next 2 days was given. After 3 days, blood pressure was 120/70 mm Hg, and oral captopril 25 mg thrice daily was started for long-term blood pressure control. A few days after the course in the hospital, she started to experience worsening shortness of breath with infrascapular bibasilar crackles. Supplemental oxygen was started, and an urgent contrast-enhanced computed tomography scan of the chest was done, which showed high-grade pulmonary edema and bilateral pleural effusion (Figure 2). Her electrocardiogram results

Table 1. Laboratory investigations of the patient.

Investigations	Report	Reference value
Hemoglobin	8.5 g/dL	12–17 g/dL
MCV	84 fl	80–100 fl
Serum LDH	415 U/L	0–248 U/L
WBC	6.13/µL	4–12 µl
Platelet count	114/µL	150–400/µL
Serum creatinine	2.22 mg/dL	0.4–1.1 mg/dL
BUN	22 mg/dL	5–20 mg/dL
Serum sodium	125 mEq/L	135–145 mEq/L
TSH	1.32 mIU/L	0.3–4.2 mIU/L
SGOT	17 U/L	30–45 U/L
SGLT	14 U/L	30–45 U/L
PT	12 s	10–14 s
INR	0.94	0.8–1.2
PTT	28 s	26–36 s

MCV: mean corpuscular volume; LDH: lactate dehydrogenase; WBC: white blood cell; BUN: blood urea nitrogen; TSH: thyroid-stimulating hormone; SGOT: serum glutamic-oxaloacetic transaminase; SGLT: sodium-glucose linked transporter; PT: prothrombin time; INR: international normalized ratio; PTT: partial thromboplastin time.

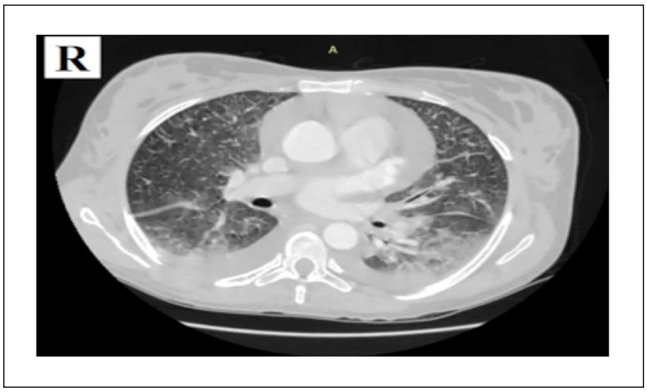

Figure 2. Axial contrast-enhanced computed tomography scan of chest indicating bilateral pleural effusion and pulmonary edema.

were normal. Echocardiography revealed concentric left ventricular hypertrophy, mild pericardial effusion, and LVDD with an ejection fraction of 53%. After intensive care unit management, the patient was hemodynamically stable. During her stay in the hospital, she also underwent hemodialysis twice (Table 2). Over 15 days of inpatient care, her condition improved gradually, and she was finally discharged. After this, the patient was lost to follow-up.

Discussion

SRC is characterized by renal involvement with a history of SSc, a multisystem autoimmune disorder affecting the connective tissue, and primarily involves skin fibrosis.[1] To diagnose SRC, SSc must be highly suspected and classified using the American College of Rheumatology–European League Against Rheumatism (ACR–EULAR) criteria comprised widespread (diffuse) skin thickening, ulcerations on the tip of the finger, and Raynaud's phenomenon due to painful fingertips in chilly hours of the morning.[2] In addition, an expert-led, in-depth diagnostic criterion by Steen and Medsger[6] aided in the diagnosis of SRC for our patient. Indicative signs of chronic hypertension include pitting edema, visual blurring from retinopathy, and pulmonary involvement, such as congestion.[3] Similarly, we also reported pitting edema, retinopathy, and pulmonary edema in our patient. Almost half of the cases of SRC have MAHA.[6] Also, elevated serum LDH can be reported in these patients.[6] A definitive diagnosis can be made by detecting ANA, which is seen in more than half of SRC patients and aided in our diagnosis.[7] In our case, MAHA, elevated LDH, and ANA positive status was found, which aided in the diagnosis of SRC.

Uddin et al.[8] demonstrated new-onset congestive heart failure as one of the major complications among SRC in comparison to the non-SRC subgroup (24/1% vs 8.8%, $p = 0.001$) and observed a strong association with SRC. Also, Kawabata et al.[9] reported pulmonary edema in SRC patients. The symptoms of heart failure are often clinically silent or may resemble the manifestations of other organ involvement, such as the lungs, which can lead to underdiagnosis or late detection of the condition.[1] SRC with LVDD is a predictor of high mortality and exceeds mortality rates associated with pulmonary hypertension.[10] In addition, the presence of left ventricular hypertrophy is also suggestive of chronic hypertension, which may have been the case in our patient.[11] Left ventricular hypertrophy is also associated with an increased risk of morbidity and mortality.[11] As a result, prompt treatment is required. The current gold-standard approach for managing SRC is rapid blood pressure control using ACEI, especially captopril.[3,4] With the induction of ACEI in the 1970s, SRC-related mortality decreased from 76% to less than 10%.[12] If blood pressure remains uncontrolled despite maximal ACEI therapy, CCB, ARB, and alpha-blockers can be added in succession.[13] Despite the addition of ACEI and CCB, the hypertensive state of our patient did not improve, prompting the addition of beta-blockers. In the current literature, beta-blockers are not routinely prescribed in SRC patients due to their theoretical effects on exacerbating Raynaud's phenomenon.[7] However, due to the risk of cardiovascular mortality coupled with renal dysfunction in our patients, beta-blockers were added for their cardio- and reno-protective effects, respectively.[14] Despite maximal pharmacological treatment, patients may require hemodialysis if renal dysfunction persists.[4,10,13] Penn et al.[7] found that higher blood pressure at presentation was associated with better long-term outcomes. Those with lower blood pressure may require long-term dialysis, sometimes without recovery.[7] In our case, hemodialysis was indicated, which resulted in the gradual improvement of the patient's overall well-being. Since ACEI use may lead to the development of SRC, these patients need to be monitored closely.[4,15]

Table 2. Parameters pre- and post-hemodialysis and at discharge.

Parameters	Before first hemodialysis	After first hemodialysis	Before second hemodialysis	After second hemodialysis	At discharge
Hemoglobin	8.9 g/dL	9.5 g/dL	8.5 g/dL	9.6 g/dL	9.4 g/dL
Serum creatinine	5.2 mg/dL	3.2 mg/dL	4.8 mg/dL	2.8 mg/dL	2.0 mg/dL
Blood urea nitrogen	60 mg/dL	35 mg/dL	62 mg/dL	32 mg/dL	28 mg/dL
Blood pressure (mm Hg)	140/90	126/88	146/90	120/86	124/90

Also, caution should be maintained while using high-dose corticosteroids to manage SRC because corticosteroids have been associated with the development of SRC.[16,17] Because of the risk of further worsening, we did not use corticosteroids in our patient. The decision for transplantation depends on renal recovery following dialysis, which may take up to 3 years.[7] Since the patient was lost to follow-up, long-term monitoring was not possible. Hence, we could not assess the possibility of worsening SRC and the requirement for long-term hemodialysis. Autoantibodies related to SRC, such as anti-topoisomerase, anti-RNA polymerase III, and anti-centromere antibodies, are associated with morbidity and mortality.[18] We were unable to report these autoantibodies with SRC due to unavailability in our setting. There were other limitations in this case. We could not conduct a renal biopsy to pinpoint the pathology for renal insufficiency due to the risk of retroperitoneal hemorrhage in uncontrolled hypertension. Also, the possibility of interstitial lung disease was not excluded, as the patient's lungs were edematous and prevented appropriate radiological interpretation.

Conclusion

We presented a 32-year-old female patient with a history of skin changes consistent with scleroderma. She presented with SSc's two possible internal organ complications: SRC and diastolic heart dysfunction. We highlighted the approach to managing SRC complicated by LVDD. Further studies focusing on managing SRC with cardiac complications are required to develop the management approach for clinicians worldwide.

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Author contributions

YAA performed data curation, original draft preparation, and reviewed and edited the manuscript. AA, HH, MT, AAK, SS, and SP performed original draft preparation, and reviewed and edited the manuscript. JM and GM reviewed and edited the manuscript.

Data availability

This manuscript has all the data relevant to this case report included.

Declaration of conflicting interests

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Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

Guarantor

YAA.

Informed consent

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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