A Woman with Swollen Fingers and New-Onset Hypertension and Renal Failure

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Figure 1. Image of the case patient's hands showing shiny, puffy-looking skin and swollen and sausage-shaped fingers.

Figure 2. Image of the case patient's hands demonstrating flexion deformity of the fingers.

CASE PRESENTATION

Initial Presentation and History

A 42-year-old woman presented to her primary care physician for routine follow-up. Her past medical history was significant for a diagnosis of systemic scleroderma 4 months ago. She denied headache, chest pain, shortness of breath, leg edema, or blurry vision. Review of systems was otherwise unremarkable. She was not taking any medications and had no known drug allergy. She reported smoking 1 pack of cigarettes per day for the last 28 years and drinking alcohol socially. She had no family history of an autoimmune disorder.

Physical Examination

Physical examination revealed a temperature of 100°F (37.8°C), blood pressure of 190/114 mm Hg, heart rate of 77 bpm, respiratory rate of 16 breaths/min, and an oxygen saturation of 99% on room air. She was alert and oriented to person, place, and time. HEENT examination revealed mild pallor, moist mucous membranes, no icterus, and a normal oropharynx, and fundoscopic examination was normal. Her skin was puffy, mainly on the hands and fingers (**Figure 1**). No lymphadenopathy was noted. Cardiac and lung examinations revealed normal heart sounds and normal breath sounds in both lungs. The abdomen was soft and nontender with no organomegaly. Joint examination was normal with no tendon friction rubs. She had flexion deformity of the fingers with a sausage-shaped appearance (**Figure 2**). Neurologic examination revealed normal sensory and motor function.

Laboratory Studies

Laboratory studies revealed a normal complete blood count but hemoglobin and hematocrit were low; additional results are listed in the **Table**. Peripheral blood smear showed slight anisocytosis and poikilocytosis with occasional tear drop cells and spherocytes. Medical records showed that the patient's basal metabolic panel was normal 1 month prior to presentation. Urinalysis revealed specific gravity of 1.006, no red or white blood cells, pH of 6.5, a trace of protein, creatinine level of 25 mg/dL (normal, 10–300 mg/dL), sodium level of 74 mEq/L (normal, 15–220 mEq/L), and no nitrites. Fractional excretion of sodium was 12.8%. Antinuclear antibody (ANA) titer was positive at 1:320 with a speckled pattern. Recent testing for anticardiolipin antibody was negative, and an extractable nuclear antigen (ENA) panel was negative for anti-Scl 70 antibody.

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Table. Results of Laboratory Testing in the Case Patient

Variable (Unit)	Result	Normal Value
Hemoglobin (g/dL)	9.5	12–15
Hematocrit (%)	28.9	36–46
Lactate dehydrogenase (U/L)	147	50–220
Sodium (mEq/L)	134	135–148
Potassium (mEq/L)	6.4	3.3–5.3
Blood urea nitrogen (mg/dL)	68	8–22
Creatinine (mg/dL)	5.8	0.7–1.5
Calcium (mg/dL)	9.4	8.4–10.4
Magnesium (mg/dL)	2.7	1.6–2.8
Phosphorus (mg/dL)	8.9	2.5–4.8
Anion gap (mEq/L)	15	8–12

WHAT IS YOUR DIAGNOSIS?

(A) Antiphospholipid antibody syndrome
(B) Hemolytic uremic syndrome
(C) Scleroderma renal crisis
(D) Thrombotic thrombocytopenic purpura

ANSWER

The correct answer is (C), scleroderma renal crisis (SRC).

DISCUSSION

All of the above conditions can present as new-onset acute kidney injury; however, this patient's recent diagnosis of scleroderma with cutaneous manifestations, new-onset hypertension, and positive ANA test with a speckled pattern strongly point toward SRC. SRC is characterized by new-onset moderate to marked hypertension (90% of patients), elevated serum creatinine (50% of patients), proteinuria (63% of patients), and signs of intravascular hemolysis (50% of patients).[1,2] SRC is typically seen in early diffuse scleroderma but rarely can present as the first sign of scleroderma in the absence of skin changes. ANA titer will be positive with a fine speckled pattern, and ENA panel for anti-Scl 70 antibody (anti-topoisomerase I antibody) is typically positive; SRC can occur in approximately 10% of patients who test negative for anti-Scl 70 antibody.[1] In addition, the possibility of SRC is increased in the presence of anti-RNA polymerase III antibody, but this is not routinely tested for in the ENA panel.[3,4] Because SRC, thrombotic thrombocytopenic purpura (TTP), and hemolytic uremic syndrome (HUS) are forms of thrombotic microangiopathy, it is often difficult to distinguish between them. In addition to progressive renal failure, both TTP and HUS are characterized by microangiopathic hemolytic anemia and thrombocytopenia. Most cases of HUS and TTP are caused by infection with *Escherichia coli* and are typically associated with diarrhea. The case patient had no gastrointestinal complaints, excluding both TTP and HUS as potential diagnoses. Renal biopsy cannot definitively distinguish between SRC and any other form of renovascular disease, such as malignant hypertension. However, adventitial and periadventitial fibrosis are seen in SRC but are rarely noted in malignant hypertension not related to scleroderma.[5] In antiphospholipid antibody syndrome, some patients have only mild proteinuria with normal renal function, while others develop acute or subacute renal failure with proteinuria and marked hypertension. The case patient had recently tested negative for anticardiolipin antibody, making antiphosholipid antibody syndrome highly unlikely.

CLINICAL COURSE OF CASE PATIENT

The patient was immediately admitted to the intensive care unit for management of SRC and was started on an intravenous infusion of enalapril to quickly and optimally control her blood pressure. However, renal function did not improve significantly and she was started on hemodialysis while continuing enalapril therapy. Intravenous enalapril was stopped, and the patient was given oral captopril. A transthoracic echocardiogram showed mild pulmonary hypertension, but right heart catheterization showed normal pressures. Blood pressure was well controlled after 48 hours, and she was transferred to the general medical floor. At 6 months postdischarge, the patient continued to undergo regular dialysis and blood pressure remained well controlled.

SCLERODERMA RENAL CRISIS

SRC is defined as the new onset of malignant hypertension or rapidly progressive oliguric renal failure during the course of systemic sclerosis. SRC is the most dangerous complication of scleroderma;[6] however, outcomes in patients with SRC have improved dramatically with the use of angiotensin-converting enzyme (ACE) inhibitors. The pathogenesis of the renal event in scleroderma appears to reflect a high renin state. Release of platelet-derived growth factors increases collagen and fibrin deposition, which increases luminal narrowing. These changes result in decreasing renal blood flow, hyperplasia of juxtaglomerular apparatus, and an ongoing increase in renin production, which subsequently leads to malignant hypertension and renal crisis.[1]

SRC occurs in approximately 10% of patients with scleroderma, with most cases occurring early in the

disease process (within 5 yr of diagnosis) and in those with rapidly progressing disease.[7] The risk for SRC is increased in men and African-American individuals and in the presence of tendon friction rubs, increasing skin scores, cardiac involvement, interstitial lung disease, use of prednisone or cyclosporine, new-onset anemia, and intravascular hemolysis.[1] SRC is rare in limited systemic sclerosis.

Clinical Presentation

Most patients (85%) with SRC have new hypertension, and approximately half present with an elevated serum creatinine level or have signs of intravascular hemolysis.[8,9] Other signs and symptoms of SRC include increased fatigue, shortness of breath, severe headache, or blurred vision with accelerated hypertension. As mentioned previously, renal crisis is most often encountered early in the course of scleroderma, especially if the patient has a high skin score or tendon friction rubs. Skin score is evaluated on a scale of 0 to 3 based on clinical palpation of skin thickness in 10 to 17 areas of the body.[10] Skin thickness can also be more objectively measured by ultrasonography[11] or forearm skin biopsy.[12] A score greater than 20 is usually associated with SRC and heart involvement.[13] Palpable tendon friction rubs are a useful sign and are associated with an increased risk of SRC, occurring in 65% of patients with diffuse scleroderma.[14] Patients with SRC may also have nail fold capillary changes, esophageal dysmotility, and recent onset of Raynaud's phenomenon.

Screening and Management

In high-risk patients, blood pressure should be checked frequently and home blood pressure monitoring should be undertaken if systolic blood pressure changes more than 10 to 15 mm Hg or diastolic blood pressure changes more than 10 mm Hg above target. If blood pressure changes are sustained after repeated measurements, a physician should be contacted for immediate management. Regular follow-up is important to assess serum creatinine and urinary protein levels.

If SRC develops, aggressive treatment of hypertension with an ACE inhibitor can stabilize or improve renal function in up to 55% to 70% of cases, if treatment is started before irreversible vascular injury has occurred.[15] Captopril is the agent of choice.[15] Initiation of ACE inhibitor therapy leads to improvement in blood pressure control in up to 90% of patients by reversing the angiotensin II–induced vasoconstriction and increasing bradykinin.[15,16] Angiotensin receptor blockers are not as effective as ACE inhibitors, possibly because they do not affect bradykinin,[17] but they can be added to ACE inhibitor therapy for additional blood pressure control. If ACE inhibitor therapy does not immediately control the hypertension, other antihypertensive agents, including calcium channel blockers and α- and β-blockers, can be added. Because intravascular volume is often depleted in patients with SRC, diuretics should not be given; an intravenous line for hydration is usually recommended. The ACE inhibitor should not be discontinued if serum potassium or creatinine increases, which may occur immediately after initiating treatment.

Rapid reduction of blood pressure is essential to reduce the need for dialysis. Despite treatment with ACE inhibitors, approximately 20% to 50% of patients with scleroderma can progress to end-stage renal disease.[9,16] Short-term hemodialysis can be started if necessary (when serum creatinine is consistently > 3 mg/dL). Improvements in renal function can be seen up to 2 years after the initiation of dialysis. In a study by Penn et al[8] involving 110 cases of SRC, dialysis was not required in 36%, was required temporarily in 23%, and was permanent in 41%. Renal transplantation should only be considered after 2 years of dialysis, as some patients may regain renal function. Lifelong ACE inhibitor therapy is required after SRC.

CONCLUSION

Progression to SRC can be prevented with frequent blood pressure monitoring and laboratory testing in all patients newly diagnosed with scleroderma. Even mild increases of blood pressure can be an indicator of SRC. Once SRC is suspected, rapid control of blood pressure with an ACE inhibitor is imperative for a good outcome. Dialysis will be required in some patients. After SRC, all patients will require lifelong ACE inhibitor therapy to maintain blood pressure control. **HP**

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