Scleroderma Renal Crisis as an Early Presentation of Systemic Sclerosis

Katya Dolnikov MD[1], Gai Milo MD[2,3], Suheir Assady MD[2,3], Robert Dragu MD[4], Yolanda Braun-Moscovici MD[1,3], and Alexandra Balbir-Gurman MD[1,3]

[1]Shine Rheumatology Institute and [2]Department of Nephrology and Hypertension, Rambam Health Care Campus, Haifa, Israel
[3]Rappaport Faculty of Medicine, Technion–Israel Institute of Technology, Haifa, Israel
[4]Department of Internal Medicine C, Galilee Medical Center, Naharia, Israel

KEY WORDS: kidney biopsy, malignant hypertension, scleroderma, scleroderma renal crisis (SRC), systemic sclerosis (SSc)
IMAJ 2020; 22: 722–723

Scleroderma renal crisis (SRC) is a life-threatening complication of systemic sclerosis (SSc), presenting with high and resistant to treatment blood pressure (BP), acute renal failure, microangiopathic hemolytic anemia, hypertensive retinopathy, encephalopathy, and cardiomyopathy [1]. SRC generally appears in early SSc accompanied by progressive skin thickening, tendon friction rub (TFR), anemia due to bleeding from gastric antral vascular ectasia (GAVE), antibodies to RNA Polymerase-3 (RNAP-3), and treatment with high doses of corticosteroids [2]. SRC as the earliest SSc presentation is very rare [3]. The approach to a hypertensive emergency depends on the cause of this complication; SRC is one such complication and must be on the list of differential diagnoses even in the absence of SSc in the medical history. We describe two patients who presented with dramatic SRC as a debut of SSc.

PATIENT DESCRIPTION

CASE 1

A 43-year-old Caucasian woman was admitted because of progressive dyspnea in the previous 3 days. She denied chest pain, palpitations, fever, or cough. Her medical history included bilateral cataracts, severe myopia, and smoking. On admission, the patient was severely dyspneic. Her oxygen saturation was 90%, BP 230/110 mmHg, and respiratory rate 30/min. Laboratory tests showed normal blood count with no schistocytes on blood smear and creatinine 2.35 mg/dl. Hemoglobin, bilirubin, haptoglobin, lactate dehydrogenase, and urinalysis were within normal limits. Chest X-rays showed pulmonary edema. ECG demonstrated sinus tachycardia 120/min. Fundus examination was impossible due to bilateral cataracts. Echo Doppler revealed left ventricular ejection fraction (EF) of 55%, pulmonary artery pressure 28 mmHg. There was no pericardial effusion.

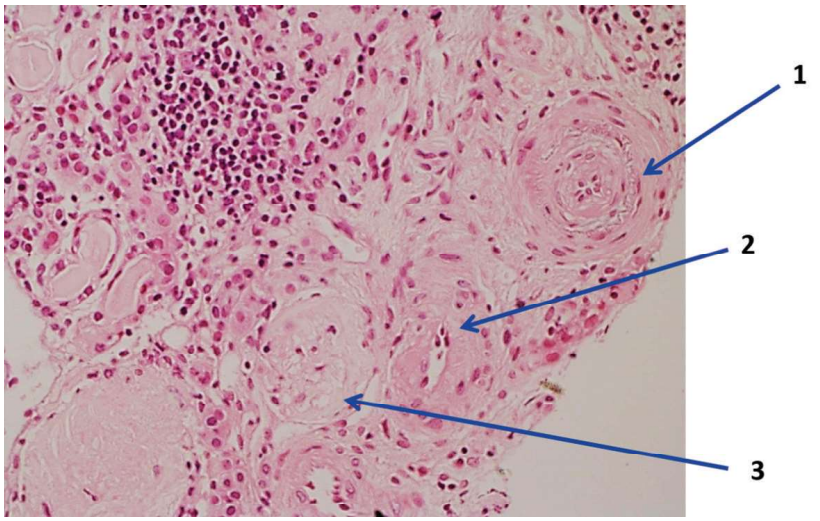
The patient underwent intubation; intravenous (IV) diuretics, nitroprusside and labetalol were started. After resolution of the pulmonary edema, the patient was extubated. The intensive care unit (ICU) staff noticed some finger changes and invited a rheumatologist consultation, who found mild fingers thickening and several telangiectasia. The patient reported strange sensations in her fingers for several months prior. Cold-water test provoked typical for Raynaud's phenomenon fingers skin color changes. Tests for creatine kinase, thyroid profile, complement, and immune tests for antinuclear antibodies (ANA), DNA, Smith, RNP, anti-topoisomerase, centromere, RNAP-3, and anti-neutrophil cytoplasmic antibodies (ANCAs) were negative. On immunofluorescence there was weak nucleolar staining. High resolution chest computed tomography did not reveal signs of interstitial lung disease.

As the patient fulfilled criteria for SRC, labetalol was discontinued; treatment with ramipril and amlodipine was started with rapid normalization of BP and renal function. During the following years, the patient's skin, joints, cardiac and pulmonary function were stable and her BP was controlled. The patient developed microcytic anemia due to GAVE that was treated with serial argon plasma coagulation and iron supplementation. Three years later, the patient developed proteinuria (1.5 g/24 hours) and renal function deterioration (creatinine 2.6 mg/dl) without further progression. Kidney needle biopsy (KNB) demonstrated typical for SSc intimal concentric hyperplasia of arcuate and interlobular arteries [Figure 1].

CASE 2

A 55-year-old Caucasian woman collapsed on arrival to the hospital with signs of pulmonary edema and asystole. She underwent resuscitation, intubation, and admission to ICU. Her spouse reported breathlessness and fatigue during the previous evening. The patient's condition rapidly deteriorated on the way to work the next morning and the couple came to the hospital. Her medical history included obesity, mild untreated hypertension, and relatively new anemia with hemoglobin of 10 g/dl scheduled for investigation. She was given IV furosemide, nitroprusside, and labetalol. After her condition improved, she was extubated. Laboratory tests revealed microcytic anemia (hemoglobin 8.6 g/dl, with no

Figure 1. Case 1, kidney biopsy showed concentric intimal hyperplasia (1), hyalinization of the intima (2), sclerotic glomerulus (3)



schistocytes or hemolysis). Creatinine was 1.6 mg/dl, and levels of troponin, electrolytes, protein albumin, and general urine were normal. Her BP remained elevated (180/100 mmHg). There were no signs of a coronary event on repeated ECG. Chest X-ray showed pulmonary edema and bilateral pleural effusion. Echo Doppler revealed EF of 65%, mild concentric left ventricle hypertrophy, and pericardial effusion. Fundus examination showed hemorrhages and cotton wool spots. Measurement of oxygen saturation was difficult due to finger skin thickening; a rheumatologist was invited and noticed skin thickening in the distal phalanges and a few telangiectasia. The patient reported recently appearing finger color changes compatible with Raynaud's phenomenon. Completed assessment revealed highly positive ANA and RNAP-3. The rest of the immune profile was negative. On gastroscopy, GAVE with active bleeding was treated with argon plasma coagulation. Previous therapy was replaced with ramipril 5 mg twice daily, nifedipin 30 mg twice daily, and omeprazole 40 mg once daily. The patient's BP and creatinine rapidly normalized.

During four years of follow-up, the patient developed TFR and skin thickening above the hands and arms with Rodnan skin score of 7; treatment with mycophenolate mofetil was added. She remained stable with normal BP and preserved kidney function without signs of lung or heart involvement.

COMMENT

The estimated incidence of SRC is 4.2% in patients with diffuse and 1.1% in limited SSc [1]. SRC as the earliest presentation of SSc is very rare [3]. Criteria for SRC include new onset or accelerated hypertension with systolic BP > 140 mmHg, diastolic BP > 90 mmHg or rise in systolic BP > 30 mmHg above baseline, rise in diastolic BP > 20 mmHg above baseline, and deterioration in renal function defined as an increase in serum creatinine by 50% over baseline [4]. Additional findings supporting the diagnosis of SRC include microangiopathic hemolytic anemia, thrombocytopenia (platelets < 100,000/mm^3), hypertensive retinopathy and/or encephalopathy, proteinuria, hematuria (> 10 red blood cells/high power field), pulmonary edema, and characteristic findings on KNB (concentric hyperplasia and hyalinization of the intima, onion-skin sign, lumen narrowing of small renal arteries without immune deposits, and sclerotic glomerulus) [4]. SRC should always be anticipated in high-risk patients with early progressive diffuse SSc, joints contractures, TFR, positivity for RNAP-3 and those treated with corticosteroids at doses above 15 mg/day [1]. SRC is associated with a poor prognosis: 60% of patients will need dialysis and the mortality rate is about 40% [1].

The incidence of SRC as an etiology of hypertensive crisis in emergency departments and ICUs is unknown [5]. When a patient with known SSc presents with a hypertensive emergency the clinical suspicion of SRC is high. Recognition of SRC in cases without prior SSc diagnosis is challenging. Signs such as Raynaud's phenomenon, mild sclerodactyly, and telangiectasia may be a clue. In presented cases detection of subtle SSc features led to changes in patient's management and a favorable outcome.

CONCLUSIONS

Though rare, SRC must be on the list of differential diagnoses when treating patients presenting with hypertensive emergency, even without known scleroderma. In these patients an active search for SSc features may be essential as well as cooperation with hospital teams. Early recognition and prompt, guided treatment could improve the outcome of SRC.

Correspondence

Dr. A. Balbir-Gurman
Shine Rheumatology Institute, Rambam Health Care Campus, Haifa 3109601, Israel
Phone: (972-4) 777-2988
Fax: (972-4) 777-2985
email: a_balbir@rambam.health.gov.il

References

1. Bose N, Chiesa-Vottero A, Chatterjee S. Scleroderma renal crisis. *Semin Arthritis Rheum* 2015; 44: 687-94.
2. Denton CP, Khanna D. Systemic sclerosis. *Lancet* 2017; 390: 1685-99.
3. Kucharz EJ, Kopeć-Mędrek M. Systemic sclerosis sine scleroderma. *Adv Clin Exp Med* 2017; 26: 875-80.
4. Hoa S, Stern EP, Denton CP, Hudson M. Towards developing criteria for scleroderma renal crisis: a scoping review. *Autoimmun Rev* 2017; 16: 407-15.
5. Ipek E, Oktay AA, Krim SR. Hypertensive crisis: an update on clinical approach and management. *Curr Opin Cardiol* 2017; 32 (4): 397-406.