CLINICAL VIGNETTE

Anti-Neutrophil Cytoplasmic Associated Vasculitis in Systemic Sclerosis

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Case Report

A 52-year-old woman with limited cutaneous systemic sclerosis (SSc) presented to her primary care doctor for leg swelling, fatigue and shortness of breath. Her laboratory tests showed elevated creatinine of 3.4 mg/dL and she was admitted to the hospital for further evaluation. She was diagnosed with SSc 14 years earlier with disease manifestations of skin induration involving face and fingers, sclerodactyly without digital ulceration, Raynaud's phenomenon, telangiectasias and interstitial lung disease. She had no history of kidney disease and a baseline serum creatinine of 0.6 mg/dL. She had mild hypertension, well controlled 120/70 mm Hg, on nifedipine and losartan. On admission her blood pressure was 201/87 mmHg, and she end inspiratory crackles in lower lung fields. Physical examination was also remarkable for pitting edema in lower extremities, induration of skin in fingers and face and sclerodactyly. She was initially felt to have scleroderma renal crisis and was started on captopril. Laboratory tests revealed a serum creatinine 3.9 mg/dL, hemoglobin of 8.8 g/dL, Platelet 340 X10E3/UL. Urinalysis showed 2 plus blood with 38 RBC in high- power-field and 3 plus protein with a urine protein creatinine ratio of 6.6. Blood smear was positive for schistocytes. Serologic tests were negative for anti-Smith, anti-RNP, dsDNA, anticentromere (ACA), anti-SSA, anti –SSB, antibodies. Antinuclear (ANA), was positive speckled pattern (1:640) as was anti-Scleroderma (Scl)-70 of 203 AU/mL, with normal < 40 AU/mL. Hepatitis B and C viruses and rheumatoid factor (RF) were negative. She had a positive myeloperoxidase-ANCA (MPO-ANCA) > 739 CU. Her proteinase-3 ANCA (PR3-ANCA) was less than 20 CU (normal value is <20 CU). Recent pulmonary function test prior showed moderate abnormalities with FVC 1.82 (53%), FEV1 1.46 (51%), DLCO 15.1 (56%), TLC 3.57 (70%). Chest CT-scan showed lower lung predominant peribronchovascular and subpleural extension of texture groundglass opacities, reticulation, and traction bronchiectasis consistent with scleroderma lung disease. The patient underwent kidney biopsy on the fourth hospital day. The biopsy showed pauci-immune crescentic glomerulonephritis, typical of rapidly progressive glomerulonephritis (RPGN). Kidney biopsy did not show any findings consistent with Scleroderma renal crisis.

Discussion

Scleroderma renal crisis (SRC) is a severe, life threatening renal disease that develops in approximately 10% to 15% of patients with SSc.[1] It usually occurs within the first few years after the onset of the disease. The use of corticosteroids,[2] diffuse cutaneous involvement[3] and presence of auto-antibodies directed against ribonucleic acid (RNA) polymerase,[4] are among the risk factors associated with SRC. Clinical manifestations of SRC include acute kidney injury (AKI) with usually normal urine sediment and abrupt onset of moderate to severe hypertension in a previously normotensive patient with normal or minimally abnormal renal function. About 10 percent of patients with Scleroderma renal crisis have normal blood pressure.[5]

The presence of hematuria, significant proteinuria, positive MPO-ANCA as well as relatively late occurrence of SRC, fourteen years after diagnosis of SSc, raised the possibility of anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) as the most likely diagnosis of AKI. The kidney biopsy did not show any features of SRC and it showed findings consistent with ANCA glomerulonephritis. The patient was started on high dose corticosteroid and plasma exchange.

AAV is a rare but serious occurrence in patients with SSc.[6,7] Diagnosis of AAV in the setting of SSc is a challenge for the clinicians. There are some clinical and laboratory features that are helpful to distinguish between AAGN and SRC in patients with SSc.[8] These include: positive anti-Scl-70 in 76% of cases of AANG vs 21% in SRC. Mean blood pressure of 140/80 mm Hg in AAGN vs 192/133 mm Hg in SRC patients; blood pressure greater than 140/90 mm Hg in 32% of patients with AAGN vs 88% in patients with SRC. Median disease duration of 7 years in patients with AAG vs 7 to 8 months in patients with SRC, and TMA in 14% of patient with AAGN vs 50% in patients with SRC. The vast majority, 97% of AAV patients are positive for MPO-ANCA and rarely positive for PR3-ANCA, 3%.[9]

Renal biopsy is not generally required to establish the diagnosis of SRC. Several features of AAV that differ from SRC may help in the prompt diagnosis of ANCA associated glomerulonephritis (AAGN) and prevent delays in appropriate treatment. Late onset AKI in a patient suffering from SSc for several years, normotensive AKI, and absence of laboratory findings consistent with thrombotic microangiopathy (TMA). Patients with Scleroderma renal crisis usually present with manifestations of TMA, moderate to severe protenuria as well as hematuria and should lead clinicians to expedite search for other causes of AKI in a patient with SSc. A kidney biopsy in addition to appropriate

laboratory tests is required to establish the diagnosis of AAGN in patients with SSc and initiate the appropriate treatment. High dose corticosteroids and immune suppression are the mainstay of treatment in patients with SSc complicated with AAV.[10,11]

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