Case Report

Scleroderma Renal Crisis in a Chinese Patient

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Abstract: Scleroderma is an uncommon connective tissue disease. Renal crisis is an even more uncommon complication of scleroderma in our locality. We reported a patient who was diagnosed to have diffuse cutaneous systemic sclerosis with interstitial lung disease. He developed rapidly deteriorating renal function despite the use of angiotensin converting enzyme inhibitor (ACEI). The pathogenesis, treatment and outcome of scleroderma renal crisis are presented.

Keywords: Angiotensin converting enzyme inhibitors, Chinese, complication, renal failure

Case Report

A 69-year-old Chinese man, enjoying good past health, presented with intermittent pain of his shoulders in January 2002, which improved with non-steroidal anti-inflammatory drugs (NSAID). He developed symmetrical polyarthritis involving the metacarpophalangeal, proximal interphalangeal, wrists, knees, ankles and metatarsophalangeal joints in May 2002. There was no history of skin rash, photosensitivity, oral ulcers or Raynaud's phenomenon. Investigations by a private rheumatologist revealed the following: strongly positive ANA (titer 1/1280), negative RF, ESR 55 mm/hr and CRP 34 mg/l. He was treated as lupus like illness with prednisolone (10 mg/day), NSAID and hydroxychloroquine. There was some improvement in the joint symptoms.

He was referred to the general medical clinic of Alice Ho Miu Ling Nethersole Hospital in October 2002. Skin tightening started a few months before his first clinic appointment, with rapid deterioration. There was also persistent arthritis of the small and large joints. He had poor appetite with significant weight loss in the past 3 months. There was no dyspnoea, dysphagia or reflux. The blood pressure was 120/67 mmHg. He was noted to have sclerodactyly, diffuse skin thickening and mild basal crackles on chest examination. Prednisolone (20 mg/day) and voltaren were prescribed for the control of his arthritis.

He was evaluated in the rheumatology clinic in November 2002 and complained of increasing cough and exertional dyspnoea. He also had mild dysphagia and developed flexion contracture of his fingers. Clinically, he was diagnosed to have diffuse cutaneous scleroderma with interstitial lung disease. He was admitted to the hospital for further investigation. His blood pressure on admission was elevated (188/94 mmHg). ACEI (lisinopril) was started and the blood pressure was brought to a satisfactory level. Further investigations revealed negative anti-dsDNA but positive anti-Scl-70 antibody. The chest X-ray showed reticulonodular shadow and bilateral pleural effusion. Pleural tapping was performed which revealed transudative effusion with negative cultures. The serum albumin was 28 g/L. This was probably related to the poor nutritional status of the patient because no significant urine loss of protein was documented. Echocardiogram revealed satisfactory left ventricular function (EF 67%). Lung function test showed a diminished KCO (67% predicted).
A high resolution CT (HRCT) scan of thorax was subsequently performed. Unfortunately, the scanning was suboptimal because of motion artefact (dyspnoea at time of examination). It revealed mild fibrotic changes at the lung apices and the right middle lobe. Intravenous cyclophosphamide was given for his interstitial lung disease. The dose of prednisolone was stepped up to 15 mg/day. He was discharged 1 week later with colchicine, lisinopril and prednisolone. The blood pressure was stable.

Our patient was admitted for the second course of intravenous cyclophosphamide in late December 2002. The blood pressure was high on this admission despite good drug compliance (187/98 mmHg). Besides, he was found to have rapidly deteriorating renal function (serum creatinine increased from 113 to 840 umol/L). Ultrasound of kidneys revealed early renal parenchymal disease. ACEI was stopped initially for suspected ACEI-related renal derangement and anti-hypertensive medication was changed to nifedipine. The renal function continued to deteriorate and he developed dropping hemoglobin and thrombocytopenia. There were also schistocytes seen in the peripheral blood smear. Renal biopsy was not attempted because of severe dyspnoea. He was treated as scleroderma renal crisis (SRC) with captopril (dose up to 50 mg tds) and diltiazem. The dose of steroid was reduced. Despite the blood pressure was under control, he required dialysis support. He remained dialysis dependent subsequently and finally succumbed in February 2003 because of bronchopneumonia.

Discussion

Scleroderma is an uncommon connective tissue disease. The most prominent feature is skin fibrosis. Patients may also have visceral organ involvement affecting the gastrointestinal tract, kidney, lung and heart. Scleroderma renal crisis (SRC) was the leading cause of death in the past. It affects about 10% of all scleroderma patients and up to 25% in patients with diffuse scleroderma. However, to our impression, this complication was uncommonly described in our local Chinese scleroderma patients. It most often occurs early in the course of disease, with 75% occurring in 4 years after diagnosis.

SRC is suggested to be triggered by endothelial cell injury. This leads to intimal proliferation and luminal narrowing which will decrease the blood flow resulting in hyperplasia of the juxtaglomerular apparatus. The increase production and release of renin leads to malignant hypertension and renal function deterioration.

The pathological change of SRC is typically seen in the small interlobular and arcuate arteries of the kidneys. The earliest change is intimal edema, proliferation and production of mucinous substance. Intramural fibrin deposition or fibrin thrombi can also be found. The thickened abnormal vessels allow platelet aggregation and cause microangiopathic hemolytic anemia. Unfortunately, we could not obtain histological evidence in our case.

Patients with SRC may be completely asymptomatic in the early stage. Common presentations include fatigue, shortness of breath, headache, blurred vision and even seizure. The blood pressure is higher than 150/90 mmHg in 90% of cases and about 30% will have a diastolic blood pressure of over 120 mmHg. Ten percent of patients are normotensive during renal function deterioration. However, even in patients with normotensive renal crisis, the blood pressure may still be high compared with their usual blood pressure. It is noteworthy that our patient did not have any symptoms initially. Progressively renal failure was only incidentally found during clinical admission for intravenous cyclophosphamide. So, a high index of suspicion is necessary.

Patients with SRC usually present with rapidly rising serum creatinine, which may increase by 0.5-1 mg/dL/day. Even when blood pressure was under control, creatinine may still continue to rise for several days. The serum renin will also increase markedly, up to 30-40 times of normal value. Urinalysis may show proteinuria, microscopic hematuria and granular casts. Our patient was found to have rapidly deteriorating renal function. The creatinine increased from 113 to 840 umol/L in 1 month despite treatment with ACEI. The occurrence of a microangiopathic hemolytic anemia picture is also compatible with SRC.

Concerning treatment of SRC, ACEI is the most important medication. It acts as a competitive inhibitor in the conversion of angiotensin I to angiotensin II. Short acting ACEI is preferred because it allows greater flexibility in controlling blood pressure. If blood pressure is not under control with a maximum dose of ACEI, other anti-hypertensive agents such as the calcium channel blockers or hydralazine should be considered. Dialysis support may also be needed. It is important to note that even with deteriorating
renal function, ACEI should be continued. Patients should continue to receive ACEI even on dialysis to prevent hyperreninemia. It was reported that 55% of patients could be weaned off dialysis with continuation of ACEI. There was report of successful use of losartan, a selective antagonist of angiotensin II receptor, in a patient with SRC who developed skin eruptions with ACEI.3 The use of intravenous infusion of iloprost, a prostacyclin analogue, in the treatment of SRC for smoother blood pressure control is also suggested.

The factors predicting SRC include diffuse skin involvement, rapid progression of skin thickening, disease duration less than 4 years, new anaemia, antecedent high dose steroid, anti-RNA polymerase antibody and new cardiac events including pericardial effusion and congestive heart failure.4-6 Our patient had at least the first four risk factors. Therefore renal complication is not too unexpected although this is uncommon in our local scleroderma patients.

Prior to the introduction of ACEI, SRC was the leading cause of death. Steen reported that the 1-year survival in SRC patients treated with ACEI was 76% comparing with 15% in those not treated with ACEI.7 She also reported that 61% of their patients had satisfactory outcomes (either receiving no dialysis or requiring temporary dialysis).8 Survival in patients with no dialysis or temporary dialysis was similar to patients with diffuse scleroderma without renal crisis. The factors reported to be associated with early death or permanent dialysis include male sex, old age, inability to control blood pressure within 72 hours, pretreatment serum creatinine over 3 mg/dL and concomitant scleroderma heart disease.

The role of ACEI in primary prophylaxis of SRC is still uncertain. The fact that our patient developed renal crisis despite ACEI illustrates that the renal protection effect of ACEI is not absolute. Further randomized trial on the efficacy of various combination therapies for the prevention of renal crisis in scleroderma is needed.

In summary, we reported a patient with diffuse cutaneous systemic sclerosis and rapid progression of skin thickening within half a year. He developed SRC despite ACEI therapy. Although SRC rarely occur in our locality, this diagnosis must be considered in scleroderma patients with rapidly progressive renal failure. Blood pressure should be regularly monitored and a high index of suspicion is needed as patients may be asymptomatic during the early stage of this renal complication.

References