Scleroderma Quebec™

THE KIDNEY IN SYSTEMIC SCLEROSIS

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The kidneys play a critical role in removing chemical waste products from the body, maintaining body fluid volume and controlling blood pressure. Kidney abnormalities encountered in systemic sclerosis are relatively common and, fortunately, most often with few consequences (e.g., small amount of protein in the urine, slight decrease in kidney function, slight increase in blood pressure). These problems are most often associated with a good prognosis and do not progress. However, there is a rarer but more urgent entity to identify: ***scleroderma renal crisis.***

WHO IS AT RISK OF DEVELOPING SCLERODERMA RENAL CRISIS?

Renal crisis occurs in 10-20% of patients with the diffuse form of systemic sclerosis. In the limited form of systemic sclerosis, its occurrence is less frequent. The risk is higher in patients with rapidly progressive skin involvement and in those with anti-RNA polymerase III autoantibodies. The use of high-dose corticosteroids (> 20 mg daily in the last 6 months) is also associated with an increased risk of developing a renal crisis. Renal crisis most commonly occurs during the first five years of disease progression. Joint contractures, new anemia and new heart problems (e.g., fluid in the envelope surrounding the heart or heart failure) may also be associated with a higher risk.

WHAT CAUSES SCLERODERMA RENAL CRISIS?

Scleroderma renal crisis is caused by a sudden narrowing of the small blood vessels of the kidneys, causing an acute decrease in blood flow to the kidneys and rapidly leading to their loss of function. The clinical consequences of the sudden narrowing of the small blood vessels of the kidneys are a very abrupt increase in blood pressure (hypertension), kidney failure (the kidneys stop working normally), anemia and a decrease in the number of platelets in the blood.

WHAT ARE THE CLINICAL FEATURES OF SCLERODERMA RENAL CRISIS?

Scleroderma renal crisis is most commonly associated with one or more of the following signs and symptoms:

- sudden and new increase in blood pressure to >150/85 mm Hg, measured at least twice in the last 24 hours; or persistent increase of 20 mm Hg in the systolic pressure (the first or upper digit) or of 10 mm Hg in the diastolic pressure (the second or lower digit);
- unusual headaches;
- blurred vision;
- difficulty breathing (a sign of the presence of fluid in the lungs, referred to as pulmonary edema);
- palpitations, or sensation of a rapid heartbeat;
- nausea and vomiting;
- decrease in the amount of urine excreted;
- drowsiness or confusion (or seizure in more severe cases).

If any of the above symptoms arise in a patient with systemic sclerosis, the blood pressure should be taken immediately. If the blood pressure is >150/85 mm Hg, measured at least twice in the last 24 hours, the patient should go to the emergency room immediately for a medical evaluation and treatment.

HOW TO DIAGNOSE SCLERODERMA RENAL CRISIS?

The presence of new and sudden hypertension, in conjunction with new and progressive kidney failure detected by blood and urine analysis in a patient with systemic sclerosis, strongly suggests the diagnosis of scleroderma renal crisis. The presence of anemia, fragmented red blood cells and a low platelet count in the blood test also supports the diagnosis. In contrast, kidney problems in systemic sclerosis may be due to other causes (see below). In cases where the diagnosis is less clear, additional tests including a kidney biopsy may be performed to help rule out alternative causes of kidney failure. Collaboration between the rheumatologist, nephrologist, hematologist and ophthalmologist is very helpful in making the diagnosis.

HOW IS SCLERODERMA RENAL CRISIS TREATED?

One of the great success stories against systemic sclerosis was the discovery of a new treatment for scleroderma renal crisis. This new treatment has significantly reduced the mortality associated with renal crisis. If left untreated, scleroderma renal crisis can lead to a severe loss of kidney function in as little as 4 to 8 weeks, and even death in less than a year.

The main objective when treating scleroderma renal crisis is to control the rise in blood pressure as quickly as possible. The drug of choice according to several studies is captopril (Capoten®), which belongs to the class of medication called angiotensin-converting enzyme inhibitor (ACE-I). The dose of captopril should be increased rapidly to bring blood pressure levels back to the patient's baseline within 72 hours. The required dose of captopril may vary from patient to patient. Treatment is started at a dose of 6.25 to 12.5 mg, and increased by 12.5 to 25 mg every four to eight hours as needed, up to 300 to 450 mg daily.

The addition of other medications to control pressure is sometimes necessary, such as calcium channel blockers (e.g., amlodipine or Norvasc®). Beta-blocker medications should be avoided given that they could theoretically worsen the narrowing of blood vessels. The treating physician should also monitor blood samples regularly to ensure that the kidney function is improving with treatment.

Some patients, especially those who were diagnosed and treated late in the course of the renal crisis, may require dialysis for varying lengths of time. In this case, there is still reason to be hopeful because we know that improvement in kidney function can be slow (up to 18-24 months), and that some patients will recover and eventually stop dialysis despite this delay. In very severe cases, some patients may need to have a kidney transplant, but with poorer short- and long-term outcomes compared to transplant patients who do not have scleroderma.

Once scleroderma renal crisis is resolved, medications in the longer-acting ACE inhibitor class should be continued indefinitely (e.g., enalapril (Vasotec®) or ramipril (Altace®)), even if the blood pressure returns to normal levels. It is also prudent to avoid medications that could be toxic to the kidneys, such as non-steroidal anti-inflammatory drugs (e.g., Advil®, Naprosyn®, Celebrex®) and contrast agents used in certain x-rays (e.g., CT scan with iodine injection).

CAN SCLERODERMA RENAL CRISIS BE PREVENTED?

No medication has been shown to be effective in protecting the kidneys and preventing scleroderma renal crisis. However, early detection of a renal crisis can help to start treatment as soon as possible and thus avoid serious complications of renal crisis. We therefore suggest to:

- check blood pressure twice a week, or daily in very high-risk patients (with a device at home);
- assess kidney function by taking blood samples and testing the urine for the presence of protein every three to six months; a deterioration in the kidney function or the persistent presence of protein in the urine could be a warning sign to the treating physician of an early scleroderma renal crisis;
- prednisone should be used with great caution. If required, prednisone should be given at a dose of 20 mg daily or less, if possible, and for the shortest time possible. However, some potentially serious conditions associated with systemic sclerosis may require higher doses of prednisone, such as inflammatory involvement of the lungs (alveolitis) or inflammatory involvement of the muscles (myositis). The dose and duration of treatment with prednisone is then at the discretion of the treating physician who prescribes and monitors the treatment.

WHAT ARE OTHER POSSIBLE RENAL MANIFESTATIONS IN SYSTEMIC SCLEROSIS?

In addition to scleroderma renal crisis, kidneys can also be affected by

- glomerulonephritis associated with ANCA or anti-GBM autoantibodies (inflammation in the wall of the small vessels of the kidneys; rare);
- thrombotic thrombocytopenic purpura (a disease in which platelets are too large and block the vessels in the kidneys; rare);
- oxalate nephropathy (in patients with severe digestive involvement and malabsorption associated with systemic sclerosis);
- other causes of kidney failure that are not directly related to systemic sclerosis, e.g., in the context of chronic high blood pressure, diabetes, medications toxic to the kidneys, dehydration, infection or blockage of the urinary system.

Therefore, depending on the patient's clinical presentation, the physician may perform additional blood, urine and imaging tests to rule out alternative causes of kidney failure. This is important because treatment depends on the diagnosis.

IN SUMMARY

Renal crisis is a relatively rare but potentially serious complication of systemic sclerosis. It is important to follow recommendations to prevent renal crisis and to recognize the early signs and symptoms of renal crisis, especially in high-risk patients. When scleroderma renal crisis is suspected, the patient should go to the nearest hospital emergency department without delay for medical evaluation and to start treatment as soon as possible, thereby minimizing the risk of serious long-term consequences.